VOLUME 9 · NUMBER 1–2 · 1975

HAEMATOLOGIA

International Quarterly of Haematology

AKADÉMIAI KIADÓ
PUBLISHING HOUSE
OF THE
HUNGARIAN ACADEMY
OF SCIENCES
BUDAPEST

HAEMATOLOGIA

is an international quarterly publishing original papers on haematology. It also provides the reader with complex and up-to-date information on both research and clinical practice. A General Survey, an Open Forum, Book Reviews, Abstracts of more important papers from other periodicals and a Documentation of the well-known and the less accessible journals are to serve this purpose.

Haematologia is published at quarterly intervals, the four issues per year make up a volume of some 500 pages.

Subscription price: $32 per volume (per year). Orders may be placed with

KULTÚRA

Trading Company for Books and Newspapers

Budapest 62. P.O.B. 149

or with its representatives abroad, listed on the verso of the cover.

Contents

VOLUME 9 · NUMBER 1–2

HAEMATOLOGIA

INTERNATIONAL QUARTERLY OF HAEMATOLOGY

AKADÉMIAI KIADÓ

PUBLISHING HOUSE OF THE HUNGARIAN ACADEMY OF SCIENCES

BUDAPEST 1975

Printed in Hungary

A kiadásért felel az Akadémiai Kiadó igazgatója
Műszaki szerkesztő: Zacsik Annamária
A kézirat nyomdába érkezett: 1975. V. 23. — Terjedelem: 16,10 (A/5) ív, 31 ábra
75.1864 Akadémiai Nyomda, Budapest — Felelős vezető: Bernát György

Haematologia 9 (1—2), pp. 3—13 (1975)

Platelet Inhibition of Human Lymphocyte PHA-Induced Blastoid Transformation

D. C. CRESS, W. K. METCALF

Department of Anatomy, Creighton University, Omaha, Nebraska 68178
and Department of Anatomy, University of Nebraska, Omaha, Nebraska 68105, United States

(Received April 2, 1975)

The reduced PHA responsiveness of human lymphocytes obtained from heparinized as compared to defibrinated blood has been shown to be due to platelet contamination in the former. Inhibition of blastoid transformation and lymphocyte death is directly related to the number of platelets added to a culture. Divalent ions partially reduce this platelet inhibitor phenomenon but do not block it completely. The "toxic" platelet components appear to be localized in the membranes and particulate matter after homogenization and hard centrifugation. Comparative studies of PHA transformation must control platelet contamination of the cultures in order to avoid severe difficulties of interpretation.

As early as 1965 it was shown that while rat lymphocytes readily respond to PHA in serum cultures, they failed to do so in cultures containing rat plasma [7]. It was suggested [8] that the toxic factor involved was probably the contamination of the plasma with platelets. The same phenomenon was later demonstrated in the guinea pig [3], but has never been fully investigated in human lymphocyte cultures. In this study, human lymphocyte cultures prepared from heparinized blood were shown to be depressed in terms of per cent of stimulation when compared to cultures derived from defibrinated blood, but not to the extent previously reported for rat and guinea pig lymphocyte cultures. In view of recent reports claiming that specific types of plasma may contain factors inhibitory to lymphocyte transformation [6] and the frequent preparation of lymphocyte suspensions from heparinized blood samples [2, 9] resulting in varying amounts of plasma and/or platelets in the subsequent cultures, it was felt there was a need for more detailed investigation of the inhibitory phenomenon of platelets in human serum lymphocyte cultures.

Materials and Methods

Lymphocyte collection: defibrinated serum

Twenty-five ml of blood was drawn by venipuncture from the median cubital vein of healthy male volunteers for defibrination in a sterile 125 ml Erlenmeyer flask that has three 8 mm lengths of 7 mm glass tubing to entrap the developing

fibrin clots. The whole was rotated on an Erbach rotator (Erbach, Ann Arbor, Michigan) for 10 min at 180 rpm. Then 3 ml of 6% Dextran (MW 200,000 – 300,000) were added and mixed for 30 sec on the rotator. The defibrinated blood was transferred to three 15 ml centrifuge tubes and allowed to stand for 30 to 40 min at room temperature for the red cells to settle. The leukocyte rich serum (LRS) was drawn off and the white cells counted according to Hepler [4] using an Improved Neubauer Counting Chamber (Hy-Life Ultra Plane, Clay Adams, New York). There is a very slight but constant red cell contamination of the LRS produced by this separation technique. The remaining serum and red cells were centrifuged at 750 g_n for 10 min and the autologous serum saved for the culture mixture.

Lymphocyte collection: heparinized plasma

Blood was drawn by venipuncture into a heparinized syringe to a final concentration of 50 units/ml (Liquaemin Sodium "100" Aqueous Sol – 1000 U.S.P. units/ml, Organon Inc., West Orange, New Jersey). Twenty-five ml of heparinized whole blood was thoroughly mixed with 3 ml of 6% Dextran in the syringe and transferred to three centrifuge tubes for red cell sedimentation. After 30 – 40 min the leukocyte rich plasma (LRP) was drawn off and the leukocytes counted [4].

Lymphocyte culture technique

The total volume of LRS was measured and diluted to a final cell concentration of 1.2 to 1.5×10 leuko/ml with 60% Minimum Essential Eagles Medium (MEM) (Microbiological Associates, Inc., Bethesda, Maryland), 40% autologous serum and 100 units of Penicillin-G per ml.

Two ml aliquots of the final culture mixture were transferred to 10 ml culture bottles siliconized with General Electric SC-87 Silicon (Silicon Products Department, Waterford, New York) [10] and 0.02 ml per ml of culture mixture of phytohemagglutinin-m (PHA-M) Difco Lab, Detroit, Michigan) was added to each bottle. Experiments that did not require the addition of PHA to the cultures were prepared following the same technique. The culture bottles were gassed with 95% CO_2 and stoppered tightly with silicon rubber corks and incubated for 72 hrs at 37°C.

Differential and absolute cell counts

Six categories of cells were selected to evaluate 72 hour leukocyte cultures. (1) Small unstimulated lymphocytes as they are on a typical smear of peripheral blood. (2) Blastoid cells – cells with enlarged nuclei and several prominent nucleoli and medium to dark blue cytoplasms (this category included cells with ruptured cytoplasmic membranes but still intact and distinct nucleoli). (3) Dead and smeared cells – cells with small pyknotic nuclei and little or no cytoplasm

and granulocytes with a number of dark spherical bodies. (4) Mitotic figures – cells in metaphase (these were added to category 2 for the total number of stimulated cells). (5) Macrophages – cells with an oval eccentric nuclei and a heavily vacuolated cytoplasm. (6) Granulocytes as they appear in a normal blood smear. At least 200 cells were counted per slide. Absolute counts of leukocyte cultures are made difficult because the cells are aggregated by the leukoagglutinating property of PHA. Too vigorous agitation [12] destroys the cells while insufficient agitation does not break up the clumps and would seriously impair the accuracy of the counts. It was, therefore, important to develop a reliable mixing technique that involved the thorough but gentle disruption of all cell clumps. Initial and terminal total nucleated cell counts were done only after gently flushing the culture fluid in and out of a Pasteur pipet 30 times to break up the aggregated leukocytes. The absolute initial and terminal number of cells in each category was calculated from a combination of the per cent differential count and the total cell count. Cultures can then be evaluated for the total number of cells that survive after 72 hr from any of the six categories above. The per cent of survival from each category can also readily be calculated from the initial and terminal absolute cell counts.

Platelet harvest

Blood was drawn by venipuncture into 3.8% sodium citrate (NaCit) from the saphenous vein in the forelimb of young healthy mongrel dogs of either sex or from the median cubital vein of healthy male medical students and mixed well by inversion. The citrated blood was emptied into a 50 ml centrifuge tube with an equal amount of 3.8% NaCit to a final concentration of 50 parts of blood and 50 parts NaCit. It was mixed well and centrifuged at 200 g_n for 20 min at 5°C. The platelet rich plasma (PRP) was drawn off with a Pasteur pipet into a clean 50 ml tube and the red cells were saved for a second and third harvest of platelets. The PRP was then centrifuged at 1000 g_n for 15 min at 5°C. The platelet poor plasma (PPP) was returned to the red cells, saving 3–4 ml of PPP to resuspend the platelet pellet. The platelet suspension was refrigerated and the harvesting procedure repeated twice more. After the third extraction, the PRP was combined with the other platelet suspension and counted according to Brecher and Cronkite [1].

Platelet homogenization

The sample of platelets to be added to a culture was first centrifuged at 1000 g_n for 20 min; then the supernatant was drawn off and discarded. The platelet pellet was mixed with 2 ml of MEM and transferred to a 5 cc Waring blender and homogenized for 3 min at 5500 rpm. The homogenized platelets were either added directly to a culture or centrifuged at 100,000 g_n for one hour in an ultracentrifuge (Beckman Ultracentrifuge Model L2-652) to separate the soluble and particulate fractions.

Results

A comparison of the mean final differential counts of 72 hour PHA cultures prepared from heparinized and defibrinated samples of peripheral blood from normal healthy male medical students is shown in Table 1. The percentage of blastoid transformation and mitotic cells is clearly higher and consequently the percentage of unchanged lymphocytes is significantly lower in the cultures prepared from defibrinated blood samples. That the difference is not due to the substances whose presence differentiates plasma from serum is shown in Table 2,

Table 1

A comparison of the 72-hour differential counts of PHA cultures prepared from human defibrinated blood with those prepared from heparinized blood (9 paired samples, standard deviations indicated)

Defibrinated Serum Cultures vs. Heparinized Plasma Cultures

Type of cells from differential	I Defibrinated serum	II Heparinized plasma	(I — II) Difference	P
Small lymphocytes	15.94 ± 5.95	27.44 ± 7.09	11.50 ± 3.27	0.005*
Stimulated lymphocytes	66.94 ± 11.9	41.0 ± 9.00	25.94 ± 5.27	0.0005*
Dead and smear	9.0 ± 5.8	14.44 ± 2.63	5.44 ± 2.26	0.025
Mitotic figure	3.05 ± 1.90	0.7 ± 0.78	2.35 ± 0.72	0.005*
Macrophages	3.5 ± 2.59	5.7 ± 3.74	2.2 ± 1.66	0.10
Granulocytes	9.90 ± 1.14	8.82 ± 12.75	7.93 ± 4.49	0.10

* Statistically significant difference

Table 2

The effect of various agents on PHA transformation of lymphocytes in cultures prepared from defibrinated human blood samples (minimum of 8 cultures per substance)

Effect of Various Agents on PHA Transformation of Lymphocytes in Defibrinated Serum Cultures

Substance	Dose per ml culture	Toxicity (FPE)*
Heparin	50 units	0
Fibrinogen	1.5 mg	0
Fibrinogen split products	1.5 mg	0
Dialysed plasmin	2500 units	0
Plasminogen	0.1 mg	0
A.T.P.	0.2 mg	0
A.D.P.	0.2 mg	0
5HT (serotonin)	0.2 mg	0

* Fresh platelet equivalents

which also confirms the inhibiting effect of the addition of platelets to serum cultures. Further, the toxic effects of platelets in serum lymphocyte cultures is demonstrated in Figure 1. After the 72 hr culture period the absolute number of

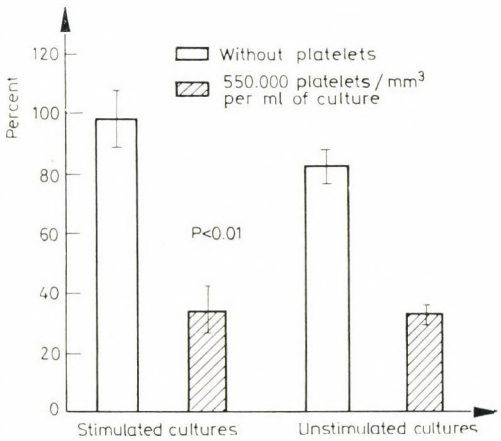


Fig. 1. Platelets in lymphocyte cultures with or without PHA kill lymphocytes at a higher rate than in cultures without platelets. Standard errors indicated

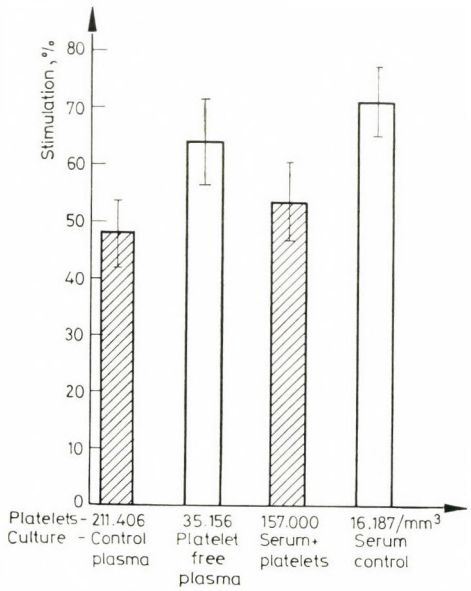


Fig. 2. Platelet inhibition of lymphocyte stimulation: As the concentration of platelets increases in either the plasma or serum cultures (shaded columns) the percentage of stimulated lymphocytes is decreased. (S. D. indicated)

lymphocytes was determined. It is clear that lymphocytes die at a much higher rate in platelet cultures than in platelet free cultures.

Heparinized plasma and defibrinated serum cultures were compared for per cent of stimulation (Fig. 2). Unaltered human cultures set up with autologous heparinized plasma were found to contain an average of 211,000 platelets/mm^3. The per cent stimulation in PHA cultures varies between 42 and 54 per cent (first column, Figure 2). When the platelet contamination was reduced (second column, Figure 2), an increase of 15% stimulation resulted. The addition of autologous platelets to PHA cultures prepared from defibrinated blood (serum cultures) resulted in an appropriate diminution in blastoid transformation (column 3, Figure 2). The fourth column in Figure 2 represents a normal serum culture showing the

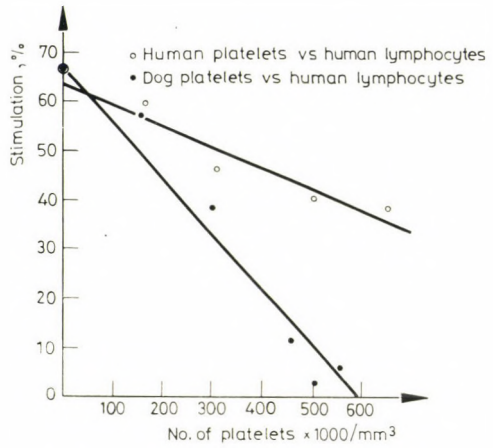


Fig. 3. The relationship between the per cent of blastoid transformation in PHA cultures and the number of added platelets

per cent stimulation and the average number of platelets that contaminate culture in this series of experiments. It was concluded from a comparison of the first and fourth column in Figure 2 that the decrease transformation rate in the heparinized plasma cultures was due to platelet contamination.

There appeared to be an inverse relationship between percentage blastoid transformation and the number of autologous or dog platelets added to human lymphocyte cultures. The purpose of these experiments was to determine whether this relationship was linear and if it could be used to develop an assay for comparing the toxicity of purified platelet products to whole platelet toxicity. Cultures with different dose levels were repeated four times and the average per cent of stimulation from each level was plotted against the number of added platelets. The total figures were subjected to least squares analysis and the calculated lines superimposed over plotted averages (Fig. 3). It was calculated that the probability of these lines not being straight is < 0.01. It is also evident that human platelets

are not as toxic as dog platelets. From this linear relationship a unit of platelet toxicity was designated fresh platelet equivalents (FPE). It is defined as the number of fresh dog platelets which, if added to 1 mm^3 of culture, would have reduced the percentage of stimulated lymphocytes to the same level as that of the material being assayed (eg. 100,000 FPE $\simeq$ 13% reduction in percentage of stimulated cells). Using this standard unit of culture, inhibition comparisons between platelet cultures and other test materials could be evaluated more accurately. Platelets in lymphocyte cultures demonstrate a toxicity which is both direct and linear. In cultures with platelets added, the results are reported in terms of FPE.

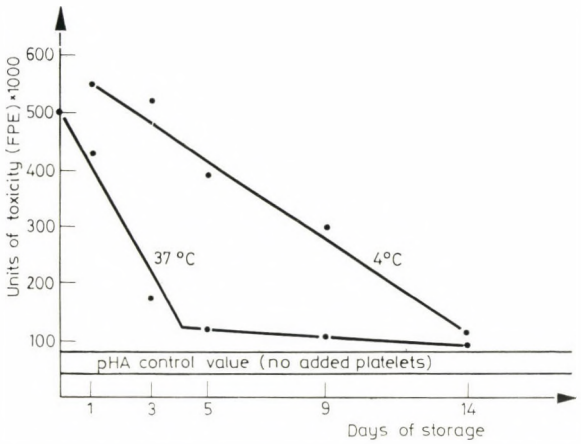


Fig. 4. The decay of the inhibitory effect of platelets on PHA blastoid transformation with storage at different temperatures. Each point represents the mean of ten cultures

The toxic constituent of platelets is thermolabile as shown in Figure 4 and in storage at 4°C it is destroyed in approximately 5 days. A large supply of dog platelets was harvested and concentrated in centrifuge tubes for addition to cultures. Half of the platelet samples were stored in plasma at 4°C and the other half in plasma at 37°C. Platelets from both cold and warm storage were evaluated for toxicity in lymphocyte cultures immediately and after 1 day, 3 days, 5 days, 9 days and 14 days storage, and the toxicity recorded as fresh platelet equivalents. A graph of the decrease in FPE with time in storage appears in Figure 4. These results are compatible with the hypothesis that the "toxic" substance is protein or lipoprotein in nature. It does not appear to be one of the better known constituents of platelets (Table 2).

The inhibitory effects of platelets on lymphocyte cultures do not depend on the presence of intact platelets. The results from cultures with frozen and thawed platelets and homogenized platelets appear in Figure 5.

Platelets prepared for lymphocyte cultures were first concentrated by centrifugation and then frozen and thawed three times in dry ice and acetone, and

homogenized in a small Waring blender. Homogenized platelets were then centrifuged at 100,000 g_n for one hour. The particulate and soluble fractions of the homogenates were tested separately for "toxic" activity and compared to the "toxicity" of frozen and thawed platelets. A summary of the results appears in Figure 5. It can be seen that frozen and thawed platelets most nearly approximate the "toxicity" of intact platelets. Separating the soluble and insoluble fractions reduced "toxicity" which appears to be localized in the insoluble fraction. The difference in total toxicity between freeze-thawed platelets and homogenized platelets may well result from proteins being denatured by shearing forces developed in the Waring blender.

Platelet "toxicity" does not depend on intact and viable platelets and appears to be a function of the insoluble platelet debris composed mainly of membrane bound vesicles and some intact granules [5].

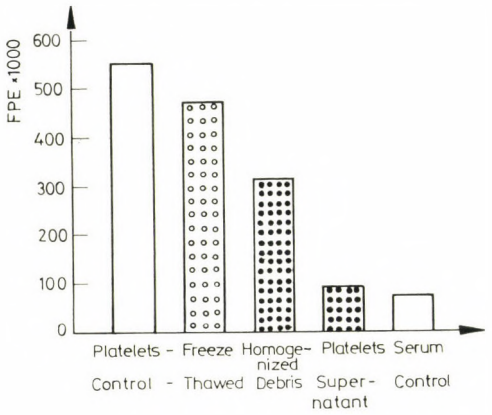


Fig. 5. The effects of freeze thawing and homogenization upon the inhibitory activity of platelets in PHA serum lymphocyte cultures

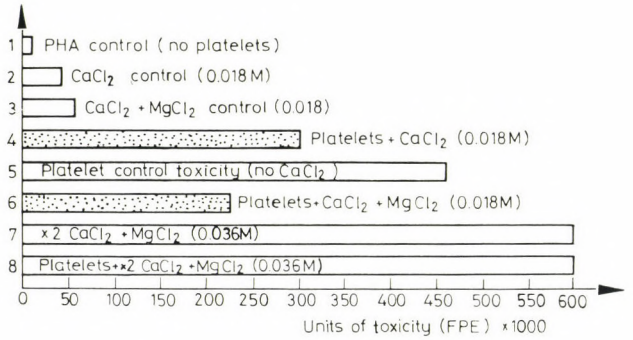


Fig. 6. The effect of the addition of calcium and magnesium ions on platelet inhibited serum PHA cultures of human peripheral blood lymphocytes. (100,000 FPE = 100,000 fresh platelets/mm^3)

The known involvement of divalent metallic ions in platelet aggregation might cause a reduction in the levels of these ions in the cultures below that are required for optimal lymphocyte growth. To investigate this possibility lymphocyte cultures were set up with a standard dose of platelets, 550×10 per ml of culture. In these cultures the concentration of $CaCl_2$ or $MgCl_2$ was increased from 0.0018 M to 0.018 M by the addition of 0.05 ml of molar solution of the respective salt (Figure 6). It can be seen that the $CaCl_2$ at a concentration of 0.018 M does not affect lymphocyte stimulation, shown in line 2, and does reduce platelet inhibition, shown in line 4, as compared to line 5. The two salts in combination at a lower concentration also reduce toxicity (line 6) but not at double the concentration (lines 7 and 8). However, increasing the number of calcium ions up to the level at which they themselves become toxic clearly inhibits the phenomenon. Further addition of magnesium ions further inhibits but does not altogether abolish platelet toxicity. Surprisingly, platelet addition does not appear to decrease the effect of toxic levels of magnesium and calcium ions. It is concluded that these two salts partially reduce platelet inhibition of lymphocyte cultures by interfering with the adsorption or inactivation of PHA produced by platelets.

The platelet experiments described above were performed using dog platelets and human blood lymphocytes. Parallel experiments were performed using human platelets and human lymphocytes with essentially identical results.

Discussion

It is apparent that the partial inhibition of blastoid transformation seen in cultures prepared from heparinized samples of blood is caused by the presence of platelets in the cultures (Figure 2). Not only is there an interference with blastoid transformation but also a lethal action on both stimulated and unstimulated lymphocytes. If the inhibitory, and toxic reactions of platelets to lymphocytes in cultures were related to the presence of a mitogen one might expect to see a higher degree of culture inhibition or death in the stimulated cultures; however, this is not true. Lymphocytes are stimulated in the presence of PHA and platelets. The normal rate of lymphocyte survival and morphology is seriously altered, however. It would appear, therefore, that the mitogen is not converted into the toxic substance and does not contribute to the inhibition of blastoid transformation. This agrees with similar experiments of Torbett [11] in which she cultured rabbit platelets with both unstimulated and PHA-M stimulated rabbit lymphocytes. Her conclusions were that autologous platelets cultured with autologous lymphocytes and serum were both inhibitory to blastoid transformation and lethal to a certain percentage of unstimulated and stimulated cells.

Yachnin [13, 14] has reported that platelets in low platelet lymphocyte ratios $3-10 : 1$ (we used ratios of $100-600 : 1$) actually potentiates the mitogenic activity of PHA-P and PWM. He also reported that platelets in MLC and in ratios of greater than 10 : 1 in PHA cultures were inhibitory to lymphocyte

transformation. Yachnin explains the platelet potentiation of lymphocyte stimulation by a cell-surface matrix theory of mitogenic concentration in which the molecules of mitogen are organized and concentrated on the surface of the platelets in a manner more accessible to the lymphocytes.

We homogenized platelets in a small blender and separated the particulate from the soluble platelet components with centrifugation at 100,000 g_n for 1 hr. Almost 75 per cent of the platelets' capacity to inhibit blastoid transformation remained with the membranous components. This does not explain or reveal the toxic substance in the platelets' membrane, but it does localize the search to the membrane.

Working with the suboptimal PHA levels and using minimal platelet doses Yachnin obtained both stimulation and inhibition depending upon PHA/platelet ratios. Our results agree with Yachnin et al. that high platelet/PHA ratios are inhibitory to blastoid transformation. Our prime concern has been the effect of physiological levels of platelets on the lymphocytes in culture with standard PHA doses as used in most laboratories. At such levels, i.e., 100,000 – 500,000 platelets/mm^3 the effect is always inhibitory.

These results may well explain some of the variability that is often found with PHA culture technics particularly in cultures prepared from heparinized plasma. Even separating the lymphocytes from their plasma and repeated washing leaves a large number of platelets as contaminants of the cell suspension. We have found rather hard centrifugation (1000 g_n for 25 min) necessary to remove all platelets from plasma samples and even defibrination leaves a small number as serum contaminants. The extent of depression of blastoid transformation which can be expected from such contamination may be seen from Figures 1 and 2. We, therefore, echo Yachnin's warning that "comparative studies of human peripheral blood lymphocyte transformation in health and disease which do not remove these contaminants or control their number are subject to the most tentative interpretation".

The mechanism of this effect of platelets is at present unexplained; it cannot be due entirely to binding of divalent metallic ions as firstly, normal transformation is not completely restored when additional divalent ions are added to the cultures, and secondly, the addition of platelets does not reduce the toxicity of toxic levels of calcium and magnesium.

References

1. Brecher, G., Cronkite, E. P.: Morphology and enumeration of human blood platelets. *J. appl. Physiol. 3*, 365 (1950).
2. Chessin, L. N., Rinehart, C. J., Douglas, S. D., Glade, P.: The response of sensitized human circulating lymphocytes following pneumococcal infection. Proc. 4th Leukocyte Culture Conference, Appleton-Century-Crofts, New York, 1969, pp. 421–428.
3. Cullen, M. H.: The response of guinea-pig lymphocytes to phytohaemagglutinin. B. Sc. Thesis, Bristol University, England, 1968.

4. Hepler, O. E.: Manual of Clinical Laboratory Methods, 4th edition. Charles C. Thomas, Springfield, Ill., 1949, p. 356.
5. Holmsen, H., Day, H. J.: The selectivity of the thrombin-induced platelet release reaction: Subcellular localization of released and retained constituents. *J. Lab. clin. Med. 75*, 840 (1970).
6. Leventhal, B. G., Buell, D. B., Yankee, R., Rogentine, G. N., Terasaki, P.: The mixed leukocyte response: The effect of maternal plasma. Proc. 5th Leukocyte Culture Conference, Academic Press, New York, 1970, pp. 473–484.
7. Metcalf, W K.: Some experiments on the phytohaemagglutinin culture of leukocytes from rats and other mammals. *Exp. Cell Res. 40*, 490 (1965).
8. Metcalf, W. K.: The PHA response of rat lymphopoietic tissue. In: The Biological Effects of Phytohaemagglutinin (ed. M. W. Elves). Charles Salt Research Centre, Oswestry, England, 1966, pp. 57–66.
9. Polgar, P. R., Cooperband, S. R., Kibrick, S.: Binding of PHA to human lymphocytes in culture. Proc. 4th Leukocyte Culture Conference, Appleton-Century-Crofts, New York, 1969, pp. 13–20.
10. Tocantins, L. M., Kazal, L. A., eds.: Blood Coagulation, Hemorrhage and Thrombosis. Grune & Stratton, New York, 1964.
11. Torbett, M.: A study of the effects, and the role of platelets in these effects, of the synthetic contraceptive, Ovral, on the culture characteristics of the blood lymphocytes of New Zealand rabbits. Ph. D. Thesis, University of Iowa, 1972.
12. Wilson, J. D., Thomson, A. E.: Death and division of lymphocytes. *Lancet 2*, 1120 (1968).
13. Yachnin, S.: The potentiation and inhibition by autologous red cells and platelets of human lymphocyte transformation induced by pokeweed mitogen, concanavalin A, mercuric chloride, antigen, and mixed leukocyte culture. *Clin. exp. Immunol. 11*, 109 (1972).
14. Yachnin, S., Allen, A. W., Baron, J. M.: The potentiation of phytohaemagglutinin-induced lymphocyte transformation cell–cell interaction. *Cell Immunol. 3*, 569 (1972).

Correspondence: Dr. D. C. Cress, Creighton University, School of Medicine, 2500 California Street, Omaha, Nebraska 68178, USA

Haematologia 9 (1—2), pp. 15—20 (1975)

Effect of Phytohaemagglutinin on Primary Immune Response in the Rat

VERA KUTAS, ELISABETH ELEKES, KATALIN MERÉTEY and L. KOCSÁR

"Fréderic Joliot-Curie" National Research Institute for Radiology and Radiohygiene, Budapest, Hungary

(Received February 15, 1973)

PHA pretreatment if given as a single stimulus exerted a stimulatory effect on SRBC haemolysin production in rats. If administered repeatedly, it proved to be immunosuppressive.

Little is known about the effects of PHA *in vivo*. Some authors found a marked immunosuppressive effect in mice and rats [1—3], others a stimulation or inhibition of antibody production, depending on the type of the antigen [4, 4a].

Petrányi et al. [5] studied the immunosuppressive and adjuvant effects of PHA after intravenous and intraperitoneal administration, and concluded that when given intravenously, PHA had an adjuvant effect on humoral antibody production. In the experiments to be reported PHA was injected intravenously to study how different PHA doses or the same dose divided into several fractions affected the primary immune response to sheep red blood cells (SRBC).

Materials and Methods

R(AxLE)Hooded F_1 hybrid male rats weighing 220 to 240 g were used. They were immunized by a single intravenous injection of 4.10^8 SRBC. PHA-treatment (PHA-P, Difco) always preceded immunization and was performed with doses defined in relation to the maximum tolerated dose (26 mg/kg) determined according to Dickson and Mood [6].

The animals were divided into 7 groups of 5 rats each. The various groups were PHA-treated and immunized as follows: 1) 4.10^8 SRBC on day 0; 2) 1/16th of the maximum tolerated dose on day −1, 4.10^8 SRBC on day 0; 3) 1/4th of the maximum tolerated dose on day −1, 4.10^8 SRBC on day 0; 4) the maximum tolerated dose on day −1, 4.10^8 SRBC on day 0; 5) the maximum tolerated dose given on days −2 and −1, 4.10^8 SRBC on day 0; 6) the maximum tolerated dose given on days −3, −2 and −1, 4.10^8 SRBC on day 0; 7) the maximum tolerated dose on day −2, 4.10^8 SRBC on day 0. The animals were sacrificed on day 5 after the antigen stimulus, except group 7, which was saved for tracing the serum titre for 1 month.

Relative spleen weight (mg spleen/g body weight) and nucleated spleen cell count were determined. The immune response was evaluated on the basis of the following parameters: the antibody producing cell count determined according to Jerne et al. [7] in the whole spleen and related to 10^6 nucleated spleen cells; the IgG-type antibody producing cell count in the spleen related to 10^6 spleen cells, determined by the indirect plaque method [8].

Humoral immune response was measured on the basis of the mercapto-ethanol-resistant (MER) and mercaptoethanol-sensitive (MES) haemolysin titres, using Takácsy's micromethod [9, 10].

Results

Low doses of PHA proved to be ineffective on relative spleen weight (Fig. 1); its significant rise was induced only by the maximum tolerated dose. The nucleated spleen cell count did not show any parallelism with spleen weight; this count was comparable in every group and ranged from 2.10^8 to 3.10^8.

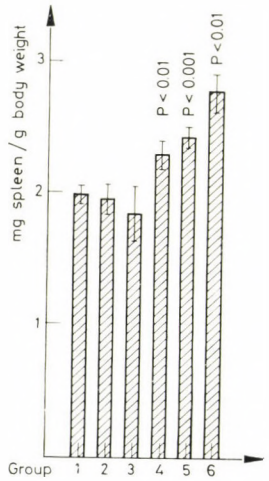


Fig. 1. Effect of different PHA doses on relative spleen weight

The relative antibody producing cell count (plaque/10^6 spleen cells) (Fig. 2a and b) was definitely high in every group where PHA was administered a single time. However, when the maximum tolerated dose was administered two or three times, a suppression of the immune response, proportional with the number of PHA doses, could be observed. This was true for both the 19S and 7S antibody producing cells measured as direct and indirect plaque number/10^6 cells.

Table 1

Serial No. of group	PHA-P-pretreatment	Immunization
1	—	4.10^8 SRBC on day 0
2	1/16 of maximum tolerated dose on day −1 (1.62 mg/kg)	4.10^8 SRBC on day 0
3	1/4 of maximum tolerated dose on day −1 (6.5 mg/kg)	4.10^8 SRBC on day 0
4	maximum tolerated dose on day −1 (26 mg/kg)	4.10^8 SRBC on day 0
5	maximum tolerated dose on days −2 and −1 (26 mg/kg on day −2) (+26 mg/kg on day −1)	4.10^8 SRBC on day 0
6	maximum tolerated dose on days −3, −2 and −1 (26 mg/kg on day −3) (+26 mg/kg on day −2) (+26 mg/kg on day −1)	4.10^8 SRBC on day 0
7	maximum tolerated dose on day −2 (26 mg/kg on day −2)	

The number of PHA-treatments affected even more markedly the total antibody producing cell count in the spleen (Fig. 3).

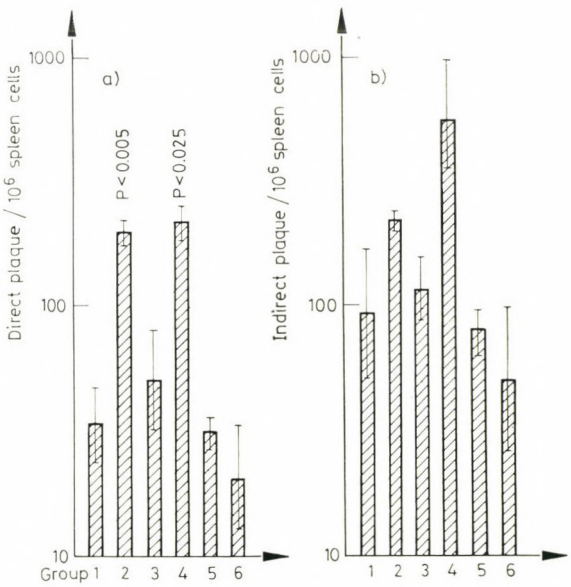


Fig. 2. Relative count of antibody producing cells after various PHA pretreatments

The changes in the serum SRBC haemolysin titre were of a lower degree. The direction of the changes was in good agreement with the rate of immune reactivity determined by the plaque method. Elevated serum titres were found after a single PHA treatment, while several PHA doses proved less effective (Fig. 4). In the time kinetics of the humoral immune response (Fig. 5a, b, group 7), in the appearance of 19S (MES) haemolysins and of the peak titre there was no difference between the control and the PHA-treated group. Still, the drop of the haemolysin

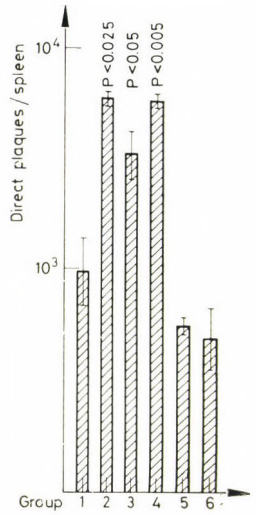


Fig. 3. Total count of antibody producing cells in the spleen after different PHA pretreatments

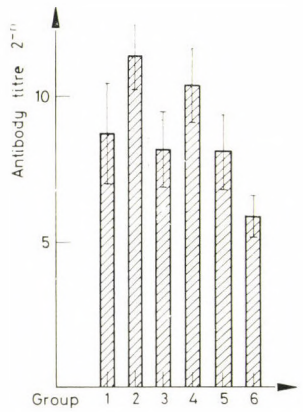


Fig. 4. SRBC haemolysin titre in serum of PHA pretreated rats

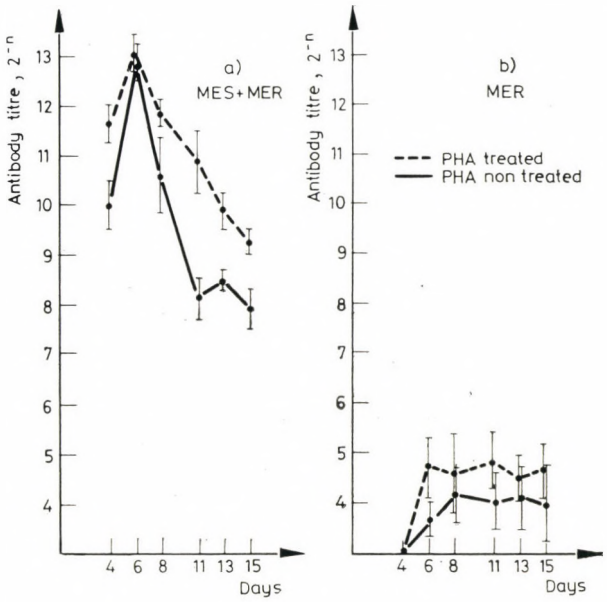


Fig. 5. Effect of PHA pretreatment on MES and MER haemolysin titres in rat sera

titre following the primary antigen stimulus was more marked in the control group. In accordance with this observation, the MER haemolysin titre reached the highest value in the PHA-P-treated group. Even the MER titre was higher in the PHA-pretreated group.

Discussion

PHA-treatment is known to exert an inhibitory effect on the immunological responsiveness of the cells [11, 12]. Its effect on the humoral response is often insignificant. On the other hand, under our experimental conditions, PHA-treatment elicited definitely adjuvant effect. Even a 16-fold difference in the single dose failed to induce an essential difference in action, but this depended on the number of doses injected. While a single administration of the maximum tolerated dose exerted an adjuvant effect, its two or three times repeated injection had a negative effect on antibody production. The phenomenon may satisfactorily explain the immunosuppressive effect in graft rejection, late hypersensitivity, graft vs. host reaction, since in such cases treatment is usually prolonged [11].

The time relation between PHA treatment and the actual antigen stimulus too might be of importance. In our experiments, however, pretreatment on days -1 or -2 did not cause any important difference in the result.

A further problem connected with the mechanism of PHA action is whether it represents some specific antigen or some aspecific stimulus for the immune mechanism. In the experiments reported, the parallelism with the endotoxin-induced adjuvant effect has automatically arisen, where endotoxin acts both as specific and as aspecific stimulus [13]. The same difference in the adjuvant effect has been observed also for endotoxin, depending on the single or serial administration of the same endotoxin dose [14]. Or, else, the repeated administration of the same dose might represent some cumulated dose which on account of its amount inhibits immune reactivity.

References

1. Markley, K., Smallman, E., Evans, G.: Decrease of mouse circulating antibodies to sheep erythrocytes by phytohemagglutinin. *Int. Arch. appl. Immunol. 321*, 482 (1967).
2. Sprefacio, F., Lerner, E. M.: The action of the primary and secondary immune response of the mouse to phytohaemagglutinin. *J. Immunol. 98*, 407 (1967).
3. Elves, M. W.: Suppression of antibody production by phytohaemagglutinin. *Nature (Lond.) 213*, 495 (1967).
4. Jasin, H. E., Ziff, M.: Effect of phytohaemagglutinin on the immune response. *Immunology 14*, 735 (1968).
5. Petrányi, Gy., Jr. Jánossy, Gy., Alföldy, P.: Effect of phytohaemagglutinin on plaque forming cells in the mouse spleen. *Nature (Lond.) 221*, 76 (1969).
6. Dickson, W. J., Mood, A. M.: Method for obtaining and analyzing sensitivity data. *J. Amer. stat. Ass. 43*, 109 (1948).
7. Jerne, N. K., Nordin, A. A., Henry, C.: The agar plaque technique for recognizing antibody-producing cells, in Amos and Koprowsky: "Cell bound antibodies", pp. 109—125. Wistar Institute Press, Philadelphia 1963.
8. Dresser, D. W., Wortis, H. H.: Use of an antiglobulin serum to detect cells producing antibody with low haemolytic efficiency. *Nature (Lond.) 208*, 859 (1965).
9. Takátsy, G.: The use of spiral loops in serological and virological micromethods. *Acta microbiol. Acad. Sci. hung. 3*, 185 (1955).
10. Hege, J. S., Cole, L. J.: Antibody plaque-forming cells: Kinetics of primary and secondary responses. *J. Immunol. 95*, 559 (1966).
11. Markley, K., Thornton, S. W., Smallman, E.: On the mechanism of action of phytohaemagglutinin in cellular immunity. *Proc. Soc. exp. Biol. (N.Y.) 139*, 37 (1972).
12. Moore, D., Slavin, R. G.: The effects of phytohemagglutinin and antilymphocyte globulin in inducing immunosuppression and tolerance in mice. *Transplantation 11*, 563 (1972).
13. Freedman, H. H.: Antibody formation in endotoxin-tolerant mice. *Proc. Soc. exp. Biol. (N.Y.) 121*, 1228 (1966).
14. Elekes, E., Merétey, K., Várterész, V.: Adjuvant effect of endotoxin on primary antibody formation in irradiated rats. *Path. et Microbiol. (Basel) 37*, 302 (1971).

Correspondence: Dr. V. Kutas, Frédéric Joliot-Curie National Research Institute for Radiobiology and Radiohygiene, Pentz Károly u. 5, 1221 Budapest, Hungary

Haematologia 9 (1—2), pp. 21—33 (1975

Lymphocyte Immunological Patterns in Leukaemia: A Review[1]

G. ASTALDI, GIULIA C. B. ASTALDI[2], ÜLKÜ TOPUZ[3], LAURA GUARINA

The Blood Research Foundation Centre,[4] Municipal Hospital, Tortona, Italy
and Division of Haematology and Oncology, Institute G. Gaslini, Genova, Italy

(Received April 10, 1975)

Investigation of the cell S—Ig in acute lymphocytic leukaemia (ALL), at the onset or relapse of the disease, shows quite marked differences from patient to patient according to the extent of the immunofluorescent-positive cells. They may vary from 0.5 to 25% or more. When these Ig-positive cells are treated with trypsin and then incubated "in vitro" for six hours, many of them are no longer Ig-positive, i.e. they do not synthesize Ig. It might be possible, that the membrane-Ig observed before trypsinization does not represent true Ig-determinants of mature B-cells (antibodies attached to leukaemia-specific determinants?). The extent of these features decrease in remission until their disappearance. Relationship between the cell immunological patterns and the treatment response in ALL could exist. In a group of ALL-patients under the same treatment, that is, vincristine and prednisone, the correlation between the course of the disease after the above-mentioned therapy showed quick and complete remission in patients with low percentage of Ig-positive cells (below 10%) and poor improvement (often without complete remission) in patients with higher percentage of Ig-positive cells. Among the most important B-lymphocyte abnormalities in chronic lymphocytic leukaemia (CLL) are the following: (a) fluorescence intensity may vary not only from patient to patient, but also from cell to cell in the same patient; (b) the Fc-receptor can be lacking; (c) the C3b-receptor is not always present, or it is from 2 to 20-folds less frequent than the C3d-receptor, whereas normal human lymphocytes do not show any outstanding differences between the number of EAC rosette-forming cells either when tested with mouse complement (C3d-receptor) or with human complement C3b-receptor); (d) the traffic capacity of peripheral-blood B-lymphocytes in CLL is quite defective. Results of the observations on lymphocytes in CLL, taken as a whole, suggest that CLL is in general given by the expansion of an abnormal clone of cells of B origin, arrested in their maturative development, non-responsive to the mitogen stimulation, accumulating in the peripheral-blood for a traffic deficiency. On the contrary, the T-cell class is apparently normal, and the T-cell extent in CLL-peripheral blood can be even greater than normal when taken as absolute value.

[1] Paper delivered at the International Symposium on the Treatment of Acute Leukaemia, Budapest, Hungary, April 10—11, 1975.

[2] Present address: Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, The Netherlands.

[3] From the University Medical School of Ankara, Turkey. Present address: The Blood Research Foundation Centre, Tortona, Italy.

[4] Supported by The Blood Research Foundation, Washington, D. C. (USA).

1. Introduction

Before discussing the immunological features of lymphocytes from lymphocytic leukaemias we would like to summarize, in the accompanying Table 1, the current status concerning the most relevant markers of immune competent cells from normal human peripheral blood, as well as the so-called "normal" values obtained in our laboratories.

Table 1

Markers of the lymphocyte classes and monocyte

Marker	Type of cells					Normal values per cent (9)
	T	B	K	Null	Monocyte	
E-rosette	+	−	−	−	−	65±15
EA-rosette	± (1)	++-(2)	+	−	+	18± 5
Aggregated IgG (3)	± (1)	++-(2)	+	−	+	18± 5
EAC^{hu}-rosette (4)	−	+	+	−	+	17±10
EAC^{mo}-rosette (5)	−	+	+	−	+	17±10
Membrane Ig	± (6)	+	−	−	+-	25±10
EB virus	−	+	−	−	−	19±10
Anti-thymus	+	−	−	−	−	68±10
Anti-brain (7)	+	−	−	−	−	70±10
Anti-B	−	+	−	−	−	20±10
Autologous rosette (8)	±	−	−	−	−	2± 1
Active rosette (8)	++−	−	−	−	−	20±13
Normal values per cent (10)	68±10	20±10	8±7	4±4		

(1) Present only on the activated and not on resting stage T cells.

(2) Present mainly on young B cells; may be absent from old ones.

(3) Studies on human peripheral blood lymphocytes and cell lines indicate that it may be a marker different from that detected by the EA-rosette.

(4) Human complement reveals C3b receptors only.

(5) Mouse complement reveals C3d receptors only.

(6) IgM-k are present on T cells at a 100- to 400-fold lower concentration than on B cells.

(7) The human brain seems to possess antigens in common vith thymocytes

(8) Both autologous and active rosettes detect subpopulations of T-lymphocytes, the function of which have not yet been identified.

(9) Human peripheral blood mononuclear cells after separation on a Ficoll-Hypaque gradient.

(10) Human peripheral blood lymphocytes after separation on a Ficoll-Hypaque gradient and monocyte removal by means of carbonyl iron.

2. Chronic lymphocytic leukaemia (CLL)

As of four years ago, it has been possible to classify most cases of CLL as disorders of B-lymphocytes. Indeed the majority of CLL-peripheral blood lymphocytes have surface membrane immunoglobulins (Ig) [1, 2, 39, 48, 73, 78, 80, 81, 85, 89, 95, 100]. Besides, few of them are E-rosette-forming cells [27]. In addition, the above-mentioned cells are minimally responsive to PHA, ConA, and PWM in three-day cell cultures [13, 71, 99]. Increased response to mitogenic stimulation is observed if the culture is prolonged up to or beyond seven days [19, 51, 52, 74, 75, 107, 108]. In the prolonged cultures (14 days), a given extent of blastic transformation of CLL-lymphocytes may even occur without any mitogen, just in the presence of homologous serum, whereas this phenomenon does not occur for normal lymphocytes [76, 83]. It is possible that the lymphocytes from CLL would not respond at all to mitogens were it not for the residual T cell population unaffected by the leukaemic process. These T cells account for the low level of tritiated thymidine incorporation seen in mitogen stimulated cultures [68, 69, 93, 108].

Several authors support the clonal nature theory of B-lymphocytes in CLL [38, 78, 87, 92], since in every patient with CLL only one Ig type of light chain determinant is present on the cell surface, and this characteristic is also seen in the patients studied by us [14]. The feature might not be constant, since the presence of both lambda and kappa determinants in the lymphocytes of the same patient was reported [73, 80]. On the other hand, after the removal of Ig by trypsinization, B-lymphocytes of CLL synthesized only one heavy chain type, primarily μ and only one light chain type, primarily kappa [86, 87, 94]. In those experiments μ, gamma and alpha but no delta determinants on the cell membrane were evaluated. Experiments for detecting the presence of IgD showed that the majority of B-lymphocytes have membrane IgD and IgM. Frequently, these two immunoglobulins coexist on the same cell [1, 14, 41, 50, 59, 77].

The clonal nature theory of B-lymphocytes in CLL has been recently substantiated by a further observation. When serum Ig monoclonality is present in CLL, it appears idiotypically identical to the surface-Ig shown by the lymphocytes of the same patient (41, 42). Again, B-lymphocyte membrane IgD and IgM have the same idiotype [84, 91, 92]. This indeed offers the final evidence that CLL is a disease characterized by clonal expansion of B leukaemic cells.

"Sandwich" radioimmunological labelling has shown the fluorescence of membrane Ig of B-lymphocytes in CLL to be less intense than that in normal subjects [106]. These data favour a maturation defect of these cells, as the number of Ig receptors on B-lymphocytes increases with their maturation. An additional proof of the defective maturation of B-lymphocytes from CLL is suggested by the above-mentioned coexistence of IgM and IgD on the surface of those cells, since IgM determinants are carried by early lymphocytes in human embryonic lymphatic tissue (105, 105). The same monoclonal proliferation of CLL B-lymphocytes is considered a sign of immaturity of these cells [78, 85–87].

Recent experiments have established that the intensity of B-lymphocyte fluorescence in CLL may vary from patient to patient [38]. It is likely that not all patients with CLL have their lymphocytes blocked at the same stage of maturation. Even the maturation of each individual lymphocyte from the same patient is not constant, since membrane fluorescence of IgD and IgM may vary considerably from cell to cell in the same patient [41].

The study of other B-lymphocyte markers has proven that a low percentage of CLL Ig-positive lymphocytes have receptors for human C_3b complement [55]. These leukaemic cells show features similar to embryonic spleen cells, many with membrane IgM and IgD, while only few have receptors for C_3 and Fc. On the other hand, some cases of CLL with many Ig-positive lymphocytes with complement receptors but without Fc receptors have also been observed [95, 96].

Other CLL patients have shown different features with regard to B cell markers, suggesting a different stage in their maturation block. Dickler et al. [32] described some cases of CLL with lymphocytes devoid of membrane Ig, unable to form E-rosettes but capable of fixing heat-aggregated IgG, therefore endowed with Fc receptors. A patient with similar features was reported also by Seligmann et al. [94]. Other CLL patients showed membrane Ig-negative lymphocytes, but had complement receptors [89].

While normal human lymphocytes do not show any outstanding differences in the number of EAC-rosette-forming cells either when tested with mouse or with human complement, in contrast CLL-lymphocytes show a big difference in favour of mouse complement. In fact, CLL-lymphocytes give from two to twenty times more EAC-rosettes with mouse complement than with human complement as Ross et al. observed [88]. They also showed that on human lymphocytes there are two distinct receptors, one for human C_3 and the other for murine C_3 [89]. Since the fraction used in the formation of EAC-rosettes with human complement is C3b, while with mouse complement it is C3d, we believe that the CLL-cells have normal or almost normal C3d receptors, but a much lower degree of C_3b receptors. This interpretation would also account for the discrepancy with the results of Jondal et al. [55] as well as of Del Giacco et al. [31] who used human complement for EAC detection.

Unlike normal subjects where the lymphocyte concentration in the thoracic duct lymph is higher than that of peripheral blood, patients with CLL have a relative lymphopenia in their thoracic duct and efferent central lymph, while in peripheral blood the lymphocyte concentration is high [20, 23]. Studies *in vitro* showed that lymph-lymphocytes from CLL are more responsive to mitogen-stimulation [35, 36, 49] than those from the peripheral blood. Subsequent studies on lymphocyte markers revealed that in the peripheral blood of CLL patients, the majority of lymphocytes has membrane Ig, while cells with membrane Ig are less than 1% in the lymph of the same patient [38]. It was also observed that CLL-lymphocytes recirculate from blood to lymph less than normal lymphocytes [24]. Transfusing leukaemic patients with their own lymphocytes drawn from their blood and lymph, and labelled differently, showed

a) that the lymph-lymphocytes disappear rapidly from the blood into which they are transfused, which indicates a normal traffic of lymphocytes between the intravascular and extravascular sectors;

b) that the peripheral blood lymphocytes remain a long time in the same blood where they are reinjected, thus showing their property of intravascular persistence, i.e. their inability to recirculate.

Other abnormalities shown by the CLL-lymphocytes concern their enzymatic features, including decreased number of lysosomes and altered patterns of beta-glucuronidase, acid-phosphates, protease, esterase activities [25, 63]. Also, the cAMP level is generally low in CLL-lymphocytes, as compared to normal lymphocytes [93].

It is therefore assumed that CLL cells are made up of an anomalous (immature?) clone of B origin which accumulates in the blood, since it is unable to recirculate normally, and of a T population which is mitogen-responsive and capable of recirculation. This thymus-derived population seems quite small in the peripheral blood of CLL patients as compared to the B cell population, but in absolute values it turns out to be greater than normal [14, 27, 64].

Thus far, only two CLL cases with lymphocytes with both T and B markers have been reported [82, 96]. More numerous, though rare, are the CLL patients whose lymphocytes had neither membrane Ig nor C3 receptors, nor Fc receptors. On the other hand, these cells formed a high percentage of E-rosettes, and were killed by a T-lymphocyte-specific antiserum [26, 32, 62, 109]. Since clinically these cases were typical CLL forms, some rare cases of CLL seem to be of T origin.

Because of space limitation, and the current state of the art, we shall confine ourselves to reporting only a few data concerning personal observation on the effect of spleen irradiation on the immunological characteristics of peripheral-blood lymphocytes in CLL. First of all, irradiation of the spleen may cause an increase in the PHA-response of blood lymphocytes in the three-day culture [12, 18]. It was suggested that the natural course of the disease, as well as chemotherapy and splenectomy may also alter the ratio of the lymphocyte population in CLL-blood [57].

We studied a group of CLL patients before and after spleen irradiation [14]. Prior to treatment, the patients had high numbers of peripheral blood lymphocytes with membrane Ig. These immunoglobulins were actively produced after trypsin treatment, too. On the majority of the lymphocytes of all the patients, delta determinants, frequently associated with μ, seldom with gamma, were present. The majority of these patients showed light chain restriction for kappa, and a minority for lambda, while there was no monoclonality in their sera. As regards the T-lymphocytes, there was a low relative percentage of E-rosette-forming cells, but in absolute value the number of E-rosettes was higher than normal. The peripheral blood lymphocytes of our patients were minimally responsive to mitogens after three-day culture, as well as to the antigens and allogenic cells after five- to seven-day culture.

After spleen irradiation, in the majority of patients the extent of cells with

surface Ig decreased both in absolute and in relative value, and the extent of cells with delta determinants also decreased. At the same time, a small percentage of cells with μ-gamma association was detected. Light chain restriction remained constant. The response to mitogens, antigens and to allogenic cells attained higher values than the initial ones in a few instances they were near that of normal controls. Moreover, the relative E-rosette count increased, while its absolute value was lower than that detected before irradiation of the spleen. Since the E-rosette values after spleen irradiation were higher than those observed after chemotherapy [27], and with the first therapy a μ-gamma association was observed in some cases, one may suppose that spleen irradiation eliminated the leukaemic cells selectively, and probably caused some changes (maturation ?) in the Ig-determinant pattern of the cells within the same leukaemic clone.

3. Acute lymphocytic leukaemia (ALL)

ALL is known to show an intense heterogeneity in clinical course, morphologic cell picture and response to therapy. These sometimes quite prominent cytologic and clinical differences might be due to a different origin of leukaemic cells. Therefore, there might be a different type of leukaemic cell population in question. Recently, different ALL forms have been proposed on the ground of morphologic criteria [37, 65]. The study of immunologic markers [3–7, 9–11, 26, 34, 43, 47, 53, 55, 60, 68, 69, 94, 95, 100, 102] might, however, provide more insight into this matter.

Many cases of ALL caused by T-lymphocytes have been reported [21, 26, 29, 43, 54, 56, 58, 70, 94, 100], but not all cases of ALL are of T-lymphocyte origin. According to Gatti [45], they do not exceed 20% of the total number of ALL. On the other hand, only two cases of ALL originating from B cells have been reported, both in adult patients [43, 47]. In addition, several cases of ALL whose lymphocytes did not show any markers, such as "null" cells, have been reported [21, 26, 58, 106]. It could therefore be assumed that a number of cases classified as ALL are not really due to immune competent lymphocytes. Theoretically, they might be formed by (*a*) lymphoid committed stem cells; (*b*) myelogenous committed stem cells; (*c*) uncommitted stem cells.

The possibility that some cases of ALL are really due to lymphoid committed stem cells which have not yet fully developed their own T or B cell markers is substantiated by some experimental evidence. "*In vitro*" preincubation of ALL-"null" cells with thymic hormone [6] caused the expression of T-lymphocyte markers, such as E-rosette formation [2, 46, 90] indicating that at least some cases of ALL are due to a T_0 cell expansion.

Terminal deoxynucleotidyl transferase is not found in peripheral-blood lymphocytes [28] even after PHA stimulation [44], as well as in lymphoblastoid cell lines [101]. The above-mentioned enzyme is found at very low concentration in normal bone marrow, in acute myelogenous leukemia, and in the chronic phase

of chronic granulocytic leukaemia [30]. Terminal deoxynucleotidyl transferase is abundant in human thymocytes, as well as in the peripheral blood cells of ALL [66, 67], and in the lymphoblastoid cell lines derived from patients with ALL [101]: this suggests that ALL-cells might arise from thymocytes.

Another problem is the association of leukaemic cells with normal lymphocytes in ALL. Clarification of the relationship between normal and leukaemic cells would decide whether ALL is a disease of all the lymphocytes, or only of a class population. It has been suggested that in untreated ALL there is a residual population of normal T-lymphocytes [15, 33]. In support of this is the fact that memory T-lymphocytes have been observed in some patients at the moment of diagnosis. These patients showed a skin reaction with delayed hypersensitivity and a normal response to anamnestic antibodies [33, 61, 97]. In addition, a blastogenic response to PHA by peripheral blood lymphocytes was also demonstrated in a high percentage of patients with early stage ALL [15, 72]. Further experiments with lymphocyte markers showed that before treatment children with ALL may have a population of lymphoid cells which appears normal, not only morphologically but also with regard to their markers. Borella and Sen [22] reported some cases of ALL in which a small percentage of lymphoblasts formed E-rosettes, while no immature lymphatic cells showed markers for B-lymphocytes, thus suggesting the T origin of the rosetting lymphoblasts of those patients.

As far as the possible presence in ALL of normal B cells together with leukaemic cells is concerned, in untreated ALL patients surface Ig-positive cells were detected, although in small number [4, 7, 8, 10, 43, 45, 94]. However, when these Ig-positive cells were treated with trypsin and incubated "*in vitro*" for six hours, many of them were no longer Ig-positive; that is, they have not synthesized surface-Ig [7–9, 11]. The membrane-Ig observed before trypsinization might therefore not represent true Ig-determinants of mature B cells, but rather antibodies attached to leukaemic determinants.

The problem of predicting the course of ALL according to the feature presented by the patients is an important issue. Pierce et al. [79], Simone [98], as well as others, tried to establish a relationship between the initial clinical picture and the response to treatment. On a morphological basis, Mathé et al. [65] proposed to divide the cases of ALL in forms characterized by small leukaemic cells (microlymphoblasts and prolymphocytes), and in forms characterized by large leukaemic cells (macrolymphoblasts and prolymphoblasts). Patients belonging to the first group seemed to be sensitive to immunotherapy, while those in the second group showed a poor response to the same treatment.

Recent studies by Astaldi A. Jr. et al. [7, 8] have shown that children with ALL may be divided into two main categories, inasmuch as the characteristics of their cells with membrane Ig are concerned. A majority of the patients with a low percentage of membrane Ig-positive cells (0.5 to 9.0%), and a minority of patients with percentage similar to normal (10 to 25%). Thus, by correlating these immunologic characteristics with the response to induction with vincristine and prednisone, it turned out that the patients of the first group

responded well to the treatment and achieved rapid complete remission, while those in the second group were less responsive and complete remission has not been always achieved.

By studying ALL cells by means of a double staining for fluorescence with anti-kappa and anti-lambda sera, it was possible to establish the simultaneous presence of lambda and kappa light chain determinants on the membrane of several lymphocytes [9]. This further supported the fact that not all Ig present on cell surface is produced actively by the tested cells.

These experiments along with the above-mentioned results obtained with trypsinization and resynthesis, show that the surface of some cells of the peripheral blood in ALL may, at least in some cases, be coated by antibodies against antigenic (leukaemic specific?) determinants. The relation between the presence of cells coated by antibodies and the failure to induce remission after vincristine–prednisone induction treatment, might mean that the more de-differentiated (therefore malignant) are the ALL cells, the more numerous (or strong) are the antigenic determinants found on their surface.

We wish to thank Dr. Alberto Astaldi for advice and criticism during the preparation of this paper.

References

1. Aisenberg, A. G., Bloch, K. J.: Immunoglobulins on the surface of neoplastic lymphocytes. *New Engl. J. Med. 287*, 272 (1972).
2. Aiuti, F., Fiorilli, M.: Effetto del fattore timico sulle cellule linfoidi in condizioni normali e patologiche. Comunicazione svolta all'"Incontro sul Linfocito" organizzato dall'Ass. Ital. contro le Leucemie. Roma, 14–15 marzo 1975.
3. Aiuti, F., La Cava, V., Fiorilli, M., Ciarla, M. V.: Lymphocyte surface markers in lymphoproliferative disorders. *Acta haemat. 50*, 275 (1973).
4. Aiuti, F., Papa, G., La Cava, V., Ciarla, M. V., D'Amelio, G., Garofalo, J.: Lymphocyte membrane markers in acute lymphoblastic leukaemia. *Brit. J. Haemat. 27*, 635 (1974).
5. Aiuti, F., Papa, G., La Cava, V., Ciarla, M. V., D'Amelio, R., Monarca, B.: Membrane markers in acute lymphoblastic leukemia. In: Proceedings of Internat. Meeting on Therapy of Acute Leukemias. Ed. by F. Mandelli, S. Amadori, G. Mariani. Minerva Medica, March 1975, p. 395.
6. Astaldi, A. Jr., Astaldi, G. C. B.: Historical review on thymic hormones. *Wadley med. Bulletin* (Special issue) *5*, 131 (1975).
7. Astaldi, A. Jr., Martini, A., Franchini, M. I.: Membrane-bound Ig-bearing cells in the peripheral blood of acute lymphocytic leukemia. *Boll. Ist. Sieroter. Milan. 53*, 294 (1974).
8. Astaldi, A. Jr., Martini, A., Franchini, M. I., Massimo, L.: Membrane immunoglobulin in acute lymphocytic leukaemia cells. *Haematologica 59*, 38 (1974).
9. Astaldi, A. Jr., Martini, A., Massimo, L.: Membrane immunofluorescence in acute lymphocytic leukemia. *New Engl. J. Med. 290*, 1438 (1974).
10. Astaldi, A. Jr., Mori, P. G., Martini, A., Giovannelli, A., Franchini, M. I., Massimo, L.: Markers and properties of a pure cell population in acute lymphocytic leukemia. *Boll. Ist. Sieroter. Milan. 52*, 306 (1973).

11. Astaldi, A. Jr., Pasino, M., Astaldi Ricotti, G., Massimo, L.: Surface immunoglobulin on lymphocytes in acute lymphocytic leukemia. Annual Report Coordinat. Committee Human Tumour Invest. Cell Tissue Organ Culture Study Group, 1974, p. 48.
12. Astaldi, G., Airò, R., Costa, G., Duarte, N.: Milzbestrahlung und immunologische Antwort peripherer Lymphozyten von chronisch-lymphatischen Leukämien. *Blut 13*, 100 (1966).
13. Astaldi, G., Airò, R., Sauli, S.: *In vitro* studies on leukaemic cells. In: Current Research in Leukaemia. Ed. by F. G. J. Hayhoe. Cambridge University 1965, p. 129.
14. Astaldi, G., Astaldi, G. C. B., Paleani Vettori, P., Astaldi, A. Jr.: Spleen irradiation and B/T cell relationship in chronic lymphocytic leukaemia. *Lancet 1*, 529 (1975).
15. Astaldi, G., Massimo, L., Dagna, F., Mori, P. G., Fossati, A.: PHA-blastogenesis in relationship to the cell-type and source in acute leukemia. *Blut 24*, 153 (1972).
16. Astaldi, G. C. B., Guarina, L., Topuz, Ü., Astaldi, A. Jr.: Immunological cell surface markers. LAB (in press).
17. Astaldi, G., Sauli, S., Ratto, L., Costa, G.: Effect of phytohemagglutinin on lymphocytes from different leukemias. *Texas Reports Biol. Med. 23*, 569 (1965).
18. Astaldi, G., Yalcin, B., Astaldi, A. Jr., Paleani Vettori, P., Bologna, P.: Spleen irradiation and lymphocyte blastogenesis in chronic lymphocytic leukemia (CLL). *Wadley med. Bull. 4* 24 (1974).
19. Bernard, C., Geraldes, A., Boiron, M.: Action de la phytohémagglutinine *in vitro* sur les lymphocytes de leucémies lymphoïdes chroniques. *Nouv. Rev. franc. Hémat. 4*, 69 (1964).
20. Bierman, H. R., Bayron, R. L. Jr., Kelly, H., Gilfillan, R. S., White, L. P., Freeman, N. E., Petrakis, N. L.: The characteristics of thoracic duct lymph in man. *J. clin. Invest. 32*, 637 (1953).
21. Borella, L., Sen, L.: T-cell surface markers on lymphoblast from acute lymphocytic leukemia. *J. Immunol. 3*, 1257 (1973).
22. Borella, L., Sen, L.: T and B lymphocytes and lymphoblast in untreated acute lymphocytic leukemia. *Cancer 34*, 646 (1974).
23. Bremer, K., Schick, P., Wack, O., Theml, H., Brass, B., Heimpel, H.: Rezirkulation von Lymphocyten bei Patienten mit malignen lymphatischen Systemerkrankungen. *Blut 24*, 215 (1972).
24. Bremer, K., Schreml, W., Flad, H. D.: Chronic lymphoid leukemia: concentration of normal lymphocytes in the lymph. *Biomed. 21*, 361 (1974).
25. Brittinger, G., Cohnen, G., Douglas, S. D., Konig, E., Augener, W.: Low number of lysosomes and low activity of lysosomal enzymes in human peripheral blood lymphocytes: a marker for B-cells? Internat. Congr. Haematol. Saõ Paulo, Brasil, July 16—21, 1972.
26. Brown, G., Greaves, M. F., Lister, I. A., Rapson, N., Papamichael, M.: Expression of human T and B lymphocyte cell surface markers on leukaemic cells. *Lancet 2*, 753 (1974).
27. Catovsky, D., Miliani, E., Okos, A., Galton, D. A.: Clinical significance of T-cells in chronic lymphocytic leukaemia. *Lancet 2*, 751 (1974).
28. Chang, L. M. S.: Development of terminal deoxynucleotidyl transferase activity in embryonic cell thymus gland. *Biochem. biophys. Res. Commun. 44*, 124 (1971).
29. Chin, A. H., Saiki, J. H., Trujillo, I. M., Williams, R. C.: Peripheral blood T- and B-lymphocytes in patients with lymphoma and acute leukemia. *Clin. Immunol. Immunopath. 1*, 499 (1973).
30. Coleman, M. S., Hutton, J. J., De Simone, P.: Terminal deoxyribonucleotidyl transferase in human leukemia. *Proc. nat. Acad. Sci. (USA) 71*, 4404 (1974).
31. Del Giacco, G. S., Manconi, P. E., Tognella, S., Mantovani, G., Floris, C., Grifoni, V.: Lymphocyte markers in chronic lymphatic leukaemia. Communic. svolta all'Incontro sul Linfocito organizzato dall'Ass. Ital. contro le Leucemia, Roma, 14—15 Marzo, 1975.

32. Dickler, H. B., Siegal, F. P., Bentwich, Z. H., Kunkel, H. G.: Lymphocyte binding of aggregated IgG and surface Ig staining in chronic lymphocytic leukaemia. *Clin. exp. Immunol. 14*, 97 (1973).
33. Dupuy, J. M., Kourilsky, F. M., Fradelizzi, D., Feingold, N., Jacquillat, C. L., Bernard, J., Bousset, J.: Depression of immunologic reactivity of patients with acute leukemia. *Cancer 27*, 323 (1971).
34. Ferrarini, M., Tonda, G. P., Risso, A., Viale, G.: Lymphocyte membrane receptors in human lymphoid leukemias. *Europ. J. Immnol. 5*, 89 (1974).
35. Flad, H. D., Huget, R. P., Bremer, K., Bruch, C.: Two populations of lymphocytes in chronic lymphocytic leukemia (CLL). *Europ. J. clin. Invest.* (Abstract) *2*, 284 (1974).
36. Flad, H. D., Huber, V., Bremer, K., Menne, H. D., Huber, M.: Impaired recirculation of B-lymphocytes in chronic lymphocytic leukemia. *Europ. J. Immunol. 3*, 688 (1973).
37. Flandrin, G., Daniel, M. T.: In: Nomenclature, Methodology and Results of Clinical Trials in Acute Leukemias. Vol. I. Ed. by G. Mathé, P. Posuillart, L. Schwarzenberg Springer, Heidelberg 1973.
38. Froland, S. S., Natwig, J. B.: Identification of three different human lymphocyte populations by surface markers. *Transpl. Rev. 16*, 114 (1973).
39. Froland, S. S., Natvig, J. B., Stavem, P.: Immunological characterization of lymphocytes in lymphoproliferative diseases. Restriction of classes, subclasses and Gm allotypes of membrane-bound Ig. *Scand. J. Immunol. 1*, 35 (1972).
40. Fu, S. M., Winchester, R. J., Feizi, I., Walzer, P. D., Kunkel, H. G.: Idiotypic specificity of surface immunoglobulin and the maturation of leukemic bone-marrow-derived lymphocytes. *Proc. nat. Acad. Sci. (USA) 71*, 4487 (1974a).
41. Fu, S. M., Winchester, R. J., Kunkel, H. G.: Occurrence of surface IgM, IgD and free light chains on human lymphocytes. *J. exp. Med. 139*, 451 (1974b).
42. Fu, S. M., Winchester, R. J., Kunkel, H. S.: Similar idiotypic specificity for the membrane IgD and IgM of human B lymphocytes. *J. Immunol. 114*, 250 (1975).
43. Gajl-Peczalska, K. J., Bloomfield, C. D., Nesbit, M. E., Kersey, J. H.: B-cell marker on lymphoblasts in acute lymphoblastic leukaemia. *Clin. exp. Immunol. 17*, 561 (1974).
44. Gallo, R. C.: Terminal transferase and leukemia. *New Engl. J. Med. 292*, 804 (1975).
45. Gatti, R. A.: Proceedings of Immunological Conference, Pavia. *Boll. Ist. Sieroter. Milan. (Suppl.) 53*, 274 (1974).
46. Goldstein, A. L., Thurman, G. B., Cohen, G. H., Hoofer, J. A.: The role of thymosin and the endocrine thymus on the autogenesis and function of T-cells. In: Molecula Approaches to Immunology. Proc., 1975. Miami Winter Symp. In press.
47. Governa, M., Massimo, L., Rosanda, C., Franchini, M. I., Tonda, G. P.: An attempt to characterize lymphocytes of acute lymphoid leukaemia as T or B cells. *Biomed. Express 19*, 384 (1973).
48. Grey, H. M., Rabellino, E., Pirofsky, B.: Immunoglobulins on the surface of lymphocytes. IV. Distribution in hypogamma-globulinemia, cellular immune deficiency and chronic lymphatic leukemia. *J. clin. Invest. 50*, 2368 (1971).
49. Hersh, E. M., Guinn, G. A., Rossen, R., Wallace, S., Rose, S., Freirech, E. J.: Two populations of lymphocytes in chronic lymphocytic leukemia (CLL). In: Proc. 4th Leukocyte Culture Conf. Ed. by O. R. McIntyre. Appleton Century Crofts, New York 1970. P. 375.
50. Hijmans, W.: Immunocytes in health and disease. *Boll. Ist. Sieroter. Milan. (Suppl.) 53*, 74 (1974).
51. Ippoliti, G. B., Marini, G., Casirola, G., Ascari, E., Invernizzi, R.: Lymphocyte reactivity in chronic lymphocytic leukaemia: effect of repeated and prolonged stimulation with PHA and PWM. Comunic. svolta all'Incontro sul Linfocito organizzato dall'Ass. Ital. contro le Leucemie. Roma, 14—15 Marzo, 1975.
52. Jaksin, B., Matera, L., Pegoraro, L.: Kinetic differences between normal and CLL-lymphocytes stimulated by phyto-hemagglutinin. In: Proc. 2nd Meeting European

and African Division of International Society of Haematology. Prague, 27—29 August, 1973. P. 383.
53. Jamra, M.: B and T lymphocytes in lymphomas and leukemias. *Wadley med. Bull.* (Special issue) *5*, 126 (1975).
54. Jata, J., Klein, G., Kobayoshi, K., Furukawa, T., Yanagisawa, M.: Human thymus lymphoid tissue antigen and its presence in leukaemia and lymphoma. *Clin. exp. Immunol. 7*, 781 (1970).
55. Jondal, M., Wigzel, M., Aiuti, F.: Human lymphocyte subpopulations. Classification according to surface markers and/or functional characteristics. *Transpl. Rev. 16*, 163 (1973).
56. Kaplan, J., Mastrangelo, R., Peterson, W. D. J.: Childhood lymphoblastic lymphoma, a cancer of thymus derived lymphocytes. *Cancer Res. 34*, 521 (1974).
57. Kay, N. E., Douglas, S. D., Estren, S.: T-cells in chronic lymphocytic leukaemia. *Lancet 2*, 1326 (1974).
58. Kersey, J. H., Sabad, A., Gajl-Peczalska, K. J., Hallgren, H. M., Junis, E. J., Nesbit, M. E.: Acute lymphoblastic leukemic cells with T (thymus-derived) lymphocyte markers. *Science 182*, 1355 (1973).
59. Kubo, R. T., Grey, H. M., Pirofsky, B.: IgD: a major immunoglobulin on the surface of lymphocytes from patients with chronic lymphatic leukemia. *J. Immunol. 112*, 1952 (1974).
60. Lancet editorial: Membrane markers in lympho-proliferative disorder. *Lancet 1*, 670 (1975).
61. Larson, D. L., Tomlinson, L. J.: Quantitative antibody studies in man. Antibody response in leukemia and other malignant lymphomate. *J. clin. Invest. 32*, 317 (1953).
62. Lille, J., Desplaces, H., Meeus, L., Saracino, R. T., Brouet, J. C.: Thymus-derived proliferating lymphocytes in a case of chronic lymphocytic leukaemia. *Lancet 2*, 263 (1973).
63. Lisiewicz, J., Cichocki, T., Astaldi, G.: The lysosomal enzymes in lymphocytes. III. Lymphocytes in lymphoproliferative disorders and some other pathological conditions. *Acta vitaminol. enzymol.* In press.
64. Macavei, I., Halmos, S.: High T-cell counts in chronic lymphatic leukaemia. *Lancet 1*, 220 (1975).
65. Mathé, G., Pouillart, P., Weiner, R. R., Mayat, M., Steresco, M., Lafleur, M.: In: Nomenclature, Methodology and Results of Clinical Trials in Acute Leukemias. Vol. 1. Ed. by G. Mathé, P. Pouillart, L. Schwarzenberg. Springer, Heidelberg 1973.
66. McCaffrey, R., Harrison, Th. A., Parkman, R., Baltimore, D.: Terminal deoxynucleoti dyl transferase activity in human leukemic cells and in normal human thymocytes. *New Engl. J. Med. 292*, 775 (1975).
67. McCaffrey, R., Smoler, D. F., Baltimore, D.: Terminal deoxynucleotidyl transferase in a case of acute lymphoblastic leukemia. *Proc. nat. Acad. Sci. (USA) 70*, 521 (1973).
68. Melief, C. J. M., Schweitzer, M., Eijsvoogel, V. P.: Studies on tumor immunity in acute lymphatic leukemia and on transformation kinetics in lymphocytic leukemia. In Proc. 7th Leukocyte Culture Conf. Ed. by F. Daguillard, Academic Press, New York 1973. P. 459.
69. Melief, C. J. M., Schweitzer, M., Zeylemaker, W. P., Verhagen, E. H., Eijsvoogel, V. P.: Some immunological properties of lymphoid cells from patients with acute lymphatic leukemia (ALL). *Clin. exp. Immunol. 15*, 131 (1973).
70. Minowada, J., Ohnuma, T., Moore, G. E.: Rosette-forming human lymphoid lines. I. Establishment and evidence for origin of thymus-derived lymphocytes. *J. nat. Cancer Inst. 49*, 891 (1972).
71. Oppenheim, J. J., Whang, J., Frei, E.: Immunologic and cytogenetic studies of chronic lymphocytic leukemic cells. *Blood 26*, 121 (1965).
72. Osamura, S., Adachi, M., Watasugi, K., Sakao, T.: Cellular immunity in acute leukemia. *Wadley med. Bull.* (Special issue) *5*, 149 (1975).

73. Papamichail, M., Brown, J. C., Holborow, E. J.: Immunoglobulin on the surface of human lymphocytes. *Lancet 2*, 850 (1971).
74. Pegoraro, L., Gavosto, F.: Phytohaemagglutinin-responsive lymphocytes in chronic lymphocytic leukaemia. *Lancet 1*, 1508 (1973).
75. Pegoraro, L., Jaksic, B., Gavosto, F.: T-cells in chronic lymphatic leukaemia. *Lancet 2*, 909 (1973).
76. Perera, D. J. B., Pegrum, G. D.: A factor causing enhanced viability of lymphatic leukaemic lymphocytes. *Acta haemat. 52*, 273 (1974).
77. Pernis, B., Ferrarini, M.: Membrane IgD and the maturation of B-lymphocytes. *Boll. Ist. Sieroter. Milan. 53*, 144 (1974).
78. Pernis, B., Ferrarini, M., Forni, L., Amante, L.: Immunoglobulins on lymphocyte membrane. In: Progress in Immunology. Ed. by B. Amos. Academic Press, New York 1971. P. 95.
79. Pierce, M. I., Borges, W. H., Heyn, R., Wolff, J. A., Gilbert, E. S.: Epidemiological factors and survival experience in 1770 children with acute leukemia. *Cancer 23*, 1296 (1969).
80. Piessens, W. F., Schur, P. H., Moloney, W. C., Churchill, W. H.: Lymphocyte surface immunoglobulins. Distribution and frequency in lymphoproliferative diseases. *New Engl. J. Med. 288*, 176 (1973).
81. Pincus, G., Bianco, G., Nussenzweig, V.: Increase proportion of complement receptor lymphocytes in the peripheral blood of patients with chronic lymphocytic leukemia. *Blood 40*, 303 (1972).
82. Polliack, A., Harven, E., Bentwich, Z., Siegel, F. P., Kunkel, H. G.: Identification of human T and B lymphocytes by scanning electron microscopy. *J. exp. Med. 138*, 607 (1973).
83. Possnerova, V., Hermansky, F., Poch, T., Fortynova, J.: The stimulating effect of some sera on lymphocytes of chronic lymphatic leukemia *in vitro*. *Neoplasma 20*, 251 (1973).
84. Preud'Homme, J. L., Brout, J. C., Clauver, J. P., Seligmann, M.: Surface IgD in immunoproliferative disorders. *Scand. J. Immunol. 3*, 853 (1974).
85. Preud'Homme, J. L., Klein, M., Verroust, P., Seligmann, M.: Immunoglobulines monoclonales de membrane dans les leucémies lymphoïdes chroniques. *Europ. J. Clin. biol. Res. 16*, 1025 (1971).
86. Preud'Homme, J. L., Seligmann, M.: Anti-human immunoglobulin C-activity of membrane-bound monoclonal immunoglobulin M in lymphoproliferative disorders. *Proc. nat. Acad. Sci. (USA) 69*, 2132 (1972/a).
87. Preud'Homme, J. L., Seligmann, M.: Surface-bound immunoglobulins as a cell marker in human lymphoproliferative diseases. *Blood 40*, 777 (1972/b).
88. Ross, G. D., Polley, M. I., Grey, H. M.: Evidence for two distinct complement receptors on the surface of human lymphocytes. *Fed. Proc. 32*, 992 (1973).
89. Ross, G. B., Rabellino, E. M., Polley, M. J., Grey, H. M.: Combined studies of complement receptor and surface immunoglobulin-bearing cells and sheep erythrocyte rosette-forming cells in normal and leukemic human lymphocytes. *J. clin. Invest. 52*, 377 (1973).
90. Sakai, H., Costanzi, J. J., Loukas, D. F., Gagliano, R. G., Ritzmann, S. E., Goldstein, A. L.: Tymosine-induced increase in E-rosette-forming capacity of lymphocytes in patients with malignant neoplasm. *Cancer* In press.
91. Salsano, F., Froland, S. S., Natvig, J. B., Michaelsen, T. E.: Some idotype of B-lymphocyte membrane IgD and IgM: Formal evidence for monoclonality of chronic lymphocytic leukemia cells. *Scand. J. Immunol. 3*, 841 (1974).
92. Schroer, K. R., Briles, D. E., Van Boxel, J. A., Davie, J. M.: Idiotypic uniformity of cell surface immunoglobulin in chronic lymphocytic leukemia. *J. exp. Med. 140*, 1416 (1974).
93. Schwarzmeier, J. D.: Purin-de-novo-Synthese und Verhalten des zyklischen AMP in normalen und pathologischen Leukozyten. *Wien. klin. Wschr. 86*, 716 (1974).

93. Schweitzer, M., Melief, G. J. M., Eijsvoogel, V. P.: The nature of transformating lymphocytes in chronic lymphocytic leukemia. *Europ. J. Immunol. 3*, 121 (1973).
94. Seligmann, M., Preud'Homme, J. L., Brouvet, J. C.: B and T cell markers in human proliferative blood diseases and primary immunodeficiencies with special reference to membrane-bound immunoglobulins. *Transplant. Rev. 16*, 85 (1973).
95. Shevach, E. M., Herberman, R., Frank, M. M., Green, I.: Receptors for complement and immunoglobulin on human leukemic cells and human lymphoblastoid cell lines. *J. clin. Invest. 51*, 1933 (1972).
96. Shevach, E. M., Jaffe, E. S., Green, I.: Receptor for complement and immunoglobulin on human and animal lymphoid cells. *Transplant. Rev. 16*, 3 (1973).
97. Silver, R. T., Utz, J. P., Fahey, J., Frie, E.: Antibody response in patients with acute leukemia. *J. Lab. clin. Med. 56*, 634 (1960).
98. Simone, J. V.: Treatment of children with acute lymphocytic leukemia. In: Advances in Pediatrics. Vol. 19. Ed. by I. Shulman. Year Book Medical, Chicago 1972. P. 13.
99. Smith, J. L., Cowling, D. C., Barker, C. R.: Response of lymphocytes in chronic lymphocytic leukaemia to plant mitogens. *Lancet 1*, 229 (1972).
100. Smith, R. W., Terry, W. D., Buel, D. N., Sell, K. W.: An antigenic marker for human thymic lymphocytes. *J. Immunol. 110*, 884 (1973).
101. Srivastava, B. I. S., Minowada, J.: Terminal deoxynucleotidyl transferase activity in a cell line (molt-4) derived from the peripheral blood of a patient with acute lymphoblastic leukemia. *Biochem. biophys. Res. Comm. 51*, 529 (1973).
102. Stevenson, R. A., Mott, M. G.: Membrane immunofluorescence in acute lymphoblastic leukemia. *New Engl. J. Med. 288*, 1127 (1973).
103. Vossen, J. M. J. J.: Age-related development of humoral immunity in normal children with immunodeficiencies. Ed. by G. R. Burgio, G. Astaldi, A. De Barbieri. *Boll. Ist. Sieroter. Milan. (Suppl.) 53*, 174 (1974).
104. Vossen, J. M. J. J.: The Development of the B Immune System in Man. Bronder Publ., Rotterdam 1975.
105. Vossen, J. M. J. J.: Membrane-associated immunoglobulin determinants on bone marrow and blood lymphocytes in the pediatric age group. *Annals N. Y. Acad. Sci.* (1974). In press.
106. Wilson, J. D., Nossal, G. J. U.: Identification of human T and B lymphocytes in normal peripheral blood and chronic lymphocytic leukaemia. *Lancet 2*, 788 (1971).
107. Wybran, I., Chanter, S., Fudenberg, H. H.: Isolation of normal T cells in chronic lymphocytic leukemia. *Lancet 1*, 126 (1973).
108. Wybran, I., Fudenberg, H. H.: T cells in chronic lymphocytic leukaemia. *Lancet 2*, 265 (1973).
109. Yodoi, J., Takatsuki, K., Masoda, T.: Two cases of T-cell chronic lymphocytic leukemia in Japan. *New Engl. J. Med. 290*, 572 (1974).

Correspondence: Mrs. Lina Feola, Istituto Sieroterapico Milanese, Via Darwin, 22—20143 Milano, Italy.

Haematologia 9 (1—2), pp. 35—38 (1975)

Rosette Formation in Acute Lymphoid Leukaemia

T. RÉVÉSZ, R. SZIGETI, D. SCHULER

Second Department of Paediatrics, Semmelweis University Medical School, Budapest, Hungary

(Received October 31, 1974)

The capacity of leukaemic lymphoblasts and remission lymphocytes, obtained from 40 children with acute lymphoid leukaemia, to form sheep red blood cell rosettes was investigated. Lymphoblasts isolated from the peripheral blood of the patients prior to antileukaemic treatment showed greatly reduced numbers of rosette-forming cells as compared to controls (4.6% *vs.* 27.5%). The ratio of rosette-forming cells during intensive induction chemotherapy was still significantly lower than the control value (15.7%), while after the achievement of complete remission the number of RFC approximated the normal value (22.5%). The presence of leukaemic serum had no significant effect on the number of RFC.

The immunological aspects of leukaemia are being extensively studied. Characterization of lymphocytes in lymphoid leukaemias as to their origin and antigenic properties is hoped to further knowledge about the malignant transformation of cells. Lymphocytes in chronic lymphoid leukaemia (CLL) carry surface immunoglobulins as judged on the basis of immunofluorescence experiments [7] or by the mixed antiglobulin reaction [4]. These cells are therefore regarded as B lymphocytes and CLL as B cell leukaemia. Lymphoblasts in acute lymphoid leukaemia (ALL), on the other hand, are somewhat ill-defined as to their T or B cell origin.

The formation of "spontaneous" rosettes by peripheral lymphocytes is a useful technique in the study of T cells. It is well recognized that varying numbers of human peripheral lymphocytes are able to bind unsensitized sheep red blood cells (SRBC), thus forming "rosettes" [2, 6, 11]. The rosette-forming cell (RFC) is a thymus-dependent lymphocyte. Rosette formation is inhibited by anti-lymphocyte serum but not by anti-immunoglobulin serum. Furthermore, RFC do not show surface fluorescence when treated with fluorescein-labelled anti-human globulin [2]. A great proportion of thymocytes forms spontaneous rosettes, while only a fraction of bone-marrow lymphocytes do so [6]. Results of rosetting tests in patients with immune deficiency conditions support the view that the RFC are T lymphocytes. Cells from patients with acquired hypogammaglobulinaemia form rosettes in normal numbers, while those from patients with cell-mediated immune disorders such as Nezelof's or Wiskott—Aldrich's syndrome, fail to show rosetting [11].

Materials and Methods

Patients

Forty children with ALL were included in the study. Diagnosis was based on bone-marrow smears stained with May–Grünwald–Giemsa and analyzed by cytochemistry using PAS and DNAse reactions. Eleven patients were tested before receiving any treatment, 10 during intensive induction chemotherapy consisting of vincristine, asparaginase and prednisolone, and 19 during maintenance therapy with 6-mercaptopurine and methotrexate after the achievement of complete remission.

Thirty-two children admitted for minor surgical interventions were studied as controls.

Rosette formation

The method of rosette formation was based on the technique of Wybran et al. [11]. Lymphocytes were obtained from heparinized peripheral blood by centrifugation on a Ficoll-Uromiro gradient, washed three times in TC-199, and resuspended to give a final concentration of 2×10^6 per ml. Viability was checked by trypan-blue exclusion. Normal human AB serum or pre-treatment ALL serum was added to the cell suspensions to a final concentration of 10%. Sheep red blood cells were washed three times in Hank's BSS and adjusted to a 1% suspension; 0.2 ml of this suspension was added to 0.2 ml of the lymphocyte suspension. After mixing, the vials were centrifuged at 500 r.p.m. for 5 min followed by an incubation at +4°C for 30 min. The cells were gently resuspended, mounted on slides and the wet preparations examined at a magnification of ×640. A RFC was defined as a lymphocyte which had 3 or more SRBC adhering to its surface, and the number of RFC was expressed per 100 lymphocytes. Statistical analysis was carried out using Student's *t*-test.

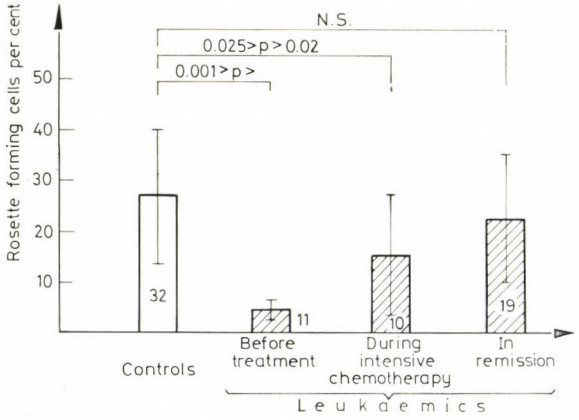


Fig. 1. Rosette formation in acute lymphoid leukaemia (mean + S.D.). Numbers in the columns refer to the number of patients studied

Results

Peripheral lymphocytes from 32 control children had a mean of 27.5% RFC, with a range of 5 to 62% (Fig. 1). Lymphoblasts obtained from children with ALL prior to treatment showed greatly reduced numbers of RFC (mean, 4.6%; range, 2 to 8%). The ratio of RFC during intensive induction chemotherapy was 15.7% (range, 3 to 41%), a figure still significantly lower than that of the controls. After achievement of complete remission the number of RFC returned to an almost normal value (mean, 22.5%; range, 5 to 60%). The presence of leukaemic serum did not significantly influence the number of RFC.

Discussion

Although some cases of ALL with lymphoblasts carrying T cell markers have been reported [1, 3, 5], the majority of ALL lymphoblasts do not seem to display T lymphocyte characteristics. Our results support this view that none of the patients studied in the initial phase of their disease had lymphoblasts which formed spontaneous rosettes with SRBC.

It was also reported that ALL lymphoblasts are immunofluorescent-negative, i.e. they lack the marker for B cells [5, 9, 10]. On the basis of these observations, most ALL lymphoblasts seem to originate from a clone, the progenitor cell of which has not begun to differentiate in either a T or B cell direction.

With the eradication of the majority of malignant cells during chemotherapy, normal lymphocytes are found again in the peripheral blood of the patients. These cells, among other functions, are able to bind SRBC.

The finding that leukaemic serum did not influence the number of RFC is in contrast to our previous observations, when a factor was demonstrated in the serum of untreated leukaemic children which inhibited the mitogen-induced transformation of both leukaemic and normal lymphocytes [8]. Conversely, the inhibitory effect of serum could not be observed in migration inhibition experiments using leukaemia associated antigens [9/a]. It seems therefore that different receptors are involved in the above functions of lymphocytes.

*

The authors wish to thank Mrs. A. Kemenes for skilled technical assistance.

References

1. Borella, L., Sen, L.: T cell surface markers on lymphoblasts from acute lymphocytic leukaemia. *J. Immunol. 111*, 1257 (1973).
2. Brain, P., Marston, R. H.: Rosette formation by human T and B lymphocytes. *Europ. J. Immunol. 3*, 6 (1973).
3. Catovsky, D., Goldman, J. M., Okos, A., Frisch, B., Galton, D. A. G.: T lymphoblastic leukaemia: A distinct variant of acute leukaemia. *Brit. med. J. 2*, 643 (1974).

4. Haegert, D. G., Hallberg, T., Coombs, R. R. A.: B and T lymphocyte subpopulations in human peripheral blood. *Int. Arch. Allergy 46*, 525 (1974).
5. Kersey, J. H., Sabad, A., Gajl-Peczalska, K., Hallgren, H. M., Yunis, E. J., Nesbit, M. E.: Acute lymphoblastic leukemic cells with T (thymus-derived) lymphocyte markers. *Science 182*, 1355 (1973).
6. Lay, W. H., Mendes, N. F., Bianco, C., Nussenzweig, V.: Binding of sheep, red blood cells to a large population of human lymphocytes. *Nature (Lond.) 230*, 531 (1971).
7. Preud'homme, J. L., Seligmann, M.: Surface-bound immunoglobulins as a cell marker in human lymphoproliferative diseases. *Blood 40*, 777 (1972).
8. Révész, T., Szigeti, R., Schuler, D.: The role of serum factors in the lymphocyte transformation test of children with acute leukaemia. *Acta paediat. scand. 63*, 715 (1975).
9. Smith, J. L., Clein, G. P., Barker, C. R., Collins, R. D.: Characterization of malignant mediastinal lymphoid neoplasm (Sternberg sarcoma) as thymic in origin. *Lancet 1*, 74 (1973).
9/a. Szigeti, R., Révész, T., Gerő-Ferencz, Éva: The inhibitory effect of leukaemia associated antigen and leukaemic serum on the leukocyte migration of children with acute leukaemia in remission. *Acta Allergol.* (Kbhv.) *29*, 288, (1974).
10. Wilson, J. D., Nossal, G. J. V.: Identification of human T and B lymphocytes in normal peripheral blood and in chronic lymphocytic leukaemia. *Lancet 2*, 788 (1971).
11. Wybran, J., Carr, M. C., Fudenberg, H. H.: The human rosette-forming cell as a marker of a population of thymus-derived cells. *J. clin. Invest. 1*, 2537 (1972).

Correspondence: Dr. T. Révész, 2nd Department of Paediatrics, Semmelweis University Medical School, Tűzoltó u. 7—9, 1094 Budapest, Hungary

Haematologia 9 (1—2), pp. 39—41 (1975)

Detection in Serum of Antilymphocyte-globulin Administered in Form of Eye-drops

A. Leövey, B. Fekete, Gy. Szegedi

First Department of Medicine, University Medical School, Debrecen, Hungary

(Received November 3, 1973)

Rosette inhibition tests indicated that similarly as in previous animal experiments, anti-human lymphocyte horse globulin (AHLG) administered in the form of eye-drops entered the systemic blood circulation in man. In the eye into which the AHLG is administered, it is expected to exert a local immunosuppressive effect.

According to preliminary animal experiments, ^{125}I-antilymphocyte-globulin (ALG) administered into one eye, can soon be detected in the other eye [3]. The phenomenon indicated that ALG enters the blood circulation, a presumption supported by radioactivity measurements. Rosette inhibition tests were performed to establish the degree of biological activity of ALG that had passed into the blood circulation, the test being suitable and for a sensitive testing of the biological activity of ALG gained from antilymphocyte serum [4—8].

Materials and Methods

Three patients were studied; they were treated with anti-human lymphocyte horse globulin eye-drops. Two of the patients (♂ D. G. 22 years; ♂ M. J. 25 years) had chronic uveitis and one patient (♂ K. K. 75 years) had hyperthyroidism associated with progressive (malignant) exophthalmus and consecutive diplopia.

One drop (= 1/20 ml) of 0.4% AHLG was given into both eyes every two hours. Blood samples were taken 15 minutes after treatment at intervals of 4, 8, 16, 24 and 48 hours (see Figure 1). Sera were inactivated for complement, and absorbed with sheep red blood cells (SRBC) and twofold serial dilutions were made.

Rosette inhibition test. Cell suspensions were made from the spleen of Balb/c mice on the 8th day after immunization with SRBC. Amounts of 2×10^7 cells/ml were incubated for 75 minutes in serum dilutions. After washing, SRBC were added to the spleen cells and thus the test was completed [9, 10].

Inhibition was considered significant when the addition of test serum caused at least a 30% decrease in the rosette count.

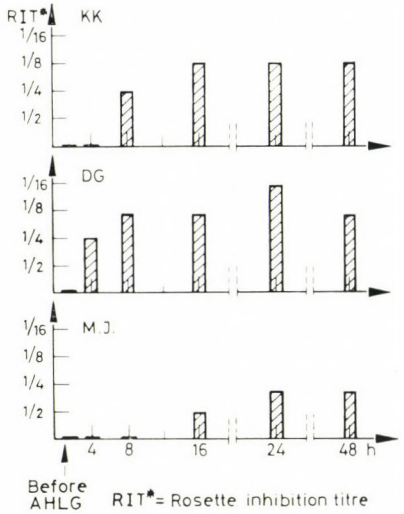


Fig. 1. Rosette inhibitory effect of serum

Results and Discussion

A positive rosette inhibition was found 4, 8 and 16 hours following the treatment.

Inhibition was most explicit between 16 and 24 hours, which means that a continuous administration of eye-drops results in an AHLG blood concentration peak at that point of time. In the subsequent 24–32 hours no change in concentration and inhibition was observed, indicating a state of equilibrium.

The present results similarly as those previously obtained in animals showed that ALG enters the blood circulation after conjunctival administration. The phenomenon is all the more interesting as in spite of the high molecule weight of equine IgG (160,000) a biologically well-defined amount is absorbed from the conjunctival sac.

In 24 hours a total of 1.2 ml of 0.4% AHLG solution was given to each patient. Had the whole amount been absorbed, 5 mg ought to have entered the organism. Naturally, only a small part, the one not bound to cells could be determined and this must have corresponded to 1 to 2% of the total. It would be essential to know the real amount of AHLG entering the blood circulation and the amount of bound AHLG, as thus more precise information concerning the biological activity and kinetics of ALG could be gained.

Since in the therapeutical sense only a low amount of AHLG (maximum 5 mg/24 hr) will enter the blood circulation, a clinical immunosuppressive effect is hardly to be expected. To obtain such an effect an amount of 100–200 mg would be necessary. In such cases, rosette inhibition will reach a titre of 1 : 1000 or higher.

As ALG will cumulate in the eye into which it is given [3], this mode of administration may result a local immunosuppressive effect in the first place.

The fact that a xenologous protein enters the blood circulation requires certain precautions, to present an antibody producing immune response. If the patient becomes sensitized, a repeated dose will result in serum sickness. It seems therefore advisable to produce antilymphocyte serum for this purpose in goats, sheep or rabbits [12].

References

1. Alberth, B., Leövey, A.: Immunosuppressio anti-human ALG-vel keratoplastica esetében. *Szemészet 108*, 81 (1971).
2. Alberth, B., Leövey, A.: Immunosuppression mit anti-humanem ALG bei Keratoplastik. In: K. E. Krüger, M. Tost eds. Augenheilkunde in Forschung und Praxis. Martin-Luther-Universität, Halle—Wittenberg 1972/2. p. 116.
3. Alberth, B., Leövey, A., Balázs, Cs., Gosztonyi, G.: Über die intraoculäre Verteilung des antilymphozytären Globulins (ALG). *Klin. Mbl. Augenheilk. 163*, 524 (1973).
4. Bach, J. F., Dormont, J., Dardenne, M., Balner, H.: *In vitro* rosette inhibition by anti-human antilymphocyte serum. *Transplantation 8*, 265 (1967).
5. Bach, J. F., Dardenne, M., Dormont, J., Antoine, B.: A new *in vitro* test evaluating anti-lymphocyte serum potency. *Transplant. Prog. 1*, 403 (1969).
6. Bach, J. F., Dormont, J., Dardenne, M., Balner, H.: *In vitro* rosette inhibition by anti-human antilymphocyte globulin. Correlation with skin graft prolongation in primates. *Transplantation 8*, 269 (1969).
7. Bach, J. F.: *In vitro* assay for antilymphocyte serum. *Fed. Proc. 29*, 130 (1970).
8. Bach, J. F., Dormont, J.: Further developments of the RIT for the testing of anti-human lymphocyte serum. *Transplantation 11*, 96 (1971).
9. Bach, J. F., Dardanne, M.: Antigen recognition by T-lymphocytes. II. Similar effects of azathioprine, antilymphocyte globulin and anti-theta serum on RFC in normal and thymectomized mice. *Cell. Immunol. 3*, 11 (1972).
10. Fekete, B., Szegedi, Gy., Szabó, G., Gergely, P., Petrányi, Gy.: A rosetta-képző sejtek felhasználása az immunosuppressio mérésére. *Magy. Pediat. 4*, 66 (1971).
11. Leövey, A., Alberth, B., Balázs, Cs., Tóth-Bagi, Z.: Az immunsuppressio és az anti-cornealis antitest szerepe a keratoplasticában. *Szemészet 109*, 259 (1972).
12. Pirofsky, B., Bardana, E. J., Bayracki, C., Porter G. A.: Antilymphocyte antisera in immunologically mediated renal disease. *J. Amer. med. Ass. 210*, 1059 (1969).

Correspondence: Prof. A. Leövey, University Medical School, I. Department of Medicine, 4012 Debrecen, Hungary

Haematologia 9 (1–2), pp. 43–47 (1975)

Immunization against Avian Proteins

* J. Brocteur, C. François-Gérard, A. André
** M. Radermecker, M. Bruwier, J. Salmon

(Received December 28, 1974)

A study of sera of pigeon breeders showed a higher ratio of antibodies with an anti-P_1 specificity in those who show clinical signs of allergic origin. By absorption of anti-P_1 antibodies it was revealed that there exist in the cells, serum and excrement of pigeons, substances with antigenic properties similar to those of human P_1 antigen. Pigeon breeders, and particularly those who show clinical signs of allergy, possess also other antibodies which precipitate specific antigens of pigeon serum.

The P blood group system was discovered in 1927 by Landsteiner and Levine [1]. At that time, it involved the P_1 and P_2 phenotypes. Family investigations showed that the P_1 antigen is transmitted as a dominant Mendelian trait [2]. The frequency of P_1 and P_2 phenotypes in the European population has been determined by Henningsen [3]; he showed that there are 78.85% of P_1 individuals and 21.15% of P_2 individuals.

Later, it was found that an antigen present in most individuals and named Tj^a, was also part of the P system [4]. Finally, the further identification of the extremely rare P^k antigen conferred to the P system a hitherto unsuspected genetic complexity [5].

While determining the P_1 phenotype of a series of individuals, it was found to display a widely varying antigenic activity [6]. It was therefore difficult to subdivide the individuals into distinct classes within the P system. Nevertheless, three categories have arbitrarily been advanced; corresponding respectively to powerful P_1, medium P_1 and weak P_1 antigens.

The first anti-P_1 reagents were obtained by immunizing rabbits and goats with P_1 human red cells. Later, anti-P_1 antibodies were discovered in human sera.

In 1957, Cameron and Staveley [7] discovered the existence of a substance similar to the P_1 antigen in hydatid fluid. Moreover, immunization of animals through injection of red cells on which the hydatid fluid is fixed, induced the formation of antibodies with an anti-P_1 specificity [8, 9].

* Blood Group and Transfusion Laboratory (Director: Prof. A. André), University of Liège (Belgium)

** Institute of Medicine, Hôpital de Bavière (Director: Prof. H. Van Cauwenberge), University of Liège (Belgium)

Another substance with an antigenecity similar to the P_1 antigen, has been detected in some worms such as *Lumbricus terrestris* and *Ascaris suum* [10].

When studying the case of a patient with respiratory disorders characterized by particularly acute attacks of bronchitis and for whom previously a pre-transfusional cross-match had shown that his serum contained a particularly active anti-P_1 antibody, we wondered whether there were similar substances in other media.

Clinicians had also been struck by the existence of similar disturbances of allergic origin in many pigeon breeders, and in the serum of some of them they demonstrated anti-pigeon precipitins. The serum of many of these patients contained anti-P_1 antibodies.

A. Study of human sera

We have made a systematic investigation for the evidence of anti-P_1 antibody in a population of pigeon breeders who, by definition, are frequently in direct contact with the antigen to be identified. We collected 205 samples of pigeon breeders' sera; they included those of healthy volunteers and those of patients treated for chronic bronchitis.

As we only had serum samples for some individuals, we were unfortunately unable to show, for each one, the P_1 or P_2 phenotype; therefore we had to undertake a global study so as to determine the distribution of P_1 and P_2 individuals in the series under study. By reference to the statistical distribution observed by Henningsen [3] we could reasonably expect to obtain $\frac{(205 \times 21.15)}{100}$ i.e. 43 P_2 individuals and $\frac{(205 \times 78.85)}{100}$ i.e. 162 P_1 individuals. A group of 51 blood donors, all belonging to the P_2 phenotype, and who had no direct and frequent contact with pigeons, served as control.

The existence and ratio of anti-P_1 antibodies has been investigated in both series. Detection and identification of anti-P_1 antibody was carried out with a panel of test cells including several P_1 and P_2 cells. The reaction was performed in 6% dextran 60,000 at 10°C.

Results are shown in Table 1.

Table 1

	P_1	P_2	Number of anti-P_1	Frequency
Pigeon breeders	162	43	16	37%
Blood donors	—	51	3	6%

$X_c^2 = 12.32$ $\quad p = 0.001$

B. Detection in pigeon blood of a substance similar to the P_1 antigen

Study of pigeon red cells

Normal human sera incubated with pigeon cells revealed in all the sera the presence of an anti-pigeon agglutinin, active up to a mean dilution of 1/32.

The same experiment, carried out with sera of patients with respiratory disorders of allergic origin, and who had anti-pigeon precipitins, showed that in some of them the normal anti-pigeon agglutinin was markedly more active than in the rest. Not all of these patients had anti-P_1 antibody.

Thus, a more specific study of pigeon red cell activity on anti-P_1 antibody was made by incubating at 4°C overnight equal volumes of anti-P_1 serum and of a pigeon red cell sediment previously washed in saline. The anti-P_1 sera so treated were titrated against P_1 cells before and after absorption.

We proceeded in the same way with 13 human sera containing anti-P_1 antibodies. These sera were either of commercial origin or prepared by ourselves. Each serum had been examined several times against pigeon red cells of various origins. In each case, we observed the total disappearance of the anti-P_1 antibody activity as well as of the anti-pigeon activity.

No significant decrease of anti-pigeon antibody was observed after absorption of these sera by human OP_1 red cells.

Results of these experiments on three different sera are recorded in Table 2.

Table 2

	+ *pigeon cells*	+ *human* P_1 *cells*
Goat anti-P_1 BIOTEST	1/256	1/16
Absorbed by pigeon cells	—	—
Absorbed by P_1 cells	1/256	—
Human anti-P_1 SPECTRA	1/8	1/4
Absorbed by pigeon cells	—	—
Absorbed by P_1 cells	1/8	—
Human anti-P_1 *VEN*	1/256	1/16
Absorbed by pigeon cells	—	—
Absorbed by P_1 cells	1/256	—

Similar control experiments have been made with sera containing antibodies of different specificities, such as anti-A, anti-B, anti-C, anti-E, anti-D, anti-I, anti-H, anti-M, anti-N, anti-Le^a and anti-Le^b. Incubation of these sera with pigeon red cells, under the same conditions as above, failed to cause a disappearance or significant decrease of the antibodies.

The study was continued with the analysis of pigeon serum by the inhibition technique applied for detecting blood group substances in saliva. In this instance the procedure consisted in detecting the last but one dilution of anti-P_1 serum, for which a complete agglutination was still observed, then by incubating the same

quantity of this serum with decreasing amounts of pigeon serum. An extract of pigeon excrement was also studied by the same method. The results obtained were in every way comparable to those observed in the case of serum.

The results, shown schematically in Table 3, indicated the presence in pigeon serum of a substance similar to the P_1 antigen, since we observed an inhibition of the activity of anti-P_1 serum.

Table 3

1. *Measurement of anti-P_1 serum activity*

1/1	1/2	1/4	1/8	1/16	1/32	1/64
+++	+++	+++	++	+	−	−

2. *Inhibition by pigeon serum of anti-P_1 serum*

1/1 to 1/32	1/64	1/128	1/256	1/512	1/1024	1/2048
−	−	+	++	+++	+++	+++

C. Detection in the blood of other birds of substances similar to antigen P_1

Similar studies were made of the blood of ganders, turkey cocks, chickens and ducks. These bloods failed to inhibit the anti-P_1 activity. On the other hand budgerigar serum proved inhibitory. We had to content ourselves with serum since we could not obtain a sufficient quantity of red cells of this bird.

Discussion

The existence of a substance similar to P_1 antigen in hydatid fluid as well as in some parasites, lead to assume its presence also in other biological fluids.

The study of the sera of healthy individuals or individuals showing disorders of allergic origin and who are constantly in contact with pigeons, compared to that of a series of healthy subjects not in contact with pigeons, has shown that in the former there is a higher ratio of immunization against the P_1 antigen. It was therefore logical to draw a parallel between the presence of anti-P_1 specific antibodies and a substance found in pigeons.

The results indicated the presence in the red cells, the serum and excrements of pigeons, of a substance inhibiting the activity of anti-P_1 antibodies. We may therefore ascribe the occurrence in pigeon breeders of anti-P_1 antibodies to a sensitization to substances having properties similar to P_1 antigen and found in the pigeon.

In addition to this antigen, there must exist in the pigeon other specific antigens, against which human individuals may become immunized. In fact, if in all human sera there are weak anti-pigeon antibodies, the latter are more active in pigeon breeders, particularly in those who suffer from allergic disorders.

The resistance of these antibodies to absorption by human OP_1 cells, and the disappearance of their activity on absorption by pigeon cells with the anti-P_1 activity disappearing at the same time, points to the presence of substances with different antigenic properties. In the present state of research, it is obviously difficult to define the relation between these antigens.

Our results together with clinical observations allow to establish a relation between these substances and the clinical manifestations of allergic origin observed in pigeon breeders. But only a more detailed study of the antigens found in pigeon blood and of the P_1 antigens of human origin, would explain the immunological manifestations observed.

References

1. Landsteiner, K., Levine, P.: Further observations on individual differences of human blood. *Proc. Soc. exp. Biol. (N.Y.) 24*, 941 (1927).
2 Landsteiner, K., Levine, P.: On the inheritance and racial distribution of agglutinable properties of human blood. *J. Immunol. 18*, 87 (1930).
3. Henningsen, K.: On the heredity of blood factor P. *Acta path. microbiol. scand. 26*, 769 (1949).
4. Sanger, R.: An association between the P and Jay systems of blood groups. *Nature (Lond.) 176*, 1163 (1955).
5. Matson, G. A., Swanson, J., Noades, J., Sanger, R., Race, R. R.: A "new" antigen and antibody belonging to the P blood group system. *Amer. J. hum. Genet. 11*, 26 (1959).
6. Landsteiner, K., Levine, P.: On the racial distribution of some agglutinable structures of human blood. *J. Immunol. 16*, 123 (1929).
7. Staveley, J. M., Cameron, G. L.: The inhibiting action of hydatic cyst fluid on anti-Tj^a sera. *Vox Sang. 3*, 114 (1958).
8. Prokop, O., Oesterle, P.: Zur Frage der P-Antigenität von Echinokokkenflüssigkeit aus Schweinelebern. *Blut 4*, 157 (1958).
9. Kerde, C., Fünfhausen, G., Brunk, R., Brunk, R.: Über die Gewinnung von hochwertigen Anti-P-Immunseren durch Immunisierung mit Echinokokkenzystenflüssigkeit. *Z. Immun.-Forsch. 119*, 216 (1960).
10. Prokop, O., Schlesinger, D.: Über das Vorkommen von P -Blutgruppensubstanz bei einigen Metazoen, insbesondere *Ascaris suum* und *Lumbricus terrestris*. *Z. Immun.-Forsch. 129*, 344 (1965).

Correspondence: Dr. J. Brocteur, Blood Group and Transfusion Laboratory, 41, rue Dos Fanchon, 4020 Liège, Belgium

Haematologia 9 (1—2), pp. 49—57 (1975)

Hemoglobin Function in Stored Blood XIII. A Citrate-adenine Preservative with Optimal pH to Maintain Red Cell 2,3-DPG (Function) and ATP (Viability)*

R. Ben Dawson, W. F. Kocholaty, R. Camp
D. Crater, T. J. Ellis, W. Spurlock, T. A. Billings, Edith B. Ledford

with the technical assistance of D. Newlon (statistics)

School of Medicine, University of Maryland, Baltimore, Maryland**
and the USA Army Medical Research Laboratory, Fort Knox, Kentucky 40121

(Received September 27, 1974)

Increasing pH by a 0.5 increment over the commonly used preservative, acid-citrate-dextrose with adenine (ACD-Ad), results in a significant improvement in 2,3-DPG, with no significant loss in concentrations of ATP. The intermediate pH preservative, 6.0, also had ATP concentrations which equaled those of the low pH preservatives, 5.0 and 5.5, from the 21st to the 42nd day of storage. A citrate-adenine preservative, with a pH between 5.5 and 6.0, would seem to be optimal for maintenance of hemoglobin function and red cell viability, as determined by measurements of 2,3-DPG and ATP concentrations.

Introduction

The dependence of normal hemoglobin function on 2,3-diphosphoglycerate (2,3-DPG) in the human red cell has been discovered [2, 5] since the preservatives – acid-citrate-dextrose (ACD) and citrate-phosphate-dextrose (CPD) – were developed for liquid (4°) storage of whole blood for 3 weeks. ACD preservatives containing adenine are used since this compound provides a substrate for ATP synthesis and results in a 5-week shelf life [1]. After demonstrating that hemoglobin function (p_{50} and 2,3-DPG) was better maintained in CPD, as compared to ACD-stored blood [7], it was determined that the higher pH of the preservative (pH of CPD 5.5) was responsible for the better maintenance of hemoglobin function [8]. In a recent study, it was shown that an ACD preservative with a pH of 5.5 or higher would be optimal for maintenance of 2,3-DPG and ATP [9]. The pH of standard ACD is 5.0.

In the present study, an attempt was made to establish the optimal pH of a preservative containing adenine for maintaining 2,3-DPG (hemoglobin function) and ATP (red cell viability) during liquid storage at 4°C under blood bank conditions. An automated analytical system for determining concentrations of 2,3-DPG and ATP allowed the study of significantly large numbers of blood units stored under various conditions of pH.

* Presented in part in abstract form in Clinical Research, Vol. 21, April, 1973.

** Supported in part by USA R and D Contract No. DA-DA-17-72-C-2005

Materials and Methods

From each of ten normal volunteers, a unit of blood was divided during donation into five, 150 ml plastic packs (PL-146, Fenwal Laboratories, Morton Grove, Ill.), containing citrate-adenine solutions of pH 5.0, 5.5, 6.0, 6.5 and 7.0. The basic preservative contained the amounts (grams per liter) of citric acid (3.27), Na citrate (26.3), and dextrose (25.5) used in CPD, plus enough NaCl (2.92), replacing phosphate, to make an isotonic solution. Recrystallized adenine (obtained from Dr. Grant Bartlett, Laboratory of Comparative Biochemistry, San Diego, Calif.) was added to give a final concentration of 0.25 mM in the blood preservative mixture. The pH was adjusted to desired levels with HCl and the preservatives were sterilized by Millipore-filtration (0.22 μ pore width). After blood collection on days 0, 3 and 7 and at weekly intervals thereafter, aliquots were removed aseptically and anaerobically for analysis of pH, 2,3-DPG, ATP and osmotic fragility.

Analyses of concentrations of 2,3-DPG and ATP-ADP were carried out by the principles of Lowry et al. [12] and Krimsky [11] using the automated scheme of Prins and Loos [13]. This procedure has been modified in our laboratories [15] using Auto-Analyzer equipment (Technicon Corporation) and enzymes and substrates obtained from the Boehringer Mannheim Corporation. Measurements of pH and H^+ ion concentration were made at 37°C under anaerobic conditions to minimize variations which might result from carbon dioxide loss.

The significance of variance with time and between preservatives was given at 95% confidence limits using the paired t test. These statistical data apply to 2,3-DPG and ATP concentrations.

Results

In Table 1 and Figure 1, 2,3-DPG concentrations are shown during the 42-day storage period. The concentrations are given in millimolar measurements and each point on the graph represents the mean DPG value from determinations on ten units of whole blood stored at 4°C after they were collected in the preservative of the pH specified. The preservatives will be referred to by the pH values which they exhibited prior to the blood collection. Significant differences between the values were determined using 95% confidence limits with the paired t test.

Changes in DPG with time

The concentration of 2,3-DPG in the 5.0 group – which corresponds to ordinary ACD plus adenine – was significantly lower at all points after day 3 than it was at days 0 and 3 and the values at days 35 and 42 were lower than the 7-day value. In addition, the 35-day value was significantly lower than the 10-day

Table 1

Mean Values and Standard Deviations for 2,3-DPG, ATP, pH and H

pH Preservative solution	Days stored	2,3-DPG	(S.D.)	ATP	(S.D.)	pH	H+ concentration ($\times 10^{-7}$
5.0	0	2.52	0.333	0.531	0.227	6.90	1.26
	3	2.54	0.286	0.706	0.144	6.82	1.51
	7	1.38	0.191	0.676	0.218	6.73	1.86
	10	1.02	0.225	0.792	0.144	6.66	2.19
	14	0.94	0.119	0.756	0.186	6.61	2.46
	21	0.96	0.237	0.692	0.153	6.53	2.95
	28	1.17	0.267	0.596	0.243	6.50	3.16
	35	0.32	0.080	0.516	0.207	6.45	3.55
	42	0.63	0.145	0.516	0.186	6.41	3.89
5.5	0	2.69	0.250	0.576	0.194	7.06	0.87
	3	3.36	0.324	0.636	0.163	6.95	1.12
	7	2.44	0.283	0.687	0.179	6.84	1.45
	10	1.48	0.224	0.728	0.243	6.75	1.78
	14	1.62	0.475	0.740	0.169	6.66	2.19
	21	1.26	0.259	0.648	0.220	6.57	2.69
	28	1.45	0.199	0.627	0.171	6.52	3.02
	35	0.37	0.094	0.512	0.159	6.48	3.31
	42	0.54	0.136	0.471	0.164	6.42	3.80
6.0	0	3.04	0.291	0.613	0.193	7.18	0.66
	3	3.72	0.283	0.481	0.147	7.04	0.91
	7	2.99	0.231	0.509	0.153	6.91	1.23
	10	1.95	0.234	0.606	0.183	6.80	1.59
	14	1.32	0.199	0.635	0.147	6.71	1.95
	21	1.46	0.260	0.663	0.209	6.58	2.63
	28	1.41	0.264	0.621	0.194	6.53	2.95
	35	0.33	0.086	0.497	0.154	6.47	3.39
	42	0.66	0.138	0.412	0.158	6.43	3.72
6.5	0	3.04	0.223	0.637	0.168	7.25	0.56
	3	3.86	0.262	0.429	0.082	7.09	0.81
	7	3.04	0.240	0.490	0.097	6.95	1.12
	10	2.03	0.206	0.529	0.101	6.83	1.48
	14	1.62	0.299	0.599	0.100	6.73	1.86
	21	1.33	0.197	0.551	0.151	6.60	2.51
	28	1.07	0.199	0.527	0.160	6.55	2.82
	35	0.46	0.107	0.406	0.109	6.48	3.31
	42	0.59	0.138	0.376	0.130	6.44	3.63
7.0	0	3.32	0.352	0.582	0.201	7.29	0.51
	3	3.77	0.347	0.411	0.164	7.11	0.78
	7	3.34	0.331	0.471	0.107	6.97	1.07
	10	2.08	0.204	0.485	0.120	6.86	1.38
	14	1.55	0.183	0.533	0.148	6.74	1.82
	21	1.57	0.161	0.544	0.173	6.61	2.46
	28	1.28	0.278	0.481	0.133	6.56	2.75
	35	0.36	0.120	0.357	0.116	6.48	3.31
	42	0.50	0.136	0.348	0.115	6.44	3.63

value and the 35 and 42-day values were lower than the values at 14, 21 and 28 days. In the other preservatives – pH 5.5 to 7.0 – the values for days 3 and 7 were not significantly different from those at day 0; however, the values for day 10 and beyond were lower than the day 0 values in each preservative. The changes

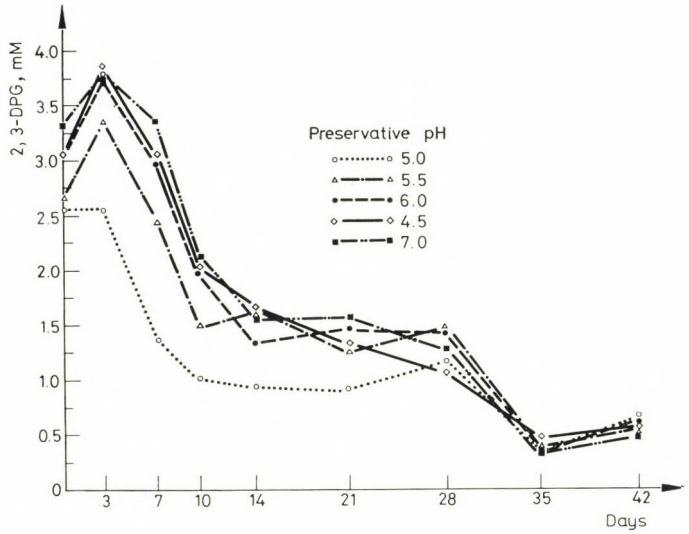


Fig. 1. Average 2,3-DPG concentrations for 42 days in blood stored in preservatives of different pHs. Each point represents the mean of ten samples. The significance of differences between means is discussed in the text

in DPG concentrations from days 7 to 14 were significant at the three higher pH values – pH 6.0 to 7.0 – but not at the lower pH values of 5.0 and 5.5. Other significant changes for the higher pH preservatives were similar to those which have been described in detail for the pH 5.0 preservative.

2,3-DPG differences between preservatives

At day 0, there were no differences between the DPG values in any of the preservatives. At day 7, the DPG value in the pH 5.0 preservative was significantly lower than the values in the other preservatives. At days 3 and 10, the DPG values in the 5.0 preservative were lower than the values in the three highest pH preservatives. The differences were not significant at days 3 and 10 between the 5.0 and 5.5 preservatives. At day 14, the 5.0 value was lower than the 6.5 and 7.0 values. At day 21, the 5.0 value was lower than the 7.0 value only.

ATP differences between preservatives

In Table 1 and Figure 2, concentrations are shown at points during the 42-day storage period. Each point on the graph represents the mean value for determinations on ten units of whole blood stored at 4°C after they were collected into the preservative with the pH specified. Differences were determined using 95% confidence limits with paired *t* tests. At day 0, there were no differences in ATP concentrations between the various preservatives. At day 3, the mean ATP

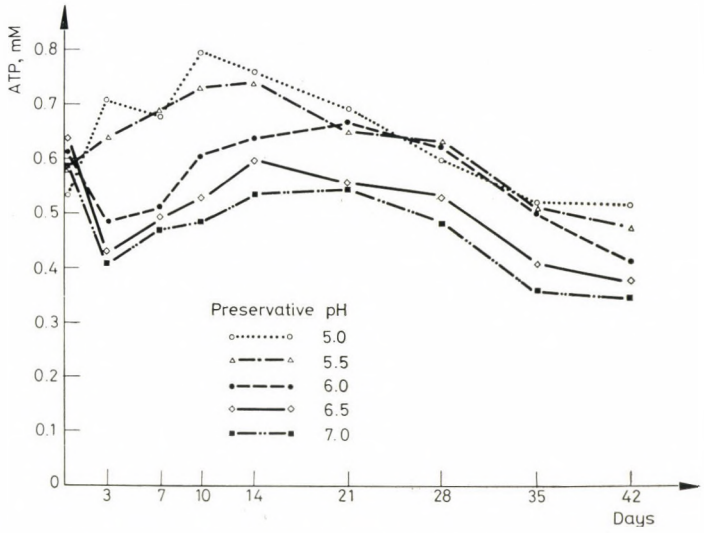


Fig. 2. Concentrations of ATP in blood stored in preservatives of different pHs. Each point is the mean of ten samples. The significance of differences is discussed in the text

concentration in the 5.0 preservative differed from the concentration in the 6.0 and 6.5 pH preservatives. The 5.5 pH preservative had a higher ATP concentration than the 6.0 preservative. At day 10, the 5.0 preservative had a mean ATP concentration which was higher than the ATP concentrations in the 6.5 and 7.0 preservatives. At day 14 the pH 5.5 preservative had a higher mean ATP concentration than the 7.0 preservative. Other differences between the mean ATP concentrations were not significant statistically at this level of confidence.

The numerical values are shown in Table 1 for the mean concentration of 2,3-DPG, ATP-ADP, and pH values, and the hydrogen ion concentrations, The values are given for each sampling time during the 6-week storage period in each of the five preservatives.

In Figure 3, the hydrogen ion concentrations show a linear increase during storage in each of the preservatives and in Figure 4, the direct correlation between blood pH measurement and red cell 2,3-DPG concentration is depicted. The pH

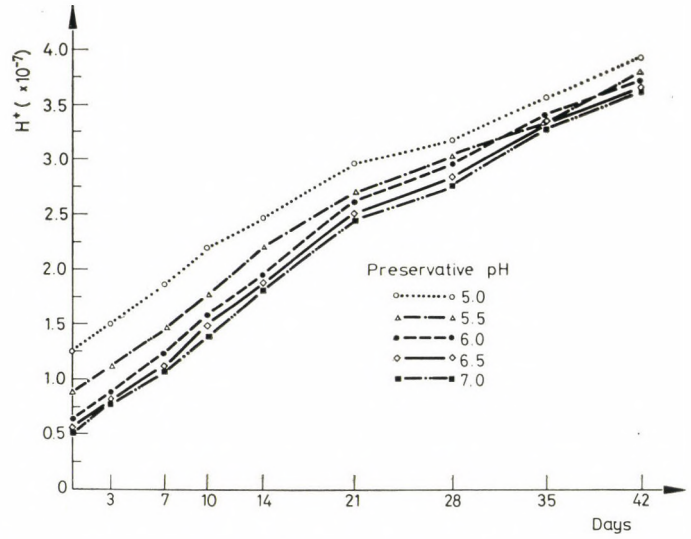


Fig. 3. Increase in hydrogen ion concentration in blood stored in different pH solutions. Each point is the mean of ten samples

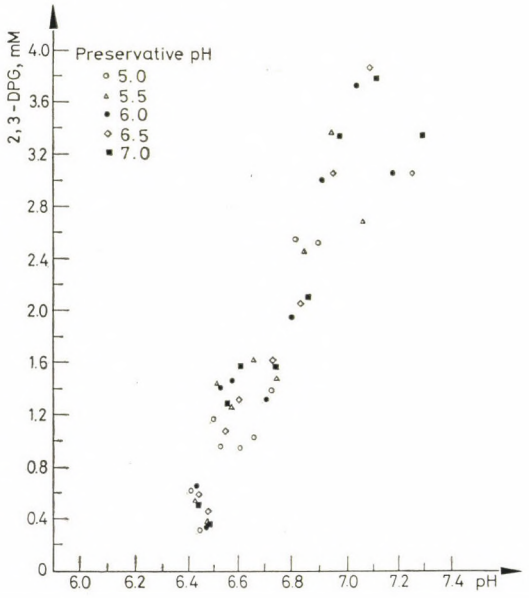


Fig. 4. Concentrations of 2,3-DPG versus pH determinations in blood stored in different pH preservatives. Each point represents the mean of ten samples

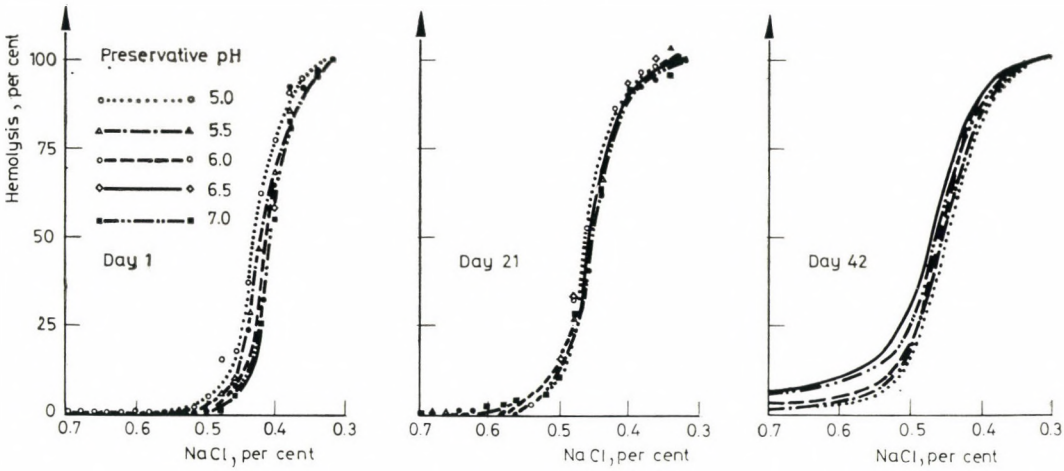


Fig. 5. Osmotic fragility (per cent hemolysis in hypotonic saline) for blood collected into preservatives of different pHs at days 1, 21, and 42

measurement was determined from a reading at 37°C in the closed-anaerobic sampling system employed in a blood gas pH meter (Instrumentation Laboratories). Hydrogen ion concentrations were calculated from pH measurements.

In Figure 5, osmotic lysis is shown as per cent hemolysis on the abscissa versus per cent saline on the ordinate. Data from one unit are shown which is representative of the three units that were studied. On day 1, the low pH cells are seen to have increased lysis, whereas on day 21 there was no apparent difference. However, on day 42 the cells in the two low pH preservatives were more resistant to lysis than the others.

Discussion

Chanutin and Curnish [6] and Beutler et al. [4] have noted that blood preservatives of high pH, for example 6.0 and 7.0, maintain near normal 2,3-DPG concentrations and thus hemoglobin function for 2 or even 3 weeks. It has also been noted that at these high pH values, ATP concentrations are not maintained well and, presumably, red cell viability or storage time would be shortened. However, adenine may be used to prevent this decrease in ATP and prolong the storage time [1].

In the present experiment, a wide range of pHs was studied using a citrate-adenine preservative to establish the optimal pH for maintaining both 2,3-DPG for hemoglobin function and ATP for red cell viability. It is clear that 2,3-DPG was not maintained during the first week of storage in the preservative of pH 5.0. In contrast, the higher pH preservatives (pH 5.5 to 7.0) maintained 2,3-DPG at

normal concentrations during the first week of storage. The intermediate preservative (pH 6.0) maintains 2,3-DPG as well as the higher pH preservatives and was more effective than the lower pH preservative (Figure 1). In addition, the pH 6.0 preservative was intermediate between the high and low preservatives with respect to maintaining ATP and ADP concentrations (Figure 2). From the results shown in these two figures, 2,3-DPG maintenance was favored by higher pH preservatives and ATP-ADP maintenance was favored by low pH preservatives. An adenine containing preservative of pH 6.0 and above was too high for maintenance of ATP during storage. A preservative with the pH as high as 5.5 was as effective at maintaining ATP when adenine was present in the preservative as was the pH 5.0 preservative. This confirms the conclusion of Beutler and Duron [3] that pH 5.5 is better than 5.0 for maintaining ATP when adenine is present.

An important recommendation could be made at this point. When adenine is used in a preservative, the pH that is optimal would seem to be 5.5. This corresponds closely to the pH of CPD which may be 5.5 or 5.67 depending on the formulation.

The correlation between red cell ATP concentrations and post-transfusion viability of stored red blood cells made by Dern et al. [10] has been extended by Strumia et al. [14] so one say that as long as the ATP concentration is within 77% of the initial, day 0, concentration, 70% of the red cells can be expected to survive in the recipient for 24 hours. Using the criterion of Strumia et al. only the preservatives with the two lowest pHs, 5.0 and 5.5, would have an acceptable shelf life or storage time at 6 weeks after collection. The intermediate pH preservative, pH 6.0, would seem to have an acceptable shelf life, according to this criterion, for a storage time of 5 weeks or 35 days. The preservatives of higher pH – 6.5 and 7.0 – would lose their acceptable storage time after 28 days. Wood and Beutler [16] have shown that DHA (dihydroxyacetone) and ascorbate are useful in helping the red cell maintain 2,3-DPG levels during four weeks of storage. The basic preservative used was CPD-adenine and effects were seen with both compounds when the pH of the preservative was 4.8, 5.6, and 7.0

The osmotic fragility at day 0 was slightly better for the higher pH preservatives (Figure 5), but by day 42, the two highest pH preservatives showed more fragility as compared to the lower pH preservatives. At day 21, there was no difference apparent between the preservatives with respect to osmotic fragility.

References

1. Akerblom, O., De Verdier, C. H., Finnson, M., Further studies on the effect of adenine in blood preservation. *Transfusion 7*, 8 (1967).
2. Benesch, R., Benesch, R. E.: The effect of organic phosphates from the human erythrocyte on the allosteric properties of hemoglobin. *Biochem. biophys. Res. Commun. 26*, 162 (1967).
3. Beutler, E., Duron, O.: Effect of pH on preservation of red cell ATP. *Transfusion 5*, 17 (1965).

4. Beutler, E., Meul, A., Wood, L. A.: Depletion and regeneration of 2,3-diphosphoglyceric acid in stored red blood cells. *Transfusion 9*, 109 (1969).
5. Chanutin, A., Curnish, R. R.: Effect of organic and inorganic phosphates on the oxygen equilibrium of human erythrocytes. *Arch. Biochem. 121*, 96 (1967).
6. Chanutin, A., Curnish, R. R.: The effect of adenosine, inosine, and adenine on the concentration of organic phosphate and an electrophoretic component (B) of human red cells during storage of blood in acid-citrate-dextrose and citrate-phosphate-dextrose. *Transfusion 5*, 254 (1969).
7. Dawson, R. B. jr.: The hemoglobin function of blood stored at 4°C in ACD and CPD. *Clin. Res. 17*, 323 (1969).
8. Dawson, R. B., Kocholaty, W. F., Gray, J. L.: The hemoglobin function and 2,3-DPG levels of blood stored at 4°C in ACD and CPD: The pH effect. *Transfusion 10*, 299 (1970).
9. Dawson, R. B., Loken, M., Crater, D.: Hemoglobin function in stored blood. IX. Preservative with pH to maintain red blood cell 2,3-DPG (function) and ATP (viability). *Transfusion 12*, 46 (1972).
10. Dern, R. J., Brewer, G. J., Wiorkowski, J. J.: Studies on the preservation of human blood. II. The relationship of erythrocyte adenosine triphosphate levels and other *in vitro* measures to red cell storage ability. *J. Lab. clin. Med. 69*, 968 (1967).
11. Krimsky, I.: In: Methods of Enzymatic Analysis. H. U. Bergmeyer (Ed.), Academic Press, New York 1963, p. 539.
12. Lowry, O. H., Passoneau, J. V., Schulz, D. W., Rock, M. D.: The measurement of pyridine nucleotides by enzymic recycling. *J. biol. Chem. 236*, 2746 (1961).
13. Prins, H. K., Loos, J. A.: Determination of energy rich phosphate, 2,3-diphosphate, lactate and glutathione in small amounts of blood cells. Personal communication 1969.
14. Strumia, M. M., Strumia, P. V., Eusebi, A. J.: The preservation of blood for transfusion. VII. Effect of adenine and inosine on the adenosine triphosphate and viability of red cells when added to blood stored from zero to seventy days. *J. Lab. clin. Med. 75*, 244 (1970).
15. White, S., Miller, G., Dawson, R. B.: Analysis of 2,3-DPG and ATP by an automated method. In preparation.
16. Wood, L., Beutler, E.: The effect of ascorbate and dihydroxyacetone on the 2,3-diphosphoglycerate and ATP levels of stored human red cells. *Transfusion 14*, 272 (1974)

Correspondence: Dr. R. Ben Dawson, University of Maryland Hospital, Blood Bank, Baltimore and Greene Streets, Baltimore, Md. 21201, USA

Haematologia 9 (1—2), pp. 59—63 (1975)

Erythropoiesis Inhibitor in a Patient with Hereditary Spherocytosis

M. ŁAZEWSKA, B. SAGANEK, Z. WOJTOWICZ, M. JÓZWIK, M. BIELECKI

Institute of Obstetrics and Gynaecology, and Department of Biophysics of the Institute of Physiology and Biochemistry, School of Medicine, Białystok, Poland

(Received November 12, 1973)

The studies dealt with the effect of plasma of a patient with congenital haemolytic anaemia on the erythropoiesis in mice. The materials included the plasma from the patient before and after splenectomy and the spleen homogenate and the spleen subcellular fractions. The effect of the materials was evaluated with the amount of the ^{59}Fe taken up by the erythrocytes of the mice. The erythropoiesis was found to be inhibited by the plasma before splenectomy and by the spleen homogenate and its subcellular fractions. The inhibition was the highest in cases when the mice were given the spleen homogenates previously incubated with plasma of healthy persons.

The activity of the erythropoietic system depends on the action of erythropoietin and the inhibitor of erythropoiesis. There are many ways to stimulate the production of erythropoietin both in men and in animals. On the other hand, the causes of increased activity of the erythropoiesis inhibitor are less known. Krzymowska [1, 2] observed that after blockade of the reticulo-endothelial and lymphatic systems by erythrocyte haemolysates or trypan blue, the blood plasma contained an erythropoiesis inhibitor substance. The formation of an erythropoiesis inhibitor in a hyperactive and enlarged spleen and the possible participation of the erythrocyte degradation products in the former process had induced us to undertake the present study.

Materials and Methods

White BALBc mice of both sexes divided into groups including 8—10 animals were used in the experiments. The spleen and the blood plasma were obtained from an 18-year-old patient with hereditary spherocytosis. From the blood taken before and on the 5th day after splenectomy, a deproteinized plasma extract was prepared according to Lowy et al. [10] as modified by Krzymowski [3]. The patient was a young man of short stature with a dome-shaped skull, gothic palate, sexual infantilism and a marked hypersplenism; his blood smears revealed the presence of spherocytes. The weight of the removed spleen was 1500 g. During the procedure 500 ml of fresh blood were transfused. Some laboratory data of the patient before and after splenectomy are presented in Table 1.

Table 1

Some Laboratory Data of a Patient with Hereditary Spherocytosis, before and after Splenectomy

	Before splenectomy	After splenectomy
Haemoglobin, g per 100 ml	6.4	14.6
Erythrocytes per cu mm	2.307.000	4.410.000
Serum bilirubin, mg per 100 ml	5.85	0.58
Erythrocyte fragility in NaCl, per cent	0.64—0.40	0.54—0.34

A piece of the dissected spleen freed from its capsule was washed with 0.9% sodium chloride solution and homogenized in a Potter—Elvehjem homogenizer in 0.34 M saccharose solution. The concentration of the initial homogenizate was 20% w/v. Its centrifugation resulted in 3 fractions, at 600 *g* — nuclear fraction, at 10.000 *g* — mitochondrial and microsomal-cytoplasmic fractions. The initial homogenate and each of its fractions were divided into two parts incubated either with 0.9% sodium chloride solution or with blood plasma of healthy persons in proportion 1 : 1 at 37°C for 60 min.

The animals of every group were given subsequently a protein-free extract of the patient's plasma in an amount of 1 ml (equivalent to 2 ml of the initial plasma volume), 1 ml of the spleen homogenate or 1 ml of the subcellular fractions. After 48 hrs the animals received 0.5 μCi ^{59}Fe in the form of 0.5 ml of isotonic citrate (product of Isocommerz GMBH, specific activity 10 mCi per mg of Fe). Forty-eight hours later the animals were sacrificed under ether anaesthesis and blood was taken for haematocrit, haemoglobin and radioactivity assay. For the latter the counts per minute were calculated per 0.5 ml of blood. The ^{59}Fe uptake by erythrocyte was measured according to Kuratowska [8]. Total circulating blood volume in the mouse was accepted as 6.2% of the body weight [1].

Results and Discussion

The activity of erythropoiesis after administration of the patient's plasma extract before (BS) and after splenectomy (AS) was compared with 1) the reactivity to a healthy person's plasma; 2) to 5 μM cobalt chloride; and 3) to 0.9% sodium chloride. The haematocrit index in mice treated with the patient's plasma extracts BS and AS did not show significant differences, and was markedly lower than in the remaining three groups. The haemoglobin level behaved in a similar manner.

^{59}Fe incorporation into erythrocytes was much lower in mice given BS deproteinized plasma extracts. After AS extract ^{59}Fe erythrocyte uptake was

Table 2

rythropoietic Activity of the Patient's Plasma Extract before and after E Splenectomy as Measured with ^{59}Fe Uptake by Mouse Erythrocytes

Preparation applied	Uptake of ^{59}Fe into erythrocytes, per cent
Patient's plasma extract before splenectomy	24.4 ± 7.19*
Patient's plasma extract after splenectomy (5th day	33.5 ± 3.25
NaCl, 0.9%	33.8 ± 3.70
Plasma extract of healthy persons	32.7 ± 4.48
$CoCl_2$ 5 μM	36.2 ± 4.90

* Mean ± S.D.

Table 3

Effect of the Subcellular Fractions from the Patient's Spleen upon Erythropoiesis in Mice. All Samples were Incubated at 37°C for 60 min

Preparations applied	Initial homogenate		Nuclear fraction		Mitochondrial fraction		Microsomal-cytoplasmic fraction		Plasma of healthy subjects	NaCl 0.9%
	plasma	NaCl 0.9%	plasma	NaCl 0.9%	plasma	NaCl 0.9%	plasma	NaCl 0.9%	NaCl 0.9%	
^{59}Fe uptake into erythrocytes, per cent	3.02 ± 1.85*	5.23 ± 1.87	2.13 ± 0.89	2.37 ± 0.84	4.56 ± 0.98	7.46 ± 2.59	2.30 ± 1.26	5.22 ± 1.57	32.75 ± 4.48	33.8 ± 3.70

* Mean ± S.D.

similar as after treatment with the plasma of healthy subjects or with 0.9% sodium chloride solution. Cobalt chloride in an amount of 5μM caused an increased uptake (Table 2). Haematocrit, reticulocyte count and haemoglobin value were lower in all groups given spleen homogenate and subcellular fractions than in the control group.

Iron uptake in mice which had received spleen homogenate was distinctly lower than in those given homogenate previously incubated with plasma of healthy persons. Uptake was lowest in mice injected with the nuclear fraction (Table 3).

The inhibition of erythropoiesis in mice given spleen homogenate or subcellular fractions appeared to be similar to the endotoxin-induced inhibition [12].

The haemolysis and the marked hypersplenism observed in hereditary spherocytosis suggested the presence in the plasma of an erythropoiesis inhibitor. Krzymowska [1, 2, 4] has shown that the products of haemolysis and the processes of their removal are connected with the formation of an erythropoiesis inhibitor.

Rytomaa and Kiviniemi [11] showed that during the disintegration of mature erythrocytes an erythropoiesis inhibiting factor was released. Lindemann [9] suggested that in its action the factor was similar or identical with the inhibitor described by Krzymowski and Krzymowska [6]. On the other hand, perfusion of the spleen but not of the liver with trypan blue containing blood elicits the formation of an erythropoiesis inhibitor [5, 7]. Thus, the spleen seems to produce substances acting on the function of the erythron.

In the present study splenectomy, apart from normalizing the patient's serum bilirubin level, caused the disappearance of the inhibitory properties of his plasma acting on the erythropoietic system of mice. After incubation with normal plasma there was an increased inhibitory activity of the spleen homogenate and of its subcellular fractions. These results support the suggestion put forward by Krzymowski that the inhibitor, like the erythropoietin, consists of two fractions. One fraction would originate from the cells of the lymphatic system. The spleen homogenate and its subcellular fractions, and a component of the erythropoiesis inhibitor which seemed to contain these fractions after incubation with normal plasma proteins, resulted in more intensive inhibition of the erythropoietic system than after incubation with physiological saline.

References

1. Krzymowska, H.: The effect of plasma from rats injected with hemolysates on erythropoiesis inhibition in mice. *Pol. Arch. weteryn. 10*, 63 (1966).
2. Krzymowska, H.: Inhibition of erythropoiesis. III. The influence of trypan blue on erythropoiesis as investigated by the tracer technique. *Folia biol. (Kraków) 14*, 115 (1966).
3. Krzymowski, T., Krzymowska, H.: Nerwowa i humoralna regulacja procesów krwiotwórczych u zwierzat. *Acta physiol. pol. 10*, 349 (1959).

4. Krzymowski, T.: Udzial inhibitora erytropoezy i erytropoetyny w regulacji wytwarzania krwinek czerwonych. *Acta physiol. pol. 22*, 719 (1971).
5. Krzymowski, T.: Studies on the site of production of the erythropoiesis inhibitor. Proc. Eighth Congr. Europ. Soc. Haemat. Vienna 1961. Part II. P. 4.
6. Krzymowski, T., Krzymowska, H.: Studies on the erythropoiesis inhibiting factor in the plasma of animals with transfusion polycythemia. *Blood 19*, 38 (1962).
7. Krzymowski, T., Krzymowska, H.: Fizjologia ukladu krwiotwórczego. PWN. Warszawa, 1963.
8. Kuratowska, Z.: Studies on the production and mode of action of erythropoietin. *Ann. med. Sect. pol. Acad. Sci. 15*, 189 (1970).
9. Lindemann, R.: Erythropoiesis inhibiting factor in urine. *Israel J. med. Sci. 7*, 1007 (1971).
10. Lowy, P. H., Keighley, G., Borsook, H.: Inactivation of erythropoietin by neuraminidase and by mild substitution reactions. *Nature (Lond.) 185*, 102 (1960).
11. Rytomaa, T., Kiviniemi, K.: Regulation system of blood cell production in control of cellular growth in adult organisms. Academic Press, London 1967.
12. Twentyman, P. R.: The effects of repeated doses of bacterial endotoxin on erythropoiesis in the normal and splenectomized mouse. *Brit. J. Haemat. 22*, 169 (1972).

Correspondence: Dr. M. Józwik, Clinic of Obstetrics, School of Medicine, ul. Warszawska 15, 15-062 Białystok, Poland

Haematologia 9 (1—2), pp. 65—72 (1975)

Corticosteroid Effect on Eosinophils *in vitro*: Ultrastructural Studies

MEIR DJALDETTI, PNINA FISHMAN, HANA BESSLER, EVA VAN DER LIJN

Department of Medicine "B", Hematology Clinic and the Unit of Electron Microscopy, Hasharon Hospital, Petah-Tiqva and Tel-Aviv University Medical School, Israel

(Received January 14, 1975)

The effect of corticosteroids, ultracortene and ACTH, on the eosinophilic cells of a patient with hypereosinophilic syndrome has been studied *in vitro*. Both drugs caused a marked decrease in the number of specific granules, a disappearance of their surrounding membrane and an almost complete destruction of their crystals. In addition, vacuolization of the cytoplasm, swelling of the mitochondria and distortion of their cristae were found. Incubation of the eosinophils with the antihistaminic drug mepyramine, did not produce ultrastructural alterations.

Introduction

The eosinopenic effect of corticosteroids is widely documented [1], but little is known concerning the mechanism of their direct effect on eosinophilic leukocytes. Kelényi et al. [2] showed that corticosteroid treatment of patients suffering from hypereosinophilic syndrome resulted in dissolution of the granules in the eosinophilic cells of the peripheral blood. Németh et al. [3] found that corticosteroids caused partial granule lysis in rat eosinophils.

In the present report, we describe *in vitro* studies on the effect of corticosteroids on the eosinophils of a patient with hypereosinophilic syndrome.

Case report

M. H., a 67-year-old female, born in Poland was admitted to our Hospital because of cough, wheezing and general malaise. The symptoms had manifested themselves half a year prior to admission.

On physical examination she was found to be pale, with a blood pressure of 160/90 mm mercury and a steady pulse rate of 100/min. A slight systolic murmur was detected over the heart apex and the liver was palpated two cm below the costal margin. The spleen and lymph nodes were not palpable.

Laboratory examinations showed: ESR 65/100; haemoglobin 11.5/100 ml., WBC count 14,800/mm^3, with 30% neutrophils, 2% band forms, 55% eosinophils, 13% lymphocytes. Platelets: 210,000/mm^3. Bone marrow aspiration biopsy showed

marked proliferation of the eosinophilic series. Eosinophils of normal appearance in every stage of maturation were seen. Serum total protein, albumin and globulin values were within normal limits. IgG was 1,800 mg, IgA 500 mg and IgM 66 mg per 100 ml. Repeated stool examinations for parasites gave negative results as did the Weinberg and Cassoni tests.

X-ray examination of the lungs, gastrointestinal tract, kidneys and gall-bladder, as well as scanning of the liver and the spleen gave no pathological findings.

Treatment with prednisone (40 mg per day) resulted in an improvement of the patient's condition and a decrease to 14% in the eosinophilic count.

The patient was followed up in our outpatient clinic. Attempts to discontinue administration of the steroids resulted in elevation of the eosinophilic counts to the pretreatment level.

Electron microscopic findings

Materials and Methods

Buffy coat was obtained from the patient's venous blood withdrawn into a heparinized syringe. The white blood cells were resuspended in autologous plasma. Six $\times 10^6$ cells/ml were used for each test. The following drugs were added to cell suspensions kept for two hours at 37°C in a moist atmosphere containing 5% CO_2: Ultracortene (Ciba, Basel, Switzerland) – 0.05 mg/ml; ACTH (Actogel, Zori, Ramat-Gan, Israel) – 0.06 units/ml; and Mepyramine (Allersan, Teva, Jerusalem, Israel) – 0.1 mg/ml. Cells incubated under the same conditions, but without the drugs served as controls.

Results

Eosinophils incubated alone

After incubation without drugs the cells appeared well preserved (Fig. 1). The nuclear structure was normal, and so was the euchromatin to heterochromatin ratio, and the nuclear envelope was intact. The cytoplasm appeared granular, but not as dense as in the non-incubated cells. The granules showed well-preserved crystals. At sites, the membrane surrounding the granules was discontinuous (Fig. 2), a feature detected also in non-incubated eosinophils. Mitochondria were normal in number and appearance.

Eosinophils incubated with ultracortene

While the nucleus and its envelope appeared unchanged, the cytoplasm and its organelles showed marked alterations (Fig. 3). The granular appearance of the cytoplasm was blurred and cytoplasmic vacuoles were frequent. The number

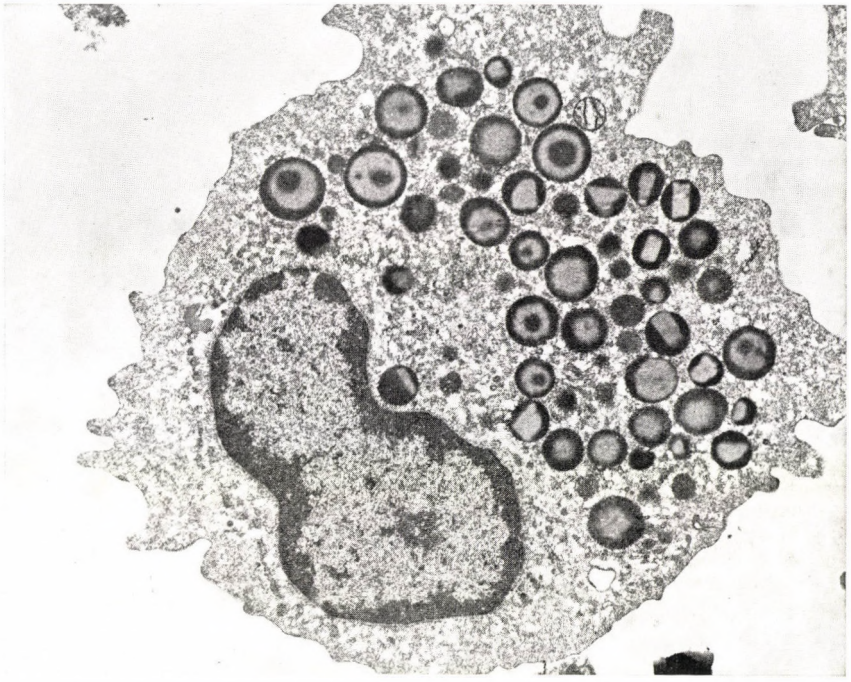


Fig. 1. Eosinophil after incubation in autologous plasma for two hours (see Methods) showing fairly normal ultrastructure. ×11,000

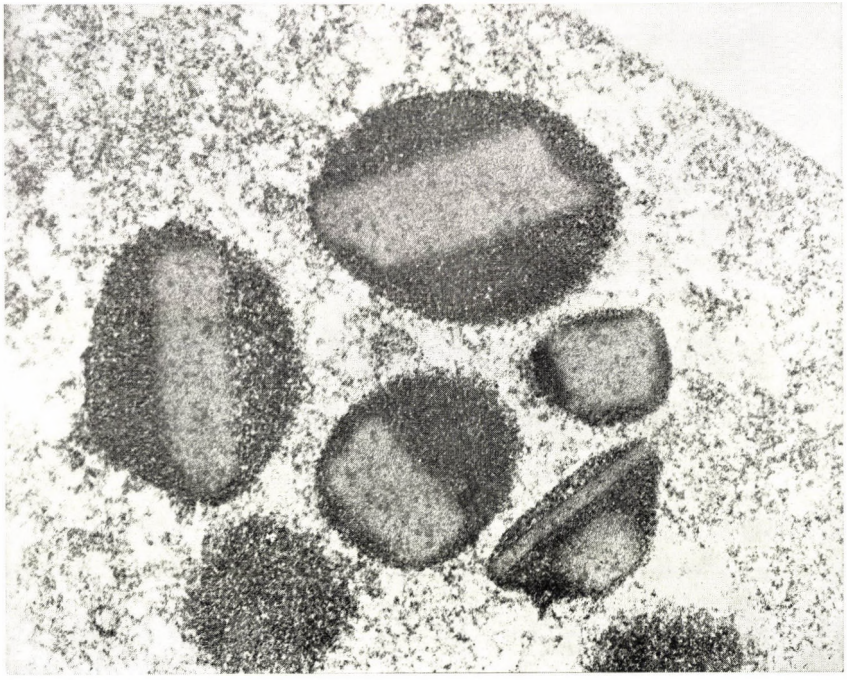


Fig. 2. Eosinophil after incubation for two hours. The granules show discontinuities of the membrane, but otherwise appear normal. ×56,000

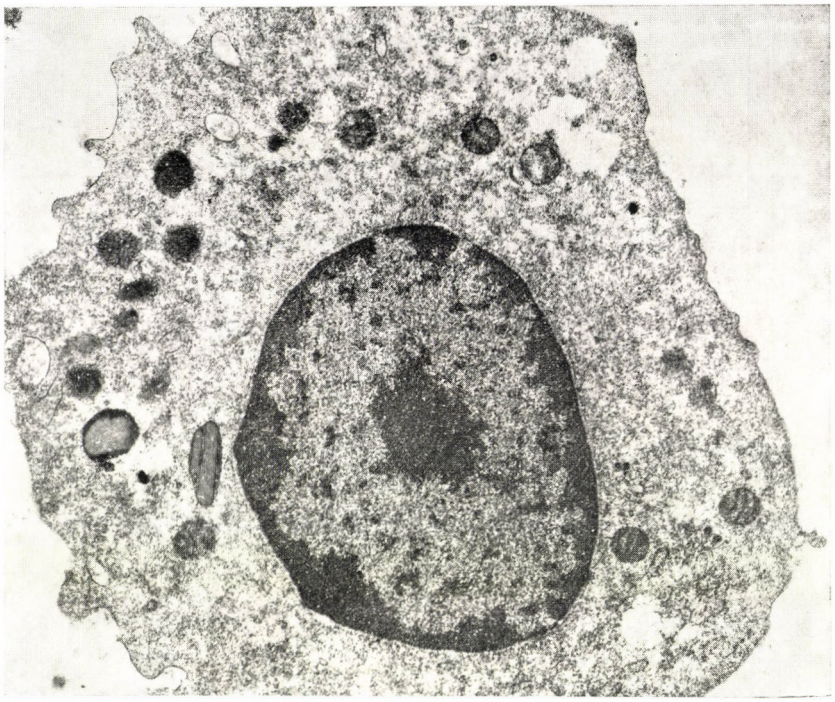


Fig. 3. Eosinophil after incubation with ultracortene. The specific granules are fewer in number and most of the crystals are destroyed. × 13,700

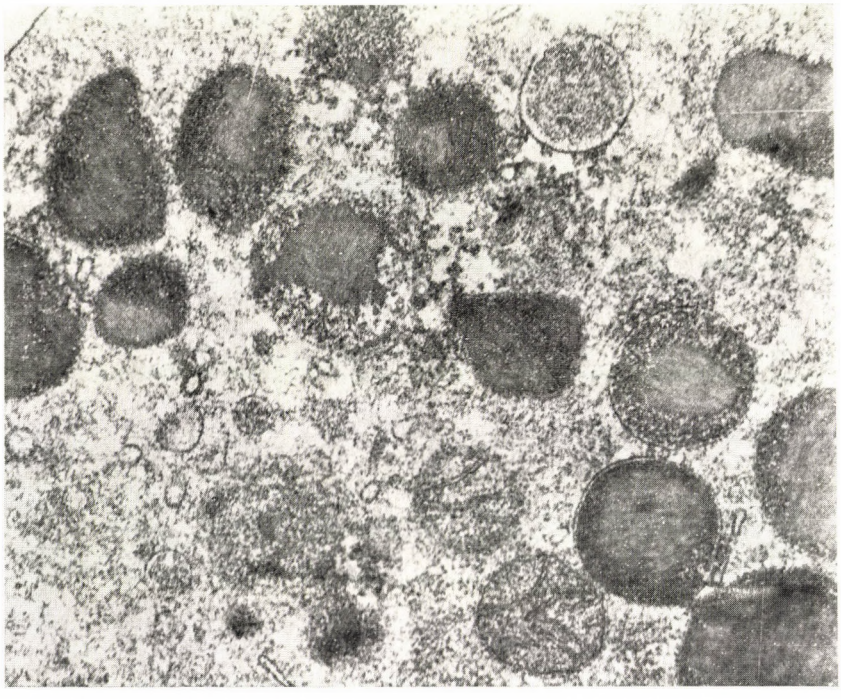


Fig. 4. Eosinophil after incubation with ultracortene. The severe damage to the granules is evident. × 36,000

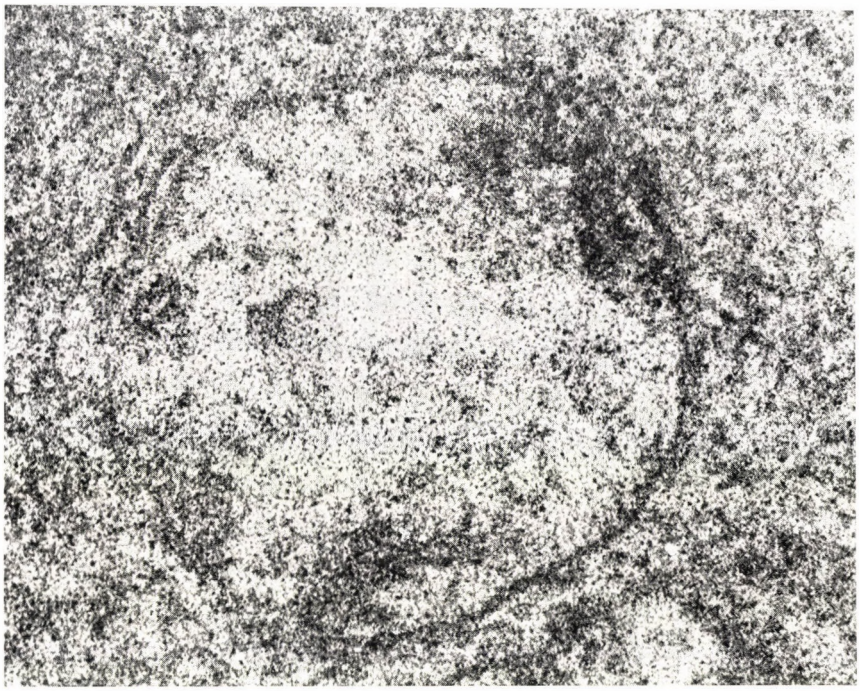


Fig. 5. Severe mitochondrial damage in an eosinophil after incubation with ultracortene. ×161,500

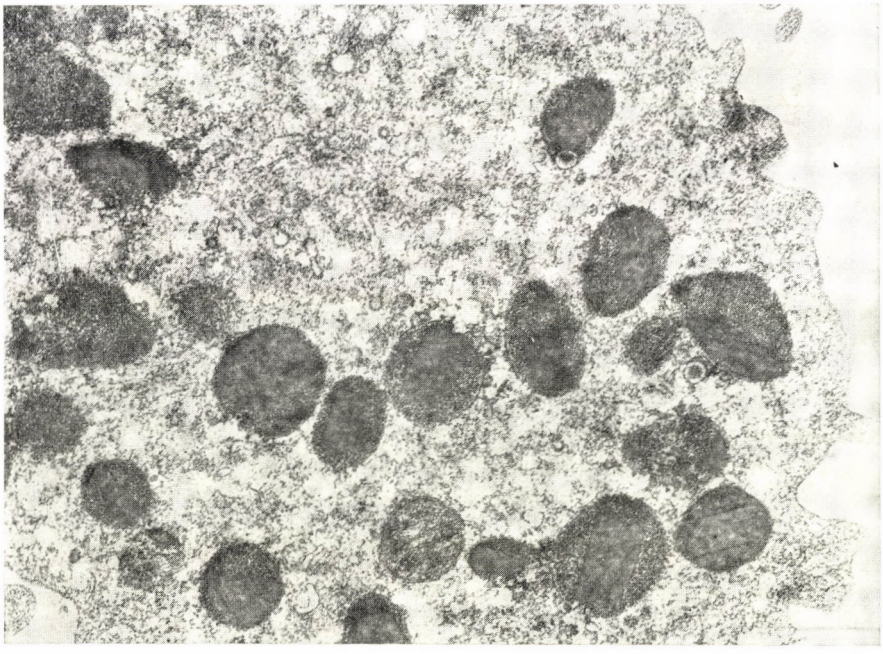


Fig. 6. Ultrastructure of the specific granules of an eosinophil after incubation with ACTH. The crystals of the specific granules are completely destroyed. ×21,600

of specific granules was markedly diminished. Their surrounding membrane had disappeared and the crystals were partly or completely destroyed (Fig. 4). The mitochondria were swollen and their cristae distorted (Fig. 5).

Eosinophils incubated with ACTH

The ultrastructural alterations of eosinophils incubated with ACTH were similar to those observed with ultracortene, although somewhat less pronounced (Fig. 6).

Eosinophils incubated with mepyramine

There was no detectable effect of this drug on the eosinophils and their appearance was similar to that of the control cells (Fig. 7).

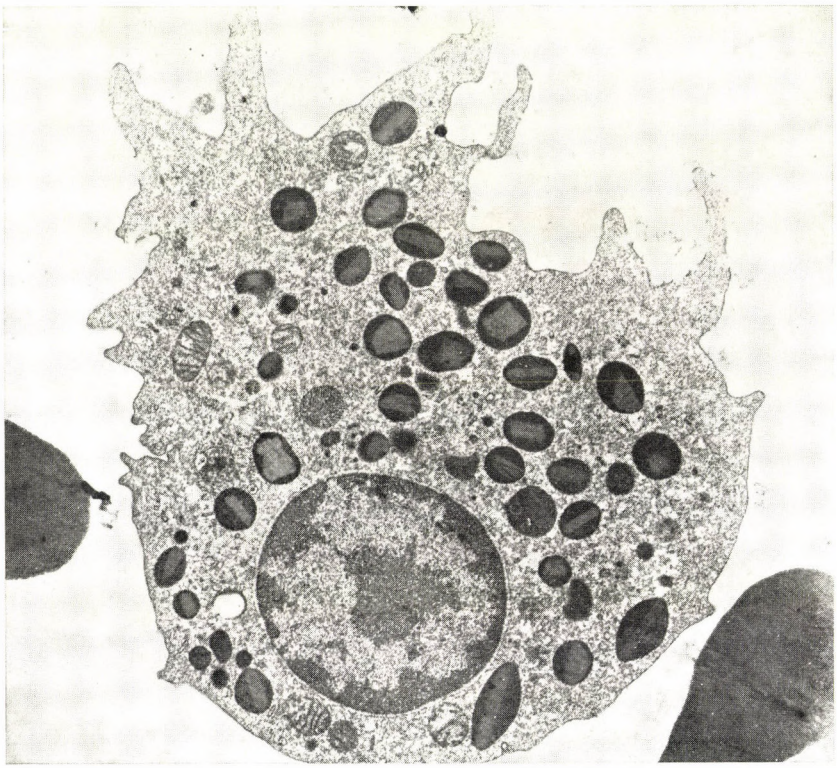


Fig. 7. Eosinophil incubated with mepyramine. The nucleus and the cytoplasmic organelles appear normal. × 11,000

Discussion

The diagnosis of our patient's illness remains obscure. Although the cough, wheezing and malaise might suggest Löeffler's syndrome, the absence of pathologi cal X-ray findings in the lungs do not support this diagnosis.

The corticosteroids possess a well-known eosinopenic effect [1]. When administered *in vivo*, the eosinopenia is believed to result from the rapid removal of such cells from the circulation [4]. Herion et al. [5] assumed a direct destructive effect on eosinophils of the steroids.

Our studies show that the main effect of the corticosteroids is on the eosinophilic granules and the mitochondria. Although these studies were not quantitative, there was no doubt that the number of granules decreased following incubation with the drug. The severe alterations in the granular matrix and crystals could explain the dissolution of the eosinophilic granules. Our observations are in accord with the effect of corticosteroids *in vivo* reported by Kelényi et al. [2], but differ with regard to the preservation of the granular membranes and unaffected mitochondria described in their study.

The fate of the destroyed granules is uncertain. Kelényi et al. [2] believe that the granular component is released in the cytoplasm. Skinnider and Ghadially [6] provided evidence of a granule discharge by eosinophilic cells. Taking into consideration that the granule content of the eosinophils is mainly peroxidase [8], acid phosphatase and hydrolases [9, 10] the action of corticosteroids on the granules seems to be an enzymic process. The lack of alterations in the eosinophils after incubation with the antihistaminic drug, mepyramine, also supports the possibility of a specific mechanism of granular destruction leading finally to eosinopenia.

This study was supported by a grant from the Chief Scientist's Bureau, Ministry of Health, of which M. D. is Established Investigator. The skilful assistance of Mr. Sadovnik is highly appreciated.

References

1. Goodman, L. S., Gilman, A.: The pharmacological basis of therapeutics. 4th ed. Collier-Mac-Millan, Ltd., London 1971.
2. Kelényi, G., Németh, A., István, L., Mohay, A.: Effect of corticosteroids on eosinophil leukocytes in hypereosinophilic syndromes. *Acta haemat. (Basel) 49*, 235 (1973).
3. Németh, A., Kelényi, G.: Die Wirkung einer Glykokorticosteroids ("Depersolon") und die des sauren pH auf die eosinophilen Leukocyten. Abstr. 13th Int. Congr. Haematology, München (1970).
4. Andersen, V., Bro-Rasmussen, F., Hougaard, K.: Autoradiographic studies of eosinophil kinetics: effects of cortisol. *Cell Tissue Kin. 2*, 139 (1969).
5. Herion, J. C., Glasser, R. M., Walker, R. I., Palmer, J. G.: Eosinophil kinetics in two patients with eosinophilia. *Blood 36*, 361 (1970).
6. Skinnider, L. F., Ghadially, F. N.: Secretion of granule content by eosinophils. *Arch. Path. 98*, 58 (1974).

7. Scott, R. E., Horn, R. G.: Fine structural features of eosinophilic granulocyte development in human bone marrow. *J. Ultrastruct. Res. 33*, 16 (1970).
8. Muller, F., de Harven, E., Palade, G. E.: The structure of eosinophil leukocyte granules in rodents and in man. *J. Cell Biol. 31*, 349 (1966).
9. Archer, G. T., Hirsch, J. G.: Isolation of granules from eosinophilic leukocytes and study of their enzymes content. *J. exp. Med. 118*, 277 (1963).
10. Ghidoni, J. J., Goldberg, A. F.: Light and electron microscopic localization of acid phosphatase activity in human eosinophils. *Amer. J. clin. Path. 45*, 402 (1966).

Correspondence: Prof. Meir Djaldetti, Department of Medicine "B" and Haematology Clinic, Hasharon Hospital, Petach-Tiqva, Israel

Haematologia 9 (1—2), pp. 73—78 (1975)

Renal Function in Polycythaemia

BOŻENA LESZKO, S. PAWELSKI

Institute of Haematology, Warsaw, Poland

(Received June 16, 1972)

In 23 patients with polycythaemia vera and symptomatic erythrocytosis, glomerular filtration rate and urine concentration ability $\left(\max U_{osm},\ C_{osm},\ Tc_{H_2O},\ \frac{Tc_{H_2O} \times 100}{GFR},\ \frac{C_{csm} \times 100}{GFR}\right)$ were determined under conditions of antidiuresis. The restriction of fluid intake caused a significant reduction of GFR and modified the osmotic function of the kidneys. The results were similar in both types of polycythaemia.

In 23 patients with true and symptomatic polycythaemia, glomerular filtration rate (GFR) and urine concentration ability were determined under conditions of antidiuresis. The results were similar in both types of polycythaemia. Restriction of fluid intake caused a significant reduction of GFR while the ability of urine concentration was less altered. Changed haemodynamic conditions in the kidneys in polycythaemia modify the glomerular as well as the osmotic function of the kidneys.

In earlier studies, an impairment of renal function has been observed in leukaemic patients [6]. This impairment could be detected a long time before the appearance of renal failure and was often present in patients with urinary findings. This early appearance of laboratory abnormalities of apparently normal kidneys has prompted us to carry out similar investigations in another myelo-proliferative syndrome, polycythaemia vera, as well as in several cases of secondary polycythaemia. Both these conditions are characterized by an increased circulating blood volume which is, probably, not without effects on the kidneys.

Material

The material included 23 polycythaemia patients aged from 26 to 70 years, 14 females and 9 males. Nine were treated with busulfan or ^{32}P and/or repeated phlebotomies; 14 patients had no treatment. Polycythaemia vera was diagnosed in 14 cases and symptomatic polycythaemia in 9 cases, of which 5 were cases of pulmonary heart disease, and 1 each of Pickwick syndrome, suspected cerebellar

tumour, uterine myoma and double renal pelvis. The disease dated back to 1 month to 15 years; 8 cases were in the period of remission, the remaining patients had exacerbations of the disease. Twenty healthy subjects served as a control group.

Methods

The controls and patients with polycythaemia were maintained under the same hospital conditions. After 16 hours of fluid deprivation the bladder was emptied spontaneously and then urine was collected without catheterization during the next 3 hours, between the 16th and 19th hours of fluid deprivation.

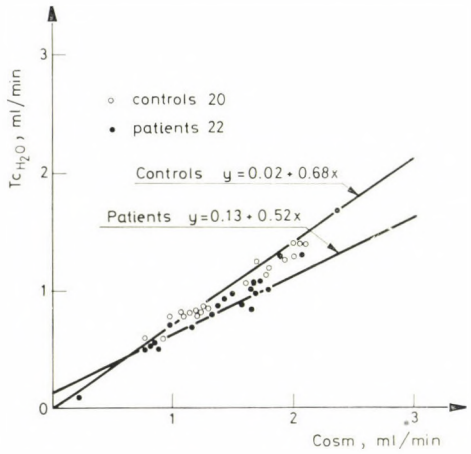


Fig. 1. Osmotic clearance and the negative clearance of free waters in controls and in polycythaemia

A venous blood sample was taken into a heparinized test tube in the middle of clearance period. Plasma and urine creatinine concentrations were determined with the Orlowski's modification of the method of Popper, Mandel and Mayer. Osmolality of plasma and urine was estimated by the cryoscopic method in Fiske's osmometer. Endogenous creatinine clearance was estimated daily in the group of patients maintained on free water intake as well. Serum urea, sodium, potassium and protein concentrations and urinary leucocyte excretion (Addis count) were measured and urinary cultures were performed.

From the obtained data, minute diuresis (V) was calculated, together with maximum urine osmolality (max U_{osm}), osmotic clearance (C_{osm}), endogenous creatinine clearance and negative clearance of free water (Tc_{H_2O}). The mean osmotic and negative free water clearances were calculated for 100 ml of GFR. Endogenous creatinine clearance was accepted as a measure of glomerular filtration rate (GFR) [8]. The material was subjected to statistical analysis using the *t* test of Student for comparison of the calculated mean values in the patients and

in the control group [2]. In order to establish the correlation between C_{osm} and Tc_{H_2O} in the control group and in patients, the correlation index was calculated and the degree of correlation between C_{osm} and Tc_{H_2O} in both groups was expressed as an equation and regression line (Fig. 1).

Mean endogenous creatinine clearance for the control group under conditions of antidiuresis was compared with the value obtained by Orlowski in a similarly large group studied by the same method under conditions of normal hydration [10].

Results

The results obtained in the group of polycythaemia vera were not significantly different from those in the group of secondary polycythaemia; they are presented in Table 1.

Table 1

Results

Studied groups	GFR antidiuresis, ml/min	GFR ml/min	V, ml/min	maxU_{osm}, mOsm/kg H_2O
Controls	116 ± 20	132 ± 41*	0.44 ± 0.62	951 ± 73
Polycythaemic patients	76 ± 34	108 ± 32	0.64 ± 1.17	798 ± 92
Statistical significance of difference	$p < 0.0001$	$p < 0.04$	$p > 0.32$	$p < 0.0001$

	C_{osm}, ml/min	Tc_{H_2O}, ml/min	$\frac{Tc_{H_2O} \times 100}{GFR}$	$\frac{C_{osm} \times 100}{GFR}$
Controls	1.52 ± 0.04	1.04 ± 0.33	0.76 ± 0.20	1.30 ± 0.03
Polycythaemic patients	1.51 ± 0.61	0.92 ± 0.47	1.22 ± 0.55	1.98 ± 0.64
Statistical significance of difference	$p > 0.05$	$p > 0.40$	$p < 0.0001$	$p < 0.001$

Mean ± S.D.
* Data from the paper of Orlowski [10].

Glomerular filtration expressed by the value of endogenous creatinine clearance under conditions of antidiuresis in the control group did not differ from those obtained by Orlowski under conditions of normal hydration [10]. GFR in patients on antidiuretic regime was considerably lower than in the controls studied under the same conditions. This value was even much lower than that obtained in the same patients during normal hydration. The differences between these values were highly significant.

Minute diuresis in both groups was not significantly different but in the group of patients a minute diuresis of over 0.5 ml/min was more frequent than in the controls.

After 19 hours of fluid deprivation the maximum osmolality of urine in polycythaemic patients was significantly lower than in the controls (798 ± 92 versus 951 ± 73 mOsm/kg H_2O, respectively).

Mean osmotic clearance was similar in both groups but its values calculated per 100 ml of GFR differed significantly ($p < 0.001$), being 1.98 ± ¼ 0.64 ml/ min for the patients and 1.30 ± 0.03 ml/min for the controls. This means that the osmotic clearance in the controls accounted for 1.3% of the value for glomerular filtration, while in patients it accounted for nearly 2% of this value.

Negative free water clearance obtained during antidiuresis with a comparable osmotic clearance was 1.04 ± 0.33 and 0.92 ± 0.47 ml/min in the controls and the patients, respectively. The difference between these values was not significant statistically ($p > 0.40$). On the other hand, the value for negative free water clearance calculated per 100 ml of GFR was higher in the polycythaemic patients than in the controls ($p < 0.0001$), its value being 1.22 ± 0.55 ml/min versus 0.76 ± 0.20, respectively.

The patients showed no abnormality in plasma urea, sodium, potassium, and protein concentrations. They showed no evidence of circulatory failure or urinary tract infection.

Discussion

It may be assumed with a fair approximation that under conditions of antidiuresis the osmotic clearance corresponds to the volume of tubular fluid reaching the collecting duct. The above presented data show that in both groups, the same amount of tubular fluid reached that part of the nephron in one minute. The passive water diffusion from collecting ducts had reduced the volume of this fluid. The value of this diffusion was similar in both groups (measured as Tc_{H_2O}) and the question why the maximum osmolality of urine was different in both groups and lower in the patients than in the controls, remains to be answered.

Since the above described abnormalities were found in polycythaemia vera as well as in secondary polycythaemia, they were not determined by proliferative changes in the kidneys.

The increased volume of erythrocytes and increased blood viscosity associated with the high haematocrit value decreases the renal plasma flow in patients with polycythaemia vera [3] as well as with secondary polycythaemia [4].

Renal function may be changed also by a relative renal ischaemia due to slow renal blood flow [5]. On the other hand, in both types of polycythaemia, renal vascular thrombosis may appear as observed by de Wardener et al. [13] in cases of polycythaemia vera and it may cause disturbances in renal functions. Theoretically, blood distribution in the kidneys must also change since blood with increased viscosity and greater cell count flows through large vessels, avoiding the capillary vessels with their considerable vascular resistance. On the other hand, certain authors point to the increase of vascular lumen in the kidneys of patients with polycythaemia [7], this vasodilatation being an evidence of the action of mechanisms

compensating the increased viscosity of blood. Probably owing to this mechanism, n the kidneys in a material of 250 cases of polycythaemia studied by Chievitz and Thiede [1] uraemia was never a cause of death. These changed conditions of renal, especially cortical, blood flow, modify the function of the kidneys. It was evident in the presented material that during antidiuresis, when the viscosity of blood increased, glomerular filtration was reduced.

Tawlas [12] observed a low creatinine clearance in 5 out of 7 cases of polycythaemia and explained this fact by nephrosclerosis. In our material (Table 1) GFR studied under conditions of normal hydration was 108 ± 32 ml/min in polycythaemia, but after 19 hours fluid restriction it decreased by 30%, to 76 ± 34 ml/min.

Reduced osmolality of urine suggests changes in blood flow in the renal medulla. However, a difference in osmotic clearance calculated per unit of filtration between controls and polycythaemia patients shows clearly that during antidiuresis a greater amount of water and sodium reaches the collecting tubules in patients than in controls and probably the amount of tubular fluid reaching the urine concentrating part of the nephron is also greater in patients than in controls.

Sodium reaching this part of the nephron in amounts greater than in healthy subjects and reabsorbed from the ascending limb of Henle's loop increased the volume per unit of GFR of free water undergoing passive diffusion from the lumen of the collecting ducts into the interstitial spaces of the renal medulla.

A normally functioning mechanism of urine concentration – despite reabsorption of probably increased amounts of sodium from the ascending limb of Henle's loop – failed to cause a final increase in urinary osmolality due to the increased amount of tubular fluid reaching the distal part of the nephron.

The efficiency of the mechanism of urine concentration in polycythaemia is evidenced by the calculated regression lines for this and for the control group (Fig. 1), as well as the correlation coefficient between C_{osm} and Tc_{H_2O} which was 0.99 in the controls and 0.94 in the patients. This shows that renal function in polycythaemia corresponds rather to the situation when for maintenance of the stability of internal environment a decrease in glomerular filtration rate modifies secondarily the tubular functions which are reducing sodium reabsorption [11]. The normal urea level found in all our patients rules out osmotic diuresis as a possible explanation of this phenomenon.

The above described reduction of glomerular filtration, the similar osmotic clearance in both groups, the greater osmotic clearance calculated per unit of filtration, and urinary osmolality being lower in the patients than in the controls, suggest rather than a certain number of nephrons have been excluded functionally or that the filtration rate in them has decreased significantly. The possibility of a slight equal decrease of filtration in every nephron seems less likely. Our study failed to supply direct data pointing to changes in renal medullary blood flow in polycythaemia. The differences in the correlation coefficient between C_{osm} and Tc_{H_2O} in patients and controls and the differences in the regression equations (Fig. 1) suggest, however, that the mechanism of urine concentration is impaired

in polycythaemia. Comparing renal function in polycythaemic and healthy subjects we suggest that it corresponds rather to a removal of part of active renal parenchyma than to e.g. renal function in heart failure or slight stenosis of renal arteries, or to the so-called prerenal uraemia.

Conclusions

1. A restriction of fluid intake during 19 hours in polycythaemic patients significantly reduced glomerular filtration.

2. The reduced filtration was due to an inhibition of filtration in a number of glomeruli or to a marked reduction of filtration in these glomeruli rather than to a slight even reduction of filtration in all glomeruli.

3. The kidneys in polycythaemia preserve their urine concentration ability but it is worse than in healthy subjects.

4. Since restriction of fluid intake impairs the renal function of patients with polycythaemia, they should be given adequate amounts of fluid to prevent the possible harmful effects of fluid restriction.

References

1. Chievitz, E., Thiede, T.: Complications and causes of death in polycythaemia vera. *Acta med. scand. 172*, 513 (1962).
2. Bancroft, H.: Introduction to biostatistics. Cassel and Co. Ltd. London 1957.
3. Doering, P., Wenker, H.: Nierenfunktion und intrarenale Haemodynamik bei der Polycythaemia rubra vera. *Klin. Wschr. 34*, 1028 (1956).
4. Herms, W., Schroeder, E., Wetzels, E.: Glomerulumfiltrat und Nierendurchblutung bei erhöhtem Haematokrit. *Dtsch. med. Wschr. 90*, 30 (1965).
5. Lawrence, J. H.: Polycythemia. Grune and Stratton, New York 1955.
6. Leszko, B.: Czynnosc nerek u chorych z białaczka. *Pol. Arch. Med. wewnęt. 41*, 633 (1968).
7. Moeller, J.: Die Niere bei Tumoren, Blutkrankheiten und Paraproteinaemien. In: Handbuch der Inneren Medizin. Vol. 8. edited by H. Schwiegk, Springer-Verlag, Berlin (1968).
8. Orlowski, T.: Czynnosc klebków i cewek nerkowach w zakresie gospodarki wodnej w stanach prawidlowach i niektórych chorobach narzadu krazenia. Poznań 1952, Prace Komisji Medycyny Doswiadczalnej, vol. 10, Nr 1.
9. Orlowski, T.: W sprawie oznaczania poziomu kreatyniny w plynach biologicznych metoda Poppera, Mandela i Mayer. *Pol. Arch. Med. wewnęt. 25*, 719 (1955).
10. Orlowski, T.: Czynnosc nerek w rozlanym klebkowym zapaleniu nerek. *Rozprawy Kom. Nauk Med. 1*, 5 (1956).
11. Slatopolsky, E., Elkan, I. O., Weerts, C.: Studies on the characteristics of the control system governing sodium excretion in uremic man. *J. clin. Invest. 47*, 521 (1968).
12. Tawlas, N.: Clearance kreatyninowy w czerwienicy prawdziwej. *Pol. Arch. Med. wewnęt. 30*, 539 (1960).
13. Wardener, H. E. de, McSwiney, R. R., Miles, B. E.: Renal haemodynamics in primary polycythaemia. *Lancet 2*, 204 (1951).

Correspondence: Dr. B. Leszko, Institute of Hematology, ul. Chocimska 5, 00-957 Warsaw, Poland

Haematologia 9 (1–2), pp. 79–84 (1975)

Iron Metabolism in Polycythaemia Rubra Vera and Secondary Polycythaemia

G. NAGY, I. DEZSŐ, MAGDOLNA VARSÁNYI

First Department of Medicine and Institute of Medical Chemistry, University Medical School, Debrecen, Hungary

(Received October 5, 1972)

Serum iron concentration, serum iron binding capacity and saturation coefficient were assayed in polycythaemia rubra vera and secondary polyglobulia. In the exacerbation stage of polycythaemia rubra, significantly lower Se Fe and SC values were found while in the remission stage and in secondary polyglobulias these values did not differ from those of the normal control.

In both normal and pathological conditions, iron metabolism is connected with haematopoiesis and haemoglobin synthesis [3, 5, 21, 29, 36, 40]. This connection is obvious if we consider the fact that under normal conditions 75–85% of the plasma iron is directed to the bone marrow [4]. Due to the close connection between iron metabolism and haematopoiesis, the various defects of haematopoiesis are reflected in the metabolism of iron. Consequently, an exact elucidation of the disturbance of iron metabolism accompanying an altered haematopoiesis may be relevant in the better understanding of the aetiopathogenetic, differential diagnostic and even therapeutic aspects of haematopoietic disease [22, 24, 25, 27, 33].

Polycythaemia rubra vera (PRV) belongs to the myeloproliferative diseases. Hyperplastic proliferation of all the three elements of haematopoiesis, especially of erythropoiesis and less of myelopoiesis and thrombocytopoiesis is an essential feature of the disease [12, 14, 24, 26, 30, 44]. Accordingly, in PRV, leucocytosis and thrombocytosis can always be detected in addition to an increased erythrocyte count, haemoglobin and haematocrit values [17, 25, 27, 44]. In the secondary polyglobulias, erythropoiesis is increased, but the white blood cell and platelet counts are normal [1, 8, 10, 11, 17, 35, 39]; the increase in erythrocyte, haemoglobin and haematocrit values is usually more moderate than in Vaquez–Osler's disease [23, 27, 44].

According to literary and our own investigations [13, 18, 26, 28–34] in Vaquez–Osler's disease plasma erythropoietin activity is increased and erythrocyte survival time is shortened [2, 6, 20, 25, 28, 29, 37]. It seemed worth-while to analyse systematically how the altered haematopoiesis is reflected in the routine parameters of iron metabolism, how consequent the changes are i.e. to what an extent they are characteristic of the disease or of its exacerbation, remission and duration, and whether they could be used for differentiating between PRV and the other secondary polyglobulias.

Material and Method

Serum iron concentration (Se Fe), serum total iron binding capacity (TIBC) and saturation coefficient (SC) were estimated in 60 PRV and 15 secondary polyglobulia patients and in 25 normal healthy controls.

Of the PRV patients, 36 were male and 24 female, with a mean age of 52.09 range, 20 to 71 years. In 25 patients the disease had been diagnosed more than 5 years, and in 16 3 to 5 years before and in 19 the last 3 years. The great majority was treated once or several times by radiophosphorus (^{32}P) and/or cytostatics. At the time of investigation, 50 of the 60 patients were in the exacerbation and 10 in the remission stage. Mean red cell count was 6,300,000; mean leukocyte count, 10,000; mean platelet count, 410,000; in patients in the exacerbation stage. The values for the remission stage were 4,460,000, 6260 and 201,000, respectively

The leucocyte and platelet counts in the patients who have had successful treatment the high values characteristic of PRV were reached only weeks after they had begun to increase in the course of exacerbations ensuing years later [27, 44].

Splenomegaly and hepatomegaly was present in the majority of the PRV patients. In the 28 cases there was a vascular complication in the history before the onset of active therapy.

Of the 15 secondary polyglobulia patients, 11 were male and 4 female. Their mean age was 48.79 years, not much different from the age of the PRV patients. Ten patients had hypoxic polyglobulia, 5 a polyglobulia associated with Cushing's disease. Their mean red cell count was 5,600,000, the leucocyte count 6450, and the platelet count 210,000.

In order to obtain results comparable to those of the secondary polyglobulia patients, the Se Fe, TIBC and SC values were determined in 25 persons displaying normal haemostasis.

Se Fe and TIBC were determined by the Bothwell–Mallett method slightly modified by one of us [7, 15, 16]. Saturation coefficient was calculated by the formula,

$$SC = \frac{\text{Se Fe}}{\text{TIBC}} \times 100$$

Blood was withdrawn into iron-free tubes, immediately before estimation, in order to eliminate errors due to haemolysis.

Results

Table 1 shows the Se Fe, TIBC and SC values and the mean red cell, leukocyte and platelet counts of PRV patients in the exacerbation and remission stage, and of the secondary polyglobulia patients and of the healthy controls.

Table 1 indicates that the Se Fe and SC values of PRV patients in the exacerbation stage were significantly lower than the corresponding values for the

Table 1

Groups \ Parameters	No. of patients	Se Fe, μg per 100 ml		TIBC, μg per 100 ml		SC, per cent	
		mean	S.D.	mean	S.D.	mean	S.D.
PRV exacerbation	50	39.6	± 13.8	300.9	± 58.2	13.69	± 5.78
PRV remission	10	106.5	± 21.0	298.4	± 59.5	36.63	± 7.03
Secondary polyglobulias	15	105.4	± 35.6	298.6	± 60.3	36.62	± 11.48
Control	25	104.4	± 34.0	323.9	± 42.8	33.71	± 33.71

Groups	No. of patients	RBC × 10^6		WBC × 10^3		Platelets × 10^5	
		mean	S.D.	mean	S.D.	mean	S.D.
PRV exacerbation	50	6.9	± 0.9	10.0	± 3.2	4.1	± 0.4
PRV remission	10	4.5	± 0.6	6.5	± 2.3	2.0	± 0.3
Secondary polyglobulias	15	5.6	± 0.7	6.5	± 1.5	2.1	± 0.3
Control	25	4.2	± 0.5	4.2	± 1.1	2.0	± 0.2

other three groups. The differences in mean Se Fe and SC of PRV patients in the exacerbation stage versus those of PRV patients in remission and of secondary polyglobulia patients was significant within 1% (P_1, P_2, P_3, P_4 were all < 0.1).

Mean TIBC of PRV patients in the exacerbation stage did not deviate significantly from the values measured in secondary polyglobulia during remission.

In some of the PRV patients in the exacerbation stage but in the initial phase of the disease, Se Fe was somewhat higher than the mean (70 – 75 μg per 100 ml), but lower than the mean for the normal controls.

Mean Se Fe, TIBC and SC of PRV patients in remission and of secondary polyglobulia patients were essentially the same as those of the normal controls.

Se Fe, TIBC and SC values in the control group agreed well with data in the literature and our previous results [3, 4, 16].

Discussion

The investigation of iron metabolism in haematological diseases accompanied by a disturbed haematopoiesis bears importance as to the essence and pathomechanism of the illness as well as the eventual therapeutic interventions [4, 5, 19, 21, 22, 29, 36]. The significance of iron assays in the differentiation of various anaemias is well-known. In addition, a study of iron metabolism may offer

important information as to the pathogenesis. Bernát [3] emphasized the role in thermal injury anaemia of the activation of the reticulo-histiocyte system, the increased iron avidity, the acceleration of iron transport, the reduced iron binding capacity of the erythroid precursors, as well as of the fact that a significant amount of iron leaving the circulation is stored in the RES instead of the bone marrow.

There are many data to indicate that haematopoiesis increases in PRV [9, 14, 19, 27, 44]. This is supported by the high plasma erythropoietin activity [20–22, 28, 29, 40] and the hyperplastic, hypercellular bone marrow of PRV patients [14, 18, 24, 27].

Pollycove et al. [37] distinguished 4 stages in the course of PRV, based on the parameters of iron transport. In the first stage, plasma iron transport and haemoglobin synthesis are enhanced. The iron administered accumulates rapidly in the bone marrow and is incorporated into the circulating erythrocytes. The survival time of erythrocytes is normal, there is no extramedullar erythropoiesis. In the second stage, erythrocyte survival time is shortened due to an increased destruction in the spleen. In the third stage, extramedullar haemolysis contributes to the shortening of erythrocyte survival. The iron administered accumulates rapidly in the marrow, but incorporation into the circulating erythrocytes is slower and partial. In the fourth stage, extramedullar haemopoiesis is detected in the spleen and liver. The iron administered accumulates in the spleen and liver is then slowly and partially incorporated by erythrocytes. Erythrocyte survival is considerably shortened. Consequently, in spite of the increased plasma iron transport and haemoglobin synthesis the volume of the erythrocyte mass and accordingly the haematocrit value is lower than in the previous stages.

Varela et al. [44] found an increased rate of plasma iron transport and a decreased Se Fe in the exacerbation stage of PRV, and an increased Se Fe level in the stage of remission. On the basis of erythrocyte survival time and the erythrocytic enzyme activities characteristic of the age of the erythrocyte population [41–43] we found a shorter erythrocyte survival in PRV, while the mean erythrocyte population was younger than normal [25, 27].

The Se Fe and SC values were found to be normal in secondary polyglobulia, although an enhanced haematopoiesis and a consequently augmented iron utilization were obvious even in that conditions. The extent of the increase of haematopoiesis is, however, significantly higher in PRV than in secondary polyglobulia, as proven, among others, by the fact that in untreated PRV, in spite of the shorter erythrocyte survival, the increase in erythrocyte count, haemoglobin and haematocrit values is more significant than in the secondary polyglobulias [26]. In our earlier studies we found that plasma erythropoietin activity was more increased in PRV patients in the exacerbation stage than in patients suffering from hypoxic polyglobulia [28].

It is therefore assumed that in secondary polyglobulia haematopoiesis is less enhanced and thus results in a more moderate iron utilization that does not manifest itself with a significant decrease of the Se Fe and SC values.

In the present study, significantly decreased Se Fe and SC values were

found in the stage of exacerbation of PRV, and these values returned to normal in the stage of remission. We found normal Se Fe and SC values in secondary polyglobulia. Although the later decrease of the Se Fe and SC values is not always so striking than in the initial stage of PRV, a study of Se Fe and SC is usually still a help in differential diagnosis. This is not the case after a therapeutic venisection, as in secondary polyglobulias. This intervention causes an increased iron loss, resulting in a lower Se Fe level.

References

1. Auerback, M. L., Wolff, J. A , Mettier, S. R.: Benign familial polycythemia in childhood. Report of two cases. *Pediatrics 21*, 54 (1958).
2. Berlin, N. J., Lawrence, H. J., Lee, H. C.: Life span of red blood cell in chronic leukemia and polycythemia. *Science 114*, 385 (1951).
3. Bernát, L.: Az égési anaemia pathogenesise. Akadémiai Kiadó, Budapest 1971.
4. Bernát, I.: A vasanyagcsere-kutatás néhány időszerű kérdése. *Orvosképzés 46*, 202 (1971).
5. Bernát, I.: A vasfelszívódás élettana és kórtana. *Honvédorvos 23*, 34 (1971).
6. Borsook, H.: A discussion of humoral erythropoietic factors. *Ann. N.Y. Acad. Sci. 77*, 225 (1959).
7. Bothwell, T. H., Mallett, B. J.: The determination of iron in plasma or serum. *Biochem. J. 59*, 599 (1955).
8. Bradley, J. E., Young, J. D., Lentz, G.: Polycythemia secondary to phenochromocytoma. *J. Urol. 86*, 1 (1961).
9. Brodsky, I.: The use of ferrokinetics in the evaluation of busulfan therapy in polycythaemia vera. *Brit. J. Haemat. 10*, 291 (1964).
10. Carpenter, G., Schwartz, H. G., Walker, A. L.: Neurogenic polycythemia. *Ann. intern. Med. 19*, 470 (1943).
11. Charache, S., Weatherhall, D. J., Clegg, J. B.: Polycythemia associated with hemoglobinopathy. *J. clin. Invest. 45*, 813 (1966).
12. Dameshek, W., Gunz, F.: Leukemia. Grune and Stratton, New York 1958.
13. Daróczy, P., Nagy, Gy.: Kapillármikroszkópos vizsgálatok polycythaemia verás betegeken. *Orv. Hetil. 110*, 593 (1969).
14. Демидова, А. В.: Новые аспекты терапии эритремии. Химиотерапии эритемии. Опыт лечения Тренимоном и Маркофаном. *Тер. Арх. ЧZ*, 64. (1966).
15. Dezső, I.: Az életkor és véreztetés hatása a serum vasszintjére, vaskötő kapacitására. A máj és lép vastartalmának változása az életkorral. D. Sc. Thesis, Debrecen 1963.
16. Dezső, I., Fülöp, T.: Vas- és rézmeghatározás vérserumban. *Kísérl. Orvostud. 12*, 327 (1960).
17. Escobar, M. A., Trobaugh, F. E.: Erythrocythemia in primary carcinoma of the liver. *Arch. intern. Med. 110*, 339 (1962).
18. Fazekas, S., Nagy, Gy., Petrányi, Gy.: A polycythaemia vera radiophosphor therapiájának későbbi eredményei. *Orv. Hetil. 104*, 214 (1963).
19. Gráf, F.: Az erythropoetin. *Orvosképzés 2*, 98 (1966).
20. Gráf, F., Takácsi-Nagy, L.: A plasma erythropoetin tartalmának vizsgálata Gordon H-R módszerével polycythaemia verában. *Orv. Hetil. 109*, 399 (1968).
21. Ярошевский, А. Я.: Фактори регулирующие эритропоэд и их изменения при некоторых внутренних болезнях. *Тер. Арх. FS*, 21, (1967).
22. Кахетелидзе, М. Г.: Эритропоэтини. *Пат. Физиол. I*, 74 (1963).
23. Kaung, D. T., Peterson, R. E.: "Relative polycythemia" or "pseudopolycythemia". *Arch. intern. Med. 110*, 456 (1962).

24. Lawrence, J. H.: Polycythaemia. Physiology, Diagnosis and Treatment Based on 303 Cases. Grune and Stratton, New York 1955.
25. Nagy, Gy.: Klinikai vizsgálatok és erythropoetin aktivitás mérések polycythaemia verás beteganyagon. Thesis. Debrecen 1968.
26. Nagy, Gy.: Polyglobuliák. *Orv. Hetil. 111*, 1743 (1970).
27. Nagy, Gy.: Polycythaemia rubra vera. Klinikai kép, pathologia és therapia. In: Az orvostudomány aktuális problémái. Medicina, Budapest 1971.
28. Nagy, Gy., Deseö, Gy.: Vergleichende Untersuchungen über die Erythropoetinaktivität bei Kranken mit Polycythaemia vera und chronischer kardiorespiratorischer Insuffizienz mittels Bestimmung der Radioeisen (Fe^{59})-Inkorporation. *Fol. Haemat.* (Lpz.) *88*, 337 (1967).
29. Nagy, Gy., Deseö, Gy., Rácz, M.: Neuere Untersuchungen über die Erythropoetinaktivität bei Polycythaemia vera. *Fol. haemat.* (Lpz.) *91*, 436 (1969).
30. Nagy, Gy., Jurgutis, R.: Chromosome studies on patients with polycythaemia vera. *Haematologia 2*, 179 (1968).
31. Nagy, Gy., Siró, B., Rácz, M.: Thrombolastographiás vizsgálatok polycythaemia verás betegeken. *Orv. Hetil. 110*, 243 (1969).
32. Nagy, Gy., Szilágyi, J., Osváth, S., Märcz, I.: Blood gases in polycythaemia vera. *Acta med. Acad. Sci. hung. 23*, 139 (1967).
33. Nagy, Gy., Terner, K.: Szájnyálkahártya elváltozások polycythaemia verában szenvedő betegeken. *Fogorv. Szle. 63*, 78 (1970).
34. Nagy, Gy., Tompa, Gy.: Műtéti tapasztalataink polycythaemia verás beteganyagon. *Magy. Seb. 23*, 345 (1970).
35. Nixon, R. K., O'Rourke, W., Rupe, Cl. E., Korst, R. R.: Nephrogenic polycythemia. *Arch. intern. Med. 106*, 797 (1960).
36. Pollycove, M.: Iron kinetics. In: Gross, F.: Iron Metabolism. Springer, Berlin—Göttingen—Heidelberg 1964.
37. Pollycove, M., Winchell, H. S., Lawrence, H.: Classification and evolution of patterns of erythropoesis in polycythemia vera as studied by iron kinetics. *Blood 28*, 807 (1966).
38. Ramsay, W. N.: The determination of the total iron binding capacity of serum. *Microchim. Acta 2*, 221 (1972).
39. Ratto, O., Briscoe, W., Morton, J. W., Comroe, J. H.: Anoxemia secondary to polycythemia and polycythemia secondary to anoxemia. *Amer. J. Med. 19*, 958 (1955).
40. Remmele, W.: Die humorale Steuerung der Erythropoese. Springer-Verlag, Berlin—Göttingen—Heidelberg 1963.
41. Sabine, J. C.: Erythrocyte cholinesterase titers in hematologic disease states. *Amer. J. Med. 27*, 81 (1959).
42. Sári, B., Prékopa, Á., Demény, P., Dán, S.: A véralakelemek enzymologiai vizsgálatának gyakorlati és elméleti problémái. *Haemat. hung. 5*, 91 (1965).
43. Sass, M., Vorsanger, E., Spear, P. W.: Enzyme activity as an indicator of red cell age. *Clin. chim. Acta 10*, 21 (1964).
44. Varela, J. E., Rochna, V. E. M., Carmena, Á. O., Etcheverry, M. A., Kremenchuzky, S.: Polycythemia vera results of repeated radioisotope studies in 53 patients during five year period. *Nucl.-Med. (Stuttg.) 3*, 1 (1962).

Addendum: After this paper had been submitted for publication an abstract of a paper entitled: The Blood Volume Changes in the Anaemia of Experimental Splenomegaly by T. Ooyirilangkumaran appeared in the British Journal of Haematology *25*, 547 (1973). The author, too, found a plasma volume expansion in rats after the administration of methylcellulose. In contrast to our results, however, red cell volume was normal in his experimental animals.

Correspondence: Dr. G. Nagy, Central Hospital, Róbert Károly krt. 44, 1134 Budapest, Hungary

Haematologia 9 (1—2), pp. 85—96 (1975)

О роли эритроцитов в процессе фибринолиза

Б. И. КУЗНИК, Я. Д. КРАСИК, П. Д. ПРАДУН

Из кафедры нормальной физиологии (зав. — профессор Б. И. Кузник)
Чистинского медицинского института (ректор-доцент В. Г. Кузьмин)

(Поступило 7, 4, 1972 г.)

Изучалось влияние разрушенных и отмытых интактных эритроцитов здоровых людей и больных с различной патологией системы крови на фибринолитическую активность цельной крови и плазмы. Выяснилось, что интактные эритроциты здоровых и больных людей тормозят растворение сгустка; гемолизированные красные кровяные тельца ускоряют лизис эуглобулинового сгустка.

Исследованиями на фибриновых плёнках в эритроцитах здоровых людей обнаружен активатор плазминогена (в жидкой фракции) и ингибитор активации (в строме).

Корреляционный анализ позволил установить зависимость между числом эритроцитов и фибринолитической активностью крови.

Результаты исследований свидетельствуют о несомненной роли эритроцитов в процессе фибринолиза у здоровых людей и при некоторых патологических состояниях.

Вопрос о роли эритроцитов в процессе фибринолиза до последних дней остаётся почти не изученным. Между тем ещё в 1903 году Dastrae (25) отмечал, что при гемолизе развёртывание сгустка осуществляется быстрее. Эти данные заставили предположить, что в составе эритроцитов имеются соединения, влияющие на переход плазминогена в плазмин. Однако дальнейшие исследования показали, что в эритроцитах преобладают вещества, тормозящие фибринолитическую активность крови [1, 4—12, 18, 19, 20, 22, 30, 33].

За последние годы в литературе вновь стали появлятся сообщения о том, что разрушенные эритроциты способны ускорять растворение кровяного сгустка [7, 10, 11, 12, 13, 15, 16, 26, 28, 31, 33]. Однако природа этих агентов остается не изученной.

В настоящем сообщении сделана попытка разрешить вопрос, какие соединения, влияющие на фибринолиз, находятся в эритроцитах. Кроме того, мы попытались выяснить, зависит ли фибринолитическая активность от содержания эритроцитов в крови.

Методика

Нами изучалось влияние разрушенных и интактных эритроцитов здоровых и больных людей (анемии различной этиологии, острые и хронические лейкозы) на скорость растворения кровяного и плазменного сгустка, а также фракции эуглобулинов. Кроме того, устанавливалась зависимость между числом эритроцитов и фибринолитической активностью крови. Наблюдения проводились следующим образом.

Из локтевой вены толстой иглой без шприца получалась кровь, которая тотчас же смешивалась с оксалатом натрия (1,34% раствор) в отношении 9 : 1, а затем центрифугировалась при 1500 об/мин в течение 10 минут. Плазма отсасывалась и в дальнейшем использовалась в опыте. Эритроциты же не менее 5 раз отмывались физиологическим раствором и повторно центрифугировались. Верхний слой их, содержащий небольшую примесь лейкоцитов и тромбоцитов, каждый раз после центрифугирования снимался. Часть отмытых эритроцитов отсасывалась и лизировалась путем замораживания при температуре —20° и последующего оттаивания при +37°. Полученный таким образом гемолизат разводился перед опытом физиологическим раствором в отношении 1 : 9. Интактные эритроциты тотчас же использовались в эксперименте.

Для изучения фибринолитической активности применялись методы, позволяющие судить о влиянии эритроцитов на фибринолитическую активность цельной крови, стабилизированной плазмы и эуглобулиновой фракции [3, 14, 24, 27]. Выявление фибринолитических компонентов в эритроцитах осуществлялось методом фибриновых пластин [21, 29].

В связи с требованиями эксперимента большинство используемых нами методик было модифицировано: в контроле к плазме или эуглобулиновой фракции добавлялся физиологический раствор хлористого натрия, в опыте такое же количество интактных или гемолизированных эритроцитов.

Полученные данные обработаны методом вариационной статистики для связанных между собой наблюдений. Кроме того, вычислялись коэффициенты корреляции.

Резуьтаты наблюдений

В первой серии наблюдений решено было проследить, как влияют разрушенные и интактные эритроциты здоровых людей на скорость растворения фибринового сгустка. С этой целью гемолизат, разведенный в 10 раз (0,1 мл) добавлялся в плазму, после чего осаждались эуглобулины. При такой постановке эксперимента из гемолизата вместе с эуглобулиновой фракцией избирательно осаждались активаторы фибринолиза. Интактные же эритроциты (0,1 мл) вносились лишь после осаждения эуглобулинов. Кроме

того, гемолизат (0,1 мл) добавлялся к цельной плазме (0,5 мл) и цельной крови (0,5 мл гемолизата на 2,5 мл крови). В контрольных пробирках гемолизат заменялся равным объёмом физиологического раствора хлористого натрия. Определялось время растворения эуглобулинов, а также степень лизиса (в %%) сгустка, образовавшегося при свёртывании плазмы и крови, за 3 часа. Полученные данные приведены в таблице 1.

Таблица 1

Влияние на фибринолиз разрушенных и интактных эритроцитов здоровых людей

Статистические показатели	Интактные эритроциты (10 наблюдений)		Разрушенные эритроциты					
			эуглобулины (20 наблюдений)		% растворения сгустка:			
					крови (13 наблюдений)		плазмы (10 наблюдений)	
	контроль	опыт	контроль	опыт	контроль	опыт	контроль	опыт
M	254	554	203	144	18,5	9,1	9,8	5,5
m±		52,9		12,8		1,4		1,1
P		<0,001		<0,001		<0,001		<0,01

Как видно из приведенной таблицы, интактные эритроциты здоровых людей обладают выраженной антифибринолитической активностью. Такое же действие присуще гемолизатам, добавленным непосредственно в кровь или плазму. Однако степень растворения сгустка, образованного из цельной крови, несколько ниже, чем свёртка плазмы, что, по-видимому, объясняется наличием эритроцитов, обладающих антифибринолитическим действием. Если же гемолизаты вносились в плазму, а затем осаждалась эуглобулиновая фракция, то скорость растворения образованного сгустка под влиянием разрушенных эритроцитов возрастала. Полученные данные позволяют предположить, что в составе красных кровяных телец имеются как ингибиторы, так и активаторы фибринолиза. Последние в кислой среде осаждаются вместе с эуглобулинами.

Соединения, активирующие и тормозяшие фибринолиз, содержатся также в эритроцитах больных с различными анемиями и лейкозами, обследованными на фоне лечения (табл. 2).

Для выяснения природы обнаруженных соединений мы воспользовались методом фибриновых пластин, предложенным Astrup, Mülertz. Отмытые интактные эритроциты, гемолизат вместе со стромой, гемолизат, частично лишенный стромы (центрифугирование при 8000 об/мин. в течение 30 мин.) и строма, разведенная в физрастворе 1 : 9, наносились на гретые и негретые пластины отдельно, а также со стрептокиназой и фибринолизином. Применяемая методика позволяла судить о наличии в интактных и разрушенных эритроцитах плазминогена, плазмина, проактиватора, активатора, а также ингибиторов фибринолиза.

Таблица 2

Влияние на фибринолиз разрушенных и интактных эритроцитов людей с различными заболеваниями крови

Группы больных	Количество наблюдений	Статистические показатели	Влияние интактных эритроцитов на время лизиса эуглобулинов (мин.)		Влияние разрушенных эритроцитов на:			
					время лизиса эуглобулинов (мин.)		степень лизиса сгустка плазмы (%)	
			контроль	опыт	контроль	опыт	контроль	опыт
Гипопластическая анемия	15	M	162	246,7	162	101,2	18,2	7,5
		m±		24,2		12,3		2,7
		P		<0,001		<0,001		<0,01
Острый лейкоз	22	M	209	421,6	209	146,1	—	—
		m±		42,1		9,9		
		P		<0,001		<0,001		
Хронический миелолейкоз	10	M	186,5	511	186,5	132,5	21	12,7
		m±		80,6		7,72		5,6
		P		<0,01		<0,001		<0,2
Хронический лимфолейкоз	12	M	212	325	212	139	—	—
		m±		28,1		19,1		
		P		<0,01		<0,01		
Постгеморрагическая анемия	17	M	253	431	253	190,5	—	—
		m±		49,5		8,7		
		P		<0,01		<0,01		
Гастрогенная анемия	21	M	223	398	223	177	—	—
		m±		50,2		17,3		
		P		<0,01		<0,01		

С интактными эритроцитами здоровых людей проведено 27 наблюдений. Данные этой серии сведены в таблице 3 и свидетельствуют об отсутствии в интактных эритроцитах активатора плазминогена (отсутствие лизиса фибрина на негретых пластинах), плазмина (отсутсвие лисиза на гретых пластинах), плазминогена (отсутствие лизиса на гретых пластинах при совместном внесении эритроцитов и стрептокиназы). Как правило, интактные эритроциты не содержат проактиватора плазминогена (лизис фибрина на негретых пластинах при внесении одной стрептокиназы и стрептокиназы совместно с эритроцитами одинаков). Однако в 11 случаях из 27 эритроциты несколько тормозили лизис фибрина, вызванный добавлением стрептокиназы. Эти данные позволяют говорить о том, что интактные эритроциты в отдельных случаях содержат ингибитор активации.

Таблица 3

Фибринолитические агенты интактных эритроцитов здоровых людей

Исследуемый субстрат	Негретые пластины	Гретые пластины
Эритроциты	−	−
Стрептокиназа	++	−
Эритроциты + стрептокиназа	+; ±	−
Фибринолизин	++	++
Эритроциты + фибринолизин	++	++

В интактных эритроцитах не обнаружен антифибринолизин (одинаковые зоны лизиса на гретых и негретых пластинах при внесении одного фибринолизина и фибринолизина совместно с эритроцитами).

Несколько иные данные получены с гемолизатом эритроцитов (табл. 4.)

Таблица 4

Фибринолитические компоненты гемолизированных эритроцитов здоровых людей

Исследуемый субстрат	Негретые пластины	Гретые пластины
Эритроциты	−	−
Стрептокиназа	++	−
Гемолизат со стрептокиназой	+	−
Фибринолизин	++	++
Гемолизат с фибринолизином	++	++

Как видно из приведенной таблицы, гемолизированные эритроциты не содержат плазминогена и плазмина. В них также отсутствует активатор и проактиватор. Вместе с тем, в разрушенных эритроцитах здоровых людей выявляется ингибитор активации (лизис, вызванный стрептокиназой, больше, чем при совместном действии стрептокиназы и гемолизата).

Таблица 5

Фибринолитические компоненты в гемолизате, частично освобожденном от стромы

Исследуемый субстрат	[illegible] пластины	Гретые пластины
Гемолизат	−; ±	−
Стрептокиназа	++	−
Гемолизат со стрептокиназой	+	−
Фибринолизин	++	++
Гемолизат с фибринолизином	++	++

Ингибитор активации обнаружен и в гемолизате, частично лишенном стромы (центрифугирование в течение 30 мин. при 8000 об/мин.). Результаты этих исследований представлены в таблице 5.

В ряде опытов этой серии был выявлен слабый активатор плазминогена (слабо выраженный лизис на негретых пластинах под влиянием гемолизата).

Других соединений, активирующих и тормозящих фибринолиз, в гемолизате, очищенном от стромы, обнаружить не удалось.

Строма эритроцитов (табл. 6) обладает более выраженным антиактиваторным действием, ибо значительно угнетает лизис фибрина, вызванный стрептокиназой. Других фибринолитических и антифибринолитических агентов в строме эритроцитов обнаружить не удалось.

Таблица 6

Фибринолитические компоненты в строме эритроцитов здоровых людей

Исследуемый субстрат	Негретые пластины	Гретые пластины
Строма	—	—
Стрептокиназа	++	++
Строма со стрептокиназой	+	—
Фибринолизин	++	++
Строма с фибринолизином	++	++

Таким образом, в гемолизате эритроцитов здоровых людей содержится активатор плазминогена, а в строме — ингибитор активации. Если гемолизат добавляется к эуглобулинам плазмы, то он, как и интактные эритроциты, ингибирует фибринолиз. При добавлении гемолизата в плазму до осаждения эуглобулинов (как это было в описанных выше опытах) в осадок выпадает активатор плазминогена, что проявляется в ускоренном растворении сгустка. Аналогичными свойствами обладают эритроциты больных различными анемиями и лейкозами (табл. 2).

Следующей задачей исследования было изучение зависимости между числом эритроцитов и фибринолитической активностью крови и плазмы у исследованных нами больных. Для этого вычислялись ранговые коэффициенты корреляции [17].

У здоровых людей, когда число эритроцитов колебалось в пределах 4—5 млн. в 1 мм^3 крови, никакой корреляции с фибринолитической активностью крови и плазмы не установлено. Результаты, полученные при исследовании больных людей, представлены в таблице 7.

Как видно из приведенной таблицы, у больных острым лейкозом и хроническим миелолейкозом установлена отчетливая, а при гипопластической анемии — достаточно тесная прямая связь между количеством красных кровяных телец и фибринолитической активностью крови. Возможно,

это связано с тем, что при анемии снижается способность эритроцитов адсорбировать антиплазмин.

Подобные соотношения не выявлены между числом эритроцитов и скоростью лизиса эуглобулинов (исключение составляет группа больных острым лейкозом). Между показателями определялась, как правило, обратная зависимость.

У больных лейкозами могло заметно влиять на фибринолиз увеличение числа лейкоцитов. Вот почему при лейкозах вычислялись коэффициенты множественной корреляции с элиминацией действия на фибринолиз повышенного количества лейкоцитов. Аналогичные расчеты были проведены при изучении соответствующих показателей у больных гипопластической анемией с исключением возможного влияния на фибринолиз сниженного числа тромбоцитов.

Расчеты показали, что независимо от количества лейкоцитов в крови больных лейкозами существует связь между фибринолитической активностью

Таблица 7

Зависимость междй числом эритроцитов и фибринолитической активностью крови и плазмы у больных анемиями и лейкозами

Группы обследованных больных	Коэффициенты корреляции (б) и показатели достоверности связи (Р) между			
	числом эритроцитов и фибринолитической активностью крови		числом эритроцитов и временем лизиса эуглобулинов плазмы	
Постгеморрагическая анемия	+0,19	<0,5	−0,293	<0,3
Гастрогенная ахлоргидрическая анемия	+0,216	<0,3	+0,142	<0,6
Гипопластическая анемия	+0,375	<0,2	−0,2	<0,5
Острый лейкоз	+0,408	<0,05	−0,396	<0,05
Хронический миелолейкоз	+0,88	<0,01	−0,17	<0,7
Хронический лимфолейкоз	+0,26	<0,4	−0,23	<0,5

Таблица 8

Зависимость между фибринолитической активностью крови и содержанием в ней эритроцитов при исключении возможного влияния на фибринолиз лейкокемии или тромбоцитопении

Группы обследованных больных	Коэффициенты множественной корреляции	Показатель достоверности связи (Р)
Острый лейкоз	+0,402	<0,05
Хронический миелолейкоз	+0,871	<0,01
Гипопластическая анемия	+0,333	<0,2

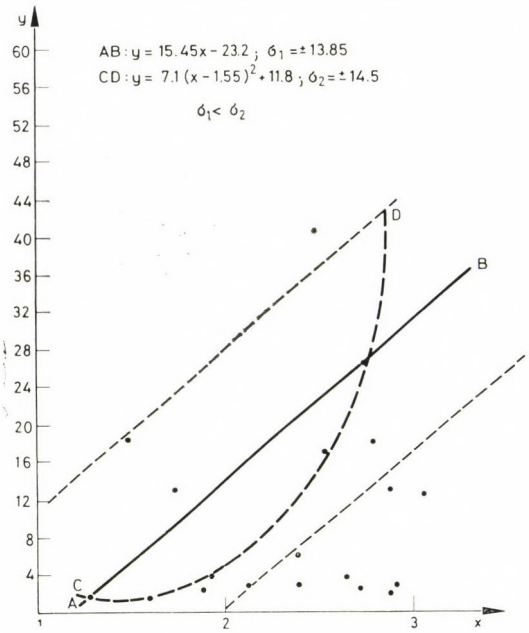


Рис.1. Зависимость между фибринолитической активностью и числом эритроцитов в крови больных острым лейкозом.

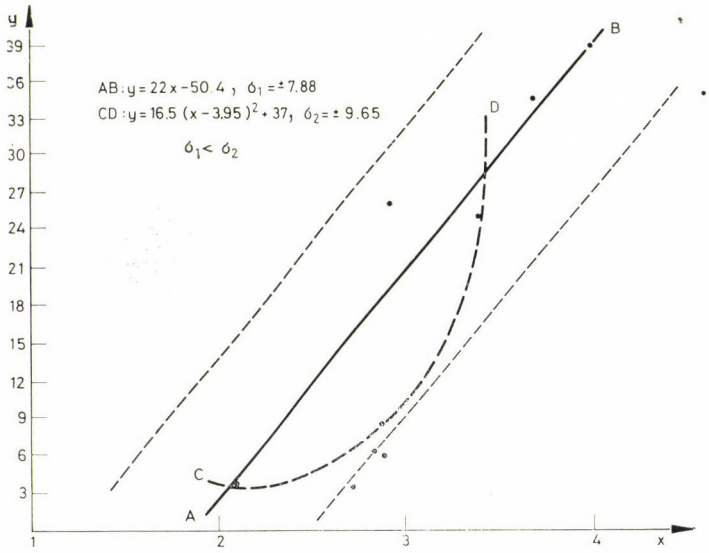


Рис. 2. Зависимость между фибринолитической активностью и числом эритроцитов в крови больных хроническим миелолейкозом.

и числом эритроцитов. Аналогичные данные установлены для больных гипопластической анемией, только по отношению к содержанию в крови тромбоцитов.

Для проверки полученных результатов мы решили проанализировать изучаемую зависимость графическим методом. При этом обнаружена прямая связь между числом эритроцитов и фибринолитической активностью крови у больных острым лейкозом (рис. 1), хроническим миелолейкозом (рис. 2), а также постгеморрагической (рис. 3) и гипопластической (рис. 4) анемиями. На представленных графиках показано, что изучаемая зависимость лучше описывается прямолинейными функциями ($\sigma_1 < \sigma_2$). Однако

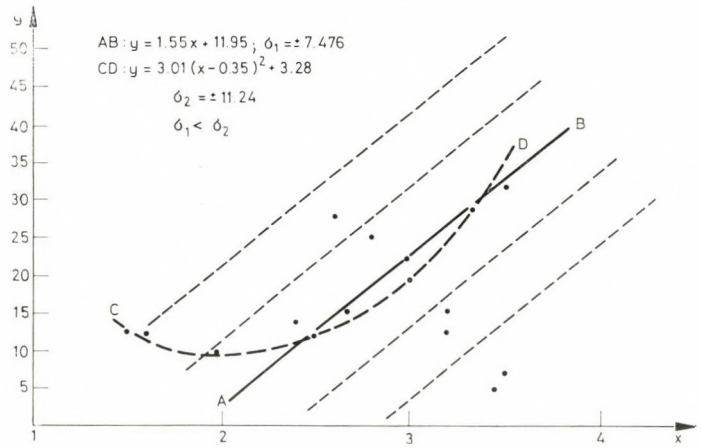


Рис. 3. Зависимость между фибринолитической активностью и числом эритроцитов в крови больных постгеморрагической анемией.

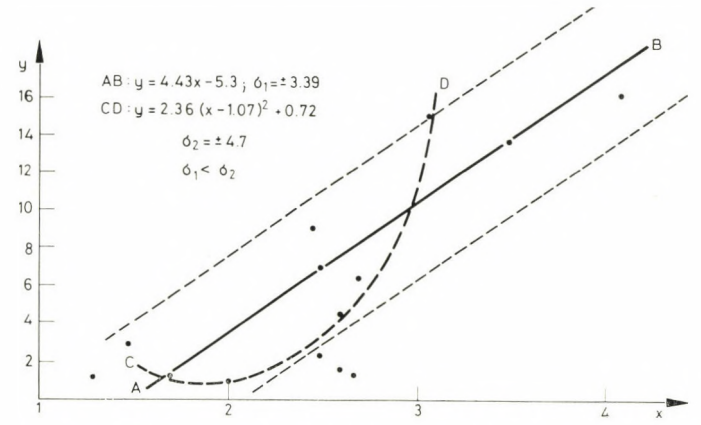


Рис. 4. Зависимость между фибринолитической активностью и числом эритроцитов в крови больных гипопластической анемией.

небольшие различия величин σ_1 и σ_2 не исключают более сложной (криволинейной) зависимости между числом эритроцитов и фибринолитичекой активностью крови больных.

Обсуждение

Приведенные данные свидетельствуют о том, что в составе эритроцитов содержатся как активаторы, так и ингибиторы фибринолиза. В жидкой части эритроцитов — гемолизате — в ряде случаев выявляется активатор плазминогена, в строме и оболочке — ингибитор активации. При разрушении эритроцитов ингибиторы и активаторы попадают в плазму и оказывают своё влияние на скорость лизиса фибринового сгустка.

Эти данные совпадают с результатами, полученными другими исследователями [1, 20, 22], выявившими ингибитор фибринолиза в составе красных кровяных телец. Наши наблюдения показывают, что это соединение относится к ингибиторам активации. Растворению сгустка может также препятствовать фибриназа, содержащаяся в эритроцитах людей и различных животных [2, 19, 23].

Вместе с тем в эритроцитах, по-видимому, находится активатор плазминогена [22], обладающий незначительной активностью [33]. Эти данные согласуются с результатами наших исследований. Однако нельзя отбросить предположение, что относительно слабое и далеко не всегда выявляемое действие активатора плазминогена в эритроцитах связано с наличием в них ингибиторов фибринолиза. Активатор плазминогена в эритроцитах напоминает урокиназу, хотя эти соединения отличаются друг от друга по своим химическим свойствам [32]. Это позволяет предполагать, что активатор плазминогена, как и ингибитор активации, являются эндогенными соединениями эритроцитов.

Литературы

1. Балуда, В. П., Цынкаловский, И. Б.: Факторы свёртывания крови, содержащиеся в эритроцитах здоровых и больных людей и животных. В кн. «Материалы XIV конференции физиологов юга». *Краснодар, 25*, (1962)
2. Балуда, В. П., Руказенкова, Ж. Н., Хнычев, С. С.: О наличии в эритроцитах фибринстабилизирующего фактора. *Бюлл. эксп. биол. и мед. 63.* 13, (1967)
3. Котовщикова, М. А., Кузник, Б. И.: Простой метод определения естественного лизиса и истинной ретракции кровяного сгустка. *Лабор. дело, 5*, 15, (1962)
4. Красик, Я. Д.: О роли эритроцитов в процессе свёртывания крови при анемиях различной этиологии. В. сб. «Материалы конференции по проблемам свёртывания крови». Баку, 1966. 151.
5. Красик, Я. Д. Изучение роли эритроцитов в процессе свёртывания крови при некоторых гематологических заболеваниях. В сб. «Лабораторная диагностика в хирургии. Пленум Всесоюзного научного общества врачей-лаборантов. 27—30 мая 1968 г. (тезисы докладов)». Ульяновск, 1968. 66.

6. Красик, Я. Д.: Роль эритроцитов в процессе свёртывания крови при постгеморрагической анемии. «Проблемы гематологии и переливания крови» *4*, 21, (1968)
7. Красик, Я. Д.: Роль эритроцитов в процессе свёртывания крови при анемиях различной этиологии. Дисс. канд. Чита, 1968.
8. Красик, Я. Д., Абдулкадыров, К. М.: Коагуляция крови и роль эритроцитов в процессе гемостаза у больных гипопластической анемией. «Проблемы гематологии и переливания крови» *2*, 35 (1971)
9. Кузник, Б. И.: Эритроцитарные факторы свёртывания крови. В кн. «Материалы конференции по проблемам физиологии и биохимии свёртывания крови и тромбообразования». Тарту, 48 (1961)
10. Кузник, Б. И.: О влиянии разрушенных эритроцитов человека на свёртываемость крови. «Физиологический журнал СССР им. Сеченова» 48, 1382 (1962)
11. Кузник, Б. И.: О роли эритроцитов в процессе свёртывания крови. «Успехи современной биологии» 56, 180, (1963)
12. Кузник, Б. И.: О роли форменных элементов крови и тканевых факторов сосудистой стенки в процессе гемостаза. Дисс. докт. Чита, 1964.
13. Кузник, Б. И., Воронянская, Л. Г.: О роли интактных и разрушенных эритроцитов в процессе свёртывания крови в условиях нормы и патологии. В сб. «Вопросы биофизики, биохимии и патологии эритроцитов» Изд. «Наука». Москва, 1967. 210.
14. Кузник, Б. И., Котовшикова, М. А.: К объективной оценке истинной ретракции кровяного сгустка. «Лабораторное дело» 10, 524 (1964)
15. Кузник, Б. И., Мишенко, В. П.: О значении интактных эритроцитов для адгезивности кровяных пластинок и фибринолиза. «Бюлл. эксп. биологии и мед.» 12, 15 (1965)
16. Кузник, Б. И., Слабожанкина, И. К.: Об участии разрушенных эритроцитов в процессе фибринолиза. «Лабораторное дело». 8, 481 (1965)
17. Лакин, Г. Ф.: Биометрия. Москва, 1968.
18. Наумов, А. Д.: Влияние разрушенных эритроцитов человека и различных животных на скорость естественного лизиса сгустка. В сб. «Вопросы экспериментальной и клинической медицины» Чита. 206 (1965)
19. Наумов, А. Д.: Эритроцитарные факторы свёртывания крови человека и различных животных. Дисс. канд. Чита, 1966.
20. Никитин, Ю. П.: Плазменные и тканевые компоненты фибринолитической системы. В кн. «Система свёртывания крови и фибринолиз» Киев, 120 (1969).
21. Astrup, T., Mülertz, S.: The fibrin late method for estimating fibrinolytic activity. *Arch. Biochem. 37*, 346 (1952).
22. Bayerle, H., Kamenhuber, K.: Über Fermenteffektoren der Fibrinolyse. 2, Mitteilung: Die Bedeutung der Erythrozyten für die Fibrinolyse. *Blut 4*, 78 (1958).
23. Buluk, K., Januszko, T., Olbromsky, J., Smrza, M., Cudnik, M.: Krwinkowy stabilisator wloknika. *Postepy Hig. Med. fósw. 17*, 743 (1963).
24. Coon, W. W., Rochon, B., Hodgson, P. E.: Fibrinolysis in surgery patients: fibrinogen — fibrinolysis relationship. *Surg. Forum 4*, 152 (1954).
25. Dastrae, M. A.: La production du fibrin-ferment. Phénomène cadavérique on phénomène d'activité normale du leucocyte vivant. *C. R. Soc. Biol. 55*, 1345 (1903).
26. Kolmen, S. N., Quest, M. M., Celander, D. R.: Evidence for the adsorbtion upon erythrocytes of urokinase and other components of the fibrinolytic system. *Arch. Biochem. 85*, 334 (1959).
27. Kowarzyk, H., Buluk, K.: Trombina, proteasa i plasmina. *Acta physiol. pol. 5*,35 (1954).
28. Künzer, W., Haberhausen, D.: Zur fibrinolytischen Aktivität von Erythrocyten des Menschen und bestimmter Tiere. *Klin. Wschr. 41*, 831 (1963).
29. Lassen, M.: Heat denaturation of plasminogen in the fibrin-plate method. *Acta physiol. scand. 27*, 371 (1953).

30. Malofieyew, M.: Znaczenie erythrozytow w systemie fibrinolitycznym. *Actn physiol· pol. 15*, 43 (1964).
31. Sacuragawa, N.: Studies on the fibrinolytic activity of red blood cells. 1. Fibrinolytic activities of bone marrow red blood cells and venous red blood cells. 2. Clinical and experimental studies. *Acta haemat. jap. 29*, 910 (1966).
32. S emar, M., Skoza, L., Johnson, A. J.: Purification properties of a plasminogen activator from human erythrocytes. *J. clin. Invest. 48*, 1771 (1969).
33. Tyminski, W., Crestochowska, E.: O czynnikach krwinkowych wplywayacych na fibrinoloza. *Postepy Hig. Med. dósw. 16*, 1119 (1962).

Effect of Erythrocytes on Fibrinolysis

The effect of destroyed and washed intact erythrocytes of normal subjects and patients with various haematological diseases was studied on the fibrinolytic activity of whole blood and plasma. Intact erythrocytes of normal and sick subjects inhibited dissolution of the clot; haemolyzed erythrocytes accelerated lysis of the euglobulin clot. Studies on fibrin films revealed in the erythrocytes of normal subjects the presence of a plasminogen activator in the fluid fraction and an inhibitor of activation in the stroma. Correlation analysis allowed to establish connections between the number of erythrocytes and the fibrinolytic activity of blood. The erythrocytes thus are affecting the process of fibrinolysis.

Correspondence: Prof. B. I. Kuznik, University Medical School, ul. Gorki, 39-a, Chita, USSR

Haematologia 9 (1–2), pp. 97–102 (1975)

Blood Volume Changes in "Hypersplenic" Rats

V. BRABEC, V. ŠEBESTÍK
Technical assistance: J. JELÍNEK, O. HLAVATÁ

Institute of Haematology and Blood Transfusion, Prague, Czechoslovakia

(Received September 30, 1973)

Blood volume in "hypersplenic" and normal rats was assessed by a simultaneous measurement of erythrocyte and plasma volumes by means of ^{59}Fe-labelled erythrocytes and ^{131}I-labelled human serum albumin, respectively. The "hypersplenic" condition was induced by prolonged intraperitoneal application of methylcellulose. Mean blood volume in normal rats was 6.3 ml/100 g body weight, the venous haematocrit being 48%. Mean blood volume in "hypersplenic" rats was 7.5 ml/100 g body weight, and the venous haematocrit lower by 22% than in normal animals. Compared with normal animals, the erythrocyte volume in "hypersplenic" rats was lower by 15% only. Plasma volume in "hypersplenic" rats exceeded the compensation in response to the reduction in erythrocyte mass. In addition to haemolysis, haemodilution due to plasma expansion seemed to be responsible for the anaemia in "hypersplenic" rats.

Introduction

Different kinds of splenic enlargement are known to be accompanied by a distinct anaemia, often with a normal or slightly lower erythrocyte volume. This discrepancy may be accounted for by haemodilution in an expanded plasma volume and/or by increased red cell pooling in the spleen [4–7, 11–13, 18, 24, 26, 29].

The present study deals with the share of hypervolaemia in the reduction of peripheral haematocrit values in hypersplenic rats. Experimental "hypersplenism" was induced by a long-term intraperitoneal application of methylcellulose and resulted in splenomegaly, anaemia and thrombocytopenia [8, 10, 15].

Material and Methods

In the experiments 31 male Wistar rats were used. One group consisting of 16 rats served as control, the other group of 15 rats was given 2 ml dosages of a 2.5% solution of methylcellulose intraperitoneally twice weekly for 16 weeks.

Erythrocyte volume was determined by dilution analysis, using ^{59}Fe-labelled red cells. These were obtained as follows: Normal rats were given 2×5 μCi of iron citrate at two days intervals. Fourteen days later their blood was col-

lected by heart puncture into ACD solution and applied intravenously to experimental animals in amounts of 0.5 ml (mean activity of ^{59}Fe being 0.3 μCi).

Plasma volume was estimated by dilution analysis using ^{131}I-labelled human serum albumin. Five minutes after the injection of ^{59}Fe-labelled erythrocytes the rats were given 0.5 ml of human serum albumin in physiological saline, with a total activity of 0.3 μCi ^{131}I. Ten minutes after the application of labelled erythrocytes, i.e. 5 min after the application of ^{131}I albumin, 0.4 ml of blood was collected from the tail vein into heparin. Blood and standard radioactivity was measured spectrometrically by means of a well-type scintillation counter Na I(Tl).

Total blood volume was obtained as the sum of erythrocyte and plasma volumes.

Venous haematocrit was measured by the microhaematocrit method, using a correlation factor 0.96 for rat blood [1, 14, 19].

Whole body haematocrit was expressed as the ratio of erythrocyte volume to total blood volume.

Results

Mean body and organ weights of the experimental animals are given in Table 1. After 16 weeks methylcellulose treatment, mean body weight was found lower by 13% in the hypersplenic rats than in the controls. Mean spleen weight was six times higher in "hypersplenic" than in normal animals, mean liver weight being higher by 11%. Mean kidney, lung, and heart weights did not differ in the two groups.

Table 1

Mean Body and Organ Weights with Standard Deviations

Group		Normal rats	"Hypersplenic" rats	Significance of differences p
No. of rats		16	15	
Body weight (g)		346 ± 36.7	302 ± 47.9	< 0.01
Organ weight (g)	Spleen	0.9 ± 0.30	5.6 ± 2.03	< 0.01
	Liver	13.1 ± 2.24	14.7 ± 1.79	< 0.05
	Kidneys	2.5 ± 0.26	2.4 ± 0.36	—
	Lungs	2.8 ± 0.43	2.8 ± 0.42	—
	Heart	1.0 ± 0.10	0.9 ± 0.08	—

Where p is not given, it was higher than 0.05.

Mean erythrocyte volume was significantly lower and plasma volume higher in the "hypersplenic" than in the normal rats. Total blood volume did not differ in the two groups (see Table 2).

Table 2

Mean Absolute Red-cell, Plasma and Total Blood Volumes, with Standard Deviations

Group	Normal rats	"Hypersplenic" rats	Significance of differences p
Red-cell volume (ml)	9.3 ± 1.33	6.9 ± 1103	< 0.01
Plasma volume (ml)	12.5 ± 1.71	15.7 ± 2.86	< 0.01
Total blood volume (ml)	21.8 ± 2.41	22.6 ± 3.39	—

Relating the volumes to 100 g of body weight (Table 3), it was discovered that erythrocyte volume in "hypersplenic" rats was by 15% lower and plasma volume by 22% higher than in the normal animals. Total blood volume in the hypersplenic animals was significantly higher than in normal rats. Compared with normal rats, in the hypersplenic rats mean venous and whole body haematocrit

Table 3

Mean Weight — Related Volumes with Standard Deviations

Group	Normal rats	"Hypersplenic" rats	Significance of differences p
Red-cell volume (ml/100 g)	2.7 ± 0.25	2.3 ± 0.45	< 0.02
Plasma volume (ml/100 g)	3.6 ± 0.46	5.2 ± 0.71	< 0.01
Total blood volume (ml/100 g)	6.3 ± 0.63	7.5 ± 1.01	< 0.01

Table 4

Mean Venous and Body Haematocrit with Standard Deviations

Group	Normal rats	"Hypersplenic" rats	Significance of differences p
Venous haematocrit, per cent	47.95 ± 3.07	37.6 ± 3.30	< 0.01
Body haematocrit, per cent	42.7 ± 4.07	30.7 ± 3.59	< 0.01

was lower by 22% and 28%, respectively (Table 4). The ratio of whole body haematocrit to venous haematocrit was 0.89 in normal and 0.82 in hypersplenic rats.

Discussion

Blood volume was assayed by the simultaneous measurement of erythrocyte and plasma volumes. This combined method seems to be more reliable than the estimation of blood volume on the basis of either of them. The lower accuracy of the latter method lies in the difference between the whole body and venous haematocrits.

Different authors found the blood volume of normal rats to range from 5 to 8 ml/100 g body weight [1, 2, 17, 19, 22, 25, 28]. The mean value of 6.3 ml/100 g body weight found by us is in the middle of that range. It is necessary to relate blood volume to unit body weight, since the weight and absolute blood volume of the animals may vary.

In the "hypersplenic" rats, an expansion of plasma volume was noted which exceeded the amount necessary for compensating the reduction in red cell mass. Mean plasma volume was higher by one-third than the volume predicted from the degree of anaemia. Total blood volume related to 100 g body weight is thus significantly higher in "hypersplenic" rats than in normal animals. This hypervolaemia must have been responsible for the discrepancy between the smaller reduction of erythrocyte volume (by 15%) and the greater reduction of venous haematocrit (by 22%) in the "hypersplenic" rats. Two components were found to have share in the pathogenesis of anaemia, 1. an increased erythrocyte sequestration in the spleen [8, 10]; 2. haemodilution arising from the increase in plasma volume. The share of the former must have exceed the share of the latter.

The cause of hypervolaemia in splenomegalic conditions is unclear. In some cases an increased production of plasma proteins is noted, leading to an increase in osmotic pressure and thus to the expansion of plasma volume [26, 30]. This mechanism was detected also in some animal experiments, where the increasing production of plasma proteins was associated with plasma expansion [3]. Other authors ascribed this condition to an expansion of the portal vascular bed [21]. According to Garnett et al. [16], an enlarged spleen acts as an arterio-venous fistula, which increases plasma volume. A combined effect of several factors is most likely involved. The problem seems to call for further investigation.

The value for venous haematocrit was significantly higher than the whole body haematocrit. The cause could be accounted for by the different ratio of red cells and plasma in organs, in small and large vessels [14, 18, 23, 27]. The ratio whole body haematocrit to venous haematocrit was lower (0.82) in "hypersplenic" rats than in normal animals (0.89); this too must have been due to blood plasma expansion.

References

1. Belcher, E. H., Harris, E. B.: Studies of plasma volume, red cell volume and total blood volume in young growing rats. *J. Physiol. (Lond.) 139*, 64 (1957).
2. Berlin, N. J., Huff, R. L., Van Dyke, D. C., Hennesy, T. C.: The blood volume of the

adult rat, as determined by ^{59}Fe and ^{32}P labelled red cells. *Proc. Soc. exp. Biol. N.Y. 71*, 176 (1949).

3. Bjørnboe, M., Jarnum, S.: The changes in serum proteins and blood volume during immunization. *J. exp. Med. 113*, 1005 (1961).
4. Blendis, L. M., Clarke, M. B., Williams, R.: Effect of splenectomy on the haemodilutional anaemia of splenomegaly. *Lancet 1*, 795 (1969).
5. Bowdler, A. J.: Theoretical consideration concerning measurement of the splenic red cell pool. *Clin. Sci. 23*, 181 (1962).
6. Bowdler, A. J.: Dilution anaemia associated with enlargement of the spleen. *Proc. Roy. Soc. Med. 60*, 44 (1967).
7. Bowdler, A. J.: Blood volume studies in patients with splenomegaly. *Transfusion 10*, 171 (1970).
8. Brabec, V., Pospíšilová, V., Šebestik, V., Jirásek, A.: Experimenteller Hypersplenismus. Hämatologische Veränderungen bei dem "makromolekulären Syndrom" der Wistar-Ratten. *Haematologia 3*, 345 (1969).
9. Brabec, V., Šebestik, V.: Sequestration von wärmealterierten Erythrozyten bei normalen und "hypersplenischen" Ratten. *Haematologia 5*, 45 (1971).
10. Brabec, V., Šebestik, V.: Survival and sites of sequestration of erythrocytes in normal and "hypersplenic" rats. *Physiol. bohemoslov. 23*, 119 (1974).
11. Christensen, B. E.: Effect of enlarged splenic erythrocyte pool in chronic lymphocytic leukaemia. Mechanism of erythrocyte sequestration in the spleen and liver. *Scand. J. Haemat. 8*, 92 (1971).
12. Donaldson, G. W. K., McArthur, M., Macpherson, A. I. S., Richmond, J.: Blood volume changes in splenomegaly. *Brit. J. Haemat. 18*, 45 (1970).
13. Eisenberg, S.: Blood volume in patients with Laennec's cirrhosis of the liver as determined by radioactive chromium-tagged red cells. *Amer. J. Med. 20*, 189 (1956).
14. Everett, N. B., Simmons, B., Lasher, E. P.: Distribution of blood (Fe^{59}) and plasma (I^{131}) volumes of rats determined by liquid nitrogen freezing. *Circulat. Res. 4*, 419 (1956).
15. Fortynová, J., Brabec, V.: Survival and localization of thrombocyte destruction in normal and hypersplenic rats. *Haematologia 5*, 273 (1971).
16. Garnett, E. S., Goddard, B. A., Markby, D., Webber, C. E.: The spleen as an arterio-venous shunt. *Lancet 1*, 386 (1969).
17. Hall, C. E., Nash, J. B.: Erythrocyte survival and blood volume in the rat as determined by labelling the red cells with ^{51}Cr. *Amer. J. Physiol. 190*, 327 (1967).
18. Huber, H., Lewis, S. M., Szur, L.: The influence of anaemia, polycythaemia and splenomegaly on the relationship between venous haematocrit and red-cell volume. *Brit. J. Haemat. 10*, 567 (1964).
19. Kee-Chang Huang, Bondurant, J.: Simultaneous estimation of plasma volume, red cell volume and thiocyanate space in unanesthetized normal and splenectomized rats. *Amer. J. Physiol. 185*, 441 (1956).
20. Lewis, A. E., Goodman, R. D., Schuck, E. A.: Organ blood volume measurements in normal rats. *J. Lab. clin. Med. 39*, 704 (1952).
21. Lieberman, F. L., Reynolds, T. B.: Plasma volume in cirrhosis of the liver: its relation to portal hypertension, ascites, and renal failure. *J. clin. Invest. 46*, 1297 (1967).
22. Loring, W. E.: A rapid simplified method for serial blood volume determinations in the rat. *Proc. Soc. exp. Biol. N.Y. 85*, 350 (1954).
23. Mejia, R. H.: Regional hematrocrit ratio and interstitial fluid volume in the normal rat. *Experientia (Basel) 24*, 43 (1968).
24. McFadzean, A. J. S., Todd, D., Tsang, K. C.: Observations on the anemia of cryptogenic splenomegaly. II. Expansion of the plasma volume. *Blood 13*, 524 (1958).
25. Montgomery, P. O'B.: A method for determining blood volume of the rat using radioactive phosphorus. *Proc. Soc. exp. Biol. (N.Y.) 77*, 445 (1951).

26. Pryor, D. S.: The mechanism of anaemia in tropical splenomegaly. *Quart. J. Med. 38*, 337 (1967).
27. Reich, J. G., Till, U., Frunder, H.: Bestimmung des Blutzell- und Blutplasmagehaltes von Leber, Niere und Milz der Ratte. *Acta biol. med. germ. 18*, 383 (1967).
28. Sharpe, L. M., Culbreth, G. G., Klein, J. R.: Blood and packed cell volume of the adult rat as measured by tagged cells. *Proc. Soc. exp. Biol. (N.Y.) 74*, 681 (1950).
29. Toghill, P. J.: Red-cell pooling in enlarged spleens. *Brit. J. Haemat. 10*, 374 (1964).
30. Weinstein, V. F.: Haemodilution anaemia associated with simple splenic hyperplasia. *Lancet 2*, 218 (1964).

Correspondence: Dr. V. Brabec, Institute of Hematology and Blood Transfusion, U nemocnice 1, Prague 2, Nové Město, Czechoslovakia

Haematologia 9 (1—2), pp. 103—110 (1975)

Auto-Hypnosis in Haemophilia*

W. L. LaBaw

Children's Hospital, Denver, Colorado, USA

(Received January 11, 1973)

A pilot study to determine the use of adjunctive trance therapy in the treatment of haemophiliacs has been carried out. Over a period of forty months, twenty randomly selected males were assigned to a control and an experimental group. All received due haematologic care. The ten patients in the experimental group utilized medical hypnosis as well, in group suggestive sessions to train and sustain them, but primarily in self-induced trance states. Results were compared at intervals on the basis of the amount of transfused blood and blood products. This provided an objective measure of the efficacy of trance therapy. Statistical analysis of the data confirmed the clinical observation of a greater improvement among patients in the experimental group.

Introduction

A psychiatric social worker and a child psychiatrist investigated the common points of view of both parents and patients in a clinical population of haemophiliacs through group encounters over several weeks [1]. Thus armed with clinical data and experience with the specific patients, who are the subjects of this report, a pilot programme was introduced to examine the usefulness of medical hypnosis in haemophiliacs [2]. The decision to embark upon a controlled study of hypnosis was based upon satisfactory initial studies. Preliminary results of the controlled study were promising [3].

There are several reports on the usefulness of encouraging children who have a haemorrhagic diathesis to reach within themselves for remedy through the utilization of their inherent suggestibility. These reports are nearly all concerned with the advantage which may be afforded to the bleeder by use of suggestion in urgent situations. Since dental surgery is such an emergency in those with a tendency to haemorrhages, there has been thoughtful consideration of the problems attending this frequently encountered crisis [4, 5]. That this interest is warranted is evident from the fact that such patients have succumbed to tooth extraction [6, 7]. In contrast, the successful employment by a haemophiliac of suggestion in

* This study was supported in part by a grant from the National Institute of Mental Health, and presented at the Medical Symposium of the 1972 Annual Meeting of the National Hemophilia Foundation in Denver, Colorado.

his recovery after gastrectomy had resulted in otherwise unassailable haemorrhage, has also been reported [8].

Most efforts to induce bleeders to enlist their suggestibility in countering untoward effects of their disorders have been expedient means of coping with emergency situations. Since these have been successful, it was conjectured that the routine use of their trance capability could be useful. Urgent matters could then be managed by them within the framework of a comfortably established way of life embellished preliminarily by the acquisition of a greater command of their suggestibility. The emergency could then be handled with more alacrity.

Coaching in his autonomous employment of trance to encourage its use by the patient whenever the need arises, independent of his suggestive therapeutist, is a paramount feature in contemporary suggestive therapy. This was anticipated in bleeders. Another useful feature sought was the return of a modicum of control of his illness directly to the patient, thereby erasing some of his helplessness and ensuing hopelessness.

The partial alleviation of anxiety and depression accompanying the usual feeling of impotence in bleeders was expected to diminish the overt manifestations of the haemorrhagic diathesis, as, along with other precipitants of haemorrhage, emotional stress has been recognized [9, 10]. Bleeding bouts have been temporally related to hospital visiting hours [4], when children are excited about communicating with parents, to name one variable. The emotionally stressed bleeder who presents a relatively benign haematological picture may conversely present a disastrous clinical image [11]. Oppositely, the calm patient with a severe problem projects a more radiant portrait than his haematological disability would predict.

While the importance of emotional factors in hereditary bleeding diseases was often dismissed until about fifteen years ago by investigators overwhelmed by their chemical elusiveness, their social, behavioural, and psychological aspects are now well-known [12–14]. This is fortunate, as clinical manifestations prescribed by seemingly immutable innate ordinance can actually be thwarted by external controls [15]. The mechanism turning emotional stress into increased haemorrhage is not known. In any case, fibrinolytic activity and blood coagulability have been found to be influenced by anxiety [16]. Spontaneous fibrinolysis associated with the specific anxieties of surgery and trauma has also been recorded [17].

Method

The patients assemble in the normally illuminated auditorium of the Psychiatric Clinic at the University of Colorado Medical Center twice each month on alternate Thursday afternoons at 5 p.m. They occupy the front row of seats and the suggestive therapeutist sits in a chair on the same level in the front aisle to their right and facing them at a right oblique angle. Interested visitors sit in rows behind the patients. Parents usually remain when they bring their children, girl-

friends and wives of older patients come frequently. Physicians, nurses, medical students and other professionals are often guests and the local chapter of the National Hemophilia Foundation is always represented. As the group is assembling small talk occurs. Professional visitors may question the suggestive therapeutist or our group participants to gain first-hand insight into feelings and experiences. The suggestive therapeutist usually relates briefly to each patient and to the group in a casual manner. He explains the programme to the uninitiated in the audience and invites inquiry prior to beginning the trance session.

The trance session is begun by asking the patients to "look intently at a point" of their choice, to attend "only to the sound" of the therapentist's voice, and to attempt to feel relaxed. A short time later eye closure is suggested; some have already closed their eyes. The wide difference in age among the group members requires repetition of remarks in more than one parlance until the rhythmicity of the procedure wholly claims their attention. So, "rest", "feel good", "fell easy", "relax", and "ultimate relaxation" may be serially suggested. While they are able to "ignore all sound but the therapist's voice", the content of what is said continues to be heard, of course. But what is said is not given listening priority: how it is said gains ascension. Extraneous sounds, as traffic noise, the ventilating system, voices in the hall, etc., are relegated to an inconsequential psychic realm from which they do not intrude. Permission to cough, move, scratch, etc., is expressly granted. There ensues a reiterative monologue, stressing rest, relaxation, comfort, and self-confidence in simple repetitive terms that drone on and on. During this period, the group embraces trance from six to ten minutes, but the time often seems longer to all concerned, as time sometimes passes slowly for one using his trance capability. Parents and spouses usually join us in the trance state. Professionals watch at first, and then indulge, also. Frequently the reflex eyelid flutter common to some in the trance state is seen. This is more common in children than in adults.

Prior to the end of the trance session, a series of pertinent comments is made by the therapist. Patients are praised for their ability to relax so well. They are reminded that they will not undergo trance with anyone except a qualified professional or by themselves. They are reassured that they will find it easy to relieve anxiety or the threat of it by relaxing through the induction of the trance state in themselves by simply recalling previous experiences, ours and theirs. They are cautioned to be ever alert for actual difficulty from their basic haemorrhagic disorder; and to have any promptly treated by their doctors [18]. They are finally told that upon "arousing" they will feel "normal, alert, but relaxed", and arousal is prompted by a slow count of three. There is a brief adjustment period of quiet as the altered state of consciousness is fully relinquished by all. Comments regarding the just finished suggestive state are offered and solicited. Visitors are invited to comment. The suggestive therapist occasionally speaks to the group about future plans. Or, an individual's sterling performance using his trance capability in some outside circumstance is recognized and applauded by the group. Toward the end of the hour, all assembled avail themselves of a second group trance.

This is the trance routine. Holidays and summer schedules have forced some variation. Some members have found a tape recording of a trance session to have a useful fortifying effect when attendance is for any reason deferred. Absent members have been included in the group endeavour by telephone on occasion.

Statistical analysis

The results were evaluated by an independent statistician [19] whose report was as follows.

Problem. The purpose of the study was to determine if there was any significant difference between a control group of male haemophiliacs who ranged in age from 6 to 33, and an experimental group of male haemophiliacs ranging in age from 5 to 48, who received trance therapy.

The statistics below represent the amount of blood used by each subject ten months prior to treatment, March 15, 1969, to January 15, 1970. Treatment was begun on January 15, 1970. Bags of blood used during treatment were tabulated for three ten-month periods – January 15, 1970, to November 15, 1970; November 15, 1970, to September 15, 1971; and September 15, 1971, to the conclusion of the study on July 15, 1972.

The null hypothesis here is that there will be no significant difference in the amount of blood used by the two groups. In other words, if the treatment is having an effect, the experimental group will have to use fewer bags of blood.

Procedure. The subjects were selected from a total of 175 haemophiliacs and

Table 1

Control						Experimental					
Bags of blood used						Bags of blood used					
Subject	Before treatment	Treatment			Total	Subject	Before treatment	Treatment			Total
	1969	1970	1971	1972			1969	1970	1971	1972	
1	89	21	175	168	364	1	0	0	0	0	0
2	16	0	6	63	69	2	60	0	0	0	0
3	56	50	56	46	152	3	24	5	69	30	104
4	12	149	133	69	351	4	0	0	0	0	0
5	41	63	30	80	173	5	50	21	12	27	60
6	0	72	27	0	99	6	210	0	0	58	58
7	54	119	251	296	666	7	134	38	50	40	128
8	12	30	72	140	242	8	13	0	0	58	58
9	100	133	217	285	635	9	89	0	75	123	198
10	292	233	420	215	868	10	20	20	115	437	567
Total	672	870	1387	1362		Total	600	84	321	768	

Note: Each bag of blood equals 90 AHF units in various products

assigned randomly to a control and an experimental group. Since variability is high within each group (note the range from 0 to 437 in the number of bags of blood used in a test period), the median test was employed to determine significance [20]. Variability is common among haemophiliacs since bleeding varies in degree.

Randomness. Blood used during surgery was neglected.

Results. First, it was studied whether the two groups were comparable prior to treatment. Using the median test and applying the chi square test with one degree of freedom, no statistically significant difference was found between the two groups; they were, therefore, comparable.

The first ten months

During this time, there was a total of 20 observations with a median of 21. Applying the same calculations, these revealed a highly significant difference showing that the chances were less than 1 in 1000 for such a difference to occur when trance therapy is having no effect.

The second ten months

The total number of observations was 20; the median was 53. Their evaluation showed a certain difference between the groups but this ($p = 0.08$) was not significant statistically.

The third ten months

In the period of September 15, 1971, to July 15, 1972, there were 20 observations with a median of 60.5. With one degree of freedom, the chi square test revealed a definite difference between the untreated control group and the experimental group. Less than 1 subject out of 100 could have reacted in this way by chance.

The total thirty months

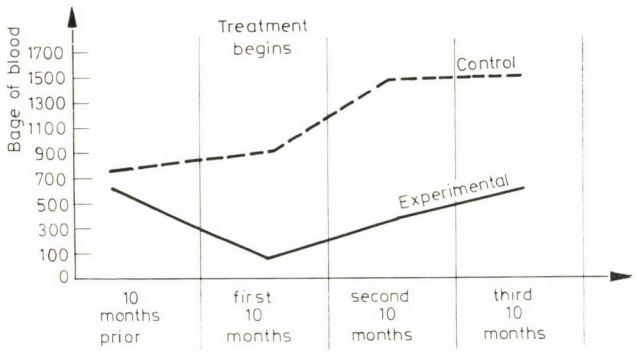
The correlated data, combining the scores of each subject, were calculated Again, the number of observations was 20 with a median of 140.

Discussion

There was then a dramatic and highly significant difference of 0.001 in 1970, a statistically not significant difference of 0.08 in 1971, a significant difference of 0.01 in 1972 and a significant 0.01 for the thirty months. A possible Hawthorne effect may have been at work here (see Table 2). This effect occurs when the subjects knowing that they are involved in an experiment, react to this novelty. After the effects of being involved in a novel situation wear off, the subjects react more normally, responding or not responding to the treatment itself. This could account for the dramatic difference in 1970 following the pretreatment where the groups showed little difference between them. But, with the novelty gone,

Table 2

The graphed experience



there is still a significant finding at 0.08 and 0.01 for the successive months and 0.01 for the correlated data.

The results would have been more significant if subject 10 would not have needed more bags of blood because he had received improper treatment prior to trance therapy. His blood needs were finally identified and he received proper treatment after many years of neglect.

Conclusion

Trance therapy had a significant effect on the subjects in the experimental group. The control group needed a statistically significantly greater number of bags of blood than the experimental group. The chances that trance therapy is having a therapeutic effect are high; statistically, the findings were significant.

Future research

The Hawthorne effect encountered in the first ten months of the study was an unexpected side effect that poses an interesting possibility for future study. The implication is that haemophiliacs may have control over their own bleeding. Trance therapy may offer them a tool with which to control the amount of bleeding.

Future research is also necessary to determine if this kind of treatment will be successful with haemophiliacs in other areas. Thus, replication of this study is highly desirable.

Comment

Use of suggestive techniques to assist chronically disabled patients such as children with haemorrhagic disorders has been based on previous work with acutely disabled children [23] and dying patients [24].

Demonstrated over the last four years has been the fact that bleeders can avail themselves of easily accomplished training in the self-induction of the

trance state for the purpose of alleviating anxiety and reducing the severity of their illnesses. The demonstration that curbing tensions in these patients is fruitful will hopefully bring forth other ataractic treatments. However, this and other techniques for permitting the patient to tap the dormant trance capability within him may remain a prominent treatment modality. For, the principle of doing something for oneself by one's own effort to modify a previously obdurate foe holds a timeless allure. The haemophiliac gains a degree of autonomy once more, for his suggestive armour is always with him. Fearful and guilty mothers, who bequeath but do not endure haemophilia themselves, have inadvertently programmed many fearful bleeders. It is a vast relief to be able to put down part of a lifelong apprehension. We have witnessed great positive changes in the mien of our haemophiliacs.

It may be noticed that a minimum of formality is coveted in these proceedings, emphasizing that suggestive techniques are natural and usual, an essential understanding for the successful suggestive therapist [25]. The therapeutist must see himself as the catalyst he is, merely assisting another to use his own innate capability. The omnipotence of the hypnotist is a myth in the present day of the suggestive therapist. To cling to a feeling of control of others is to adhere to nonsense which will doom more proposed aid than it helps, for patients will sense and resent this ignorance in the therapist.

The presence of interested persons at the trance session deserves comment. Mothers were included from the onset, as our pilot experience showed that the mothers needed at least as much relief from anxiety as their male offspring. Thus, mothers sometimes utilize trance therapy as much as their sons, to cut down the vicarious transmission of their tension to their boys. Girl-friends and spouses participate in the anxiety of their males similarly, but in a slighter degree, presumably because their concern is great but their genetic "offense" is nil.

The presence of professional observers and newsmen has positively affected the group, as they are quite prone to want to share their success.

The reason for the second trance at each session is that the first seems preliminary to some patients, who achieve a greater sense of equanimity at the second experience.

It should be noted that nothing is done to alter the presence of the genetic mandate in the haemophiliacs. We simply modify an environmental variable which limits the expression of the hereditary command with resulting lower morbidity which saves pain, time, effort and money.

References

1. Walker, H., LaBaw, W. L.: Group endeavor with hemophiliacs and their parents at the University of Colorado Medical Center. Unpublished observations, 1968.
2. LaBaw, W. L.: Regular use of suggestibility by paediatric bleeders. *Haematologia 4*, 419 (1970).,
3. LaBaw, W. L.: Trance therapy with hemophiliacs at the University of Colorado Medical Center, Denver, U.S.A.: A preliminary report. Unpublished data presented at the Seventh Congress of the World Federation of Haemophilia in Teheran, Iran 1971.

4. McIntyre, H.: Dental extractions in patients with hemophilia syndrome. *Oral Surg. 19*, 163 (1965).
5. Middleton, S. S., Davies, S. H., Cumming, R. A., Kamel, K., Cameron, A.: Experience with thirty-six dental extractions in patients with hemophilia and Christmas disease. *Oral Surg. 19*, 283 (1965).
6. Archer, W. H., Zubrow, H. J.: Fatal hemorrhage following regional anesthesia for operative dentistry in a hemophiliac. *Oral Surg. 7*, 464 (1954).
7. Parnell, A. G.: Danger to haemophiliacs of local anaesthesia. *Brit. dent. J. 116*, 183 (1964).
8. Fredericks, L. E.: The use of hypnosis in hemophilia. *Amer. J. clin. Hypn. 10*, 52 (1967).
9. Spaet, T. H.: Recent progress in the study of hemophilia. *Stanford med. Bull. 13*, 24 (1955).
10. Brown, W. J., Mally, M. A., Kane, R. P.: Psychosocial aspects of hemophilia: a study of twenty-eight hemophilic children and their families. *Amer. J. Orthopsychiat. 30*, 730 (1960).
11. Lucas, O. N.: Dental extractions in the hemophiliac, control of emotional factors by hypnosis. *Amer. J. clin. Hypn. 7*, 301 (1965).
12. Goldy, F. B., Katz, A. H.: Social adaptation in hemophilia. *Children 10*, 189 (1963).
13. Mattson, A., Gross, S.: Social and behavioral studies on hemophilic children and their families. *J. Pediat. 68*, 952 (1966)
14. Agle, D. P., Mattson, A.: Psychiatric and social care of patients with hereditary hemorrhagic disease. In: Treatment of Hemorrhagic Disorders. Ed. by O. D. Ratnoff. Harper and Row, New York 1968, pp. 111—124.
15. LaBaw, W. L.: Genetics in medicine. *Cincinn. J. Med. 35*, 114, (1954).
16. Ogston, D., McDonald, G. A., Fullerton, H. W.: The influence of anxiety in tests of blood coagulability and fibrinolytic activity. *Lancet 2*, 521 (1962).
17. Macfarlane, R. G., Biggs, R.: Observations on fibrinolysis, spontaneous activity associated with surgical operations, trauma etc. *Lancet 2*, 862 (1946).
18. Dr. William Hathaway and Dr. Roger Hamstra are primarily in charge of haemophiliacs at the UCMC. Other patients of our groups were treated by haematologists in private practice.
19. Dr. Robert N. Rothstein, a professor at Temple Buell College in Denver, performed this analysis.
20. Source for the median test (sign test for independent samples) can be found in George A. Ferguson: Statistical Analysis in Psychology and Education. McGraw-Hill, New York 1966, pp. 357—358.
21. All calculations were computed for accuracy on the Marchant Cogito 566 PR The Programable Electronic Computer.
22. Ferguson, G. A.: Op. cit. 20, p. 407.
23. LaBaw, W. L.: Adjunctive trance therapy with severely burned children, presented to the Fifth World Congress of Psychiatry in Mexico City, 1971. *Int. J. Child Psychiat. 2*, 1 (1973).
24. LaBaw, W. L.: Terminal hypnosis in lieu of terminal hospitalization. *Geront. Clin. 11*, 312 (1969).
25. LaBaw, W. L.: Assisting adults and children with remedial uses of their trance capability, a frequent imperative for health professionals. *Behav. Neuropsychiat. 1*, 24 (1969).
26. LaBaw, W. L.: Medical hypnosis with children. Presented to the annual meeting of the American Association of Psychiatric Clinics for Children in Boston, 1969.

Correspondence: Dr. W. L. LaBaw, Suite 709, 2045 Franklin St., Denver, Colorado 80205, USA

Obituary

Gordon Carl de Gruchy
1922 – 1974

Dr. G. C. de Gruchy, emeritus professor of medicine at St. Vincent's Hospital Melbourne, died on October 12th, 1974, after a long illness.

Gordon Carl de Gruchy, an Australian by birth, graduated in medicine at Melbourne University in 1944. In 1951 he was appointed a research fellow in the university department of medicine at St. Vincent's and was subsequently appointed in 1962 to the university chair of medicine. His main interest throughout his professional life was haematology and he made many notable contributions to the knowledge of hereditary and acquired haemolytic anaemias and aplastic anaemia. He founded the Haematology Society of Australia of which he was the first honorary secretary. He was president of the XI Congress of the International Society of Haematology, held in Sydney in 1966. The high level and excellent organization of the Congress did not only give evidence of his intellectual gifts but manifested the appreciation of his associates.

He was a brilliant author, and it is not mere chance that his book "Clinical Haematology in Medical Practice" is appreciated by physicians and specialists working in this field throughout the world because it gives an excellent concise presentation of the most important knowledge in clinical haematology. Because of ill health he retired from his chair in medicine to devote his time mainly to writing.

Prior to his death Professor de Gruchy had completed the text of a new monograph "Drug-induced Blood Diseases" which will soon be out of press. Working on this book gave him much pleasure till the last days of his life.

He was a member of the Editorial Board of Haematologia from the year of its foundation in 1967.

I first met Carl at the Congress of the European Society of Haematology in Lisbon. It was a pleasure to talk with him, he was a likeable person extremely cultured who radiated a rich spiritual wealth.

It was staggering when in 1970 he spoke about the malignancy of his illness. His human greatness became more distinct during the last years of his life.

Although we have been aware of his fatal illness, it was a shock to all of us to learn of his early death. It was hoped by everyone who knew him and held him in high esteem that he would remain with us for some time to come. He is a great loss to the medical world and to his many friends.

Susan R. Hollán

Frederick Stohlman, Jr.
1926 – 1974

On September 8, 1974, the world of hematology lost one of its outstanding leaders. A brutal tragedy has ended the lives of Frederick Stohlman, Jr. and his wife Bernadette Bush Stohlman. The Stohlmans were on their way to Italy from Jerusalem when their plane plunged into the Ionian Sea off the coast of Greece.

Frederick Stohlman, Jr., was born on August 19, 1926, in Washington, D.C., and graduated from Georgetown University Medical School receiving his M.D. in 1948. After three years of house staff training at Boston City Hospital and a year of fellowship in medicine at Georgetown University Hospital, he became an Instructor at his alma mater. In 1953, he moved to the National Institutes of Health as a Senior Investigator and served as Chief of the Section of Hematology of the National Institute of Arthritis and Metabolic Diseases from 1960 to 1962. In 1962, he became Director of Research and Hematology at St. Elizabeth's Hospital and Associate Professor of Medicine at Tufts University. In 1965, he was promoted to Professor of Medicine at Tufts. Between 1963 and 1966, he was also a Lecturer in Medicine at Harvard Medical School. Fred was a member of countless national and international committees, editorial boards, and advisory groups. In 1964, he received the Parke-Davis Award of the American Society of Experimental Pathology.

This recitation of the bare facts of Fred's outstanding academic career cannot possibly describe his real contributions to medicine and hematology. While at the National Institutes of Health, he initiated fundamental studies on the control of erythropoiesis, the effects of irradiation, and the kinetics of cellular proliferation, as well as working on problems of erythrocyte lifespan determinations and hemolytic disorders. With his characteristic vigor and enthusiasm, he continued these investigations after his move to Boston and directed his attention not only to erythrocytes and leukocytes, but, with Dr. Shirley Ebbe, to platelets as well. He contributed over 156 papers to the scientific literature and edited three major books. He guided the research work of an unusually gifted group of hematology fellows and young investigators who have gone on to make their own important contributions to the understanding of hematopoietic cell differentiation and kinetics.

To all of these important duties he added another in 1970, Editor-in-Chief of BLOOD, The Journal of Hematology. During his almost five years as Editor-in-Chief, Fred expanded the size of the journal and significantly improved the quality of the publication. His stewardship of BLOOD will go down as a permanent memorial to his wisdom, energy, and equanimity.

A true friend to all who knew him, Frederick Stohlman's gentle, warm, and compassionate touch can never be replaced, only remembered with fondness and respect.

ERNST R. JAFFÉ

Tadeusz Tempka
1885–1974

Professor Tempka was born on October 15th, 1885, in Cracow. In 1911 he graduated from the Faculty of Medicine, Jagello University, and received his M.D. with the highest state honours. From 1912–1914 he worked at the St. Lazarus Hospital in Cracow. In 1920 he was appointed assistant and in 1928 associate professor and director of the First Department of Internal Diseases, Jagello University. In 1939 he was appointed professor and head of the Second Department of Internal Diseases. Professor Tempka could not, however, accept the appointment because he was arrested together with other professors of Jagello University by the Gestapo and sent to the concentration camp of Oranienburg. He was released from the camp before the end of the war but he did not return to his Department, which at that time was headed by Professor L. Heilmeyer, the well-known German haematologist, until the end of the War. Working at home he wrote the first Polish textbook on clinical haematology in two volumes which was published in 1956 by the Polish Medical Publishers.

In 1945 he returned to the University and took charge of the Second Department of Internal Diseases, and remained its director until his retirement in 1962.

Professor Tempka devoted his scientific investigations almost exclusively to clinical haematology. He was the second haematologist (after the Russian clinician Arinkin) to introduce cytological examination of bone marrow punctates in haematologic diagnosis. He was the first to point out that the morphological changes in the myelogram in pernicious anaemia are not limited to the erythroblastic system but include also the leucoblastic series. He had world priority in demonstrating the presence of an anti-anaemic factor, i.e. the Castle's factor in saliva and in his studies on the haemolytic syndrome in pernicious anaemia with its disappearance during treatment with liver extracts. He was undoubtedly the first to study the morphological features of the normal spleen by biopsy and the value of histological examination of the spleen in blood diseases.

Professor Tempka's untiring energy, organizational ability and medical experience qualified him to hold leading positions in Polish scientific life. In the years 1938–1939 he was Dean of the Medical Faculty of Jagello University. During the years between the two World Wars he was President of the Cracow and Lublin Medical Societies. From 1955, he took active part in the work of the

Academy of Sciences becoming later president of the Committee of Medical Sciences of the Cracow Division of the Polish Academy of Sciences. He was President of the Scientific Council of the Institute of Haematology in Warsaw. He founded the Polish Society of Haematology, acting as its President for a considerable time, becoming later Honorary President of the Society. He was a member of numerous editorial boards. He published over 100 scientific papers.

With Professor Tadeusz Tempka, Polish science has lost one of its outstanding representatives.

H. KOWARZYK

Book Reviews

Bessis, M.: *Living Blood Cells and their Ultrastructure*
XXIII + 767 pages. 521 figures and 2 coloured plates. Translated by Robert J. Weed. Springer-Verlag, Berlin—Heidelberg—New York 1973.

Many excellent atlases on haematology and bone marrow electron microscopy have been published but this volume differs from all of them. Besides presenting excellent illustrations on the subject, blood cells are discussed from the point of integrity of structure and physiology. A desciption of their anatomy, physiology, pathology and biology is followed by a review of the newest demographical data.

The volume consists of 10 chapters. The first discusses function and structure of blood cells in general. Besides the ultrastructure and the differentiation of blood cells, maturation, embryonic haemopoiesis, cell physiology, cell-ageing and cell-death are described and demonstrated in a rich series of illustrations. The 10th chapter discusses technical problems. Chapters 2—9 discuss the cytology of the different blood cells and of the malignant haematological diseases. Each chapter is divided into two main parts: description of the normal series and description of pathological cells. Besides the usual light microphotographs, many diagrams, phase-contrast and interference micrograms, transmission- and scanning electron microphotos are presented, making the volume indispensable for both the beginner and the experienced haematologist.

The rich and well selected list of references is a substantial aid to the haematomorphologist gathering information on the subject.

The photos of excellent quality are a specially attractive force of the volume.

This splendid book should not be missing from the bookshelves of haematologists and morphologists.

Susan R. Hollán

Radioimmunoassay and saturation analysis. British Medical Bulletin, Volume *30*, Number 1, 1974. Medical Department, The British Council, 65 Davies Street, London W1Y 2AA. 103 pages, 32 figures, 7 tables. Price: £ 2.25

This number of the British Medical Bulletin is an excellent review of the saturation analysis techniques including radioimmunoassays. The compilation was planned by a committee chaired by Dr. J. D. N. Nabarro. Prof. R. P. Ekins (a pioneer in developing the technique), V. H. T. Jame J. Landon and Dr. P. H. Sönksen participated in the committee's work. Dr. Sönksen has also acted as Scientific Editor of this issue, that comprises 16 essays by various authors.

The first part containing 7 papers covers the theory and practice of saturation analysis. The basic principles are described by R. P. Ekins himself, who first applied the technique for thyroxine and thyroxine-binding globulin in 1960, the same year as Yalow and Berson had elaborated their assay for insulin and insulin-antibodies. All these techniques are based on the fact that the biological material e.g. hormone to be de-

termined is in competition with its radioactively labelled form (added in known amounts) for combining with a specific binding protein. Free and bound compounds can be separated after binding, and from the amount of bound radioactivity the amount of the non-radioactive compound to be measured can be calculated. Ways of designing assays of this type are described, and their sensitivity and reproducibility are analyzed. Technical difficulties in raising antibodies or obtaining other specific binding proteins, problems in standardization, labelling and preparation methods are reviewed by various authors. The fact that radioimmunoassays measure immunological and not biological activity is emphasized (by Woodhead, Addison and Hales). The comparatively high intra- und inter-assay variations, i.e. the relative inaccuracy of the tests are stressed: A drawback that has to be taken into consideration, when making use of the technique (the only technique in the majority of cases) which claims to measure picogram quantities of materials (e.g. complex polypeptides) in a composite mixture of proteins. Further developments, such as automation and expansion of the analytical technique into new fields are recommended (by Challand, Goldie and Landon).

The second half of the Bulletin consists of five papers on recent developments of radioimmunoassays in endocrinology (glycoproteins, posterior pituitary, thyroid, gastrointestinal tract hormones and steroids), and four further papers reporting on the use of saturation analysis outside the field of endocrinology, i.e. in oncology, haematology and virology.

The applications in haematology are summarized by P. A. Newmark and Y. B. Gordon on three pages. In addition to the first radioimmunoassay in haematology, the vitamin B_{12} determination in serum elaborated by Barakat and Ekins in 1961, a wide variety of compounds: transcobalamins, intrinsic factor, folic acid, iron, transferrin, ferritin, erythropoietin in the field of erythropoiesis, fibrinogen, fibrin(ogen) degradation products, fibrinopeptides, plasminogen, plasmin, the antihaemophilic factor and prothrombin in the field of coagulation and fibrinolysis, and the anti-D immunoglobulin in the field of isoserology, can be determined by this technique. The authors underline that in addition to their sensitivity the great advantage of radioimmunoassays consists in their specificity that eliminates the influence of other factors of the system. This may be a great advantage when e.g. a component of the coagulation system is to be measured. Some techniques described, on the other hand, are not considered to be preferable to the traditional procedures. E.g. the determination of serum iron is simpler, cheaper and more precise with colorimetry than with saturation analysis. The authors emphasize that there are many areas of haematology where the possibilities of these techniques are still unexplored.

Transfusiologists may also be interested in the progress of a virological application of saturation analysis. Hepatitis B-antigen can be tested very sensitively with the radioimmunoassay (including, however, high number of false positive results). Various methods are suggested for checking validity. One approach involves the subtyping of the antigens, in which field a radioimmunoassay is also available.

No separate chapter deals with biochemical applications. The cyclic AMP protein-binding assay, however, is treated within the scope of endocrine tissue (radioligand) receptors, and the cyclic AMP kit (Radiochemical Centre, Amersham) is well advertised in text and picture, drawing attention to broader horizons of further application of the technique.

This number of the British Medical Bulletin introducing the benefits and restrictions of the saturation analysis technique at present and in perspective is undoubtedly of great value for workers of scientific and medical research. In addition to the precise and detailed descriptions and discussion clear conclusions are drawn in the papers meeting thus every demand. Beyond its use, this number of the British Medical Bulletin is an enjoyable piece of reading.

Ilma Szász

Untersuchungen von Blut und Knochenmark (Examination of blood and bone marrow) by H. Stobbe. Verlag Volk und Gesundheit, Berlin 1974. 319 pages, 70 figures, 25 tables, 6 illustrations in colour. Price: 20.40 M

The previous edition of this practical haematology was written for technical assistants. This new edition contains many data useful also for the practising haematologist. The pathological relations are discussed systematically, earlier methods are summarized and the standardization procedures are also listed. Up-to-date techniques are described in full detail together with the evaluation of results. The methods described are practical and can easily be performed in every modern haematological laboratory. The volume consists of 14 chapters. Synoptic tables, coloured illustrations and a list of basic literature complete the methodological descriptions. The first chapter reviews fundamental knowledge and the techniques required in the haematological laboratory. The second chapter presents cytological and cytochemical methods. The next chapter contains a concise summary of bone marrow examinations. The review of counting methods is indispensable and precise. Chapter 5 presents special haematomorphological examinations. The description of haematocrit and haematoglobinometry is also up-to-date. The more complicated methods such as measuring of cell diameter or specific microscopic examinations are easy to understand. The descriptions of osmotic and other examinations of resistance are useful, the review of thrombocyte and LE cell examinations is indispensable. A short summary of statistical methods and calculations, the methods of evaluation and finally a summary of everyday laboratory practice are extremely useful.

The volume presents fundamental knowledge to those interested in the subject, on the basis of which the attainment of more specific haematological methods is greatly facilitated.

E. Benedek

Abstracts

The use of exogenous δ-aminolaevulinic acid for the studies of the regulation of haem synthesis in rabbit reticulocytes. P. Poňka, J. Neuwirt, J. Borová (Department of Pathological Physiology, Faculty of General Medicine, Charles University, Prague, Czechoslovakia). *Biochim. biophys. Acta (Amst.) 304*, 123 (1973).

δ-Amino (4-^{14}C)-laevulinate added to reticulocytes incubated *in vitro* is incorporated into haem. Exogenous δ-aminolaevulinate restores the incorporation of ^{59}Fe into haem in reticulocytes which had been treated with isonicotinic acid hydrazide (INH) or penicillamine and were hence unable to synthetize δ-aminolaevulinate. On the other hand, addition of δ-aminolaevulinate does not restore the incorporation of Fe into reticulocytes incubated with haemin. The inhibition of iron incorporation is restored by δ-aminolaevulinate in reticulocytes incubated with cycloheximide (which inhibits globin synthesis and thus elevates the free intracellular haem pool). These suggest that in intact reticulocytes haemin does not inhibit δ-aminolaevulinate synthetase. This conclusion is further supported by the finding that the pattern of incorporation of (2-^{14}C)-glycine and δ-amino (4-^{14}C)-laevulinate into haem differs in reticulocytes incubated with an inhibitor of δ-aminolaevulinate synthetase (INH) and in reticulocytes incubated with haemin and cycloheximide.

A. Egyed

Study of intracellular iron distribution in rabbit reticulocytes with normal and inhibited haem synthesis. J. Borová, P. Poňka, J. Neuwirt (Department of Pathological Physiology, Faculty of General Medicine, Charles University, Prague, Czechoslovakia). *Biochim. biophys. Acta (Amst.) 320*, 143 (1973).

Iron compartments in which iron accumulates during inhibited haem synthesis after treatment with isonicotinic acid hydrazide were studied in rabbit reticulocytes. A considerable accumulation of ^{59}Fe radioactivity was found in mitochondria, low molecular weight iron compounds and non-haemoglobin proteins, especially ferritin. In a case experiment, approximately 50% of the ^{59}Fe radioactivity accumulated in mitochondria and low molecular weight iron compounds was re-utilized for the synthesis of haemoglobin. Although some iron is incorporated into ferritin, it apparently is not utilized for haem synthesis. In control reticulocytes, only traces of ^{59}Fe activity were detected in mitochondria and only a minute amount was detected in low molecular weight iron compounds. The release of low molecular weight iron from ^{59}Fe-transferrin occurred in intact reticulocytes to a larger extent than in the stroma-free haemolysate. An attempt was made to establish the possible pathway of iron transport inside the reticulocyte. It is suggested that an iron-transferrin complex enters the reticulocyte cytoplasm, and the majority of released iron is taken up by mitochondria for haem synthesis. When protoporphyrin IX is not available, iron accumulates inside the mitochondria.

A. Egyed

The reaction of ferric salts with transferrin. G. W. Bates, M. R. Schlabach (Department of Biochemistry and Biophysics, College of Agriculture, and Texas Agricultural Experiment Station, Texas A M University, College Station, Texas, USA). *J. biol. Chem. 248*, 3228 (1973).

Fe^{3+} salts are often used for saturating apotransferrin in buffer solutions and serum in basic research and clinical procedures, despite a lack of adequate documentation. The authors investigated the reaction of Fe^{3+} salts with apotransferrin, using the absorption peak of Fe^{3+}-transferrin at 470 nm to monitor the reaction. While titration of apotransferrin with Fe^{3+}-nitrilotriacetic acid gives a linear function with a clear end point, titration with $FeCl_3$ results in a sigmoid curve and no clear end point is reached. The spectral data indicate that only 5 to 25% of the iron becomes bound when 1 Eq of $FeCl_3$ is added to apotransferrin at neutral pH. The remaining sites of the protein are vacant and available for reaction with Fe^{3+}-nitrilotriacetic acid. Several methods have been applied separating unbound $FeCl_3$ from transferrin but all have failed and often yielded misleading results. A stoichiometric reaction of Fe^{3+} salts with apotransferrin is obtained only when the reactants are mixed initially at a low pH and then carefully adjusted to neutrality. A method is also described for obtaining fully saturated, chelate-free Fe^{3+}-transferrin, using Fe^{3+}-nitrilotriacetic acid as the iron reagent. In view of the poor reactivity of Fe^{3+} salts with apotransferrin at neutral pH, proton release studies have been re-examined with Fe^{3+}-nitrilotriacetic acid. A value close to 2.6 H^+ released per Fe^{3+} bound was obtained by two methods.

A. Egyed

Exchangeability of bicarbonate specifically bound to transferrin. Ph. Aisen, A. Leibman, R. A. Pinkowitz, S. Pollack (Departments of Biophysics and Medicine, Albert Einstein College of Medicine, Bronx, N. Y., USA). *Biochemistry 12*, 3679 (1973).

The Fe(III) and anion binding functions of transferrin are interdependent, with specific binding of either dependent on the presence of the other. Under physiological conditions, bicarbonate is the anion preferentially bound by transferrin, although a variety of other anions is also capable of occupying the specific anion-binding site of the protein. In view of its probable role in the uptake of iron from transferrin by the reticulocyte, studies were undertaken of the exchangeability of transferrin-bound bicarbonate with bicarbonate free in solution. The rate of exchange depends on the anionic composition of the medium. At physiological pH and ambient p-CO_2, bicarbonate exchange is slow, with a half-time of about 20 days. The presence of millimolar concentrations of citrate or nitrilotriacetate increases the rate of exchange by two orders of magnitude. On increasing the bicarbonate concentration the exchange rate is also increased in an approximately proportional manner. The exchange of bicarbonate from monoferric transferrin prepared by isoelectric focussing is describable by a simple first-order plot. However, exchange from diferric transferrin is more complex and requires two exponential terms to fit the data satisfactorily. In every case studied, the half-time for monoferric transferrin exchange has a value intermediate between the two half-times for exchange in diferric transferrin. These results point to an interaction between the two specific anion-binding sites of the protein. They may account, in part, for the observed difference in the rates at which iron is taken up by the reticulocyte from the two iron-binding sites of transferrin.

A. Egyed

Effect of 2,4-dinitrophenol and azide on the erythrocyte membrane. I. Mirčevová (Institute of Haematology and Blood Transfusion, Prague, Czechoslovakia). *Acta biol. med. germ. 30*, 835 (1973).

In human erythrocytes the activity of Mg^{2+}-dependent ATPase was found to increase with DNP concentration, parallel with the increase in haemolysis. On reaching a maximum at 5–8 mM DNP concentration, the activity of the enzyme declines, and the haemolysis of erythrocytes also decreases. In erythrocytes, where the Mg^{2+}-dependent ATPase activity is stimu-

lated by saponin, DNP exerts only an inhibitory action. 10^{-2} M azide mildly stimulates the Mg^{2+}-dependent ATPase activated by saponin, and in the absence of saponin it has no statistically significant effect on the enzyme.

Ilma Szász

The interaction of 1-fluoro-3,4-dinitrobenzene with amino-phospholipids in membrane of intact erythrocytes, modified erythrocytes, and erythrocyte ghosts. S. E. Gordesky, G. V. Marinetti, G. B. Segel (Departments of Biochemistry and Pediatrics, University of Rochester School of Medicine and Dentistry, Rochester, N. Y., USA). *J. Membrane Biol. 14*, 229 (1973).

1-Fluoro-2,4-dinitrobenzene (FDNB) has been used to study the availability of amino-containing phospholipids in erythrocyte membranes and ghosts in an aqueous isotonic medium. Addition to the medium of bovine serum albumin (BSA) protected the cells from cation leak and some of the amino-phospholipids from reacting with the probe. In isotonic medium without BSA, 46% of the phosphatidylethanolamine and 12% of the phosphatidylserine of erythrocytes and 73% and 21% of these respective lipids of ghosts reacted with the probe. In the presence of 70 μM BSA, 31% of phosphatidylethanolamine and 6.5% of phosphatidylserine of the erythrocytes and 59% and 16% of these respective lipids of ghosts reacted with the probe. Labelling of these lipids did not change under conditions of varying tonicity, or after treatment of erythrocytes with pronase or lysolecithin. The data suggest that 46% of phosphatidylethanolamine and 12% of phosphatidylserine of the erythrocyte membrane are free in a lipid bilayer; 27% and 9% of these respective lipids are loosely bound to proteins which are lost during the preparation of ghosts and 27% of the phosphatidylethanolamine and 79% of the phosphatidylserine are tightly bound to core proteins which remain in the erythrocyte membrane even after haemolysis.

G. Gárdos

A study of the dependence of the human erythrocyte glucose transport system on membrane sulfhydryl groups. R. P. R. Smith, G. L. Ellman (Department of Biochemistry and Biophysics, University of California, San Francisco, and Langley Porter Neuropsychiatric Institute, San Francisco, Calif. USA). *J. Membrane Biol. 12*, 177 (1973).

A brief review of the data relating the glucose transport system and other membrane functions of red cells to surface sulfhydryl groups is presented. The effect of a variety of sulfhydryl reagents on glucose efflux rates from loaded red cells was studied. Neither iodoacetate nor iodoacetamide at 5 mM inhibited efflux. Several maleimide derivatives and disulfides inhibited efflux at 0.7 to 2.0 mM concentrations. Organic mercury compounds, on the other hand, were active in the 0.07 to 0.1 mM range. These data suggest that, if sulfhydryl groups are important in the glucose efflux process, they are not equally accessible for the above reagents; and that the primary effect of these reagents may be on structural elements near membrane sulfhydryl groups.

G. Gárdos

Comparative aspects of phosphate transfer across mammalian erythrocyte membranes. W. Gruber, B. Deuticke (Abteilung Physiologie, Medizinische Fakultät, Technische Hochschule Aachen, Aachen, BRD). *J. Membrane Biol. 13*, 19 (1973).

Magnitude and characteristics of phosphate transfer through the erythrocyte membranes of ten mammalian species were measured using tracer exchange techniques. Remarkable quantitative species differences could be demonstrated, with the permeabilities (at an extracellular phosphate concentration of 10 mM) increasing from 0.2×10^{-8} cm/sec (sheep) to 2.2×10^{-8} cm/sec (rabbit) in the sequence sheep < ox < cat < horse < pig < man < dog < guinea pig < rat < rabbit. In contrast, the characteristics of the phosphate transfer system, such as temperature dependence, dependence on anion composition and pH of the media and sensitivity to amphiphilic inhibitors proved to be very similar in every species studied, suggestive of a uniform transfer mechanism. The quantitative differences in permeability which

roughly parallel those reported for a number of non-electrolytes could be correlated with the phosphatidylcholine and sphingomyeline contents of the membranes. The possible molecular basis of a causal relationship between phosphate permeability and phospholipid patterns is discussed.

G. Gárdos

The inactivation by fluorodinitrobenzene of glucose transport across the human erythrocyte membrane. The effect of glucose inside or outside the cell. P. A. W. Edwards (Department of Pharmacology, University of Cambridge, Cambridge, Great Britain). *Biochim. biophys. Acta (Amst.) 307*, 415 (1973).

The inactivation of glucose transport in human red cells by fluorodinitrobenzene is accelerated by 120 mM glucose outside the cell but retarded to at least 50% by 120 mM glucose inside the cell. This suggests that the transport system is predominantly in one conformation when there is glucose inside the cell, and in another conformation when there is glucose outside the cell.

G. Gárdos

Reduced glutathione and glutathione reductase. A comparative study of erythrocytes from various species. P. G. Lankisch, R. Schroeter, L. Lege, W. Vogt (Max-Planck-Institut für Experimentelle Medizin, Abt. Biochemische Pharmakologie, Göttingen, BRD). *Comp. Biochem. Physiol. 46 B*, 639 (1973).

Reduced glutathione and glutathione reductase were measured in man, guinea pig, sheep, rat, rabbit, cattle and dromedary. Reduced glutathione was present in all species tested but at different concentrations. If the species are placed in order of increasing glutathione concentration, the sequence is: dromedary, man, cattle, sheep, rat, guinea pig, rabbit, while in order of increasing glutathione reductase activity the sequence is rat, cattle, sheep, dromedary, rabbit, man, guinea pig. Glutathione reductase was also estimated in the erythrocyte membrane of some species which could be placed in the following order of increasing activity: rat, rabbit, guinea pig, man. These species differences may be of help in further studies on the different susceptibility to haemolysis of erythrocytes from various species.

Ilma Szász

NAD(P) glycohydrolase deficiency in human erythrocytes and alteration of cytosol NADH-methemoglobin diaphorase by membrane NAD glycohydrolase activity. H. Frischer, R. Nelson, C. Noyes, P. E. Carson, J. E. Bowman, K. H. Rieckmann, F. Ajmar (Department of Medicine, Rush University, and Department of Medicine and Pathology, University of Chicago, Chicago, Ill.). *Proc. nat. Acad. Sci. (Wash.) 70*, 2406 (1973).

Erythrocytic NADH methaemoglobin diaphorase acquires NADH dichlorophenolindophenol diaphorase activity when enzyme-associated NAD is removed. This transformation is reversible and is mediated by membrane NAD glycohydrolase in haemolysates as well as in intact cells exposed to hydrogen peroxide. It is abolished either in NADH methaemoglobin diaphorase deficiency of in NAD(P) glycohydrolase deficiency which is common in Afro-American but not in European-American adults. Activities of erythrocytic NADP glycohydrolase and NAD glycohydrolase appear to depend on a single membrane enzyme.

Ilma Szász

Multiple forms of cyclic adenosine 3',5'-monophosphate phosphodiesterase from human blood platelets. I. Kinetic and electrophoretic characterization of two molecular species. A.-L. Pichard, J. Hanoune, J.-C. Kaplan (Institut de Pathologie Moléculaire, Faculté de Médecine Cochin, Paris, France). *Biochim. biophys. Acta (Amst.) 315*, 370 (1973).

The soluble cyclic adenosine 3',5'-monophosphate (cyclic AMP) phosphodiesterase of human blood platelets consists of two forms with distinct electrophoretic mobility in starch gel. The less anodic form (form I) has a high K_m ($5 \cdot 10^{-4}$ M) for cyclic AMP, is stable at 50°C and competitively inhibited by aminophylline. The more anodic form (form II) has a low K_m ($5 \cdot 10^{-5}$ M) for cyclic AMP, is thermolabile at 50°C and is less inhibited by aminophylline. Both forms are strongly inhibited by dipyridamole and 6-mercaptopurine.

Ilma Szász

Haematologia 9 (1—2), pp. 125—176 (1975)

From the International Literature of Haematology

Acta Haematologica (Basel) **49** (1973) No. 6

Oxymetholone treatment in hypoproliferative anaemia. I. Frequency of response. *Skårberg, K. O., Engstedt, L., Jameson, S., Killander, A., Lundh, B., Pers, B., Reizenstein, P., Udén, A.-M., Wadman, B.* (Department of Internal Medicine, Karolinska Hospital, 10401 Stockholm 60, Sweden), p. 321

Correlation between oestriol levels and serum iron-binding capacity in pregnancy. *Vrettos, A., Mantzos, J., Kokini, G., Gyftaki, E.* (Maternity Hospital Alexandra, Athens, Greece), p. 331

Quantitative studies of macrophages in blood cultures in chronic lymphocytic leukaemia. *Navone, R., Mazzucco, G., Stramignoni, A.* (I° Istituto di Anatomia e Istologia Patologica dell'Università, I-10126 Torino, Italia), p. 335

A new anomaly of platelet aggregation. A report of two families. *Sanderson, J. H., Dodsworth, H., Shorrock, M., Israëls, M. C. G.* (Department of Clinical Haematology, Royal Infirmary, Manchester, M13 9WL, England), p. 340

Thrombocytopathia with abnormalities in platelet release reaction. Some evidence for platelet factor 4 deficiency. *Kubisz, P.* (Hemostasis Laboratory, Departmental Hospital, Čadca, Czechoslovakia), p. 349

Acta Haematologica (Basel) **50** (1973) No. 1

The treatment of terminal metamorphosis of chronic granulocytic leukaemia with corticosteroids and vincristine. *Marmont, A. M., Damasio, E. E.* (Centro di Ematologia, Ospedali Civili, Genova—Sampierdarena, Italy), p. 1

A comparison of the three in vivo assays for haemopoietic stem cells. *Dunn, C. D. R., Constable T. B.* (Department of Haematology, Welsh National School of Medicine, Cardiff CF4 4XW, Wales, Great Britain), p. 9

Granulocyte alkaline phosphatase activity: A measure of the emergence time of mature marrow neutrophils? *Kelemen, E.* (1st Department of Medicine, Semmelweis University, Budapest VIII., Hungary), p. 19

Spontaneous platelet aggregation in myeloproliferative disorders. A preliminary study. *Barbui, T., Battista, R., Dini, E.* (Division of Haematology, Regional Civil Hospital, Vicenza, Italy), p. 25

Haemoglobin O Indonesia (α116 glutamic acid → lysine) in an Iranian family. *Rahbar, S., Berelian, F., Nowzari, G., Daneshmand, P.* (Department of Immunology, University of Tehran, Tehran, Iran), p. 30

Übergang einer Polycythaemia vera in eine akute Monozytenleukämie. *Hauswaldt, Ch., Douwes, F.-R., Ziesemer, G., Rahlf, G.* (Medizinische Universitätsklinik, D-34 Göttingen, BRD), p. 36

Ropalocytosis in a patient with acute lymphoblastic leukaemia. *Djaldetti, M., Rubinstein, I., Lewinski, U., Mandel, M.* (Hematology Clinic, Hasharon Hospital, Petah Tiqva, Israel), p. 44

The effects of irradiation on the haematopoietic tissues of anaesthetized mice. *Riches, A. C., Sharp, J. G., Littlewood, V., Thomas, D. B.* (Department of Anatomy, The Medical School Birmingham B15 2TJ, Great Britain), p. 50

Morphologie de l'érythropoïèse chez *Lacerta muralis* (Laurenti). *Taib-Cazal, E.* (Institut d'Hématologie, F-34010 Montpellier, France), p. 56

Acta Haematologica (Basel) **50** (1973) No. 2

Pyroglobulinemia. A report of eight patients with associated paraproteinemia. *Invernizzi, F., Cattaneo, R., Rosso Di San Secondo, V., Balestrieri, G., Zanussi, C.* (Institute of Medical Pathology II, University of Milan, I-20123 Milan, Italy), p. 65

Viskositätsuntersuchungen mit Fibrinogenspaltprodukten. *Leonhardt, H., Bungert, H.-J.* (Klinikum Steglitz der Freien Universität Berlin, D-1 Berlin 45, BRD), p. 75

Binding of folic acid to serum proteins. I. The effect of pregnancy. *Markkanen, T., Himanen, P., Pajula, R.-L., Ruponen, S., Castrén, O.* (Department of Medical Microbiology, University of Turku, 20520 Turku 52, Finland), p. 85

Spezifische Mikrogranula in Eosinophilen. Eine vergleichende elektronenmikroskopische Untersuchung an verschiedenen Säugern zur Charakterisierung einer besonderen Granulationsform bei eosinophilen Granulozyten. *Schaefer, H. E., Hübner, G., Fischer, R.* (Pathologisches Institut der Universität Köln, D-5 Köln 41, BRD), p. 92

Glucose-6-phosphate dehydrogenase electrophoresis in Ghanaians with AA and SS haemoglobin. *Lewis, R. A.* (University of Ghana Medical School, PO Box 4236, Accra, Ghana), p. 105

Haemoglobin C in Arabs in Kuwait. *Mulla, N., Chrobak, L.* (Haematology Department, Sabah Hospital, P. O. Box 177, Kuwait, Arabia), p. 112

Congenital thrombocytopathy (platelet factor 3 defect) with prolonged bleeding time but normal platelet adhesiveness and aggregation. *Girolami, A., Brunetti, A., Fioretti, D., Gravina, E.* (Institute of Semeiotica Medica, University of Padua Medical School, Padua, Italy), p. 116

Hereditary persistence of fetal hemoglobin and β-thalassemia in a Turkish child. *Yamak, B., Özsoylu, S., Altay, C., Hicsönmez, G., Say, B.* (Hacettepe University School of Medicine, Department of Pediatrics, Ankara, Turkey), p. 124

Acta Haematologica (Basel) **50** (1973) No. 3

Ultrastructural features of phytohemagglutinin and concanavalin A. Responsive lymphocytes in chronic lymphocytic leukemia. *Douglas, S. D., Cohnen, G., König, E., Brittinger, G.* (Department of Medicine, Mount Sinai School of Medicine, City University of New York, New York, N. Y. 10029), p. 129

Diisopropylfluorophosphate uptake by granulocytopoietic cells in chronic myeloid leukaemia and in normal individuals. *Brostrøm, J.* (The Institute of Cancer Research, Radiumstationen, DK-8000 Aarhus C, Denmark), p. 143

Serum haemopexin concentration in patients with various haemoglobinopathies. Effect of splenectomy. *Fertakis, A., Panitsas, G., Angelopoulos, B.* (Department of Pathologic Physiology, University of Athens, Athens 609, Greece), p. 149

Splenic function and infection in sickle cell anemia. *Falter, M. L., Robinson, M. G., Kim, O. S., Go, S. Ch., Taubkin, S. P.* (Department of Pediatrics, State University of New York, Downstate Medical Center, Brooklyn, N.Y. 11203), p. 154

Ribonucleic acid and phytohemagglutinin on rat leukocyte cultures within diffusion chambers. *Conesa, L. C. G., Rumi, L., Colmerauer, M. E. M., Pasqualini, C. D.* (Instituto de Investigaciones Hematológicas, Academia Nacional de Medicina, Buenos Aires, Argentina), p. 162

Study of the effect of actinomycin D on the thrombocytopoiesis of mice, using ^{75}Se-labelled methionine. *Cserháti, I., Tóth, S.* (1st Department of Medicine, University Medical School, 6701 Szeged, Hungary), p. 168

Unreifzellige Panmyelose. *Meister, H., Trux, F.* (Medizinische Abteilung des St. Vincenz-Krankenhauses, DDR-563 Heiligenstadt), p. 174

Hemoglobin H-β-thalassemia. *Özsoylu, S., Hicsönmez, G., Altay, C.* (Hacettepe University, School of Medicine, Ankara, Turkey), p. 184

Acta Haematologica (Basel) **50** (1973) No. 4

Studies on bone marrow transplantation in experimental ^{32}P-induced aplastic anemia

after conditioning with antilymphocyte serum. *Speck, B., Kissling, M.* (Medizinische Universitätsklinik, Kantonsspital, Basel, Switzerland), p. 193

Säulenchromatographische Anreicherung von DNA-Polymerase-Aktivitäten bei Leukämie. *Rainer, H., Höcker, P., Pittermann, E., Moser, K.* (I. Medizinische Universitätsklinik, A-1097 Wien, Österreich), p. 200

Le syndrome de Richter. Rapport de quatre observations et essai de démembrement. *Hoerni, B., Brunet, R., Hoerni-Simon, G.* (Fondation Bergonié, F-33076 Bordeaux Cedex France), p. 213

Untersuchungen über den Einfluss des Cyclophosphamids auf Enzyme der Megakaryozyten. *Hein, K., Kühner, U.* (Universitäts-Kinderklinik, D-8700 Würzburg, BRD), p. 217

Some aspects of leucocyte behaviour in haemodialysis. *Buscarini, L., Bassi, F.* (Ente Ospedaliero di Fiorenzuola d'Arda, Fiorenzuola, Italia), p. 223

Congenital hypoproconvertinemia (factor VII deficiency). A report of two cases belonging to two different kindreds. *Girolami, A., Scorza, P., Brunetti, A., Morgagni, C., Santini, G.* (Istituto di Semeiotica Medica, Padova, Italy), p. 228

Platelet defect in a case of Ehlers—Danlos syndrome. *Onel, D., Ulutin, S. B., Ulutin, O. N.* (Physico-Therapy and Rehabilitation Clinic, Division of Haematology, Istanbul, Turkey), p. 238

Neuartige Einschlüsse im Ergastoplasma peripherer Lymphozyten bei Virusinfekt. *Huhn, D., Asamer, H.* (Institut für Hämatologie, D-8 München 2, BRD), p. 245

Pyknocytosis in heat-stroke. *Gomperts, E. D., Kew, M. C., Katz, J.* (Department of Haematology, School of Pathology, University of the Witwatersrand, Johannesburg, South Africa), p. 249

Acta Haematologica (Basel) **50** (1973) No. 5

Mechanism of action of L-asparaginase on the cell cycle and growth in acute lymphoblastic leukemia. *Pagliardi, G. L., Gabutti, V., Gavosto, F.* (Hematology Division of the General Medical Clinic, University of Turin, Turin, Italy), p. 257

The effect of L-asparaginase on DNA and RNA synthesis by lymphoblasts of acute lymphocytic leukemia. *Leinonen, E. A.* (University of Michigan Medical School, Department of Anatomy, Medical Science II, Ann Arbor, Mich. 48104), p. 269

Lymphocyte surface markers in lymphoproliferative disorders. *Aiuti, F., Lacava, V., Fiorilli, M., Ciarla, M. V.* (Department of Clinical Medicine III, Department of Infectious Disease, University of Rome, 00161 Rome, Italy), p. 275

Binding of folic acid to serum proteins. II. The effect of diphenylhydantoin treatment and of various diseases. *Markkanen, T., Himanen, P., Pajula, R.-L., Molnár, G.* (Department of Medical Microbiology and Medicine, University of Turku, SF-20520 Turku 52, Finland), p. 284

The prevalence of Australia antigen and antibody in haemophilia. *Essien, E., Smith, J. A., Francis, T. I.* (Department of Haematology, University College Hospital, Ibadan, Nigeria), p. 293

Blood group and tissue mosaicism in a natal Indian woman. *Moores, Ph.* (Natal Blood Transfusion Service, Durban, South Africa), p. 299

Acquired factor IX deficiency. A report of two cases. *Özsoylu, S., Özer, F. L.* (Departments of Pediatrics and Medicine, University of Hacettepe School of Medicine, Ankara, Turkey), p. 305

Haemoglobin D Punjab in a Cuban family and its interaction with haemoglobin S. *Uriarte, A., Perez, A. R., Colombo, B.* (Instituto de Hematologia e Immunologia, Hospital E. Cabrera, Altahabana, La Habana, Cuba), p. 315

Acta Haematologica (Basel) **50** (1973) No. 6

The value of laparotomy and splenectomy in the staging of 56 patients with Hodgkin's disease. *Rozman, C., Triginer, J., Ribas-Mundo, M., Ferran, C., Visa, J., Gonzales, E.* (Escuela de Hematologia, Universidad de Barcelona, Barcelona 11, Spain), p. 321

Erythrodermia, mycosis fungoides, skin reticulosis-autonomous disorders of the monocytopoietic macrophage system? *Meuret, G., Lowka, K., Brand, E. T., Kalkoff, K. W.* (Medizinische Klinik C,

Kantonsspital, 9006 St. Gallen, Switzerland), p. 329

Synthese von Hämoglobin, RNS und Proteinen in der normalen Erythropoese. *Müller, D., Lauterbach, H., Pouillon, H. G., Hahn, E.* (Stadtkrankenhaus Hof, Medizinische Klinik, D-8670 Hof/Saale, BRD), p. 340

Chromosome studies in paroxysmal nocturnal haemoglobinuria. *Zaccaria, A., Ricci, P., Baccarani, M., Tura, S.* (Division of Haematology, St. Orsola's University Hospital, 40138 Bologna, Italy), p. 350

A new unstable haemoglobin: Hb Buenos Aires, β85 (F1) phe → ser. *Weinstein de, B. I., White, J. M., Wiltshire, B. G., Lehmann H.* (Request reprints from: Lehmann, H., MRC Abnormal Haemoglobin Unit, Department of Biochemistry, Addenbrooke's Hospital, Cambridge CB2 2QR, Great Britain), p. 357

Blood (New York) **41** (1973) No. 6

Normal granulocyte colony-forming cells in the bone marrow of Yemenite Jews with genetic neutropenia. *Mintz, U., Sachs, L.* (Department of Medicine D, Beilinson Hospital, Tel Aviv University Medical School, Tel Aviv, Israel), p. 745

Granulopoiesis in neutropenic disorders. *Greenberg, P. L., Schrier, S. L.* (Department of Medicine, Division of Hematology, Stanford University School of Medicine, Stanford, Calif. 94305), p. 753

Cyclic leukocytosis in chronic myelogenous leukemia: New perspectives on pathogenesis and therapy. *Gatti, R. A., Robinson, W. A., Deinard, A. S., Nesbit, M., McCullough, J. J., Ballow, M., Good, R. A.* (Department of Tumor Biology, Karolinska Institutet, Stockholm, Sweden), p. 771

The origin of bone marrow fibroblasts. *de la Chapelle, A., Vuopio, P., Borgström, G. H.* (Folkhälsan Institute of Genetics, Helsinki, Finland), p. 783

Kinetic parameters of bone marrow stem cells using in vivo suicide by triatiated thymidine or by hydroxyurea. *Vassort, F., Winterholer, M., Frindel, E., Tubiana, M.* (Institut de Recherche de Radiobiologie Clinique, Villejuif, France), p. 789

The role of granulocytes in endotoxin-induced vascular injury. *Gaynor, E.* (Hematology Division, Department of Medicine, Montefiore Hospital and Medical Center, Albert Einstein College of Medicine, Bronx, N. Y. 10461), p. 797

Properties of the platelet retention (von Willebrand) factor and its similarity to the antihemophilic factor (AHF). *Weiss, H. J., Rogers, J., Brand, H.* (Columbia University College of Physicians and Surgeons, New York, N. Y. 10019), p. 809

Isoantibody specificity in post-transfusion purpura. *Gockerman, J. P., Shulman, N. R.* (Department of Hematology, Walter Reed Army Institute of Research, Washington, D. C.), p. 817

Influence of cytochalasin B on the shape change induced in platelets by cold. *White, J. G., Krumwiede, M.* (Department of Pediatrics, University of Minnesota School of Medicine, Minneapolis, Minn. 55455), p. 823

The biconcavity of the red cell: An analysis of several hypotheses. *Bull, B. S., Brailsford, J. D.* (Loma Linda University School of Medicine, Loma Linda, Calif. 92354), p. 833

Effect of smoking on tissue oxygen supply. *Sagone, A. L., Jr., Balcerzak, S. P.* (Ohio State University College of Medicine, Columbus, Ohio 43210), p. 845

The effect of iron deficiency on the expression of hemoglobin H. *O'Brien, R. T.* (Department of Pediatrics, Yale University School of Medicine, New Haven, Conn. 06410), p. 853

Dyserythropoiesis, refractory anemia, and "preleukemia": metabolic features of the erythrocytes. *Valentine, W. N., Konrad, P. N., Paglia, D. E.* (Department of Pediatrics, University of California, Los Angeles, Calif. 90024), p. 857

Regulation of glucose-6-phosphate dehydrogenase activity in red blood cells from hemolytic and nonhemolytic variant subjects. *Yoshida, A., Lin, M.* (Department of Biochemical Genetics, City of Hope National Medical Center, Duarte, Calif. 91010), p. 877

Effects of vitamin A on the erythrocyte membrane surface. *Murphy, M. J., Jr.* (Department of Immunology, John Curtin School of Medical Research, Australian

National University, Canberra, Australia), p. 893

Storage cells of spleem and bone marrow in thalassemia: An ultrastructural study. *Beltrami, C. A., Bearzi, I., Fabris, G.* (Division of Pathological Anatomy, Arcispedale S. Anna, Ferrara, Italy), p. 901

The importance of bone marrow biopsy in the staging of patients with lymphosarcoma. *Vinciguerra, V., Silver, R. T.* (New York Hospital, New York, N. Y. 10021), p. 913

Nitroblue tetrazolium reduction: False positive and false negative results. *Ashburn, Ph., Cooper, M. E., McCall, Ch. E., DeChatelet, L. R.* (Bowman Gray School of Medicine, Winston-Salem, N. C. 27103), p. 921

Nucleotide profiles of the formed elements of human blood determined by high-pressure liquid chromatography. *Scholar, E. M., Brown, Ph. R., Parks, R. E., Jr., Calabresi, P.* (Brown University, Providence, R. I. 02912), p. 927

Blood (New York) **42** (1973) No. 1

Hereditary hemolytic anemia associated with abnormal membrane lipid. II. Ion permeability and transport abnormalities. *Shohet, S. B., Nathan, D. G., Livermore, B. M., Feig, S. A., Jaffé, E. R.* (Division of Hematology, Department of Medicine, Children's Hospital Medical Center, San Francisco, Calif. 94122), p. 1

In vivo aging of transfused erythrocytes and 2,3-diphosphoglycerate levels. *Dickerman, J. D., Ostrea, E. M., Jr., Zinkham, W. H.* (University of Vermont College of Medicine, Burlington, Vt. 05401), p. 9

The effect of periodic mixing on the preservation of 2,3-diphosphoglycerate (2,3-DPG) levels in stored blood. *Wood, L. A., Beutler, E.* (Department of Hematology, City of Hope Medical Center, Duarte, Calif. 91010), p. 17

Treatment of thrombotic thrombocytopenic purpura with antiplatelet drugs. *Amir, J., Krauss, S.* (University of Tennessee Memorial Research Center and Hospital, Knoxville, Tenn. 37920), p. 27

Metabolism of human prothrombin and fibrinogen in patients with thrombocytosis secondary to myeloproliferative states. *Martinez, J., Shapiro, S. S., Holburn, R. R.* (Cardeza Foundation, Jefferson Medical College, Philadelphia, Pa. 19107), p. 35

Thrombogenic activity of leukocytes. *Niemetz, J., Fani, K.* (Department of Medicine, Veterans Administration Hospital, Bronx, N. Y. 10468), p. 47

Ultrastructure of presumptive hematopoietic stem cells. *Rubinstein, A. S., Trobaugh, F. E., Jr.* (Loyola University Dental School, Department of Oral Pathology, Maywood, Ill. 60153), p. 61

Hematopoietic stem cell regulation. I. Acute effects of hypoxic-hypoxia on CFU kinetics. *Murphy, M. J., Jr., Lord, B. I.* (Department of Immunology, The John Curtin School of Medical Research, Australian National University, Canberra, Australia), p. 81

Hematopoietic stem cell regulation. II. Chronic effects of hypoxic-hypoxia on CFU kinetics. *Lord, B. I., Murphy, M. J., Jr.* (Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester, England), p. 89

Immunologic rebound after cessation of long-term chemotherapy in acute leukemia. II. In vitro response to phytohemagglutinin and antigens by peripheral blood and bone marrow lymphocytes. *Green, A. A., Borella, L.* (Laboratories of Virology and Immunology, St. Jude Children's Research Hospital, Memphis, Tenn. 38101), p. 99

IgA-induced anaphylactic transfusion reactions: A report of four cases. *Leikola, J., Koistinen, J., Lehtinen, M., Virolainen, M.* (Department of Immunobiology, Central Public Health Laboratory, Helsinki, Finland), p. 111

Evaluation of opsonic and leukocyte function with a spectrophotometric test in patients with infection and with phagocytic disorders. *Stossel, T. P.* (Children's Hospital Medical Center, Harvard Medical School, Boston, Mass. 02115), p. 121

Radioautographic observations on iron absorption by the duodenum of mice with iron overload, iron deficiency, and X-linked anemia. *Bédard, Y. C., Pinkerton, P. H., Simon, G. T.* (New Mount Sinai Hospital, University of Toronto, Toronto, Canada), p. 131

Studies on the uptake of synthetic conjugated folates by human marrow cells. *Hoffbrand, A. V., Tripp, E., Houlihan,*

C. M., Scott, J. M. (Department of Hematology, Royal Postgraduate Medical School, London, England), p. 141

Sickle cell safari. *Bemis, E. L.* (Medical College of Wisconsin, Milwaukee, Wis. 53233), p. 147

Blood (New York) **42** (1973) No. 2

Hodgkin's disease in childhood. *Young, R. C., DeVita, V. T., Johnson, R. E.* (National Cancer Institute, Bethesda, Md. 20014), p. 163

Leukocyte interferon production, RNA synthesis, and PHA response in patients with infectious mononucleosis. *Pidot, A. L. R., Maurer, L. H., McIntyre, O. R.* (Darthmouth-Hitchcock Medical Center, Hanover, N. H. 03755), p. 175

Pyridoxine-responsive anemia: Influence of tryptophan on pyridoxine responsiveness. *Horrigan, D. L.* (Case Western Reserve University School of Medicine, Cleveland, Ohio 44106), p. 187

Identification of cells in primate bone marrow resembling the hemopoietic stem cell in the mouse. *Dicke, K. A., Van Noord, M. J., Maat, B., Schaefer, U. W., Van Bekkum, D. W.* (Radiobiological Institute TNO, Rijswijk [ZH], The Netherlands), p. 195

Correlation between cytokinetically resting lymphocytes and bone marrow restoration: Experiments using a discontinuous albumin gradient. *Haas, R. J., Flad, H.-D., Fliedner, Th. M., Fache, I.* (Departments of Clinical Physiology and Pediatrics, University of Ulm/Donau, FRG), p. 209

Platelet production in experimental iron deficiency anemia. *Choi, S. I., Simone, J. V.* (St. Jude Children's Research Hospital, Memphis, Tenn. 38101), p. 219

Cytogenetic studies in myeloma. *Dartnall, J. A., Mundy, G. R., Baikie, A. G.* (Department of Medicine, University of Tasmania, Royal Hobart Hospital, Hobart, Tasmania, Australia 7000), p. 229

Gm allotype preference in erythrocyte IgG antibodies of patients with autoimmune hemolytic anemia. *Litwin, S. D., Balaban, S., Eyster, M. E.* (Cornell University Medical College, New York, N. Y. 10021), p. 241

Methyldopa: Physicochemical characterization of the erythrocyte autoantibody. *Wenz, B., Lalezari, P.* (Montefiore Hospital and Medical Center, Bronx, N. Y.), p. 247

Effect of phenylhydrazine-induced hemolytic anemia on nuclear RNA polymerase activity of the mouse spleen. *Spivak, J. L., Toretti, D., Dickerman, H. W.* (Department of Medicine, The Johns Hopkins University School of Medicine, Baltimore, Md. 21205), p. 257

An electron microscopic study of spleen in myelofibrosis with myeloid metaplasia. *Tavassoli, M., Weiss, L.* (Scripps Clinic and Research Foundation, La Jolla, Calif. 92937), p. 267

Measurement of serum folate levels and serum folic acid-binding protein by ^{3}H-PGA radioassay. *Waxman, S., Schreiber, C.* (Cancer Chemotherapy Laboratory, Division of Oncology, Department of Medicine, Mount Sinai School of Medicine, City University of New York, New York, N. Y. 10029), p. 281

Characteristics of folic acid-binding protein infolate-deficient serum. *Waxman, S., Schreiber, C.* (Cancer Chemotherapy Laboratory, Division of Oncology, Department of Medicine, Mount Sinai School of Medicine, City University of New York, New York, N. Y. 10029), p. 291

A comprehensive modeling procedure for the human granulopoietic system: Overall view and summary of data. *Blumenson, L. E.* (Department of Biostatistics, Roswell Park Memorial Institute, Buffalo, N. Y. 14203), p. 303

Blood (New York) **42** (1973) No. 3

Differences in inducing activity for human bone marrow colonies in normal serum and serum from patients with leukemia. *Mintz, U., Sachs, L.* (Department of Medicine D, Beilinson Hospital, Tel Aviv University Medical School, Tel Aviv, Israel), p. 331

A new human low molecular weight granulocyte colony stimulating activity. *Price, G. B., McCulloch, E. A., Till, J. E.* (Ontario Cancer Institute, Toronto, Canada), p. 341

Comparison of two methods of preventing

central nervous system leukemia. *Aur, R. J. A., Hustu, H. O., Verzosa, M. S., Wood, A., Simone, J. V.* (St. Jude Children's Research Hospital, Memphis, Tenn. 38101), p. 349

5-azacytidine: A new active agent for the treatment of acute leukemia. *Karon, M., Sieger, L., Leimbrock, S., Finklestein, J. Z., Nesbit, M. E., Swaney, J. J.* (Division of Hematology, Children's Hospital of Los Angeles, Los Angeles, Calif. 90027), p. 359

Survival in chronic lymphocytic leukemia. *Zippin, C., Cutler, S. J., Reeves, W. J., Jr., Lum, D.* (Cancer Research Institute, Department of International Health, University of California, San Francisco, Calif. 94143), p. 367

Lymphoblastic leukemia with marked eosinophilia: A report of two cases. *Spitzer, G., Garson, M. O.* (St. Vincent's Hospital, Fitzroy, Victoria, Australia), p. 377

"Foreign serum" heterophile antibodies in patients receiving antithymocyte antisera. *Pirofsky, B., Ramirez-Mateos, J. C., August, A.* (Division of Immunology and Allergy, University of Oregon Medical School, Portland, Oreg. 97201), p. 385

The influence of thymus cells in hemopoiesis: Stimulation of hemopoietic stem cells in a syngeneic, in vivo, situation. *Lord, B. I., Schofield, R.* (Paterson Laboratories, Christie Hospital, Manchester M20 9BX, England), p. 395

Immunologic response of patients with acute leukemia to platelet transfusions. *Tejada, F., Bias, W. B., Santos, G. W., Zieve, P. D.* (P. D. Zieve, Department of Medicine, Baltimore City Hospital, Baltimore, Md. 21224), p. 405

Cholinesterase as a possible marker for early cells of the megakaryocytic series. *Jackson, C. W.* (St. Jude Children's Research Hospital, Memphis, Tenn. 38101), p. 413

A hypertransfused mouse assay for thrombopoietic factors. *Cooper, G. W., Cooper, B., Ossias, A. L., Zanjani, E. D.* (City College of the City University of New York, New York, N. Y.), p. 423

Von Willebrand's syndrome presenting as an acquired bleeding disorder in association with a monoclonal gammopathy. *Mant, M. J., Gauldie, H. J., Bienenstock, J., Pineo, G. F., Luke, K. H.* (St. Joseph's Hospital, Hamilton, Ontario, Canada), p. 429

Antibodies to factor VIII. I. Variations in stability of antigen-antibody complexes in hemophilia A. *Allain, J.-P., Frommel, D.* (Medico-Pedagogical Center for Hemophiliacs, Croix-Rouge Française, Paris, France), p. 437

Autoantibodies in acquired hemolytic anemia with special reference to the LW system. *Vos, G. H., Petz, L. D., Garratty, G., Fudenberg, H. H.* (Natal Institute of Immunology, Durban, South Africa), p. 445

Hemoglobin D Iran $\alpha_2^A \beta_2^{22 \rightarrow Glu \rightarrow Gln}$ in association with thalassemia. *Rohe, R. A., Sharma, V., Ranney, H. M.* (Division of Hematology, Department of Medicine, E. J. Meyer Memorial Hospital, Buffalo, N. Y.), p. 455

Chronic hemolytic anemia due to cold agglutinins: A 20-year history of benign gammopathy with response to chlorambucil. *Evans, R. S., Baxter, E., Gilliland, B. C.* (Veterans Administration Hospital, Seattle, Wash. 98108), p. 563

Hemoglobin function in the horse: The role of 2,3-diphosphoglycerate in modifying the oxygen affinity of maternal and fetal blood. *Bunn, H. F., Kitchen, H.* (H. Kitchen, Center for Laboratory Animal Resources, Colleges of Human and Veterinary Medicine, Michigan State University, East Lansing, Mich.), p. 471

Blood (New York) **42** (1973) No. 4

Thrombotic thrombocytopenic purpura. Coagulation parameters in twelve patients. *Jaffe, E. A., Nachman, R. L., Merskey, C.* (Cornell University Medical College, New York, N. Y. 10021), p. 499

The effects of injection of human factor VIII antibody into rabbits. *Shen, S. M.-C., Feinstein, D. I., Rapaport, S. I.* (Department of Medicine, University of Southern California School of Medicine, Los Angeles, Calif. 90033), p. 509

Intravascular clotting after endotoxin in rabbits with impaired intrinsic clotting produced by a factor VIII antibody. *Shen, S. M-C., Rapaport, S. I., Feinstein, D. I.* (Department of Medicine, University of

Southern California School of Medicine, Los Angeles, Calif. 90033), p. 523

Atypical megakaryocytes in preleukemic phase of acute myeloid leukemia. *Smith, W. B., Ablin, A., Goodman, J. R., Brecher, G.* (Department of Pediatrics, University of California, San Francisco, Calif. 94122), p. 535

Pseudothrombocytopenia: Manifestation of a new type of platelet agglutinin. *Shreiner, D. P., Bell, W. R.* (Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pa. 15213), p. 541

Induction of aggregation of human blood platelets by ultraviolet light: Action spectrum and structural changes. *Doery, J. C. G., Dickson, R. C., Hirsh, J.* (Department of Pathology, McMaster University, Hamilton, Ontario, Canada), p. 551

The effect of cold on platelets. III. Adenine nucleotide metabolism after brief storage at cold temperature. *Kattlove, H. E.* (Division of Hematology, Harbor General Hospital, Torrance, Calif. 90509), p. 557

Effect of platelets stored at 22°C for 24 hours in patients with acute leukemia. *Vallejos, C. S., Freireich, E. J., Brittin, G. M., de Jongh, D. S.* (Department of Developmental Therapeutics, University of Texas at Houston, M. D. Anderson Hospital and Tumor Institute, Houston, Texas 77025), p. 565

Pancytopenia and leukemia in Hodgkin's disease: Report of three cases. *Weiden, P. L., Lerner, K. G., Gerdes, A., Heywood, J. D., Fefer, A., Thomas, E. D.* (Department of Medicine, Division of Oncology, University of Washington School of Medicine, Seattle, Wash. 98195), p. 571

Tissue immunoglobulins in nodular lymphomas as compared with reactive follicular hyperplasias. *Braylan, R. C., Rappaport, H.* (University of Chicago, Chicago, Ill. 60637), p. 579

Pokeweed mitogen response of lymphocytes in chronic lymphocytic leukemia: A fine structural study. *Cohnen, G., Douglas, S. D., König, E., Brittinger, G.* (Division of Hematology, Department of Medicine, University of Essen, Essen, FGR), p. 591

Treatment of established graft-versus-host disease in dogs by antithymocyte serum or prednisone. *Storb, R., Kolb, H. J., Graham, T. C., Kolb, H., Weiden, P. L., Thomas, E. D.* (Division of Oncology, Department of Medicine, University of Washington, Seattle, Wash. 98144), p. 601

Lymphocytosis induced in mice by supernatant fluids of *Bordetella pertussis* cultures: A histopathological study. *Athanassiades, Th. J., Morse, S. I.* (Department of Pathology, State University of New York, Downstate Medical Center, Brooklyn, N. Y. 11203), p. 611

Kinetics of lymphocytes in chronic lymphocytic leukemia: Studies using continuous ^{3}H-thymidine infusion in two patients. *Themi, H., Trepel, F., Schick, P., Kaboth, W., Begemann, H.* (Medical Division. Municipal Hospital of Munich-Schwabing, FGR), p. 623

The elevation of adenosine-triphosphate levels in human erythrocytes. *Warrendorf, E. M., Rubinstein D.* (Department of Biochemistry, McGill University, Montreal, Canada), p. 637

Blood (New York) **42** (1973) No. 5

Hematopoiesis versus osteogenesis in ectopic bone marrow transplants. *Meck, R. A., Haley, J. E., Brecher, G.* (Medical Department, Brookhaven National Laboratories, Upton, Long Island), p. 661

Defective capacity of bone marrow from nude mice to restore lethally irradiated recipients. *Zipori, D., Trainin, N.* (Department of Cell Biology, The Weizmann Institute of Science, Rehovot, Israel), p. 671

Serial in vitro marrow culture in acute myelocytic leukemia. *Bull, J. M., Duttera, M. J., Stashick, E. D., Northup, J., Henderson, E., Carbone, P. P.* (National Cancer Institute, Bethesda, Md.), p. 679

Serial in vitro bone marrow culture in acute lymphocytic leukemia. *Duttera, M. J., Bull, J. M., Northup, J. D., Henderson, E. S., Stashick, E. D., Carbone, P. P.* (Duke University, Durham, N. C.), p. 687

Interacting cell populations affecting granulopoietic colony formation by normal and leukemic human marrow cells. *Messner, H. A., Till, J. E., McCulloch, E. A.* (Institute of Medical Science, University of Toronto, Toronto, Canada), p. 701

Granulocyte-monocyte colony-forming capacity of human marrow: A clinical study.

Craddock, C. G., Hays, E. F., Forsen, N. R., Rodensky, D. (University of California, Department of Medicine, Los Angeles, Calif.), p. 711

Chloroma and other myeloblastic tumors. *Muss, H. B., Moloney, W. C.* (Peter Bent Brigham Hospital, Boston, Mass. 02115), p. 721

Tissue factor activity of normal and leukemic cells. *Garg, S. K., Niemetz, J.* (Hahnemann Medical College, Philadelphia, Pa.), p. 729

Immunologic studies of antihemophilic factor (AHF, factor VIII). V. Immunologic properties of AHF subunits produced by salt dissociation. *Rick, M. E., Hoyer, L. W.* (University of Connecticut, School of Medicine, Farmington, Conn.), p. 737

Inhibition of human platelet aggregation by plasmin digests of human factor VIII. *Donati, M. B., de Gaetano, G., Vermylen, J., Verstraete, M.* (Mario Negri Institute, Milano, Italy), p. 749

Lymphocytes forming red cell rosettes in the cold in patients with chronic cold agglutinin disease. *Feizi, T., Wernet, P., Kunkel, H. G., Douglas, S. D.* (The Rockefeller University, New York, N. Y.), p. 753

Genetic implications of the interaction of two types of beta-thalassemia genes in a patient with thalassemia major. *Russo, G., Mollica, F., Pavone, L., Musumeci, S., Baglioni, C.* (Pediatric Clinic, University of Catania, 92125 Catania, Italy), p. 763

Hemoglobin Köln in a black: Pre- and postsplenectomy red cell survival ($DF^{32}P$ and ^{51}Cr) and the pathogenesis of hemoglobin instability. *Pedersen, P. R., McCurdy, P. R., Wrightstone, R. N., Wilson, J. B., Smith, L. L., Huisman, T. H. J.* (William Beaumont General Hospital, El Paso, Texas), p. 771

The interaction of hemoglobin E with β thalassemia: A study of hemoglobin synthesis in a family of mixed Burmese and Iranian origin. *Feldman, R., Rieder, R. F.* (New York Medical College, Metropolitan Hospital Center, New York, N. Y.), p. 783

Two cases of familial erythrocytosis with increased erythropoietin activity in plasma and urine. *Yonemitsu, H., Yamaguchi, K., Shigeta, H., Okuda, K., Takaku, F.* (First Department of Medicine, Chiba University of Medicine, Chiba, Japan 280), p. 793

A "Philadelphia-like" chromosome derived from the Y in a patient with refractory dysplastic anemia. *Warburton, D., Bluming, A.* (Department of Human Genetics and Development, College of Physicians and Surgeons, Columbia University, New York, N. Y.), p. 799

Thrombotic thrombocytopenic purpura: Report of a case with disseminated intravascular platelet aggregation. *Neame, P. B., Lechago, J., Ling, E. T., Koval, A.* (McMaster University, Department of Laboratory Medicine, Hamilton General Hospital, Hamilton, Ontario, Canada), p. 805

Blood (New York) **42** (1973) No. 6

Globin messenger RNA in hemoglobin H disease. *Benz, E. J., Swerdlow, P. S., Forget, B. G.* (Peter Bent Brigham Hospital, Boston, Mass. 02115), p. 825

The role of red cell energy metabolism in the generation of irreversibly sickled cells in vitro. *Jensen, M., Shohet, S. B., Nathan, D. G.* (Children's Hospital Medical Center, Boston, Mass.), p. 835

Unbalanced globin chain synthesis in congenital dyserythropoietic anemia. *Hruby, M. A., Mason, R. G., Honig, G. R.* (Abraham Lincoln School of Medicine, University of Illinois Medical Center, Chicago, Ill. 60612), p. 843

Sensitivity of human and murine hemopoietic precursor cells to chemotherapeutic agents assessed in cell culture. *Ogawa, M., Bergsagel, D. E., McCulloch, E. A.* (Department of Medicine, The Ontario Cancer Institute, University of Toronto, Toronto, Canada), p. 851

Abnormalities of megakaryocytes in W/W^V mice. *Ebbe, Sh., Phalen, E., Stohlman, F., Jr.* (St. Elizabeth's Hospital, Boston, Mass. 02135), p. 857

Abnormalities of megakaryocytes in SI/SI^d mice. *Ebbe, Sh., Phalen, E., Stohlman, F., Jr.* (St. Elizabeth's Hospital, Boston, Mass. 02135), p. 865

Cyclic hematopoiesis in grey collie dogs: A stem-cell problem. *Patt, H. M., Lund, J. E., Maloney, M. A.* (Laboratory of

Radiobiology, University of California, San Francisco, Calif. 94143), p. 873

Change in marrow and spleen CFU compartments following leukemia virus infection: Comparison of Friend and Rauscher virus. *OKunewick, J. P., Phillips, E. L.* (Cellular and Radiation Biology, Allegheny General Hospital, Pittsburgh, Pa. 15212), p. 885

Effects of cobalt on the renal erythropoietic factor and kidney hydrolase activity in the rat. *Smith, R. J., Fisher, J. W.* (Tulane University School of Medicine, New Orleans, La. 70112), p. 893

Erythropoiesis in carotid body resected cats. *Gillis, D. B., Mitchell, R. A.* (Department of Physiology, University of California, San Francisco, Calif.), p. 907

Isolation and properties of human platelet mitochondria. *Fukami, M. H., Salganicoff, L.* (Specialized Center of Thrombosis Research, School of Medicine, Temple University, Philadelphia, Pa. 19140), p. 913

Failure of combined factor VIII and cyclophosphamide to suppress antibody to factor VIII in hemophilia. *Hruby, M. A., Schulman, I.* (Department of Pediatrics, Abraham Lincoln School of Medicine, University of Illinois, Chicago, Ill. 60612), p. 919

Biological effects of repeated leukopheresis of patients with chronic myelogenous leukemia. *Vallejos, C. S., McCredie, K. B., Brittin, G. M., Freireich, E. J.* (Department of Developmental Therapeutics, University of Texas at Houston, M. D. Anderson Hospital and Tumor Institute, Houston, Tex. 77025), p. 925

Factors that influence the appearance of central nervous system leukemia. *Pavlovsky, S., Eppinger-Helft, M., Muriel, F. S.* (Instituto de Investigaciones Hematologicas, Melo 3081, Buenos Aires, Argentina), p. 935

Enhanced binding of neuraminidase-treated sheep erythrocytes to human T lymphocytes. *Weiner, M. S., Bianco, C., Nussenzweig, V.* (Department of Pathology, New York University School of Medicine, New York, N. Y. 10016), p. 939

The Ausria test: Critical evaluation of sensitivity and specificity. *Alter, H. J., Holland, P. V., Purcell, R. H., Gerin, J. L.* (Immunology Section, Blood Bank Department, Clinical Center, NIH, Bethesda, Md. 20014), p. 947

Iron in the duodenal mucosa of normal, iron-loaded, and iron-deficient rats. *Mattii, R., Mielke, C. H., Levine, P. H., Crosby, W. H.* (Hematology Laboratory [Tufts], Boston City Hospital, Blood Bank Research Laboratory, Tufts-New England Medical Center, Boston, Mass. 02111), p. 959

Blut (Munich) **27** (1973) No. 3

Der Transfer-Faktor und seine therapeutische Bedeutung. *Zitzig, W. H.* (Kinderspital, CH-8032 Zürich, Schweiz), p. 145

Factor X Friuli coagulation disorder. *Girolami, A., Carli, A., Falomo, R., de Marco, L.* (Medical School, Institute of Semeiotica Medica, University of Padova, Italy), p. 151

Morphologische phasenkontrast-kinematographische Studien zum Verhalten von Knochenmarkzellen in vitro. VII. Reifung von Myeloblasten zu Promyelozyten und Myelozyten bei myeloischen Leukämien. *Boll, I.* (Städtisches Krankenhaus Neukölln, D-1 Berlin 47, BRD), p. 159

The effect of cyclophosphamide, ^{32}P and ^{60}Co irradiation on rabbit bone marrow cells. *Kissling, M., Speck, B.* (Department of Haematology, Kantonsspital Basel, CH-4004 Basel, Switzerland), p. 167

Zur Natur und ontogenetischen Entwicklung von Carboanhydrase-Isoenzymen in menschlichen Erythrozyten. *Wehinger, H.* (Universitäts-Kinderklinik, D-78 Freiburg i. Brsg., BRD), p. 172

Eine Schnellmethode zur photometrischen Bestimmung des Gesamtbilirubins und des direkten Bilirubins im menschlichen Serum. *Schmidt, M., Stich, W.* (Institut für Hämatologie, 8 München 2, BRD), p. 186

Erythrozytenaggregation bei Nichtrauchern, Rauchern und Herzinfarktpatienten. *Boss, N., Chmiel, H., Kachel, V., Ruhenstroth-Bauer, G.* (Max-Planck-Institut für Biochemie, D-8033 Martinsried bei München, BRD), p. 191

Blut (Munich) **27** (1973) No. 4

Chalone. Endogene Inhibitoren der Zellteilung? *Paukovits, W. R.* (Institut für Krebs-

forschung der Universität, A-1090 Wien, Österreich), p. 219

Kinetics of lymphocytes in Hodgkin's disease. *Schick, P., Trepel, F., Theml, H., Benedek, Sz., Trumpp, P., Kaboth, W., Begemann, H., Fliedner, Th. M.* (I. Medizinische Abteilung, Städtische Krankenhaus, München-Schwabing, 8 München 40, BRD), p. 223

Congenital factor VII deficiency. A case report. *Girolami, A., Cattarozzi, G., Mengarda, G., Lazzarin, M.* (Medical School, Institute of Semeiotica Medica, University of Padova, Padova, Italy), p. 236

Cytochemistry and ultrastructure of pathologic granulation in myelogenous leukemia. *Schmalzl, F., Huhn, D., Asamer, H., Rindler, R., Braunsteiner, H.* (University of Innsbruck, Department of Medicine, A-6020 Innsbruck, Austria), p. 243

Serumeisen-Normalwerte und statistische Verteilung der Einzelwerte bei Mann und Frau. *Weippl, G., Pantlitschko, M., Bauer, P., Lund, S.* (Universitätskinderklinik, A-1090 Wien, Österreich), p. 261

Eine elektronische Methode zur Verbesserung der Volumenauflösung des Coulter-Partikelvolumenmessverfahrens. *Kachel, V.* (Max-Planck Institut für Biochemie, 8033 Martinsried bei München, BRD), p. 270

Ferritin: Struktur, Funktion und medizinische Aspekte. *Wetz, K., Crichton, R. R.* (Max-Planck-Institut für Molekulare Genetik, 1 Berlin-Dahlem, BRD), p. 275

Blut (München) **27** (1973) No. 5

Bone marrow transplantation. Clinical results and problems. *Speck, B.* (Section of Hematology, Kantonsspital Basel, 4000 Basel, Switzerland), p. 297

Zur Typenverteilung, Alters- und Geschlechtsdisposition der akuten Leukämien des Erwachsenen. *Abbrederis, K., Schmalz, F., Braunsteiner, H.* (Medizinische Universitäts-Klinik, A-6020 Innsbruck, Österreich), p. 302

Ultrastructural studies in a particular case of congenital dyserythropoietic anemia (CDA). *Morgenstern, E., Schatanek, W., Meiser, J. R., Hufnagl, D.* (Medizinische Biologie, Universität des Saarlandes, D-665 Homburg/Saar, BRD), p. 307

Blutgruppen bei Bantu-Populationen aus Angola, zugleich ein Beitrag zur Berechnung der Vaterschaftswahrscheinlichkeit bei Gutachten mit Negern als Eventualvätern. *Spielmann, W., Teixidor, D., Matznetter, T.* (Institut für Immunhämatologie und Transfusionskunde der Universität, 6 Frankfurt/Main-Niederrad, BRD), p. 322

Identity for the strong MLC-locus in HL-A different unrelated pairs. *Mempel, W., Grosse-Wilde, H., Albert, E. D.* (Institut für Hämatologie der GSF, 8 München 2, BRD), p. 336

Entwicklung eines Erythropoese-Regelkreismodells zur Computer-Simulation. *Düchting, W.* (Lehrstuhl für Elektrotechnik der Gesamthochschule Siegen, D-59 Siegen, BRD), p. 342

Ein Beitrag zur Plasmazell-Leukämie. *Leibetseder, F., Samitz, H., Sorgo, G.* (II. Medizinische Abteilung der Landeskrankenanstalten Salzburg, A-5020 Salzburg, Österreich), p. 351

Blut (München) **27** (1973) No. 6

MLC-Eigenschaften, ein eigenes Histokompatibilitätssystem. *Mempel, W., Grosse-Wilde, H.* (Institut für Hämatologie, Abteilung Immunologie, 8 München 2, BRD), p. 269

Normalwerte und Verteilung von Transferrin beim Erwachsenen. *Weippl, G., Pantlitschko, M., Priebe, H.* (Universitäts, Kinderklinik, A-1090 Wien, Österreich), p. 376

Über die Beziehungen zwischen basophilen und hellen, azurgranulierten Blutzellen der lymphatischen Reaktion, auf Grund von Leukozytenkulturversuchen beim Pfeifferschen Drüsenfieber. *Drescher, J., Diedenhofen, H.* (Universitäts-Kinderklinik, 23 Kiel, BRD), p. 384

Ultrastructural studies on the acute leukemic lymphoblast. *Schumacher, H. R., Székely, I. E., Park, S. A., Fisher, D. R.* (Harrisburg Hospital, Harrisburg, Penn. 17101), p. 396

Granulozytenmobilisation durch Endotoxin bei Mäusen nach Infektion mit Rauscher-Virus. *Seidel, H. J., Müller-Stöcker, E.* (Zentrum für Klinische Grundlagenforschung der Universität Ulm, 79 Ulm/Donau, BRD), p. 407

pH Wert, Ammoniakgehalt, Eiweißzusammensetzung und Osmolalität Faktor-VIII-haltiger Substitutionspräparate. *Göbel, U., Jasper, F.-J.* (Universitäts-Kinderklinik, 4000 Düsseldorf, BRD), p. 416

Blutgruppen und Lepra bei angolanischen Völkerschaften. *Spielmann, W., Teixidor, D., Matznetter, Th.* (Institut für Immunhämatologie und Transfusionskunde der Universität, 6 Frankfurt/Main-Niederrad, BRD), p. 426

Blut (München) **28** (1974) No. 1

Impulszytophotometrie in der Hämatologie. *Büchner, Th.* (Medizinische Klinik und Poliklinik, Universität Münster, D-44 Münster/Westf., BRD), p. 1

Morphologische phasenkontrast-kinematographische Studien zum Verhalten von Knochenmark und Blutzellen in vitro. VIII. Das Monozyten-System beim Menschen. *Boll, I.* (Städtische Krankenhaus Neukölln, D-1 Berlin 47, BRD), p. 8

Thrombozytäre Funktionsanalyse bei Hyperlipoproteinämien. *Zöller, H., Schramm, A., Gross, W.* (Medizinische Poliklinik der Universität Würzburg, D-87 Würzburg, BRD), p. 24

Congenital combined factor V and factor, VIII deficiency in a male born from a, brother-sister incest. *Girolami, A., Brunetti, A., de Marco, L.* (Istituto di Semeiotica Medica dell'Università, Padova, Italy), p. 33

Entstehungsmechanismus von L-Asparaginase-Nebenwirkung und deren Bekämpfung. *Kodama, J., Higashino, K., Kobayashi, S. Izumi, K., Satani, M., Takamitsu, Y. Yoshioka, K., Bando, K., Kawai, K., Wada, H.* (2-1 Hoenzakacho, Higashiku 540, Osaka, Japan), p. 43

Unterdrückung der primären und sekundären Immunantwort durch Antilymphozytenserum (ALS), gemessen an der antigenspezifischen Proliferationsaktivität im graft-versus-host-Modell. *Baumann, P., Thierfelder, S.* (Abteilung Immunologie, Institut für Hämatologie, D-8000 München, BRD), p. 51

Studies on hypo-and hypercoagulability I. Evidence for the occurrence of "incomplete" consumption coagulopathy. *Kunz, F., Hörtnagl, H., Kroesen, G., Rumpl, E., Holzknecht, F.* (Medizinische Universitäts-Klinik für Neurologie, A-6020 Innsbruck, Austria), p. 56

Blut (München) **28** (1974) No. 2

Immunologische Untersuchungen über Faktor XIII und das FSF-bindende Globulin. *Bohn, H.* (Behringwerke AG, Marburg/Lahn, BRD), p. 81

Hemmung der Blutgerinnung in vitro durch Protease von *Pseudomonas aeruginosa. Scharmann, W., Kraft, W.* (Institut für Bakteriologie und Immunologie, 63 Giessen, BRD), p. 90

Multi-channel preparation of fresh blood. An economic therapy with blood components. *Schneider, W., Glassner, K., Fröhlich, Ch., McCarty, L. J.* (German Red Cross Blood Transfusion Service Hagen Institute, D-58 Hagen, FGR), p 100

Morphologie der Megakaryozyten bei Blutkrankheiten. *Albrecht, M., Fülle, H.-H.* (II. Innere Abteilung des Städtischen Krankenhauses Moabit, Berlin 21, FGR), p. 109

Methodik und klinische Wertigkeit der Fibrinogenbestimmung mit der quantitativen Immunelektrophorese nach Laurell. *Barthels, M., Kiessler, G.* (Abteilung für Hämatologie des Departments Innere Medizin, Medizinische Hochschule Hannover, Hannover, BRD), p. 122

Lymphozytenmembranen im Gefrierätzbild. *Ruzicka, F., Huhn, D., Steidle, Ch.* (Ludwig-Boltzmann Institut für Leukämieforschung. A-1140 Wien, Österreich), p. 131

Das beginnende Plasmozytom. *Brücher, H.* (Klinikum Steglitz der Freien Universität Berlin, BRD), p. 136

Blut (München) **28** (1974) No. 3

Therapiebedingte Veränderungen zytochemischer Befunde akuter Leukämien. *Litwin, J., Stacher, A.* (I. Medizinische Abteilung, Hanusch-Krankenhaus, A-1140 Wien, Österreich), p. 161

Der Retikulozyt als zelluläres Modell eines adrenergischen β-Rezeptor-Effektor-Systems. *Quiring, K., Kaiser, G., Gauger, D.* (Zentrum der Pharmakologie, Klinikum

der Universität, D-6000 Frankfurt 70, BRD), p. 166

Gefäßveränderungen im Knochenmark bei granulozytären Myelosen. *Demmler, K., Burkhardt, R.* (Abteilung für Knochenmarksdiagnostik, D-8 München, BRD), p. 178

Untersuchungen über die DNA-synthese peripherer Lymphozyten bei progredient chronischer Polyarthritis. *Klein, G., Altmann, H., Wottawa, A., Tuschl, H., Eberl, R.* (Universitätsklinik für Innere Medizin Graz, A-8036 Graz, Österreich), p. 187

Zur Präparation von Blut- und Knochenmarkzellen für die Impulszytophotometrie. *Büchner, Th., Hiddemann, W., Schneider, R., Kamanabroo, D.* (Medizinischen Klinik und Poliklinik, Westfälischen Wilhelms-Universität Münster, 44 Münster/Westf., BRD), p. 191

Zur gelchromatographischen Trennung von kompletter (IgM-) und inkompletter (IgG-) Antikörperaktivität blutgruppenspezifischer Antiseren. *Mühlfeld, J., Sachs, V.* (Blutspendezentrale am Hygiene-Institut der Universität, D-23 Kiel, BRD), p. 196

Cyclic neutropenia. *Haghshenas, M., Banihashemi, A., Mohallatee, E. A.* (Department of Medicine, Reza Pahlavi Medical Center, Teheran-Tajrisch, Iran), p. 199

Hämatologen-Kongreß Wien, 21.—23. März 1974, p. 203

Blut (München) **28** (1974) No. 4

Entwicklung von Di Guglielmo-Syndromen aus chronischen myeloischen Leukämien. *Aust, Ch., Boll, I.* (Städtische Krankenhaus Neukölln, 1 Berlin 47, BRD), p. 245

Biochemische Unterschiede der DNA-Polymerasen leukämischer Zellen. *Rainer, H., Höcker, P., Deutsch, E., Stacher, A., Moser, K.* (I. Medizinische Universitätsklinik, A-1097 Wien, Austria), p. 256

Etude du taux du facteur VIII dans les vaisseaux profonds de l'organisme. *Mayer, G., Kalogjera, V., Witz, J.-P., Tongio, J., Waitz, R.* (Centre de Transfusion Sanguine, Université de Strasbourg, Strasbourg, France), p. 264

Cryoprotective effects of polyvinylpyrrolidone and dextran in the preservation of murine bone marrow cells. *Dobry, E., Livora, J.* (Institute of Hematology and Blood Transfusion, Prague, Czechoslovakia), p. 282

Leukämie L 5222 des Rattenstammes BD IX. Eine durch Äthylnitrosoharnstoff induzierte monozytärmyeloische, transplantierbare Form für zytochemische und chemotherapeutische Studien. *Ivankovic, S., Zeller, W. J.* (Institut für Toxikologie und Chemotherapie am Deutschen Krebsforschungszentrum, Heidelberg, BRD), p. 288

Chronic exposure to benzene as a possible contributory etiologic factor in Hodgkin's disease. *Aksoy, M., Erdem, S., Dincol, K., Hepyüksel, T., Dincol, G.* (Internal Clinic of Istanbul Medical School, Capa, Istanbul, Turkey), p. 293

Accumulation of S-phase cells in the bone marrow of patients with acute leukemia by cytosine arabinoside. *Büchner, Th., Barlogie, B., Asseburg, U., Hiddemann, W., Kamanabroo, D., Göhde, W.* (Medizinische Klinik und Poliklinik der Universität Münster, 44 Münster/Westf. BRD), p. 299

Blut (München) **28** (1974) No. 5

Klinische Gnotobiotik in der Hämatologie. *Dietrich, M.* (Zentrum für Innere Medizin und Kinderheilkunde der Universität Ulm, Abteilung Hämatologie, 7900 Ulm/Donau, BRD), p. 317

Zur Aufhebung des zytostatischen Effekts von Amethopterin (Methotrexat) durch Methyl-Tetrahydrofolsäure. *Sauer, H., Jaenicke, L.* (Robert-Bosch-Krankenhaus, Stuttgart, Zentrum für Innere Medizin, Abteilung für Hämatologie, Onkologie und Immunologie, D-7000 Stuttgart 50, BRD), p. 321

Hemoglobin Lepore: Its significance for thalassemia and clinical manifestations. *Quattrin, N., Ventruto, V.* (Department of Hematology and Social Centre for Thalassemia, Ospedale Cardarelli, Naples, Italy), p. 327

Etude ultrastructurale des mégacaryocytes dans la thrombasthénie de Glanzmann. *Falcao, L.* (Centre de Microscopie Electronique de l'Université de Lausanne, CH-1011 Lausanne. Suisse), p. 337

Dilution curves studies in coumarin plasmas and in artificially depleted abnormal control plasmas. *Girolami, A., Brunetti, A., Patrassi, G.* (Istituto di Semeiotica Medica dell'Università di Padova, Padova, Italy), p. 351

Studies on hypo- and hypercoagulability II. Coagulation and fibrin analyses in severe infectious and toxic conditions. *Kunz, F., Hörtnagl, H., Kroesen, G., Schennach, W., Egg, D., Rumpl, E., Aschauer, R., Holzknecht, F.* (Department of Internal Medicine, University of Innsbruck, A-6028 Innsbruck, Austria), p. 360

Anti-T agglutinin in primary malignant blood disease. *Boccardi, V., Attinà, D., Girelli, G.* (Istituto di Patologia Medica I dell'Università di Roma, 00100 Roma, Italy), p. 370

Blut (München) **28** (1974) No. 6

Long-term preservation of hematopoietic tissue for marrow transplantation. *Lewis, J. P.* (Section of Hematology and Oncology, School of Medicine, University of California, Davis, Calif. 95616), p. 389

Therapeutische, funktionelle und kinetische Aspekte der Leukopheresetherapie chronischer lymphatischer Leukämien. *Höcker, P., Pittermann, E., Gobets, M., Haist, B., Gazda, M., Stacher, A.* (Hanusch-Krankenhaus, A-1140 Wien, Austria), p. 396

Ungewöhnlicher Chromosomensatz (46, XX, Dq-) bei Osteomyelofibrose. *Ganner-Millonig, E.* (Medizinische Universitätsklinik Innsbruck, 6020 Innsbruck, Austria), p. 411

Immunhistochemische Untersuchungen an T-Lymphozyten der Maus. *Huhn, D., Rodt, H., Thierfelder, S.* (I. Medizinische Klinik der Universität, 8 München 2, BRD), p. 415

Morphologische Phasenkontrast-kinematographische Studien zum Verhalten von Knochenmark- und Blutzellen in vitro. IX. Spontane Zellfusion beim Menschen, zugleich ein Beitrag zur Pathogenese einer leukämoiden Reaktion. *Boll, I.* (I. Innere Abteilung der Städtischen Krankenhauses Berlin-Neukölln, D-1000 Berlin 47), p. 430

Elektronenmikroskopische Untersuchung über die Blutbildung in der fetalen Rattenleber (Tag 14 a. p.) nach Gabe von Chloramphenicol und Oxytetrazyklin. *Noack, W., Borowski, R., Elbrecht, B.* (II. Anatomisches Institut der Freien Universität Berlin, 1 Berlin 33), p. 435

Standardisierung des Quick-Testes Referenz-Thromboplastin oder Referenz-Plasmen? *Averdunk, R., Borner, K.* (Institut für Klinische Chemie u. Klinische Biochemie, Klinikum Steglitz, D-1 Berlin 45), p. 445

Histochemical findings on preleukemic states. *Heller, A., Gross, R.* (Medizinische Universitätsklinik Köln, D-5 Köln, BRD), p. 452

British Journal of Haematology (Oxford) **25** (1973) No. 2

Annotation. The blastic crisis of chronic myeloid leukaemia: acute transformation of a preleukaemic condition? *Pedersen, B.* (Cancer Research Institute, Danish Cancer Society, The Radium Station, DK-8000 Aarhus C, Denmark), p. 141

Reticuloendothelial phagocytic function in human liver disease and its relationship to haemolysis. *Cooksley, W. G. E., Powell, L. W., Halliday, J. W.* (Department of Medicine, University of Queensland, Royal Brisbane Hospital, Brisbane, Australia 4029), p. 147

Gaucher-like cells and congenital dyserythropoietic anaemia, type II (HEMPAS). *Van Dorpe, A., Broeckaert-Van Orshoven, A., Desmet, V., Verwilghen, R. L.* (Laboratory of Physiopathology and Laboratory of Histochemistry and Cytochemistry, Department of Medical Research, University of Leuven, Leuven, B-3000 Belgium), p. 165

Acute plasma cell leukaemia following chronic lymphatic leukaemia: Transformation or two separate diseases? *Fitzgerald, P. H., Rastrick, J. M., Hamer, J. W.* (Cytogenetics Unit, Christchurch Hospital, Christchurch, New Zealand), p. 171

Case report: Studies on the mechanism of erythrocytosis associated with a uterine fibromyoma. *Ossias, A. L., Zanjani, E. D., Zalusky, R., Estren, S., Wasserman, L. R.* (Departments of Physiology and Medicine, Mount Sinai School of Medicine, City University of New York, N. Y. 10029), p. 179

Sustained erythropoietin production in nephrectomized rats subjected to severe hypoxia. *Peschle, C., Rappaport, I. A., Jori, G. P., Chiariello, M., Gordon, A. S., Condorelli, M.* (Laboratory of Experimental Hematology, Department of Biology, Graduate School of Arts and Science, New York University, New York, N. Y. 10003), p. 187

Effect of isopropyl methane sulphonate (IMS) on haemopoietic colony-forming cells. *Schofield, R., Lajtha, L. G.* (Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester M20 9BX, England), p. 195

Chronic lymphocytic leukaemia associated with acute myelomonocytic leukaemia. *Roberts, P. D., Forster, P. M.* (Haematology Department, West Middlesex Hospital, Isleworth, Middlesex, England), p. 203

Quantitative haemagglutination. IV. Effect of neuraminidase treatment on agglutination by blood group antibodies. *Greenwalt, T. J., Steane, E. A.* (American National Red Cross, Washington, D. C. 20006), p. 207

Quantitative haemagglutination. V. Influence of in vivo ageing and neuraminidase treatment on the M and N antigens of human red cells. *Greenwalt, T. J., Steane, E. A.* (American National Red Cross, Washington, D. C. 20006), p. 217

Quantitative haemagglutination. VI. Relationship of sialic acid content of red cells and aggregation by polybrene, protamine and poly-l-lysine. *Greenwalt, T. J., Steane, E. A.* (American National Red Cross, Washington, D. C. 20006), p. 227

The exchangeable splenic platelet pool studied with epinephrine infusion in idiopathic thrombocytopenic purpura and in patients with splenomegaly. *Branehög, I., Weinfeld, A., Roos, B.* (Unit of Medical Oncology, Department of Medicine II, 41345 Göteborg, Sweden), p. 239

The erythropoietic response to pregnancy in β-thalassaemia minor. *Schuman, J. E., Tanser, C. L., Péloquin, R., De Leeuw, N. K. M.* (Division of Haematology, McGill University Medical Clinic, Royal Victoria Hospital, Montreal, Canada), p. 249

Glucose-6-phosphate dehydrogenase deficiency in Maltese newborn infants. *Grech, J. L., Vicatou, M.* (Department of Pathology, St. Luke's Hospital, Malta), p. 261

Abstracts of papers presented at a meeting of the British Society for Haematology held in Aberdeen, 30-31 March, 1973. p. 271

British Journal of Haematology (Oxford) **25** (1973) No. 3

Annotation. Viruses and leukaemia. *Jarrett, W. F. H.* (Department of Veterinary Pathology, University of Glasgow, Glasgow, Scotland), p. 287

Skin window macrophages in malignant lymphomas. *Ghosh, M. L., Hudson, G., Blackburn, E. K.* (University Department of Haematology, Royal Infirmary, Sheffield, England), p. 293

Phagocytic function of leucocytes from patients with acute myeloid and chronic granulocytic leukaemia. *Goldman, J. M., Th'ng, K. H.* (M. R. C. Leukaemia Unit, Royal Postgraduate Medical School, London W12 oHS, England), p. 299

Ouabain-sensitive and oligomycin-sensitive adenosine-triphosphatase activities of normal human lymphocytes. *Ellegaard, J., Dimitrov, N. V.* (Marselisborg Hospital, DK-8000 Aarhus C, Denmark), p. 309

Evaluation of ^{51}Cr as a leucocyte label. *Spivak, J. L., Perry, S.* (Department of Medicine, Johns Hopkins University Medical School, Baltimore, Md.), p. 321

Fine structure and peroxidase activity of circulating micromegakaryoblasts and platelets in a case of acute myelofibrosis. *Breton-Gorius, J., Daniel, M. T., Flandrin, G., Kinet Denoel, G.* (Unité de Recherches sur les Anémies, U. 91. I.N.S.E.R.M., Hôpital Henri Mondor, 94010 Créteil, France), p. 331

^{52}Fe studies of the effects of treatment on erythropoiesis in megaloblastic anaemia. *Bruce-Tagoe, A. A., Hoffbrand, A. V., Short, M. D., Szur, L.* (Departments of Haematology, Medical Physics and Radiotherapy, Royal Postgraduate Medical School, London W12 oHS, England), p. 341

Significance of large red blood cells. *Chanarin, I., England, J. M., Hoffbrand, A. V.* (Department of Haematology, Northwick

Park Hospital, Harrow, Middlesex HA1 3UJ, England), p. 351

A comparison of the properties of chicken serum with other vitamin B_{12} binding proteins used in radioisotope dilution methods for measuring serum vitamin B_{12}. *Newmark, P. A., Green, R., Musso, A. M., Mollin, D. L.* (Department of Haematology, St Bartholomew's Hospital and Medical College, London, E.C.1, England), p. 359

The clinical and haematological findings in children inheriting two types of thalassaemia: High-A_2 type β-thalassaemia, and high-F type or $\delta\beta$-thalassaemia. *Kattamis, C., Metaxotou-Mavromati, A., Karamboula, K., Nasika, E., Lehmann, H.* (Department of Pediatrics, Choremis Research Laboratory, Athens University, St, Sophie's Hospital, Athens 608, Greece), p. 375

Glucose-6-phosphate dehydrogenase Johannesburg: A new variant with reduced activity in a patient with congenital non-spherocytic haemolytic anaemia. *Balinsky, D., Gomperts, E., Cayanis, E., Jenkins, T., Bryer, D., Bersohn, I., Metz, J.* (The South African Institute for Medical Research, P. O. Box 1038, Johannesburg, South Africa), p. 385

Renal mechanisms underlying cyclic AMP action on erythropoiesis. *Peschle, C., Rappaport, I. A., D'Avanzo, A., Russolillo, S., Marone, G., Condorelli, M.* (Institute of Medical Pathology, II Faculty of Medicine and Surgery, University of Naples, Naples, Italy), p. 393

Sialic acid deficiency of human red blood cells associated with persistent red cell, leucocyte and platelet polyagglutinability. *Lalezari, P., Al-Mondhiry, H.* (Division of Immunohematology, Montefiore Hospital and Medical Center, Bronx, N. Y. 10467), p. 399

British Journal of Haematology (Oxford) **25** (1973) No. 4

Annotation. The diagnosis of systemic lupus erythematosus. *Hughes, G. R.* (Department of Medicine, Royal Postgraduate Medical School, London W12 oHS, England), p. 409

A red cell membrane protein abnormality in hereditary elliptocytosis. *Gomperts, E. D., Cayannis, F., Metz, J., Zail, S. S.* (Department of Haematology, School of Pathology, University of the Witwatersrand, Johannesburg, South Africa), p. 415

Red cell membrane protein in antibody-induced haemolytic anaemia. *Gomperts, E. D., Metz, J. Zail, S. S.* (Department of Haematology, Johannesburg, South Africa), p. 421

Linolenoyl sorbitol and the fragility of hereditary spherocytes. *Livne, A., Aloni, B., Moses, S., Kuiper, P. J. C.* (Department of Biology, University of the Negev, Beer Sheva, Israel), p. 429

The prevalence of the rarer inherited haemoglobin defects in adult Jamaicans. *Ahern, E. J., Swan, A. V., Ahern, V. N.* (Department of Pathology, University of the West Indies, Kingston 7, Jamaica), p. 437

Monitoring successive batches of British comparative thromboplastin. *Hills, M., Ingram, G. I. C.* (Biometrics Section, British Museum [Natural History], London SW7 5BD, England), p. 445

Quality control trials in the national reference thromboplastin scheme. *Leck, I., Thomson, J. M., Poller, L.* (Department of Social and Preventive Medicine, University of Manchester, Manchester M20 8LR, England), p. 453

Erythrokinetic studies as a guide to the value of splenectomy in primary myeloid metaplasia. *Milner, G. R., Geary, C. G., Wadsworth, L. D., Doss, A.* (Department of Haematology, Manchester Royal Infirmary, Manchester M13 9WL, England), p. 467

Plasma lysozyme in drug-induced and spontaneous cyclic neutropenia. *Hansen, N. E., Andersen, V., Karle, H.* (Division of Haematology, Department of Medicine A, Rigshospitalet, 2100 Copenhagen, Denmark), p. 485

Transport of methotrexate into normal haemopoietic cells and into leukaemic cells and its effects on DNA synthesis. *Hoffbrand, A. V., Tripp, E., Catovsky, D., Das, K. C.* (Department of Haematology, Royal Postgraduate Medical School, London W12 oHS, England), p. 497

The availability of food folate in man. *Tamura, T., Stokstad, E. L. R.* (Department of Nutritional Sciences, University

of California, Berkeley, Calif. 94720), p. 513

Plasma clearance of ^{125}I-labelled haemopexin in normal and haem-loaded rabbits. *Lane, R. S., Rangeley, D. M., Liem, H. H., Wormsley, S., Muller-Eberhard, U.* (Department of Haematology, St George's Hospital, London, S. W. 17, England), p. 533

British Journal of Haematology (Oxford) **25** (1973) No. 5

Annotation. Red cell 2,3-diphosphoglycerate. *Bellingham, A. J., Grimes, A. J.* (Department of Clinical Haematology, University College Hospital Medical School, London, WC1, England), p. 555

Glutathione peroxidase in human red cells in health and disease. *Hopkins, J., Tudhope, G. R.* (Department of Pharmacology and Therapeutics, University of Dundee, Dundee, England), p. 563

Reduced glutathione, glutathione reductase, glutathione peroxidase, and pyruvate kinase in erythrocytes of human newborns and adults in Malaysia. *Eng, L.-I. L., Wan, W. P., Ng, T.* (Department of International Health, University of California, San Francisco, CA 94143), p. 577

The attachment of Heinz bodies to the red cell membrane. *Winterbourn, Ch. C., Carrell, R. W.* (Department of Clinical Biochemistry, Christchurch Hospital, Christchurch, New Zealand), p. 585

Bone marrow and bone mineral scintigraphic studies in sickle cell disease. *Hammel, C. F., DeNardo, S. J., Lewis, J. P.* (Section of Hematology, School of Medicine, University of California, Davis, Calif. 95616), p. 593

Depression of bone marrow delta-aminolaevulic acid synthetase activity in erythroleukaemia. *Tanaka, M., Hotta, T., Yamada, H.* (VA Hospital, Hematology Section, Oklahoma City, Oklahoma 73104), p. 599

Haemoglobin Perth: β_{32} (B14) leu → pro, an unstable haemoglobin causing haemolysis. *Jackson, J. M., Yates, A., Huehns, E. R.* (Department of Haematology, Royal Perth Hospital, Perth, Australia), p. 607

The effect of ascorbate on the maintenance of 2,3-diphosphoglycerate (2,3-DPG) in stored red cells. *Wood, L. A., Beutler, E.* (Hematology Department, City of Hope National Medical Center, Duarte, Calif. 91010), p. 611

A tanned cell haemagglutination test for the detection of hepatitis-associated-antigen (Au-Ag) and antibody (Anti-Au). *Hopkins, R., Das, P. C.* (South-East Scotland Regional Transfusion Centre, Edinburgh EH3 9HB, Scotland), p. 619

Oxygen transport in anaemia. *Pollock, A., Cotter, K. P.* (Department of Haematology, The General Hospital, Birmingham B4 6NH, England), p. 631

The metabolism of intravenously administered iron-dextran. *Kanakakorn, K., Cavill, I., Jacobs, A.* (Department of Haematology, University Hospital of Wales, Cardiff CF4 4XW, England), p. 637

Factor-VIII antigen and platelet retention in a glass bead column. *Bouma, B. N., Sixma, J. J., De Graaf, S., Wiegerinck, Y., Van Mourik, J. A., Mochtar, I. A.* (Division of Haemostasis, Department of Internal Medicine, University Hospital, Utrecht, The Netherlands), p. 645

Energy metabolism in washed human platelets responsive to ADP: Comparison with platelets in plasma. *Doery, J. C. G., Hirsh, J., Mustard, J. F.* (Department of Pathology, McMaster University, Hamilton, Ontario, Canada), p. 657

Effect of repeated treatment of rabbit platelets with low concentrations of thrombin on their function, metabolism and survival. *Reimers, H. J., Pakham, M. A., Kinlough-Rathbone, R. L., Mustard, J. F.* (Department of Pathology, McMaster University, Hamilton, Ontario, Canada), p. 675

British Journal of Haematology (Oxford) **25** (1973) No. 6

Annotation. The immune interaction between red cells and leucocytes and the pathogenesis of spherocytosis. *Brown, D. L.* (Department of Immunology, Royal Postgraduate Medical School, London W12 0HS, England), p. 691

Storage iron kinetics. V. Iron exchange in the rat. *Cook, J. D., Hershko, Ch., Finch, C. A.* (Division of Hematology, Department of Medicine, University of Washing-

ton School of Medicine, Seattle, Wash. 98195), p. 695

Effects of inflammation on iron and transferrin metabolism. *O'Shea, M. J., Kershenobich, D., Tavill, A. S.* (Departments of Haematology and Medicine, Royal Free Hospital, Hampstead, London N. W. 3, England), p. 707

Reappraisal of the role of anti-i in haemolytic anaemia in infectious mononucleosis. *Wilkinson, L. S., Petz, L. D., Garraty, G.* (Harkness Community Hospital and Medical Center, San Francisco, Calif. 94117), p. 715

Phenobarbitone sensitivity of jaundice in haemolytic patients. *Perona, G., Corrocher, R., Frezza, M., Falezza, G. C., Cellerino, R., Tiribelli, C., Fusaro, A., de Sandre, G.* (Istituto di Patologia Speciale Medica dell'Università di Trieste, Ospedale Maggiore, Trieste, Italia), p. 723

Studies on the transcobalamins. *England, J. M., Clarke, H. G. M., Down, M. C., Chanarin, I.* (MRC Experimental Haematology Unit, St. Mary's Hospital Medical School, London, W.2, England), p. 737

Early onset of pernicious anaemia in two siblings: Genetic and autoimmune aspects. *Hall, Ch. A., Beebe, R. T.* (Haematology Section, Medical Service, Veterans Administration Hospital, Albany Medical College, Albany, N. Y. 12208), p. 751

Assessment of the value of lysozyme assay in neutropenia. *Levi, J. A., Macqueen, A., Vincent, P. C.* (National Cancer Institute, Baltimore Cancer Research Center, Baltimore Md. 22211), p. 757

The relationship between the turnover rate of neutrophilic granulocytes and plasma lysozyme levels. *Hansen, N. E.* (Division of Haematology, Department of Medicine A, Rigshospitalet, University Hospital, DK 2100 Copenhagen, Denmark), p. 771

Instantaneous and continuous measurement of phagocytosis-stimulated glucose oxidation in human granulocytes by an ionization chamber method. *Davidson, W. D., Tanaka, K. R.* (Department of Medicine, Harbor General Hospital, Torrance, Calif. 90509), p. 783

Tuberculosis and blood disorders. *Coburn, R. J., England, J. M., Samson, D. M., Walford, D. M., Blowers, R., Chanarin, I., Levi, A. J., Slavin, G.* (Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex HA1 3UJ, England), p. 793

Standard techniques for the measurement of red-cell and plasma volume. *Glass, H. I.* (Department of Medical Physics, Royal Postgraduate Medical School, London W12 OHS, England), p. 801

Experimental Hematology (Copenhagen) **1** (1973) No. 1

Adaptive phenomena in bone marrow transplantation. *Goujet-Zalc, C., Ilbery, P. L. T.* (University of Sydney, School of Public Health, Sydney 2006, New S. Wales, Australia), p. 3

Survival of rat marrow cells after treatment with myleran and endoxan. *Dunjic, A., Cuvelier, A.-M.* (University College of Leuven, Institute for Cancer, 8-3000 Leuven, Belgium), p. 11

Inhibition of graft-versus-host-reaction (GVHR) by in vitro incubation of donor lymphocytes with thymic or splenic chalone(s). *Kiger, N., Florentin, I., Garcia-Giralt, E., Mathé, G.* (Paul Brousse Hospital, Institute of Cancerology and Immunology Genetics, 94800 Villejuif, France), p. 22

Studies on the source of hematopoietic tissue in the marrow of subcutaneously implanted femurs. *Fried, W., Husseini, S., Knospe, W. H., Trobaugh, F. E., Jr.* (University of Illinois, College of Medicine, Department of Medicine, Chicago, Ill. 60680), p. 29

Attempts at morphological identification of the hemopoietic stem cell in rodent and primates. *Dicke, K. A., Noord, M. J. van, Bekkum, D. W. van* (Radiobiology Institute, Ruswuk, The Netherlands), p. 36

Experimental Hematology (Copenhagen) **1** (1973) No. 2

Planning cooperation in human bone marrow transplant research. *Congdon, C. C., Bortin, M. M., Morris, W. C.* (Oak Ridge National Laboratory, Biology Division, Oak Ridge, Tenn. 37830), p. 85

Evidence suggesting identity of CFU-spleen and cells producing colonies in a specially designed tissue culture system. *Dicke,*

K. A., Engh, G. van den, Bekkum, D. W. van (TNO, Radiobiology Institute, Ryswyk ZH, The Netherlands), p. 98

Brain associated erythrocyte antigen: An antigen shared by brain and erythrocytes. *Golub, E. S.* (Purdue University, Department of Biological Science, Lafayette, Ind., 47907), p. 105

Active immunotherapy in spontaneous leukemia of AkR mice. *Mathé, G., Halle-Pannenko, O., Bourut, C.* (Paul Brousse Hospital, Institute for Cancer and Immunogenetics, 94800 Villejuif, France) p. 110

Cytological studies of granulopoietic colonies from two patients with chronic myelogenous leukemia. *Aye, M. T., Till, J. E., McCulloch, E. A.* (Ontario Cancer Institute, Toronto 5, Ontario, Canada), p. 115

Immunosuppression with ethidium bromide: Effect on lymphocyte blastogenesis and antibody plaque forming spleen cells. *Khan, A., Hill, J. M.* (Wadley Institute of Molecular Medicine, Dallas, Texas 75235), p. 119

Studies on the erythropoietic activity of steroid metabolites. *Gorshein, D., Murphy, S., Gardner, F. H.* (University of Pennsylvania, Presbyterian Hospital, Medical College of Pennsylvania, Philadelphia, Pa. 19104), p. 123

Assay of granulocytic progenitor cells in human peripheral blood. *Rubin, S. H., Cowan, D. H.* (Ontario Cancer Institute, Toronto M4X 1K9, Ontario, Canada), p. 127

Experimental Hematology (Copenhagen) **1** (1973) No. 3

Development of tumors as a result of graft-versus-host reaction. *Cornelius, E. A.* (Yale University School of Medicine, Department of Radiology, New Haven, Conn. 06510), p. 135

Lymphoid cell dependence of eosinophil response to antigen II. *Speirs, R. S., Gallaher, M. T., Rauchwerger, J., Heim, L. R.* (Downstate Medical Center, Department of Anatomy, Brooklyn, N. Y. 11203), p. 150

A test of osteoblasts for hematopoietic competence. *Meck, R., Mel, H. C.* (University of California, Division of Medical Physics, Berkeley, Calif. 94720), p. 159

Sedimentation velocities of cells mediating two different GVH lesions. *Bain, G. O., Pezzot, D. E., Asquith, P. R.* (University of Alberta, Department of Pathology, Edmonton, Alberta, Canada), p. 165

Altered responsiveness to erythropoietin in mice following infection with polycythemia-inducing Friend virus. *McGarry, M. P., Mirand, E. A.* (Roswell Park Memorial Institute, Department of Biological Resources, Buffalo, N.Y. 17440P2), p, 174

Experimental Hematology (Copenhagen) **1** (1973) No. 4

Regulation of granulocyte and monocyte-macrophage proliferation by colony stimulating factor (CSF). A review. *Metcalf, D.* (Walter and Eliza Hall Institute, Cancer Research Unit, Melbourne, Australia), p. 185

Delayed secondary disease in mice after early or late therapy with antithymocyte serum. *Kinnamon, K. E., Blackwell, L. H., Ledney, G. D.* (Walter Reed Army Medical Center, Institute of Research, Department of Biology, Washington, D. C. 20012), p. 202

Splenectomy and radiation sensitivity. *O'Grady, L. F., Lewis, J. P.* (University of California, School of Medicine, Section Hematology, Davis, Calif. 95616), p. 215

Precipitating antibodies in anti-erythropoietin sera. *Pavlovic-Kentera, V., Ichiki, A. T., Lange, R. D.* (University of Tennessee, Membrane Research Center, Knoxville, Tenn. 37920), p. 222

Experimental Hematology (Copenhagen) **1** (1973) No. 5

Relative roles of genetic histocompatibility determinants in bone marrow transplantation. *Bachvaroff, R., Rapaport, F. T., Cannon, F. D., Mollen, N., Blumenstock, D. A., Ayvazian, J. H., Ferrebec, J. W.* (New York Medical Center, Institute for Reconstructive Plastic Surgery, Department of Surgery, New York, N. Y. 10016), p. 233

Abstracts from the Second Annual Conference of the International Society for Experimental Hematology, p. 239

Folia Haematologica (Leipzig) **100** (1973) No. 1/2

Übersicht. Neues aus der Milzforschung. *Hittmair, A. M.* (Kaiser-Josef-Strasse 15, A-6020 Innsbruck, Österreich), p. 1

Morphological aspects of myelofibrosis, observed in rats following sublethal whole body irradiation and subsequent allogeneic bone marrow cell transfusion. *Stodtmeister, R., Fliedner, T. M.* (Abteilung für klinische Physiologie, Zentrum für klinische Grundlagenforschung, Universität Ulm, Ulm/Donau, BRD), p. 23

Blastoid lymphocyte transformation assay in malignant tumours of lymphopoietic tissue: in Hodgkin's disease, reticulosarcoma, lymphosarcoma and chronic lymphatic leukaemia. Relationship to the clinical status and to the delayed type of hypersensitivity. *Libánský, J.* (Institute of Hematology and Blood Transfusion, Prague 2, Czechoslovakia), p. 51

Gastrointestinal lesions and complications in haemoblastoses. *Klener, P., Donner, L., Bočanová, M., Ort, J.* (Second Department of Medicine, Charles University Hospital, 128 08 Prague 2, Czechoslovakia), p. 57

Die Splenektomie bei der Panzytopenie. *Hesse, P., Lehmann, K.* (Kreiskrankenhaus, DDR-285 Parchim), p. 67

Zum Enzymgehalt der Leukozyten des peripheren Blutes bei perniziöser Anämie. *Kolarz, G., Vormittag, W., Pietschmann, H.* (II. Medizinische Universität-Klinik, A-1097 Wien, Österreich), p. 72

Kryptogenetische perniziöse Anämie mit Vitiligo bei einem jugendlichen Patienten. *Meister, H., Lehmann, K.* (Medizinische Abteilung des St. Vincenz-Krankenhauses, DDR-563 Heiligenstadt), p. 76

Leiterkriterien der Retikulozytenreifung: Osmotische Fragilität von im Dextrandichtegradienten getrennten roten Blutzellen im Verlaufe einer Entblutungsanämie. *Gross, J., Pietsch, L., Rosenthal, S.* (Institut für Physiologische und Biologische Chemie, Bereich Medizin (Charité) der Humboldt-Universität zu Berlin, DDR-104 Berlin), p. 81

Ladungsänderung an menschlichen Erythrozyten während der Lagerung von Blutkonserven. *Linn, W., Helmke, U., Richter, H., Geyer, G.* (Anatomisches Institut der Friedrich-Schiller-Universität, DDR-69 Jena), p. 90

Schädigungen der Hämatopoese durch Thorium-X-Therapie. *Stieglitz, R., Thiele, M., Stobbe, H., Wegener, G.* (Hämatologische Abteilung, I. Medizinische Klinik der Charité, DDR-104 Berlin), p. 95

Measurement of the labile iron stores with Singh's technique and chemical determination of iron contents in organs of rats. *Bobeck-Rutsaert, M. M., Wiltink, W. F., op den Kelder, M., Van Eijk, H. G., Leijnse, B.* (Akademie Hospital Rotterdam-Dijkzigt, Rotterdam, The Netherlands), p. 104

Tierexperimentelle Untersuchungen zur Pathogenese des Morbus Werlhof. *Sundermann, A., Mey, U., Meister, H., Sundermann, U., Malik, B.* (Medizinische Klinik der Medizinischen Akademie Erfurt, DDR-50 Erfurt), p. 110

Herstellung und klinische Anwendung von Plättchen- und Faktor-VIII (AHG)-Konzentraten. *Vopatová, M., Vlčková, M., Fortýnová, J., Pudlák, P.* (Institut für Hämatologie und Bluttransfusion, Prag 2, CSSR), p. 122

Die Thrombozyten der Hämophilen. *Weinbach, G., Bührdel, P., Domula, M.*, (Universitäts-Kinderklinik, DDR-705 Leipzig), p. 131

Ausscheidung von Gruppensubstanzen ABO (H) mit dem Harn bei verschiedenen Nierenkrankheiten. *Kalinowski, M.* (Woiwodschafts-Blutspendezentrum, Gdansk, Polen), p. 144

Folia Haematologica (Leipzig) **100** (1973) No. 3

Übersicht über die Standardisierung und Qualitätskontrolle in der klinischen Hämostaseologie. *Vogel, G.* (Medizinische Klinik der Medizinischen Akademie Erfurt, DDR-50 Erfurt), p. 177

Angewandte Zytochemie in der Hämatologie. *Meister, H.* (Medizinische Abteilung des St. Vincenz-Krankenhauses, DDR-563 Heilbad Heiligenstadt), p. 186

Familial myeloma. *Boga, M., Jákó, J., Domán, J., Magyar, É., Konyár, É.* (IV. Department of Medicine, Postgraduate

Medical School, 1135 Budapest, Hungary), p. 201

Die Monozytose bei Benzolarbeitern und chronischer Benzolvergiftung. *Roth, L., Turcanu, P., Dinu, I., Moise, G.* (Bega Krankenhaus, Timişoara, Rumänien), p. 213

Sekundäre Immunphänomene in der Hämatologie. *Hadnagy, Cs.* (II. Medizinische Universitätsklinik, Tg. Mureş, Rumänien), p. 225

Phagozyten im Hautexsudat. *Ruffert, K., Jahn, H., Friebel, U., Jorke, D.* (Städtisches Krankenhaus Jena, Fachkrankenhaus für Innere Medizin, DDR-69 Jena), p. 237

Lymphozytentransformationsrate bei "low birth weight infants". *Wiersbitzky, S., Dierschke, R.* (Universitäts-Kinderklinik, DDR-22 Greifswald), p. 252

Ultrastrukturelle Besonderheiten von roten Blutzellen Neugeborener. *David, H., Gross, J., Uerlings, I., Grauel, E. I., Syllm-Rapoport, I.* (Pathologisches Institut des Bereichs Medizin [Charité] der Humboldt-Universität zu Berlin, DDR-104 Berlin), p. 261

Der Nachweis von Histokompatibilitätsantigenen bei Lymphozyten mit Hilfe proteolytischer Fermente. *Bube, F. W., Heumann, H., Siebel, E.* (Blutspendezentrale der Universitätskliniken Köln, 5 Köln 41, BRD), p. 269

Comparative study of platelet kinetics with ^{75}Se-methionine and ^{51}Cr in ITP and congestive splenomegaly. *Burger, T., Schmelzer, M.* (Medical University of Pécs, First Department of Medicine, Pécs, Hungary), p. 278

In-vitro-untersuchungen über den Einfluß verschiedener Pharmaka auf die Aktivität der Streptokinase. *Fuchs, R.* (Medizinische Klinik der Medizinischen Akademie Erfurt, DDR-50 Erfurt), p. 290

Elektrophoretische Untersuchungen der Untereinheiten des Fibrinogens und durch Faktor XIII stabilisierten Fibrins von normalen und kobaltbehandelten Kaninchen. *Krantz, S., Lober, M.* (Physiologisch-chemisches Institut, DDR-22 Greifswald), p. 295

Einfluß der Wasserstoffionenaktivität auf die Blutgerinnung. *Neef, H., Richter, M., Fischer, U.* (Chirurgische Universitätsklinik, DDR-402 Halle), p. 303

Folia Haematologica (Leipzig) **100** (1973) No. 4

Der Einfluß von Phytohämagglutinin und heterologen Antilymphozytensera auf kultivierte Nagerlymphozyten in Abhängigkeit von Dosierung und Zeit. *Kaden, K., Kaden, J.* (Akademie der Wissenschaften der DDR, Abteilung für Zoo- und Wildtierkrankungen, DDR-1136 Berlin), p. 321

Vergleichende Untersuchungen zur Wirkung xenogener Antilymphozytensera bzw.-globuline auf das periphere Blutbild von Maus, Hund und Mensch. *Kaden, J., Preussner, S., Frick, G.* (Abteilung für Transfusions- und Transplantationswesen, des Bereiches Medizin, Humboldt-Universität, DDR-104 Berlin), p. 337

DNA synthesis in cells infiltrating a skin allograft in mice. *Jakóbisiak, M., Abramczuk, J., Kossakowska, A. E., Rowinski, J.* (Department of Transplantology, Biostructure Institute, Medical School, Warsaw, Poland), p. 354

Die Lysozymurie bei Leukosen. *Jaworkovsky, L., Grant, H.* (Spirgus iela 1, Riga 2, USSR), p. 358

Die Wirkung ionisierender Strahlen auf die Aktivität der alkalischen Phosphatase in Zellen des hämatopoetischen Systems von Maus und Ratte. *Bartnikowa, W.* (Instytut Onkologii, Gliwice, Polen), p. 377

Über den Einfluß ionisierender Strahlen auf die Aktivität der alkalischen Phosphatase in den Leukozyten des peripheren Blutes und den Knochenmarkzellen des Menschen. *Bartnikowa, W.* (Instytut Onkologii, Gliwice, Polen), p. 385

ABO and RhD blood group in leukemic patients. *Moszczyński, P., Lisiewicz, J.* (Department of Internal Diseases, County Hospital, Brzesko-Czechów, Poland), p. 395

Cytogenetic study of erythromyelosis and erythroleukaemia. *Demin, A. A., Degtjareva, M. M., Metelkina, N. V., Radgabli, S. I., Kabardina, V. A.* (Gorki, 26 a, KV 5, Novosibirsk, USSR), p. 401

Nachweisbare Stoffwechsel- und Strukturanomalien der roten Blutzellen von Diabetikern. *Heller, H.* (Katholisches Krankenhaus, DDR-501 Erfurt, Pf. 587, DDR), p. 417

IgM anti-i cold agglutinins in hepatitis

mononucleosa. *Ambrus, M., Bajtai, G., Péley, I.* (Bezirks-Institut für Blutspende- und Transfusionswesen, Pécs, Ungarn), p. 429

A quantitative study of the erythrocytes and haemoglobin in the blood of an air-breathing fish, *Anabas testudineus* (Bloch), in relation to its body size. *Dube, S. C., Munshi, J. S. D.* (Post-Graduate Department of Zoology, Bhagalpur-7 [Bihar], India), p. 436

Haemostasis (Basel) **3** (1974) No. 1

Effect of the polyene antibiotic filipin on the lipid-dependent intrinsic pathway of blood coagulation. *van der Plas, P. M., Kraan, L., van Es, G., Stibbe, J., Hemker, H. C.* (Department of Haematology, Division of Haemostasis, University Hospital Dijkzigt, Rotterdam, The Netherlands), p. 1

Induction of aggregation and of the release reaction in human platelets by polylysine. *Massini, P., Metcalf, L. C., Näf, U., Lüscher, E. F.* (Theodor Kocher Institut, CH-3000 Bern 9, Switzerland), p. 8

Effect of contact factor (factor XII + factor XI) on aggregation of platelets. *Aznar, J., Mayans, J., Aznar, J. A.* (Department of Clinical Pathology, Ciudad Sanitaria "La Fe", Valencia, Spain), p. 20

Some effects of a microcrystalline collagen preparation on blood. *Mason, R. G., Read, M. S.* (Department of Pathology, University of North Carolina, Chapel Hill, N. C. 27514), p. 31

Hemostatic defects in experimental leukemia. *Rasche, H., Hoelzer, D., Dietrich, M., Keller, A.* (Service of Haemostaseology, Center of Internal Medicine and Pediatrics, University of Ulm, D-7900 Ulm/Donau, FRG), p. 46

In vitro effects of aspirin in fibrinolysis. *Iatridis, P. G., Iatridis, S. G., Markidou, S. G., Ragatz, B. H.* (Department of Physiology, Indiana University School of Medicine, Northwest Center for Medical Education, Gary, Ind. 46408), p. 55

Nouvelle Revue Française d'Hématologie (Paris) **13** (1973) No. 5

Le rôle des cellules dans la viscosité sanguine. *Weed, R. I.* (University of Rochester, Rochester, N. Y. 14642), p. 605

Leucémie à "tricholeucocyte" (hair cell leukemia). Etude clinique et cytologique de 55 observations. *Flandrin, G., Daniel, M. T., Fourcade, M., Chelloul, N.* (Laboratoire de Cytologie, Institut de Recherche sur les Leucémies et les Maladies du Sang, Hôpital Saint-Louis, 65475 Paris Cedex 10), p. 609

Etude des leucémies aiguës myéloblastiques en poussée et en rémission par culture de moëlle "in vitro". *Sultan, C., Marquet, M., Joffroy, Y.* (Hôpital Henri-Mondor, F 94010 Créteil, France), p. 641

Un nouveau cas de dysérythropoïese congénitale de type. II. Caractères immunologiques et transmission héréditaire de l'antigène de polyagglutinabilité distinct des antigènes T, Tn et Cad. *Rochant, H., Minh N'Go, M., Ton That, H., Henri, A., Basch, A., Sultan, C., Dreyfus, B.* (Unité de Recherches sur les Anémies, Hôpital Henri-Mondor, F 94000 Créteil, France), p. 649

Teneurs en ADN, ultrastructure et activité peroxydasique des mégacaryocytes médullaires dans un cas d'anémie réfractaire. *Kinet-Denoël, C., Breton-Gorius, J.* (Institut d'Histologie et d'Embryologie, 4000 Liège, Belgique), p. 661

Complications neurologiques de la maladie de Burkitt. Étude clinique et biologique. *Bonhomme, J. S., Bureau, J. P., Schmitt, T.* (Faculté de Médecine, B. P., 20632 Abidjan, Côte d'Ivoire), p. 681

Nouvelle Revue Française d'Hématologie (Paris) **13** (1973) No. 6

L'absorption du fer par la muqueuse duodénale. *Bédard, Y. C., Pinkerton, P. H., Simon, G. T.* (Département de Pathologie de l'Université de Toronto, Banting Institute, Toronto, Ontario M5G1Ld, Canada), p. 727

Leucémies aiguës à basophiles. *Quattrin, N.* (Département d'Hématologie, Ospedale Cardarelli, Naples, Italy), p. 745

A propos de la leucémie à promyélocytes. *Bernard, J., Flandrin, G.* (Institut de Recherches sur les Maladies du Sang, Hôpital Saint-Louis, 75475 Paris, France), p. 755

Traitement dans les observations de leucémies aiguës promyélocytaires de la coagulation intravasculaire disséminée. *Dreyfus,*

B., *Varet*, *B.*, *Heilmann-Gouault*, *M.*, *Sultan*, *C.*, *Reyes*, *F.*, *Gluckman*, *E.*, *Basch*, *A.*, *Beaujean*, *F.* (Département d'Hématologie Biologique, Centre Départemental de Transfusion Sanguine du Val-de-Marne, Hôpital Henri-Mondor, F. 94010 Créteil, France), p. 761

Etude au microscope électronique à balayage, de la migration des cellules sanguines à travers les parois des sinusoïdes spléniques et médullaires chez le rat. *Leblond*, *P.-F.* (Institut de Pathologie Cellulaire, I.N.S.E.R.M., Unité 48, Hôpital de Bicêtre, 94270 Le Kremlin-Bicêtre, France), p. 771

Scintigraphie de la moëlle osseuse. I. Etude expérimentale du marquage médullaire par l'indium. Résultats préliminaires obtenus chez l'homme. *Rain*, *J.-D.*, *Eberlin*, *A.*, *Boulard*, *M.*, *Dresch*, *C.*, *Najean*, *Y.* (Service de Médecine Nucléaire de l'Hôpital Saint-Louis, 75475 Paris Cedex 10, France), p. 789

Anémies hémolytiques dues à des hémoglobines instables présentant des délétions. Etude clinique, hématologique et biochimique de deux cas: Hb Tours (Thr β 87 (F3) délétée) et Hb Saint-Antoine (Gly-Leu β 74—75 (E18—19) délétée. *Najman*, *A.*, *Duhamel*, *G.*, *André*, *R.*, *Buc*, *H.*, *Wajcman*, *H.*, *Labie*, *D.*, *Schapira*, *G.* (Service d'Hématologie C.H.U. Saint-Antoine, 75012 Paris, France), p. 803

The effects of pH, oxygen tension and 2,3-diphosphoglycerate concentration upon the binding of adenosine triphosphate to concentrated hemoglobin A solutions. *Udkow*, *M. P.*, *Lacelle*, *P. L.*, *Weed*, *R. I.* (University of Rochester, Medical Center, Department of Internal Medicine, Rochester 14642, N. Y.), p. 817

Essai d'interprétation pathogénique de l'hémolyse au cours d'un hémangio-endothéliosarcome à début splénique. *Potron*, *G.*, *Hopfner*, *C.*, *Dufour*, *M.* (Laboratoire Central d'Hématologie, 51100 Reims, France), p. 835

Influence des réactions croisées dans l'immunisation fœto-maternelle anti-HL-A. *Mayer*, *S.*, *Tongio*, *M. M.* (Centre de Transfusion Sanguine, Institut d'Hématologie, Hôpital Civil de Strasbourg, 67000 Strasbourg, France), p. 847

Dysérythropoïese congénitale de type II avec anémie hémolytique néo-natale chez deux sœurs: Etude hématologique et ultrastructurale. *Mouriquand*, *C.*, *Bachelot*, *C.*, *Louis*, *J.*, *Beaudoing*, *A.*, *Berthier*, *R.* (Laboratoire d'Histologie de la Faculté de Médecine de Grenoble, 38700 La Tronche, France), p. 857

La forme des érythrocytes dans la sphérocytose héréditaire. Etude au microscope à balayage. Relation avec leur déformabilité. *Leblond*, *P.-F.*, *de Boisfleury*, *A.*, *Bessis*, *M.* (Institut de Pathologie Cellulaire, I.N.S.E.R.M., Unité No. 48, Hôpital de Bicêtre, 94270 Le Kremlin-Bicêtre, France), p. 873

Symposium sur le chimiotactisme des leucocytes, 6 et 7 juillet 1973, Hôpital de Bicêtre, 94270 Le Kremlin-Bicêtre, France, p. 885

Проблемы гематологии и переливания крови (Москва) 16 (1971) № 7

К вопросу о лечении острого лейкоза. *Рынская Л. М.* (Научная группа акад. АМН СССР проф. И. А. Кассирского, Москва.) с. 3. — Treatment of acute leukemia. *Rynskaya*, *L. M.*, p. 3

Применение неробола в комплексном лечении больных агранулоцитозом и гипопластической анемией. *Вогралик В. Г.*, *Егорова Г. А.*, *Новикова Л. Е.*, *Донскова Г. С.*, *Петренко А. М.* (Клиника госпитальной терапии лечебного факультета Горьковского медицинского института им. Кирова С. М.) с. 10. — Application of Nerobol in complex treatment of agranulocytosis and hypoplastic anemia. *Nogralik*, *V. G.*, *Egorova*, *G. A.*, *Novikova*, *L. E.*, *Donskova*, *G. G.*, *Petrenko*, *A. M.*, p. 10

Применение циклофосфана при лечении больных миелофиброзом. *Климова Н. Ф.*, *Индосова Э. Н.* (Гематологическая клиника Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва.) с. 11. — Cyclophosphane treatment of myelofibrosis. *Klimova*, *N. F.*, *Indosova*, *E. N.*, p. 11

К вопросу о цитологической характеристике бластного криза при хроническом миелолейкозе. *Терентьева Э. И.*, *Кореневская М. И.*, *Козинец*, *Г. И.*,

Мокеева Р. А., Дульцина С. М., Бартащук Е. И., Альперович В. В., Сусоева В. М. (Цитологическая лаборатория и гематологическая клиника Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва.) с. 16. — Cytologic characteristics of blastic crisis in chronic myeloid leukemia. *Terentieva, E. I., Korenevskaya, M. I., Kozinetz, G. I., Mokeyeva, R. A., Dultsina, S. M., Bartastchuk, E. I., Alperovitch, V. V., Susoyeva, V. M.*, p. 16

Применение метода лимфографии при злокачественных лимфомах. *Зисман И. Ф.* (Отделение общей онкологии и гематологии Молдавского научно-исследовательского института онкологии.) с. 23. — Significance of lymphography in malignant lymphomas. *Zisman, I. F.*, p. 23

Изменения белков сыворотки крови у больных с различными формами лейкоза. *Серикова, А. З., Дыгин, В. П.* (Кафедра факультетской терапии Военно-медицинской академии им. С. М. Кирова, Ленинград.) с. 26. — Change of serum proteins in various forms of leukemia (Data of analytic ultracentrifugation). *Serikova, A. Z., Dygin, V. P.*, p. 26

Образование L-форм бактерий у больных лейкозом. *Мартинова В. А., Голосова Т. В., Каган, Г. Я., Чумакова Л. П.* (Бактериологическая лаборатория Центрального института гематологии и переливания крови Министерства здравоохранения СССР, лаборатория микроплазм и L-форм бактерий Института экспериментальной микробиологии им. Н. Ф. Гамалеи АМН СССР.) с. 32. — Formation of L-form bacteria in leukemia. *Martinova, V. A., Golosova T. V., Kagan, G. Ya., Chumakova, L. P.*, p. 32

Иммунобиологическая и микробиологическая характеристистика пневмоний при лейкозах. *Голосова, Т. В., Мартинова, В. А., Ковалева Л. Г., Ермакова Г. Л., Абакумов Е. М.* (Бактериологическая лаборатория и гематологическая клиника Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва.) с. 35. — Immunobiological and microbiological characteristics of pneumonia in leukemias. *Golosova, T. V., Martinova, V. A., Kovaleva, L. G., Ermakova, G. L., Abakumov, E. M.*, p. 35

Оценка гемостатических свойств кровяного сгустка при лейкозах и геморрагических диатезах. *Иванов Е. П.* (Белорусский научно-исследовательский институт гематологии и переливания крови, Минск.) с. 40. — Assessment of hemostatic properties of blood clot in leukemias and hemorrhagic diatheses. *Ivanov, Ye. P.*, p. 40

Гемолитическая болезнь новорожденного при несовместимости крови матери и плода по фактору М. *Михайлова, А. А., Ичаловская, Т. А.* (Горьковская областная станция переливания крови, лаборатория (центр) по изучению и стандартизации групп крови Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва). с. 46. — Hemolytic disease of the newborn from M factor incompatibility. *Mikhailova, A. A., Ichalovskaya, T. A.*, p. 46

Распределение резусположительного и резусотрицательного населения Минска по группам крови системы АВО. *Толочко, Г. В., Розина, И. В.* (Белорусский научно-исследователеьский институт гематологии и переливания крови, Минск.) с. 48. — Distribution of Rh-positive and Rh-negative population of Minsk according to AB0 blood groups. *Tolochko, G. V., Rozina, I. V.* p. 48

К вопросу о возможности переноса сифилиса с кровью дорона, страдающего латентной формой этого заболевания. *Михайлова, А. А., Градова, Л. И.* (Горьковская областная станция переливания крови.) с. 50. — Possibility of transmission of syphilis with blood of a donor suffering from latent form of this disease. *Mikhailova, A. A., Gradova, L. I.*, p. 50

Опыт лечения острого лейкоза трансфузиями крови, содержащей большое количество лейкоцитов. *Элькис, Н. Я., Берман, М. А., Вакуленко, С. А.* (Гематологическое отделение Харьковского областного онкологического диспансера.) с. 51. — Experience in the treatment of acute leukemia with transfusions of blood containing many leukocytes.

Elkis, N. Ya., Berman, M. A., Vakulenko, S. A., p. 51

Случай первичного амилоидоза с портальной гипертонией и эритроцитозом. *Гуглин, Э. Р., Денисова, О. П.* (Кафедра факультетской терапии Волгоградского медицинского института и Клиническая больница, Вольгоград.) с. 52. — A case of primary amyloidosis with portal hypertension. *Guglin, E. R., Denisova, O. P.*, p. 52

Рефрактерная сидероахрестическая анемия как промежуточная фаза перехода хронической парциальной гипопластической анемии в острый эритромиелоз. *Берлинер, Г. Б.* (Кафедра терапии медицинского факультета Петрозаводского университета и гематологическое отделение Республиканской больницы Министерства здравоохранения КАССР.) с. 54. — Refractory sideroachrestic anaemia as an intermediate phase of a change of chronic partial hypoplastic anaemia into acute erythromyelosis. *Berliner, G. B.*, p. 54

Случай парциальной мегакариоцитарной гипоплазии. *Геллер, Л. И.*, (Кафедра госпитальной терапии Хабаровского медицинского института.) с. 55. — A case of partial megakariocytic hypoplasia. *Geller, L. I.*, p. 55

Вопросы организации диспансеризации больных лейкозами. *Лебедев, В. Н.* (Гематологическое отделение Сочинского онкологического диспансера.) с. 57. — Dispensary system for patients suffering from leukemia. *Lebedev, V. N.*, p. 57

Проблемы гематологии и переливания крови (Москва) 16 (1971) №8

Морфологическая, биохимическая характеристика и жизнеспособность отмытых эритроцитов, предназначенных для операций с искусственным кровообращением. *Виноградов-Финкель, Ф. Р., Терентьева, Э. И., Сухова, А. Г., Воробьева, Г. С., Тальская, И. Н., Лифляндский, Д. Б. Дорофеева, Т. Н., Самсонова, Н. Н.* (Центральный институт гематологии и переливания крови Минздрава СССР и Институт сердечно-сосудистой хирургии АМН СССР, Москва) с. 3. — Morphological and biochemical characteristics and viability of washed erythrocytes intended for extracorporeal circulation. *Vinograd-Finkel, F. R., Terentieva, E. I., Sukhova, A. G., Vorobieva, G. S., Talskaya, I. N., Liflyandsky, D. B., Dorofeeva, T. N., Samsonova, N. N.*, p. 3.

Изучение приживаемости эритроцитов крови, консервированной по реценту ЦОЛИПК 12А. *Олдурова, С. В., Голубев, В. Л.* (Лаборатория консервирования крови Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 7. — Viability of erythrocytes preserved by the Tsolipk 12A method. *Oldurova, S. V., Golubeva, V. L.*, p. 7.

Поиски новых способов консервирования крови с целью улучшения сохранности ее гемостатических свойств. *Федорова, З. Д., Котовщикова, М. А., Кацадзе Ю. Л.* (Лаборатория свертывания крови Ленинградского научно-исследовательского института гематологии и переливания крови). с. 11. — New methods of blood preservation for improved preservation of haemostatic properties. *Fedorova, Z. D., Kotovtstchikova, M. A., Katadze, Yu. L.*, p. 11

Изоиммунизация к форменным элементам крови при гемотрансфузиях и беременностях. *Нерсисян, В. М., Шамирханян, С. Т., Погосян, А. С., Щербакова Л. П. Акопян, Л. П., Балаян, Л. Х.*, (Армянский научноисследовательский институт гематологии и переливания крови и кафедра акушерства и гинекологии Ереванского медицинского института) с. 18. — Isoimmunization to formed elements in hemotransfusion and pregnancy. *Nersisyan, V. M., Shamirkhanyan, S. T., Pogosyan, A. S., Stcherbakova, L. N., Akopyan, L. P., Balayan, L. A.*, p. 18.

Влияние различных режимов замораживания на пролиферативную активность и дифференцировку родоначальных клеток костного мозга. *Федотенков, А. Г., Дашлова Л. А., Алеексеева Л. П* (Лаборатория консервирования и культивирования костного мозга Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 21. — The effect of various freezing methods on

proliferative activity and differentiation of bone marrow stem cells. *Fedotenkov, A. G., Danilova, L. A., Alexeeva, L. P.*, p. 21

К вопросу и влиянии многократного плазмофереза на организм донора. *Константинов, В. Н., Куренкова, Л. В., Зайцева, Л. В.* (Кафедра патологической физиологии Актюбинского медицинского института и Областная станция переливания крови) с. 25. — Effect of numerous repeated plasmapheresis on the donor. *Konstantinov, V. N., Kurenkova, L. V., Zaytseva, L. V.*, p. 25

Вазоактивные свойства консервированной крови. *Кузьмин, И. В.* (2-я кафедра хирургии Центрального института усовершенствования врачей, Москва) с. 27. — Vasoactive properties of preserved blood. *Kuzmin, I. V.*, p. 27

Механизмы активации фибринолитической системы при хирургических вмешательствах. *Уманский, М. А.* (Киевский научно-исследовательский институт гематологии и переливания крови) с. 33. — Mechanism of activation of fibrinolytic system in surgical interventions. *Umansky, M. A.*, p. 33

Влияние комплексной терапии на гемокоагуляцию при хроническом лимфо- и миелолейкозе. *Серикова, А. З.* (Кафедра факультетской терапии Военно-медицинской академии им. С. М. Кирова, Ленинград) с. 38. — Influence on coagulation of complex therapy of chronic lympho- and myeloleukemia. *Serikova, A. Z.*, p. 38

О неврологических изменениях при геморрагической тромбоцитемии. *Певзнер, Т. Н., Фриновская, И. В.* (Гематологическая клиника Центрального института гематологии и переливания крови Минздрав СССР, Москва) с. 42. — Neurologic changes in hemorrhagic thrombocytemia. *Pevzner, T. N., Frinovskaya, I. V.*, p. 42

Тромбопоэтическая активность крови и реактивный тромбоцитоз. *Баранов, А. Е.* с. 47. — Thrombopoietic activity of blood and reactive thrombocytosis. *Baranov, A. E.*, p. 47

Ультрабыстрое замораживание крови человека в виде гранул и изучение ее серологических свойств. *Киселев, А. Е., Подольский, М. В., Смирнова, Л. С., Скуръят, Э. Н., Ичаловская, Т. А., Пискунова, Т. М.* (Лаборатория лиофилизации биопрепаратов и лаборатория по изучению и стандартизации групп крови Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 52. — Ultra-rapid freezing of human blood in the form of granules and a study of its serolog ical properties. *Kiselev, A. E., Podolsky, M. V., Smirnova, L. S., Skuryat, E. N., Itchalovskaya, T. A., Piskunova, T. M.*, p. 52

Экспресс-метод выявления антигенов системы Rh—Hr с помощью протеина. *Сахаров, Р. С., Лазаренко, Ю. П.* (Лаборатория по изучению и стандартизации групп крови Центрального института гематологии и переливания крови Минздрава ССВР, Москва) с. 54. — Express method of detection of antigens of the Rh—Hr system with the aid of protein. *Sakharov, R. S., Lazarenko, Yu. P.*, p. 54

Проблемы гематологии и переливания крови (Москва) 16 (1971) №9

Противотканевые антитела у больных с заболеваниями системы крови. *Базарнова, М. А.* (Харьковский институт усовершенствования врачей) с. 3 — Antitissue antibodies in blood diseases. *Bazarnova, M. A.*, p. 3

D-парапротеинемия. *Андреева, Н. Е., Фузайлова, Л. М., Герман, Г. П., Миронова, И. В.* (3-я кафедра терапии Центрального института усовершенствования врачей, Научно-исследовательский институт эпидемиологии и микробиологии Минздрава РСФСР, Московская клиническая больница № 6) с. 8. — D-Paraproteinemia. *Andreeva, N. E., Fuzailova, L. M., German, G. P., Mironova, I. V.*, p. 8

Цитогенетические исследования при моноклоновых гаммапатиях. *Захарова, А. В., Мокеева, Р. А.* (Цитологическая лаборатория и гематологическая клиника Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 13 — Cytogenetic studies in monoclonic gammopathies. *Zakharova, A. V., Mokeeva, R. A.*, p. 13

К вопросу клинико-цитологической диффе-

ренциации острых лейкозов. *Терентьева, Э. И., Ковалева, Л. Г., Дульцина, С. М., Исаев В. Г.* (Гематологическая клиника, цитологическая лаборатория Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 23. — Clinico-cytologic differentiation of acute leukemias. *Terentieva, E. I., Kovaleva, L. G., Dultsina, S. M., Isaev, V. G.*, p. 23

К вопросу о саркоматозе лимфатических узлов при хроническом миелолейкозе. *Флейшман, Е. В., Волкова, М. А., Дубровская, В. С., Маргулис, М. И., Крыщенко, Г. П.* (Академическая группа при Акад. МН СССР, Москва) с. 30. — Lymph node sarcomatosis in chronic myeloid leukemia. *Fleischman, E. V., Volkova, M. A., Dubrovskaya, V. S., Margulis, M. I., Kravchenko, G. P.*, p. 30

К вопросу о морфологических особенностях хронического лимфолейкоза. *Базарнова, М. А.* (Харьковский институт усовершенствования врачей) с. 36. — Morphologic peculiarities of chronic lymphoid leukemia. *Bazarnova, M. A.*, p. 36

Некоторые особенности лимфоцитов при лимфопролиферативных заболеваниях. *Каюмова, М. Г.* (Гематологическое отделение Института экспериментальной и клинической онкологии АМН СССР, Москва) с. 41. — Peculiarities of lymphocytes in lymphoproliferative diseases. *Kayumova, M. G.*, p. 41

Радиоизотопное сканнирование печени у больных лимфогранулематозом. *Зубовский, Г. А., Филькова, Е. М., Рязанская, Г. В.* (Рентгенотерапевтический отдел и лаборатория радиоизотопной диагностики Московского научно-исследовательского рентгенорадиологического института Министерства здравоохранения РСФСР) с. 44. — Radioisotopic scanning of the liver in lymphogranulomatosis. *Zubovsky, G. A., Filkova, E. M., Ryazanskaya, G. V.*, p. 44

Лечение лимфогранулематоза натуланом. *Кондратьева, А. П., Лорие, Ю. Г.* (Институт экспериментальной и клинической онкологии АМН СССР, Москва) с. 49. — Natulan treatment of lymphogranulomatosis. *Kondratieva, A. P., Lorie, Yu. G.*, p. 49

Изменения глюкокортикоидной функции коры надпочечников у больных хроническим лимфолейкозом при лечении преднизолоном и нероболом. *Леонова, В. Н.* (Кафедра факультетской терапии Казанского медицинского института им. С. В. Курашева) с. 55. — Glucocorticoid function in chronic lymphoid leukemia treated with prednisolone and nerobol. *Leonova, V. N.* p. 55

Об аэробном гликолизе миелоидных клеток в связи с возможностью использования этого показателя для идентификации тканевой принадлежности малодифференцированных клеток крови. *Свирновский. А. И.* (Лейкозологическая лаборатория Белорусского научно-исследовательского института гематологии и переливания крови) р. 58. — Aerobic glycolysis of myeloid and lymphoid cells: use of this index for identification of undifferentiated blood cells. *Svirnovsky, A. I.*, p. 58

Проблемы гематологии и переливания крови (Москва) 16 (1971) № 10

К вопросу о нарушении обмена железа у больных гипо- и апластической анемией. *Турбина, Н. С., Родина, Р. И., Соболева, Ю. Г., Воронина, А. Н., Шитикова, М. Г., Розанова, Н. С., Фетисов, В. В., Реук, В. В., Орлов, Г. П., Лаврова, О. П., Фром, А. А., Файнштейн, Ф. Э.* (Гематологическое отделение, клиническая лаборатория, цитологическая лаборатория, производственно-экспериментальная лаборатория Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 3. — Causes of iron metabolism disturbance in hypo- and aplastic anemia. *Turbina, N. S., Rodina, R. I., Soboleva, Yu. G., Voronina, A. N., Shitikova, M. G., Rozanova, N. S., Fetisov, V. V., Reuk, V. V., Orlov, G. P., Lavrova, O. P., From, A. A., Fainshtein, F. E.*, p 3

Сидеробластоз как показатель нарушения обмена железа при гипо- и апластической анемии. *Фетисов, В. В., Турбина, Н. С., Соболева, Ю. Г.* (Цитологическая лаборатория, гематологическая клиника и клиническая лаборатория Центрального института гематологии и перели-

вания крови Минздрава СССР, Москва) с. 9. — Sideroblastosis as an index of disturbed iron metabolism in hypo- and aplastic anemia. *Fetisov, V. V., Turbina, N. S., Soboleva, Yu. G.*, p. 9

О критерии эритропоэтической активности костного мозга пти анемических состояниях. *Мосягина Е. Н., Репина Ф. Б.* (Гематологическая лаборатория Института педиатрии АМН СССР, Москва) с. 15. — Criterion of bone marrow erythropoetic activity in anemic conditions. *Mosyagina, E. N., Repina, F. B.*, p. 15

Содержание церулоплазмина при циррозах печени и анемиях. *Баронина, М. А., Замчий, А. А., Жеребцов, Л. А., Михайлова, Л. И.* (Гемотерапевтическая клиника Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 18. — Coeruloplasmin content in liver cirrhosis and anemias. *Baronina, M. A., Zamchy, A. A., Zherebtsov, L. A., Mikhailova, L. I.*, p. 18

Эритропоэз и синтез ДНК эритроиндными клетками костного мозга больных хроническими диффузными гломерулонефритами. *Каримова Г. Т., Плоткин, В. Я.* (Пропедевтическая терапевтическая клиника I Ленинградского медицинского института им. И. П. Павлова) с. 22. — Erythropoiesis and DNA synthesis by marrow erythroid cells in chronic diffuse glomerulonephritis. *Karimova, G. T., Plotkin, V. Ya.*, p. 22

Роль эритроцитов в ретракции кровяного сгйстка. *Кузник, Б. И., Красик, Я. Д.* (Кафедра нормальной физиологии и кафедра факультетской терапии Читинского медицинского института) с. 25. — Role of erythrocytes in blood clot retraction. *Kuznik, B. I., Krasik, Ya. D.*, p. 25

Влияние переливаний крови различных сроков хранения на некоторые функции организма больных железодефицитной анемией. *Михайлова, Л. И., Родина, Р. И., Шарова, Ю. А., Дубровина, Н. А., Мелихова, О. П., Кочина, Е. Н., Иванова, А. Н.* (Гемотерапевтическое отделение Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 29. — Effect of transfusion of blood stored for various periods in patients suffering from iron deficiency anemia. *Mikhailova, L. I., Rodina, R. I., Sharova, Yu. A., Dubrovina, N. A., Melikova, O. P., Kochina, E. N., Ivanova, A. N.* p. 29

Экспериментальное изучение действий массивных обменных гемотрансфузий. *Скачилова, Н. Н., Рудаев, Я. А., Гласко, Е. Н., Позина, М. С.* (Центральный институт гематологии и переливания крови Министерства здравоохранения СССР и Институт сердечно-сосудистой хирургии им. А. Н. Бакулева АМН СССР, Москва) с. 34. — Experimental study of the action of massive exchange transfusions. *Skachilova, N. N., Rudayev, Ya. A., Glasko, E. N., Pozina, M. S.*, p. 34

Применение рингер-лактатного раствора при лечении острой кровопотери в эксперименте. *Смирнова, И. Л., Козинер, В. Б., Розенберг, Г. Я., Хайло, Г. В.* (Лаборатория кровезаменителей и фракционирования белков крови и патологической физиологии Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 36. — Use of Ringer-lactate in the treatment of acute experimental blood loss. *Smirnova, I. L., Koziner, V. B., Rozenberg, G. Ya., Khailo, G. V.*, p. 36

Экспериментальное изучение механизма действия переливания крови на функциональное состояние печени. *Абесадзе, А. И., Эгнаташвили, Ш. В.* (Экспериментальное отделение Института гематологии и переливания крови Министерства здравоохранения Грузинской ССР, Тбилиси) с. 42. — Effect of blood transfusion on liver function. *Abesadze, A. I., Egnatashvili, Sh. V.*, p. 42

Гистохимические изменения в печени под влиянием полиглюкина. *Туревской, А. А., Маслаков, Д. А., Лагодский, Я. В., Шаланда, Т. И.* (Кафедра гистологии и кафедра патофизиологии Гродненского медицинского института) с. 45. — Histochemical change in the liver under the effect of polyflucine. *Turevskoy, A. A., Maslakov, D. A., Lagodsky, Ya. V., Shalanda, T. I.*, p. 45

Получение стандарта эритропоэтина С и изучение его активности. *Гудим, В. И., Москалева, Г. П., Корецкая, Т. И.,*

Иванова, В. С., Розенберг, Г. Я. (Лаборатория кровезаменителей и фракционирования белков крови и лаборатория патофизиологии Центрального института гематологии и переливания кррови Минздрава СССР, Москва) с. 48. — Standard erythropoietin C and its activity. *Gudim, V. I., Moskaleva, G. P., Koretskaya, T. I., Ivanova, V. S., Rozenberg, G. Ya.*, p. 48

Взаимодействие фактора Хагемана с поверхностями. *Зубаиров, Д. М., Ассадулина, З. З., Попова, Л. Г.* (Кафедра биохимии Казанского медицинского института) с. 49. — Surface effet of Hageman's factor. *Zubairov, D. M., Assadulina, Z. Z., Popova, L. G.*, p. 49

Некоторые вопросы консервирования костного мозга с поливинилпирролидоном при температуре —40°. *Михайлов, В. Г., Иоффе, А. Л.* (Лаборатория консервирования тканей Узбекзкого института гематологии и переливания крови, Ташкент) с. 53. — Certain problems of bone marrow preservation with polyvinylpyrrolidone at a temperature of —40°C. *Mikhailov, V. G., Joffe, A. L.*, p. 53

Применение типирующих антилейкоцитарных сывороток для подбора доноров костного мозга. *Климова, К. Н., Локтев, А. Ф., Серова, Л. Д., Шабалин, В. Н., Абдулкадыров, К. М., Бэм, Э. К.* (Лаборатория изосерологии Ленинградского института гематологии и переливания крови) с. 56. — Typing of antileucocytic sera for the choice of marrow donors. *Klimova, K. N., Loktev, A. F., Serova, L. D., Shabalin, V. N., Abdulkadyrov, K. M., Bem, E. K.*, p. 56

Случай несфероцитарной гемолитической анемии, обусловленной дефицитом активности пируваткиназы эритроцитов. *Ермильченко, Г. В., Идельсон, Л. И., Щербак, Е. М.* (Группа акад. АМН СССР проф. И. А. Кассирского на базе Центральной клинической больницы № 2 МПС и Московский областной научно-исследовательский клинический институт) с. 58. — Nonspherocytic haemolytic anaemia caused by deficient erythrocytic pyruvate kinase activity. *Ermilchenko, G. V., Idelson, L. I., Shcherbak, E. M.*, p. 58

Случай гемотрансфузионного шока с геморрагическим диатезом. *Женчевский, Р. А.* (Кафедра хирургических болезней Ставропольского медицинского института) с. 60. — Blood transfusion shock with hemorrhagic diathesis. *Zhenchevsky, R. A.*, p. 60

Замер и транспортировка белковых растворов в производстве препаратов крови. *Скобелев, Л. И., Фром, А. А., Михайлов, Г. В.* (Эксперимательно-производственная лаборатория Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 61. — Volumetric assessment of protein solutions and their transportation in the production of blood preparations. *Skobelev, L. I., From, A. A., Mikhailov, G. V.*, p. 61

Приспособление к замораживателю ZZ 150/50. *Лущенков, Н. Д., Денисов, А. В.* (Севастопольская станция переливания крови) с. 63. — A device for the freezer ZZ 150/50. *Lushchenkov, N. D., Denisov, A. V.*, p. 63

Проблемы гематологии и переливания крови (Москва) 16 (1971) № 11

Анализ теории переливания крови академика А. А. Богомольца с позиций диалектического материализма. *Белова, А. А.* (Центральный институт гематологии и переливания крови Минздрава СССР, Москва) с. 3. — Analysis of academician A. A. Bogomoletz's theory of blood transfusion from the aspects of dialectic materialism. *Belova, A. A.*, p. 3

Наш опыт хирургического лечения заболеваний системы крови. *Карташевский, Н. Г., Сенчило, Е. А.* (Хирургическая клиника Ленинградского института гематологии и переливания крови). с. 7. — Surgical treatment of haematologic diseases. *Kartashevsky, N. G., Senchilo, E. A.*, p. 7

Пути снижения риска спленэктомии при гематологических заболеваниях. *Епифанов, Н. С., Журавлев, В. А., Молчанов Ю. И.* (Кировский институт гематологии и переливания крови) с. 11. — Ways of reducing the hazard of splenectomy in hematological diseases. *Epifanov, N. S., Zhuravlev, V. A., Molchanov, Yu. I.*, p. 11

К вопросу о клинике, диагностике и терапии болезни Гоше. *Покровский, П. И., Цела, Л. С.* (Хирургическая клиника Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 15. — Clinical picture, diagnosis and therapy of Gaucher's disease. *Pokrovsky, P. I., Tseia, L. S.*, p. 15

Профилактика и лечение кровотечений при оперативных вмешательствах у больных гемофилией. *Караванов, А. Г. Уманский, М. А., Демидюк, П. Ф., Скляренко, Е. Т., Гранул Ю. Л., Стаковецкая, З. С.* (Киевский институт гематологии и переливания крови) с. 19. — Prophylaxis and treatment of hemorrhage in surgical interventions in hemophilics. *Karavanov, A. G., Umansky, M. A., Demidyuk, P. F., Sklyarenko, E. T., Granul, Yu. L., Stakovetskaya, Z. S.*, p, 19

Особенности гемокоагуляции у больных, оперированных в условиях искусственного кровообращения с включением в состав перфузата отмытых эритроцитов. *Бураковский, В. И., Лифляндский, Д. Б., Поспелова, Е. П., Воробьева, Г. С., Дорофеева, Т. Н., Самсонова, Н. Н.* (Институт сердечно-сосудистой хирургии АМН СССР и Центральный институт гематологии и переливания крови Минздрава СССР, Москва) с. 23. — Peculiarities of hemocoagulation in patients operated under extracorporeal circulation with washed erythrocytes. *Burakovsky, V. I., Lifliandsky, D. B. Pospelova, E. P., Vorobyeva, G. S., Dorofeeva, T. N., Samsonova, N. N.*, p. 23

Вопросы переливания крови при искусственном кровообращении. *Соловьев, Г. М., Радзивил, Г. Г.* (Иститут трансплантации органов и тканей АМН СССР, Москва) с. 27. — Problems of blood transfusion in extracorporeal circulation. *Soloviov, G. M., Radzivil, G. G.*, p. 27

Лечение осложнений со стороны почек и легких у больных с тяжелой травмой. *Золотокрылина, Е. С.* (Лаборатория экспериментальной физиологии по оживлению организма и отделение реанимации при больнице им С. П. Боткина, Москва) с. 34. — Treatment of renal and pulmonary complications in patients suffering from traumatic shock. *Zolotokrylina, E. S.*, p. 34

Кровь внезапно умерших и ее применение при лечении больных с травматическим шоком. *Пафомов, Г. А., Жилис, Б. Г.* (Лаборатория крови и тканей и отдел анестезиологии и реанимации Института скорой помощи им. Н. В. Склифосовского, Москва) с. 38. — Blood of persons who died suddenly and its use in the treatment of traumatic shock. *Pafomov, G. A., Zhilis, B. G.*, p. 38

Особенности трансфузионной терапии при реанимации акушерских больных с массивной кровопотерей на фоне нарушения гемокоагуляции. *Сполуденная, С. Т.* (Московский городской выездной центр реанимации при больнице им. С. П. Боткина и лаборатория экспериментальной физиологии по оживлению организма АМН СССР) с. 42. — Blood transfusion in reanimation of obstetric patients with massive blood loss due to coagulation disturbances. *Spoludennaya, S. T.*, p. 42

Опыт переливания консервированной крови разных сроков хранения с гемостатической целью. *Романяк, М. И Ротенберг, Д. Л., Кулевник, И. И.* (Кафедра общей хирургии Ивано-Франковского медицинского института) с. 46. — Transfusion for hemostatic purposes of blood stored for various periods. *Romanyak, M. I., Rotenberg, D. L., Kulevnik I. I.*, p. 46

Трансфузионная терапия белковой недостаточности у больных при ожоговом истощении. *Федоровский, А. А., Клименко, Л. Ф., Шмушко, Р. Я.* (Киевский ожоговый центр на базе Клинической больяицы № 23 им. М. И. Калинина и Киевский институт гематологии и переливания крови). с. 48. — Transfusion therapy of protein deficiency in burns. *Fedorovsky, A A., Klimenko, L. F., Shmushko, R. Ya.*, p. 48

Использование венозного русла костей для многократного введения крови и других жидкостей при лечении больных с обширными ожогами. *Атясов, Н. И.* (Всероссийский ожоговый центр на базе Горьковского института травматологии и ортопедии) с. 53. — The

use of venous bed of the bones for multiple transfusion of blood and other fluids in the treatment of extensive burns. *Atyasov, N. I.*, p. 53

Изменение проницаемости капилляров и белкового равновесия между кровью и лимфой при термических ожогах. *Фарманов, Р. Т.* (Азербайджанский институт гематологии и переливания крови, Баку) с. 56. — Changes in capillary permeability and of protein equilibrium between the blood and lymph in thermal injuries. *Farmanov, R. T.*, p. 56

Лейкоцитарные антигены человека. *Белоцкий, С. М., Говалло, В. И.* (Центральный институт травматологии и ортопедии Минздрава СССР, Москва) с. 59. — Human leukocytic antigens. *Belotsky, S. M., Govallo, V. I.*, p. 59

Проблемы гематологии и переливания крови (Москва) 16 (1971) № 12

Длительные ремиссии острого лейкоза у детей. *Курмашов, В. И., Кошель, И. В.* (2-е отделение старшего детского возраста Института педиатрии АМН СССР, Москва) с. 3. — Prolonged remissions of acute leukemia in children. *Kurmashov, V. I., Koshel, I. V.*, p. 3

Кинетические аспекты химиотерапии острого лейкоза у детей. *Владимирская, Е. Б., Кошель, И. В., Курмашев, В. И.* (2-я клиника старшего детского возраста, клинико-гематологическая лаборатория Института педиатрии АМН СССР, Москва) с. 6. — Kinetic aspects of chemotherapy of acute leukemia in children. *Vladimirskaya, E. B., Koshel, I., V. Kurmashov, B. I.*, p. 6

Анеуплоидные линии клеток у больных хроническим миелолейкозом в не бластных кризов. *Флейшман, Е. В., Волкова, М. А.* (Академическая группа при акад. АМН СССР проф. И. А. Кассирском, Москва) с. 10. — Aneupioid cell lines in chronic myeloleukemia not during blastic crises. *Fleishman, E. V., Volkova, M. A.*, p. 10

Некоторые морфологические и функциональные особенности лимфоцитов при лимфогранулематозе. *Каюмова, М. Г., Лорие, Ю. И.* (Гематологическое отделение Института экспериментальной и клинической онкологии АМН СССР, Москва) с. 16. — *Kayumova, M. G., Lorie, Yu. I.*, p. 16

К вопросу о частоте выявления и классе парапротеинов у гематологических больных. *Яворковский, Л. И., Удрис, О. Ю., Пушкарев, И. А., Яворковская, Е. К., Корт, С. С.* (Кафедра терапии факультета усовершенствования врачей и отдел лейкозологии Центральной научно-исследовательской лаборатории Рижского медицинского института) с. 20. — Detection and class of paraproteinemia in hematological patients. *Yavorkovsky, L. I., Udriz, O. Yu., Pushkarev, I., A., Yavorkovskaya, E. K., Kort, S. S.*, p. 20

Изменения аминокислотного состава сыворотки крови больных острым лейкозом. *Абрамович, А. Б., Ковалева, Л. Г.* (Гематологическая клиника Центрального института гематологии и переливания крови Минздрава СССР и отдел кинетики химических и биологических процессов Института химической физики АН СССР., Москва) с. 22. — Amino acid composition of serum in acute leukemia. *Abramovich, A. B., Kovaleva, L. G.*, p. 22

Бактериальная флора у больных острым лейкозом при специфическом лечении. *Дронова, О. М., Смолянская, А. З., Хватова, Н., Хватова, Н. В., Лорие, Ю. И.* (Институт экспериментальной и клинической онкологии АМН СССР, Москва) с. 27. — Bacterial flora in acute leukemia subjected to specific therapy. *Dronova, O. M., Smolyanskaya, A. Z., Khvatova, N. V., Lorie, Yu. I.*, p. 27

Серологическая характеристика атипичных микробных агентов, выделяемых из крови и костного мозга больных лейкозом. *Мартынова, В. А., Голосова, Т. В., Ермакова, Г. Л.* (Бактериологическая лаборатория Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 30. — Serological characteristics of atypical microbial agents isolated from the blood and marrov of leukemic Patients. *Martynova, V. A., Golosova, T. V. Ermakova, G. L.*, p. 30

Хроническое течение перевивного лейкоза Мазуренко. *Яковлева, Л. С., Жарова,*

Е. И. (Лаборатория вирусологии лейкозов и лаборатория системных заболеваний крови Института экспериментальной и клинической онкологии АМН СССР, Москва) с. 34. — Chronic course of transplanted leukemia. *Yakovleva, L. S., Zharova, E. I.*, p. 34

Активность дегидрогеназ лимфоцитов в иммуногенезе. *Нарциссов, Р. П., Катосова, Л. К.* (Лаборатория цитохимии и лаборатория микробиологии Института педиатрии АМН СССР, Москва. с. 37. — Activity of lymphocyte dehydrogenases in immunogenesis. *Nartsissov, R. P., Katosova, L. K.*, p. 37

Содержание нуклеиновых кислот в субклеточных структурах в норме и при экспериментальном лейкозе у крыс. *Бала Ю. М., Лифшиц, В. М.*, (Кафедра факультетской терапии и Центральная научно-исследовательская лаборатория Воронежского медицинского института) с. 41. — Nucleic acid content of subcellular structures under normal conditions and in experimental leukemia in rats. *Bala, Yu. M., Lifshitz, V. M.*, p. 41

Влияние антилимфоцитарной сыворотки на репопулирующие стволовые кроветворные клетки. *Чертков, И. Л., Леменева, Л. Н.*, (Лаборатория миелогемотерапии лучевой болезни Центрального института гематологии и переливания крови Минздрава СССР, Москва) с. 44. — Effect of antilymphocytic serum on repopulating stem cells. *Chertkov, I. L., Lemeneva, L. N.*, p. 44

Высушивание растворов альбумина в лотках из нержавеющей стали. *Поздняков, В. А., Гельфанд, Э. М., Фойгель, Г. А.* (Одесская областная станция переливания крови) с. 53. — Desiccation of albumin solutions in stainless steel containers. *Pozdnyakov, V. A., Gelfand, E. M., Foigel, G. A.*, p. 53

К вопросу о получении водонерастворимых протеолитических ферментов. *Антонян, Р. К., Никитенко, А. А., Фром, А. А.* (Экспериментально-производственная лаборатория компонентов и препаратов крови Минздрава СССР, Москва) с. 55. — Water-insoluble proteolytic enzymes. *Antonyan, R. K., Nikitenko, A. A., From, A. A.*, p. 55

Revue Française de Transfusion (Paris) **16** (1973) No. 3

Thrombopénie néonatale avec incompatibilité fœto-maternelle dans le système HL-A. *Salet, J., Colombani, J., Girot, R., Beaufils, C., Lejeune, C., Fajgenbaum, J.* (Hôpital Bretonneau, 75018 Paris, France), p. 243

Observations sur un anticorps rare: l'anti-Gerbich. *Muller, A., André-Liardet, J., Garretta, M., Brocteur, J., Moullec, J.* (Centre National de Transfusion Sanguine, 75739 Paris Cedex 15, France), p. 251

Variabilité d'expression d'un gène A faible dans les érythrocytes et les sécrétions dans une même fratrie. *Garretta, M., Muller, A., André, J., Moullec, J.* (Centre National de Transfusion Sanguine, 75739 Paris Cedex 15, France), p. 259

Fréquence des déficits isolés en IgA dans la population normale. Etude sur 15 200 donneurs de sang. *Fine, J. M., Moullec, J., Lambin, P., Frommel, D.* (Centre National de Transfusion Sanguine, 75739 Paris, France), p. 269

Anti-immunoglobulines humaines. Présence d'anti-IgD et d'anti-IgA dans les sérums humains. *Rivat, L., Rivat, C., Ropartz, C.* (Centre Départemental de Transfusion Sanguine, 76230 Bois-Guillaume, France), p. 279

Etudes sur les contrôles de stérilité du plasma. *Arnaud, R., Borderon, E., Borderon, J. C., Loulergue, J.* (Centre Régional de Transfusion Sanguine de Tours, Centre Hospitalier Régional "Bretonneau", 37033 Tours Cedex, France), p. 289

Evolution des indications de l'exsanguino-transfusion chez le nouveau-né. Critères de renouvellement (A propos de 1200 cas). *Streiff, F., Raffoux, C., Genetet, B., Dejean, M.* (Centre Régional de Transfusion Sanguine, 54-Nancy, France), p. 299

Surprises du groupage de routine. *Chauvat, D., Mauze, J., Richard, A., Lescaroux, A.* (Centre Départemental de Transfusion Sanguine, 36 Châteauroux, P. B. 136, France), p. 311

Revue Française de Transfusion (Paris) **16** (1973) No. 4

Dépistage automatique de la syphilis sur Groupamatic. Résultats préliminaires.

Garretta, M., Paris-Hamelin, A., Gener, J., Muller, A., Matte, C., Vaisman, A., Moullec, J. (Centre National de Transfusion Sanguine, 75739 Paris Cedex 15, France), p. 349

Recherche d'anticorps anti HL-A après transfusions lors de circulation extracorporelle. *Tongio, M. M., Falkenrodt, A., Weill, D., Kieny, R., Kieny, M. T., Mayer, S.* (Institut d'Hématologie, Centre de Transfusion Sanguine, Hôpital Civil, 67000 Strasbourg, France), p. 365

Quelques aspects des anti-immunoglobulines chez les polytransfusés. *Salmon, Ch., Ropars, C., Gerbal, A., Habibi, B., Andreu, G., Salmon, D.* (Centre Départemental de Transfusion Sanguine, 75571 Paris Cedex 12, France), p. 373

Teneurs en IgE des sérums de malades polytransfusés. *Cartron, J.-P., Ropars, C., Salmon, Ch., Salmon, D.* (Centre Départemental de Transfusion Sanguine, 75012 Paris, France), p. 385

Anticorps anti-immunoglobulines chez les sujets atteints de déficit immunitaire. *Caldera, L. H., Ropars, C., Griscelli, C., Homberg, J. C., Salmon, Ch.* (Centre Départemental de Transfusion Sanguine, 75012 Paris, France), p. 393

Groupes sanguins ABO et Rh (D) dans la population turque. *Büyükyüksel, C.* (Kizilay Kan Merkezi, Topkapi, Istanbul, Turkey), p. 403

Revue Française de Transfusion (Paris) **17** (1974) No. 1

Trois observations de phénotype érythrocytaire "B acquis". L'acquisition de la spécificité pseudo-B paraît s'effectuer aux dépens de la spécificité A_1. *Reznikoff-Etievant, M. F., Garretta, M., Sylvestre, R., Reviron, J., Tonthat, H., Rochant, H.* (Centre d'Hémobiologie C.H.U. Henri Mondor, 94010 Créteil, France), p. 15

Sous-groupes faibles de A et de AB. Fréquences calculées sur 150.000 échantillons. *Garretta, M., Muller, A., Gener, J., Moullec, J.* (Centre National de Transfusion Sanguine, 75739 Paris Cedex 15, France), p. 41

Etude de quelques propriétés de la lectine anti (A + B) d'Hygrophorus hypothejus Fr. Fixation, élution, inhibition. *Guillot, J., Coulet, M.* (Faculté de Pharmacie, B. P. 38 63001 Clermont-Ferrand, Cedex, France), p. 49

Recherche de l'antigène Australia (HB) et de l'anticorps correspondant chez les mères et leur nouveau-né à Dakar. *Diébolt, G., Linhard, J., Darassé, D., Diadhiou, F.* (Centre de Transfusion Sanguine, Hôpital Le Dantec, Dakar, Senegal), p. 59

Etude clinique, épidémiologique et biochimique d'une population de donneurs de sang porteurs de l'antigène de l'hépatite B. *Chicot, D., Delaruelle, S.* (Centre de Transfusion et d'Hémobiologie du Groupe Hospitalier Pitié-Salpêtrière, 75013 Paris, France), p. 75

Recherche de l'antigène Australia dans les produits de fractionnement du plasma humain. *Lévêque, Ph., North, M. L., Malgras, J., Drouet, J., Amouch, P.* (Centre de Transfusion Sanguine, 67000 Strasbourg, France), p. 87

Scandinavian Journal of Haematology (Copenhagen) **11** (1973) No. 1

Pathophysiology of "hypersplenism syndrome". Remarks about definition and estimation of the splenic erythrocyte pool. *Christensen, B. E.* (Medical Department C, Gentofte Hospital, DK-2900 Copenhagen, Hellerup, Denmark), p. 5

Levels of transcobalamin II in normal human serum measured with zirconyl phosphate gel. *Sonneborn, D. W., Baskerville, A. B., Regelson, W.* (Department of Anatomy, Virginia Commonwealth University, Medical College of Virginia, Richmond, Va. 23219), p. 8

Perturbation of generation cycle of human leukaemic blast cells in vivo by daunomycin. *Ernst, P.* (Division of Haematology, Department of Medicine A, Rigshospitalet, DK-2100 Copenhagen Ø, Denmark), p. 13

Difference in uptake tritiated thymidine by myelocytes from bone marrow and spleen in chronic myeloid leukaemia. *Brandt, L.* (Department of Internal Medicine, University Hospital, 220 05 Lund 5, Sweden), p. 23

Inheritance of selective malabsorption of vitamin B_{12}. *Furuhjelm, U., Nevanlinna H. R.* (FRC Blood Transfusion Service, 00310 Helsinki 31, Finland), p. 27

Ultrastructural visualization of the thrombin-induced platelet release reaction. *Droller, M. J., Fox, M. C.* (Stanford University Medical Center, Palo Alto, Calif. 94305), p. 35

The laboratory diagnosis of low-graded disseminated intravascular coagulation. A study in rabbits. *Slaastad, R. A., Jeremic, M.* (Haematological Research Laboratory, Medical Department IX, Ullevål Hospital, Oslo 3, Norway), p. 50

Effect of cortisol on the eosinophils in the rat spleen. Autoradiographic studies. *Bro-Rasmussen, F.* (Anatomy Department B, University of Copenhagen, DK-2100 Copenhagen Ø, Denmark), p. 59

The increase in the number of circulating megakaryocytes and blood platelets in rats after surgery. *Pedersen, N. T.* (University of Copenhagen, Anatomy Department C, DK-2200 Copenhagen N, Denmark), p. 71

Haematopoiesis in busulphan-treated mice. A comparison between two different stem cell assays. *Josvasen, N., Bøyum, A.* (Institute for Medical Biology, N-9001 Tromsø, Norway), p. 78

IgA deficiency and autoimmune haemolytic anaemia. *Bergström, K., Britton, M., Hanson, L. A., Holm, G., Kardos, M., Wester, P. O.* (Department of Clinical Chemistry, Seraphimer Hospital, Stockholm, Sweden), p. 87

Demonstration of spleen colonies on grafted spleens in the radiation chimera. *Boynton, A. N., Crouse, D. A., Sharp, J. G.* (Radiation Research Laboratory, University of Iowa, Iowa City, Iowa 52240), p. 92

Scandinavian Journal of Haematology (Copenhagen) **11** (1973) No. 2

Chronic lymphocytic leukaemia in 5 siblings. *Schweitzer, M., Melief, C. J. M., Ploem, J. E.* (Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, P.O.B. 9190, Amsterdam, The Netherlands), p. 97

Glucose-6-phosphate dehydrogenase deficiency and myelofibrosis. *Selroos, O., Vuopio, P.* (Fourth Department of Medicine, Helsinki University Central Hospital, 00170 Helsinki 17, Finland), p. 106

Periodic acid-Schiff positive myeloblasts in chronic myelogenous leukaemia: Relation to karyotype evolution. *Pedersen, B.* (Institute of Cancer Research, Radium Station, DK-8000 Aarhus C, Denmark), p. 112

Comparative studies on the in vitro uptake of ^{3}H-cytidine and ^{3}H-uridine by normal and leukaemic lymphocytes. *Bremer, K., Schreml, W., Harriss, E. B.* (Department of Medicine, Division of Haematology, University of Essen, D-4300 Essen 1, FRG), p. 122

Autoimmune haemolytic anaemia with positive Ham and Crosby's test and scleroderma. *Loft, B., Olsen, F.* (Bispebjerg Hospital, Medical Department B, DK-2400 Copenhagen NV, Denmark), p. 131

The induction of chromosome abnormalities by melphalan in rat bone marrow cells. *Wantzin, G. L., Jensen, M. K.* (Division of Haematology, Medical Department A, Rigshospitalet, University Hospital, DK-2100 Copenhagen, Denmark), p. 135

Red cell size and uric acid in Down's syndrome. *Howell, A., Mason, A. S., Brown, E., Watts, R. W. E., Chanarin, I., McPherson, K., Ridler, M. A.* (Division of Inherited Metabolic Diseases, Medical Research Council Clinical Research Centre Harrow, Middlesex HA1 3UJ, England), p. 140

Antihaemophilic factor A (F VIII) and serum fibrin-fibrinogen degradation products in hepatic cirrhosis. *Van Outryve, M., Baele, G., De Weerdt, G. A., Barbier, F.* (Department of Internal Medicine, University of Ghent, Akademisch Ziekenhuis, B-9000 Ghent, Belgium), p. 148

Selective malabsorption of vitamin B_{12} in a Negro boy. *Buchanan, N., Geefhuysen, J., Cassel, R., Green, R.* (Department of Haematology, School of Pathology, The South African Institute for Medical Research, P.O. Box 1038, Johannesburg, South Africa), p. 153

Effect of anticonvulsive drugs on folate absorption and the cerebrospinal folate pump. *Reizenstein, P., Lund, L.* (Medical Department, Karolinska Sjukhuset, S-10401 Stockholm 60, Sweden), p. 158

Electrophoresis of blood platelets and erythrocytes. A study in healthy persons and patients with haematological diseases, prosthetic heart valves, virus infections

and hyperlipaemia. *Grøttum, K. A.* (Medical Department A, Rikshospitalet, Oslo, Norway), p. 166

Scandinavian Journal of Haematology (Copenhagen) **11** (1973) No. 3

The activation of fetal lymphocytes. *Weber, T. H., Santesson, B., Skoog, V. T.* (Minerva Institute, P.O. Box 819, 00101 Helsinki 10, Finland), p. 177

Immunological characterization of anti-haemophilic factor A related antigen in haemophilia A. *Bouma, B. N., Van Mourik, J. A., Wiegerinck, Y., Sixma, J. J., Mochtar, I. A.* (Division of Haemostasis, Department of Internal Medicine, University Hospital, Utrecht, The Netherlands), p. 184

Normal red cell survival in the rabbit. *Smith, G. N., Mollison, P. L.* (MRC Experimental Haematology Unit, St. Mary's Hospital Medical School, London, W2 1PG, England), p. 188

Blood lymphocytes in Hodgkin's disease. Increase of B-lymphocytes following extended field irradiation. *Engeset, A., Fröland, S. S., Bremer, K., H st, H.* (Det Norske Radiumhospital, Montebello, Oslo 3, Norway), p. 195

Levodopa induced Coombs positive haemolytic anaemia. *Gabor, E. P., Goldberg, L. S.* (Department of Medicine, UCLA Medical Center, Los Angeles, Calif. 90024), p. 201

Quantitation of plasma fibrinogen in the presence of fibrinogen degradation products. *Arnesen, H.* (Haematological Research Laboratory, Department IX, Ullevål Hospital, Oslo, Norway), p. 204

Red blood cell acetylcholinesterase activity and lysis in various dyshaemopoietic disorders. *Stathakis, N., Papayannis, A. G., Scliros, Ph., Gardikas, C.* (Medical Unit, Evangelismos Hospital, Athens 140, Greece), p. 210

Failure to trigger intravascular coagulation by water-induced haemolysis in rabbits. *Slaastad, R. A., Eika, C.* (Haematological Research Laboratory, Ullevål Hospital, Oslo 1, Norway), p. 217

Controlled trial of oral contraceptives in haemophilia. *Brandt, N. J., Cohn, J., Hilden, M.* (University Clinic of Pediatrics, Børnehospitalet på Fuglebakken, DK-2000 Copenhagen F, Denmark), p. 225

The relationship between red cell acetylcholinesterase activity and Ii antigenicity in leukaemia. *Scott, G. L., Dornhorst, A., Rasbridge, M. R.* (Louis Jenner Laboratories, St. Thomas' Hospital, London S.E.1. England), p. 230

The effect of iron and folic acid therapy on combined iron and folate deficiency anaemia: The results of a clinical trial. *Izak, G., Levy, Sh., Rachmilewitz, M., Grossowicz, N.* (Haematology Department, Hadassah Medical School, P.O.B. 499, Jerusalem, Israel), p. 236

Nucleotide leakage from platelets in artificial media: Prevention by albumin and other macromolecules and relation to ADP-induced platelet aggregation. *Tangen, O., Andrae, M.-L., Nilsson, B. E.* (Department of Experimental Medicine, Pharmacia AB, Box 604, S-75125 Uppsala 1, Sweden), p. 241

Hypergranular acute promyelocytic leukaemia with intravascular coagulation. *Stavem, P.* (Section of Haematology, Medical Department A, Rikshospitalet, Oslo 1, Norway), p. 249

Phagocytic tumour cells. *Spivak, J. L.* (Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Md. 21205), p. 253

Scandinavian Journal of Haematology (Copenhagen) **11** (1973) No. 4

A case of acute myelomonocytic leukaemia associated with myelomatosis. *Parker, A. C.* (Department of Medicine and Therapeutics, Royal Infirmary, Edinburgh, Scotland), p. 257

Clasmatocytosis in rat bone marrow lymphocytes. *Ben-Ishay, Z.* (Department of Anatomy, Hadassah Medical School, P.O.B. 1172, Jerusalem, Israel), p. 261

The NBT test using venous and capillary blood. *Björkstén, B.* (Department of Clinical Virology, University of Umea, S-90185 Umea, Sweden), p. 270

Effects of adrenergic alpha- and beta-receptor stimulation on the release of lymphocytes and granulocytes from the spleen. *Ernström, U., Sandberg, G.* (Department of Histology, Karolinska Insti-

tutet, S-10401 Stockholm 60, Sweden), p. 275

Ultrastructure of ristocetin aggregated normal human platelets: Tortuous boundaries and swollen granules. *Ts'ao, C. H., Green, D., Rossi, E. C.* (Department of Pathology, Northwestern Memorial Hospital Wesley Pavilion, Chicago, Ill. 60611), p. 287

Quantitative aspects of post-irradiation granulocytic recovery. The effect of the erythropoietic suppression subsequent to hypoxia and hypertransfusion. *Beran, M., Tribukait, B.* (Department for Medical Radiobiology, Karolinska Institutet, S-10401 Stockholm 60, Sweden), p. 298

Immunological deficiency in myelofibrosis. *Selroos, O., Skrifvars, B., Wasastjerna, C.* (Fourth Department of Medicine, Helsinki University Central Hospital, 00170 Helsinki 17, Finland), p. 307

Aplastic anaemia complicating infectious mononucleosis. *Mir, M. A., Delamore, I. W.* (Department of Clinical Haematology, Manchester Royal Infirmary, Manchester, M13 9WL, England), p. 314

Frythropoiesis inhibiting factor (EIF). The inhibitory effect of oestrogens on erythropoiesis and the content of oestrogens in the urinary EIF. *Lindemann, R.* (Barneklinikken, Rikshospitalet, Oslo 1, Norway), p. 319

Heterogeneity of enzymes in leukaemic eosinophils. *Pajdak, W., Lisiewicz, J.* (Haematological Clinic, Institute of Internal Medicine, Medical Academy, 31-501 Cracow, Poland), p. 325

IgM-producing lymphocytes in peripheral nerve in a patient with benign monoclonal gammopathy. *Forssman, O., Björkman, G., Hollender, A., Englund, N.-E.* (Department of Medicine, Central Hospital, S-501 15 Borås, Sweden), p. 332

Scandinavian Journal of Haematology (Copenhagen) **11** (1973) No. 5

The etiocholanolone test for prediction of the leukopenic effect of cytotoxic drugs. *Karjalainen, J., Wasastjerna, C.* (Department of Medicine, Kivelä Hospital, 00260 Helsinki, 26, Finland), p. 337

Iron state in regular blood donors. *Liedén, G.* (Blood Centre, Regional Hospital, S-58185 Linköping, Sweden), p. 342

Coexistence of a myelo- and lymphoproliferative disorder. *Louwagie, A. C., Desmet, V. J., Van Den Berghe, H.* (Laboratory for Physiopathology-Haematology, Department of Medicine, Akademisch Ziekenhuis St.-Rafael, B-3000 Leuven, Belgium), p. 350

A method for concentrating platelets for direct studies of platelet aggregation in thrombocytopenia. *Sanderson, J. H.* (I.C.I. Ltd., Industrial Hygiene Research Laboratories, N. Macchesfield, Cheshire, England), p. 356

The influence of fibrinogen degradation products on the Reptilase-time of plasma. *Arnesen, H., Kierulf, P., Godal, H. C.* (Haematological Research Laboratory, Department IX, Ullevål Hospital, Oslo, Norway), p. 360

The influence of haemoglobin on the fibrinolytic enzyme system. *Ogston, D., Herbert, R. J.* (Department of Medicine, Foresterhill, Aberdeen, Scotland), p. 367

Kinetic distinction of two mechanisms for platelet retention. *Cronberg, S., Holmberg, L.* (Allmänna Sjukhuset, S-21401 Malmö, Sweden), p. 372

Fibrin deposits in the Kiil dialyser. *Björnson, J., Kierulf, P., Eika, C., Godal, H. C.* (Medical Department VII, Ullevål Hospital, Oslo 1, Norway), p. 379

Clinical classification and evaluation of treatment response in acute myeloid leukaemia on the basis of differences of leukaemic cell differentiation. *Brincker, H.* (Radium Centre, Odense University Hospital, DK-5000 Odense, Denmark), p. 383

Food iron absorption in man — III. Effect of iron salt, ascorbic acid and desferrioxamine on the isotopic exchange between native food iron and an extrinsic inorganic iron tracer. *Björn-Rasmussen, E.* (Medical Department II., Sahlgrenska sjukhuset, S-41345 Göteborg, Sweden), p. 391

Pattern of the activator inhibitor in carcinoma and renal diseases. *Hedner, U., Nilsson, I. M.* (Coagulation Laboratory, Allmänna sjukhuset, S-21401 Malmö, Sweden), p. 398

The effects of antiinflammatory drugs on myeloperoxidase mediated iodination in human granulocytes. *Olofsson, T., Olsson, I.* (Research Department II., E-blocket,

Hospital of Lund, S-22005 Lund, Sweden), p. 405

Seminars in Hematology (New York) **10** (1973) No. 3

Introduction. *Miescher, P. A.* (Division of Hematology, Cantonal Hospital, 1205 Geneva, Switzerland), p. 179

Hematologic aspects of alcoholism. *Straus, D. J.* (Department of Medicine, Division of Hematology, Beth Israel Hospital, Boston, Mass. 02215), p. 183

Drug-induced aplastic anemia. *Williams, D. M., Lynch, R. E., Cartwright, G. E.* (Department of Medicine, University of Utah College of Medicine, Salt Lake City, Utah 84112), p. 195

Chloramphenicol-induced bone marrow suppression. *Yunis, A. A.* (Department of Medicine, University of Miami School of Medicine, Miami, Fla.), p. 225

Drug-induced megaloblastic anemias. *Stebbins, R., Scott, J., Herbert, V.* (Department of Medicine, VA Hospital, Bronx, N. Y. 10468), p. 235

Drug-induced methemoglobinemia. *Smith, R. P., Olson, M. V.* (Department of Pharmacology and Toxicology, Dartmouth Medical School, Hanover, N. H.), p. 253

Seminars in Hematology (New York) **10** (1973) No. 4

Drug-induced oxidative denaturation of hemoglobin. *Nagel, R. L., Ranney, H. M.* (Department of Medicine, Albert Einstein College of Medicine, Bronx, N. Y. 10461), p. 269

Immune and toxic mechanisms in drug-induced agranulocytosis. *Pisciotta, A. V.* (Blood Research Laboratory, Medical College of Wisconsin, Milwaukee, Wisc. 53226), p. 279

Drug-induced thrombocytopenia. *Miescher, P. A.* (WHO Research Centre, Hôpital Cantonal, Geneva, Switzerland), p. 311

Immune drug-induced hemolytic anemias. *Worlledge, Sh. M.* (Royal Postgraduate Medical School, London, England), p. 327

Drug-induced lupus erythematosus. *Blomgren, S. E.* (Division of Rheumatology, Scripps Clinic and Research Foundation, La Jolla, Calif. 92037), p. 345

Thrombosis et Diathesis Haemorrhagica (Stuttgart) **29** (1973) No. 2

Editorial. Molecular variants of haemophilia B. *Denson, K. W. E.* (No address)

In the beginning there were no thrombocytes blood vessels or scientists and so it was good. *Shepro, D.* (Departments of Biology and Surgery, Boston University Graduate School, and School of Medicine, Boston, Mass.) p. 220

Calibration of five different thromboplastins, using fresh and freeze-dried plasma. *Bangham, D. R., Biggs, R., Brozovic, M., Denson, K. W. E.* (Division of Biological Standards, National Institute for Medical Research, London, NW7 1AA, England), p. 228

Immunoreactive factor VIII in carriers of hemophilia A^+ and A^-. *Lechner, K.* (Central Coagulation Laboratory, First Department of Medicine, University of Vienna, Vienna, Austria), p. 240

Studies on the prolonged prothrombin time in haemophilia B. *Előd, S.* (Laboratory of Blood Coagulation, National Institute of Haematology and Blood Transfusion, 1113 Budapest, Hungary), p. 247

Studies on the mechanism of action of synthetic antifibrinolytics. A comparison with the action of derivatives of benzamidine on the fibrinolytic process. *Landmann, H.* (Institute of Pharmacology and Toxicology, Medical Academy of Erfurt, GDR), p. 253

Amidase activity of urokinase. I. Hydrolysis of α-N-acetyl-L-lysine p-nitroanilide. *Petkov, D., Christova, E., Karadjova, M.* (Laboratory of Protein Chemistry, Institute of Organic Chemistry, Bulgarian Academy of Sciences, Sofia 13, Bulgaria), p. 276

In vitro effects of lipids on fibrinolysis. *Chopin, S. F., Beard, E. L.* (Department of Biological Sciences, Loyola University, New Orleans, La. 70118), p. 286

Insulin and blood fibrinolytic activity. *Hedlin, A. M.* (Department of Physiology, Faculty of Medicine, Medical Sciences Building, University of Toronto, Toronto, Canada), p. 293

Release of fibrinopeptides from fibrinolytic fibrinogen fragment E. *Peyer, A., Straub, P. W.* (Department of Medicine, Kantons-

spital, University of Zurich, Zurich, Switzerland), p. 300

A comparative study of cross linked and non-cross-linked fibrin from the major classes of vertebrates. *Schwartz, M. L., Pizzo, S. V., Sullivan, J. B., Hill, R. L., McKee, P. A.* (Department of Biochemistry, Duke University Medical Center, Department of Medicine, Veterans Administration Hospital, Durham, N. C. 27710), p. 313

Acquired resistance to ancrod, its evaluation and clinical occurrence. *Vinazzer, H.* (Blood Coagulation Laboratory, A-4020 Linz, Austria), p. 339

Human fibrinopeptides as antithrombins. *Gorman, J. J., Castaldi, P. A.* (Haematology Department and Departments of Pathology and Medicine, Austin Hospital, University of Melbourne, Heidelburg, Victoria, 3084, Australia), p. 347

The local Sanarelli-Shwartzman phenomenon in rats induced by human leukaemic cells. *Lisiewicz, J., Pituch, A., Litwin, J. A.* (Haematological Clinic of the Institute of Internal Medicine, Medical Academy, Cracow, Poland), p. 353

Fibrin derivatives, plasma hemoglobin and glomerular fibrin deposition in experimental intravascular coagulation. *Beller, F. K., Theiss, W.* (Department of Obstetrics and Gynecology, New York University School of Medicine, New York, N. Y.), p. 363

Induction of glomerular microclot formation by fibrin monomer infusion. *Müller-Berghaus, G., Róka, L., Lasch, H. G.* (Department of Medicine, Justus Liebig-Universität, Giessen, FGR), p. 375

Disappearance of ellagic acid induced hypercoagulability in the dog after Trasylol administration. *Girolami, A., Brunetti, A., Cella, G., Pedrazzoli, S., Bernardi, R.* (University of Padua Medical School, Institute of Semeiotica Medica, Padua, Italy), p. 384

Studies on thrombolysis with streptokinase. IV. Immunofluorescent investigations on the fibrin pattern and the content of plasminogen and of plasma-plasmin-inhibitors in clots and thrombi of various age. *Gottlob, R., Nashef, B. E., Donas, P., Piza, F., Kolb, R.* (Department of Experimental Surgery of the 1st Surgical Clinic Vienna University, Vienna IX, Austria), p. 393

Sensitive method for the detection and characterization of platelet isoantibodies. *Hirschman, R. J., Yankee, R. A., Coller, B. S., Gralnick, H. R.* (Hematology Service, Clinical Pathology Department, Clinical Center, National Institutes of Health, Bethesda, Md.), p. 408

On the mechanism by which bovine fibrinogen induces the release and availability reaction of human blood platelets. *Kubisz, P., Suranová, J.* (Hemostasis Laboratory, Department Hospital, Čadca, Czechoslovakia), p. 416

Platelet Fc receptor as a mechanism for Ag—Ab complex-induced platelet injury. *Israels, E. D., Nisli, G., Paraskevas, F., Israels, L. G.* (Department of Medicine, University of Manitoba, Winnipeg, Manitoba, R3E0V9, Canada), p. 434

Enhancement by ADP of thrombin-induced aggregation in ADP-refractory platelets. *Simard-Duquesne, N.* (Ayerst Research Laboratories, Montreal, Quebec, Canada), p. 445

Lipid infusions in man. Ultrastructural studies on blood platelet uptake of fat particles. *Hovig, T., Grøttum, K. A.* (Institute of Pathology, Electron Microscopic Laboratory and Section of Haematology, Medical Department A, Rikshospitalet, Oslo 1, Norway), p. 450

Neuraminidase injections in rabbits. Reduced platelet surface charge, aggregation and thrombocytopenia. *Grøttum, K. A., Jeremic, M.* (Section of Haematology, Medical Department A, Rikshospitalet, Oslo, Norway), p. 461

Platelet thrombosis and non-traumatic intimal injury in mouse aorta. *Jørgensen, L., Haerem, J. W., Moe, N.* (Ullevål Hospital, Department of Pathology, University of Oslo, Oslo, Norway), p. 470

Enhancement of ADP-induced platelet aggregation by adrenaline *in vivo* and its prevention. *Yamazaki, H., Kobayashi, I., Sano, T., Shimamoto, T.* (Institute for Cardiovascular Diseases, Tokyo Medical and Dental University, School of Medicine, Yushima, Tokyo, Japan), p. 490

Clotting mechanisms in patients with hypertriglyceridemia during therapy with anabolic or progestational drugs. *Glueck, H. I., Glueck, Ch. J.* (Department of Internal Medicine, Coagulation Labora-

tory, J-4, Cincinnati General Hospital, Cincinnati, Ohio 45229), p. 499

Influence of pregnancy and oral contraceptives on platelets in relation to coagulation and aggregation. *Lecompte, F., Renaud, S.* (Laboratory of Experimental Pathology, Montreal Heart Institute and Department of Pathology, University of Montreal, Canada), p. 510

Thrombosis et Diathesis Haemorrhagica (Stuttgart) **29** (1973) No. 3

Editorial. Dysfibrinogenaemia. *Biggs, R.* (Haemophilia Centre, Churchill Hospital, Oxford, England), p. 523

Abnormal fibrinogens. A review. *Ménaché, D.* (Central Service for Immunology and Haematology, Hôpital Beaujon, 92 Clichy, France), p. 525

Fibrinogen Montreal. A new case of congenital dysfibrinogenaemia with defective aggregation of monomers. *Lacombe, M., Soria, J., Soria, C., d'Angelo, G., Lavallée, R., Bonny, Y.* (Haematology Laboratory, Hôpital Maisonneuve Montreal, Montreal, Canada), p. 536

Congenital dysfibrinogenemia (fibrinogen Giessen). *Krause, W. H., Heene, D. L., Lasch, H. G.* (Department of Medicine, University of Giessen, Giessen, FGR), p. 547

A new congenital abnormality of human fibrinogen. Fibrinogen Bethesda II. *Gralnick, H. R., Givelber, H. M., Finlayson, J. S.* (Hematology Service, Clinical Pathology Department, National Institutes of Health, Bethesda, Md. 20014), p. 562

The determination of optimum glycine concentration for the preparation of human fibrinogen at ambient temperatures. *Silberstein, E. B., Ingraham, S. C., III, Kereiakes, J. G.* (Radioisotope Laboratory, Department of Radiology, University of Cincinnati Medical Center, Cincinnati, Ohio), p. 572

Intravascular coagulation in experimental acute renal failure. Assessment by radiofibrinogen technique. *Wardle, E. N.* (Department of Medicine, Royal Victoria Infirmary, Newcastle upon Tyne, NE1 4LP, England), p. 579

The effect of fibrinogen degradation products on plasmin activity. *Mysliwiec, M., Arnesen, H., Godal, H. C.* (Hematological Research Laboratory, Department IX, Ullevål Hospital, University Clinic, Os'o, Norway), p. 592

Plasminogen depletion during administration of epsilon-aminocaproic acid. *Nibbelink, D. W., Jacobsen, C. D.* (Department of Neurology and Pathology, University of Iowa, Iowa City, Iowa 52240), p. 598

The effect of exocrine pancreas stimulation on the coagulation and fibrinolytic system in dogs. *Gabryelewicz, A., Prokopowicz, J., Szalaj, W., Wolosowicz, N., Laszewicz, W., Szmitkowski, M.* (Institute of Medicine, Gastrology Clinic, Białystok, Poland), p. 603

Decreased fibrinolysis in Behcet's disease. *Chajek, T., Aronowski, E., Izak, G.* (Departments of Hematology and Medicine B, Hadassah University Hospital, Jerusalem, Israel), p. 610

Action of coagulation factors on experimental thrombogenesis and their changes after thrombosis. *Marbet, G. A., Duckert, F.* (Department of Internal Medicine, First University Medical Clinic, Coagulation and Fibrinolysis Laboratories, Kantonsspital, Basle, Switzerland), p. 619

Cold promoted activation of factor VII. VI. Effect of Inhibitors. *Gjonnaess, H.* (Institute for Thrombosis Research, University of Oslo, Rikshospitalet, Oslo, Norway), p. 633

Coagulation factors of the newborn and his mother. *Biland, L., Duckert, F.* (Department of Internal Medicine, First University Medical Clinic, Coagulation and Fibrinolysis Laboratories, Kantonsspital, Basle, Switzerland), p. 644

The specificity of antibodies to factor VIII produced in the rabbit after immunization with human cryoprecipitate. *Kernoff, P. B. A., Rizza, C. R.* (Oxford Haemophilia Centre, Churchill Hospital, Oxford OX3 7LJ, England), p. 652

A simple indirect method to evaluate platelet aggregation. The clot retraction inhibition (CRI) test. *de Gaetano, G., Vermylen, J., Verstraete, M.* (Laboratory of Blood Coagulation, Department of Internal Medicine, University of Leuven, Leuven, Belgium), p. 661

Retention of platelets by glass beads. Varia-

tion with the age of the individual. *Bucher, U., Robert, Y., Riedwyl, H.* (Central Laboratory of Hematology, Inselspital, University of Bern, Bern, Switzerland), p. 671

Retention of platelet fibrin stabilizing factor during the platelet release reaction and clot retraction. *Joist, J. H., Niewiarowski, S.* (Department of Pathology and Blood Components, Developmental Laboratory, McMaster University, Hamilton, Ontario, Canada), p. 679

Enhancement of ADP-induced platelet aggregation by cholesterol and its prevention by pyridinolcarbamate. *Sano, T., Yamazaki, H., Shimamoto, T.* (Institute for Cardiovascular Disease, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo, Japan), p. 684

The effect of dipyridamole and RA233 on human platelet function in vitro. *Rifkin, P. L., Zucker, M. B.* (Department of Medicine and Pathology, New York University School of Medicine, New York, N. Y. 10016), p. 694

Lipid infusions in man. Blood platelet uptake of lipid and effects on platelet functions. *Grøttum, K. A., Nordøy, A., Hellem, A.* (Section of Haematology, Medical Department A, Institute for Thrombosis Research, Rikshospitalet, Oslo Norway), p. 701

The in vitro effects of mithramycin on the aggregation and the calcium uptake of human platelets. *Chao, F. C., Tullis, J. L.* (Cytology Laboratory, Center for Blood Research, Harvard Medical School, Boston, Mass.), p. 712

Platelet coagulant activities and clinical severity in haemophilia. *Walsh, P. N., Rainsford, S. G., Biggs, R.* (Oxford Haemophilia Center, Churchill Hospital, Oxford, England), p. 722

Platelet aggregation in patients with cerebral vascular disease and in control subjects. *Danta, G.* (Department of Neurology, North Staffordshire Royal Infirmary, Stoke-on-Trent, England), p. 730

Thrombosis Research (New York) **2** (1973) No. 6

Cross-linking of α-chain remnants in human fibrin. *Finlayson, J. S., Mosesson, M. W.* (Bureau of Biologics, Food and Drug Administration, Bethesda, Md.), p. 467

Properties of two types of solid-phase urokinase preparations. *Capet-Antonini, F. C., Grimard, M., Tamenasse, J.* (Faculty of Pharmacy, University of Montreal, Montreal, Canada), p. 479

Studies of snake venoms on blood coagulation. I. The thromboserpentin (thrombin-like) enzyme in the venoms. *Copley, A. L., Banerjee, S., Devi, A.* (Hemorrhage and Thrombosis Research Laboratories, Departments of Medicine and Pharmacology, New York Medical College, New York, N. Y. 10029), p. 487

The factor V activating enzyme of Russell's viper venom. *Esmon, Ch. T., Jackson, C. M.* (Department of Biological Chemistry, Washington University School of Medicine, St. Louis, Mo. 63110), p. 509

The influence of the surface charge of phospholipids on the activity of the prothrombin converting complex. *Janssen, C. L., Wijngaards, G., van Leeuwen, W. H.* (Department of Blood Coagulation Research, Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, The Netherlands), p. 525

A comparative study of precipitation and paracoagulation by protamine sulfate and ethanol gelation tests. *Gurewich, V., Lipinski, B., Lipinska, I.* (Vascular Laboratory, Lemuel Shattuck Hospital, Department of Medicine, Tufts University School of Medicine, Boston, Mass. 02130), p. 539

Consumption of abnormal prothrombin in the presence of different types of thromboplastin. *Brozovic, M., Gurd, L., Howarth, D. J.* (National Institute for Biological Standards and Control, London N.W.3 6RB, England), p. 557

On the model for the fibrinogen molecule. Consecutive stages of fibrin polymerization. *Belitser, V. A., Varetska, T. V., Manjakov, V. Ph.* (Institute of Biochemistry, Academy of Sciences of the Ukrainian S.S.R., Kiev, U.S.S.R), p. 567

Thrombosis Research (New York) **3** (1973) No. 1

Density distribution of ^{51}Cr-labelled platelets within the circulating dog platelet popula-

tion. *Busch, Ch., Olson, P. S.* (Department of Forensic Medicine, University of Uppsala, Uppsala, Sweden), p. 1

Bleeding times and antiaggregating drugs: A controlled study in elderly patients. *Praga, C., Malisardi, P., Pollini, C., Cortellaro, M., Mars, G.* (Clinica Medica I, Università di Milano, Milano, Italy), p. 13

Autoprothrombin II-A: Thrombin removal and mechanism of induction of fibrinolysis. *Zolton, R. P., Seegers, W. H.* (Department of Physiology, Thrombosis Specialized Center of Research, Wayne State University School of Medicine, Detroit, Mich.), p. 23

Effects of dipyrodamole and five related agents on human platelet aggregation and adenosine uptake. *Philip, R. B., Francey, I., McElroy, F.* (Department of Pharmacology, University of Western Ontario, London, Canada), p. 35

The systemic release of plasminogen activator to intravenous adrenaline in man: Dose reponse studies. *Gader, A. M. A., da Costa, J., Parker, Sh. M., Cash, J. D.* (S-E Scotland Regional Blood Transfusion Centre, Royal Infirmary, Edinburgh, Scotland), p. 51

Tensile strength of clots of recalcified plasma and fibrinogen-thrombin-calcium systems. *Rubin, H., Levine, S., Alter, A., Lipton, S., Estrin, J.* (Division of Hematology, Department of Medicine, Maimonides Medical Center, Brooklyn, N. Y.), p. 59

Coagulation studies in *Neisseria meningitidis* group A meningitis in Egypt. *Fresh, J. W., Girgis, N. I., Yassin, M. W., Lewis, J. H.* (U.S. Naval Medical Research Unit Number 3, Cairo, Egypt), p. 67

Platelet response to laser-induced microvascular injury in the rabbit mesentery and the rabbit ear chamber. A statistical comparison. *Arfors, K.-E., Bergqvist, D., McKenzie, F. N., Nilsson, G.* (Department of Experimental Medicine, Pharmacia AB, Uppsala, Sweden), p. 75

Determination of the surface energy of proteinated polymer surfaces. *Lee, R. G., Adamson, C., Kim, S. W., Lyman, D. J.* (Division of Materials Science and Engineering, University of Utah, Salt Lake City, Utah 84112), p. 87

Thrombosis Research (New York) **3** (1973) No. 2

The change of activity and molecular weight of thrombin by modification of aminogroups and tyrosine residues. *Baskova, I. P., Strukova, S. M.* (Laboratory of Blood, Moscow State University, Moscow, U.S.S.R), p. 91

Hemmung der ADP-induzierten Aggregation beim Meerschweinchen. *Deutsch, E., Gasic, S.* (I. Medizinische Universitätsklinik, A-1097 Wien, Austria), p. 103

Fetal fibrinogen and fibrinogen Paris I: Comparative fibrin monomers aggregation studies. *Guillin, M.-C., Menache, D.* (C.H.U. Xavier Bichat, Service Central d'Immunologie et Hématologie, Hôpital Beaujon, 92110 Paris, France), p. 117

Fibrinolytic, factor VIII and pulse rate responses to intravenous adrenaline during chronic oral salbutamol administration. *Gader, A. M. A., Parker, Sh., Crompton, G. K., Cash, J. D.* (S-E Scotland Regional Blood Transfusion Centre, University Department of Medicine, Royal Infirmary, Northern General Hospital, Edinburgh, Scotland), p. 137

A modified beta-alanine precipitation procedure to prepare fibrinogen free of antithrombin-III and plasminogen. *Jakobsen, E., Kierulf, P.* (Hematological Research Laboratory, Department IX, University Clinic, Ullevål Hospital, Oslo, Norway), p. 145

Vein graft surgery in Defibrase^{R}-defibrinogenated dogs. *Olsson, P., Ljungqvist, A., Göransson, L.* (Thoracic Surgery Research Laboratory, Department of Pathology, Karolinska Hospital, S-104 01 Stockholm 60, Sweden), p. 161

Consumption coagulopathy caused by a boomslang bite. A case report. *Matell, G., Nyman, D., Werner, B., Wilhelmsson, S.* (Department of Medicine, Södersjukhuset, Swedish Poison Information Centre, Karolinska Sjukhuset, Stockholm, Sweden), p. 173

Formation of soluble fibrin monomer complexes in human plasma. *von Hugo, R., Graeff, H.* (First Department of Obstetrics and Gynecology, Munich University, 8 Munich 2, FGR), p. 183

On fibrin distribution in organs of dogs during defibrination with the thrombin-like enzyme from bothrops atrox. *Egberg, N., Ljungqvist, A.* (Department of Blood Coagulation Research, Karolinska Institutet, Karolinska Sjukhuset, Stockholm, Sweden), p. 191

Observations on late stages of fibrinogen polymerization in human plasma. *Boyd, T. H. III, Stoner, G. E.* (Department of Materials Science, University of Virginia, Charlottesville, Va. 22901), p. 209

The fibrinolytic response to venous occlusion in hypoproteinaemic patients. *Gader, A. M. A., Anderton, J. L., Cash, J. D.* (S-E Scotland Regional Blood Transfusion Centre, Medical Renal Unit, Royal Infirmary, Edinburgh, Scotland), p. 219

Thrombosis Research (New York) **3** (1973) No. 3

Editorial. Thrombolytic therapy in acute myocardial infarction. *Fletcher, A. P.* (Washington University School of Medicine, St. Louis, Mo.), p. 233

The inactivation of factor XIII during blood coagulation. *Triantaphyllopoulos, D. C.* (American National Red Cross Blood Research Laboratory, Bethesda, Md.), p. 241

Estimation of the specific inhibitors of fibrin polymerization. Inhibitory units. *Belitser, V. A., Varetska, T. V., Tsinkalovska, S. N.* (Institute of Biochemistry, Academy of Sciences of Ukrainian S.S.R., Kiev, U.S.S.R.), p. 251

Susceptibility of early and late stages of fibrin self-assembly to specific inhibitors. *Belitser, V. A., Varetska, T. V., Manyakov, V. Ph., Manko, N. I., Degtyaryova, I. I., Smechova, E. A., Galanova, T. F.* (Institute of Biochemistry, Academy of Sciences of Ukrainian S.S.R., Kiev, U.S.S.R.), p. 265

Significance of kaolin-induced arginine esterase in human plasma during septic shock: Depletion in prekallikrein and prekallikrein activator. *Marcel, G. A., Caspar, C., Sabatier, C., Rapin, M.* (Service de Réanimation Médicale, Hôpital Henri Mondor, 94-Créteil, France), p. 281

Variation in commercial heparin and its relation to the problem of heparin standardization for clinical use. *Jaques, L. B., Kavanagh, L. W., Kuo, S. H.* (Hemostasis-Thrombosis Research Unit, Department of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO), p. 295

Investigations on the time dependence of platelet functions. I. General methodical investigations. *Reuter, H., Podolsak, B., Hagen, I., Linker, H., Ströder, J., Gross, R.* (Medizinische Universitätsklinik, Köln, BRD), p. 307

Prevention of aspirin inhibition of platelet release reaction by the fatty acid precursor of platelet prostaglandins. *Leonardi, R. G., Alexander, B., White, F.* (Coagulation Laboratory, New York Blood Center, New York, N. Y. 10021), p. 327

Determination of fibrinogen degradation products using anti-fibrinogen serum and anti-fragment E serum. *Soria, J., Soria, C., Fabiani, P., Samama, M.* (Haematology Laboratory, Hôtel-Dieu, Paris IV^{e}, France), p. 339

Demonstration of platelet fibrinogen secretion via the surface connecting system. *Holme, R., Sixma, J. J., Mürer, E. H., Hovig, T.* (Electron Microscopic Laboratory, Institute of Pathology, Rikshospitalet, Oslo, Norway), p. 347

Prothrombin and the ultimate formation of thrombin. *McCoy, L. E., Walz, D. A., Seegers, W. H.* (Department of Physiology, Wayne State University, School of Medicine, Detroit, Mich.), p. 357

Thrombosis Research (New York) **3** (1973) No. 4

Relationship of factor VIII to ristocin-induced platelet aggregation; effect of heterologous and acquired factor VIII antibodies. *Thomson, C., Forbes, C. D., Prentice, C. R. M.* (University Department of Medicine, Royal Infirmary, Glasgow G4 OSF, Scotland), p. 363

Antibody-induced "thrombocytopathy". *Clancy, R., Firkin, B.* (Department of Medicine, McMaster University, Hamilton, Ontario L8S 4J9, Canada), p. 375

The presence and reactions of high and lower-molecular-weight procoagulant factor VIII in the plasma of patients with von Willebrand's disease after treatment:

Significance for a structural hypothesis for factor VIII. *Bloom, A. L., Peake, I. R., Giddings, J. C.* (Department of Haematology, University Hospital of Wales, Cardiff, Wales), p. 389

Disseminated intravascular coagulation in septicemia caused by beta-hemolytic streptococci. *Cronberg, S., Skånsberg, P., Nivenius-Larsson, K.* (Department of Infectious Diseases, Coagulation Laboratory, University of Lund, Allmänna Sjukhuset, S-214 01 Malmö, Sweden), p. 405

Fibrin/fibrinogen degradation products in amniotic fluid. *Svanberg, L., Astedt, B., Ekelund, L.* (Department of Obstetrics and Gynecology, Malmö Allmänna Sjukhuset, Malmö, Sweden), p. 413

Variations in abilities of animal fibrinogens to clump staphylococci. *Lewis, J. H., Wilson, J. H.* (Department of Medicine, University of Pittsburgh, Pittsburgh, Pa. 15213), p. 419

Effect of platelets on clot structuration. A thrombelastographic study. *de Gaetano, G., Bottecchia, D., Vermylen, J.* (Laboratory of Blood Coagulation, Medical Research Depertment, Academisch Ziekenhuis St. Rafael, University of Leuven, Leuven, Belgium), p. 425

Factor XIII activity of platelets and plasma in health and disease. *Mandel, E. E., Minn, S. K.* (Isaac Albert Research Institute and Department of Medicine, Kingsbrook Jewish Medical Center, Brooklyn, N. Y.), p. 43

Studies of actions of snake venoms on blood coagulation. II. Electrophoretic analysis of venoms of viperidae, crotalidae, elapidae and hydrophidae. *Banarjee, S., Devi, A., Copley, A. L.* (Hemorrhage and Thrombosis Research Laboratories, Departments of Medicine and Pharmacology, New York Medical College, New York, N. Y. 10029), p. 451

Thrombosis Research (New York) **3** (1973) No. 5

In vivo formation of soluble fibrin monomer complexes in human plasma. *Graeff, H., von Hugo, R., Hafter, R.* (First Department of Obstetrics and Gynecology, University of Munich, 8 Munich 2, FRG), p. 465

Platelet migration and chemotaxis demonstrated in vitro. *Lowenhaupt, R. W., Miller, M. A., Glueck, H. I.* (Department of Physiology and Coagulation Laboratory, College of Medicine, University of Cincinnati, Cincinnati, Ohio 45219), p. 477

The influence of sodium salts of fatty acids on the fibrinolytic enzyme system. *Ogston, D., Herbert, R. J., Akinsete, F. I., Douglas, A. S.* (Department of Medicine, University of Aberdeen, Aberdeen, Scotland), p. 489

Ristocetin-induced aggregation of gel filtered platelets. A study of von Willebrand's disease and the effect of aspirin. *Olson, J. D., Fass, D. N., Bowie, E. J. W., Mann, K. G.* (Mayo Clinic and Mayo Foundation, Rochester, Minn. 55901), p. 501

Conversion of NH_2-terminal glutamic acid to NH_2-terminal lysine human plasminogen by plasmin. *Claeys, H., Molla, A., Verstraete, M.* (Laboratory of Blood Coagulation, Academisch Ziekenhuis St. Rafael, 3000 Leuven, Belgium), p. 515

Analysis of gel exclusion chromatographic data by chromatographic plate theory analysis: Application to plasma fibrinogen chromatography. *Alkjaersig, N., Roy, L., Fletcher, A.* (Washington University School of Medicine, St. Louis, Mo.), p. 525

Laser induced microvascular thrombosis in mice treated with oral contraceptives. *Kovács, I. B., Csalay, L.* (Ottó Korvin Hospital, Budapest, Hungary), p. 545

Plasmic degradation of fibrinogen: The preparation of a low molecular weight derivative of fragment D. *Kemp, G., Furlan, M., Beck, E. A.* (Central Hematology Laboratory, Inselspital, Berne, Switzerland), p. 553

Effect of Arvin on rabbit platelet activity in vitro and in vivo. *McKenzie, F. N., Arfors, K.-E., Tangen, O.* (Department of Experimental Medicine, Pharmacia AB, Uppsala, Sweden), p. 565

Flurbiprofen, a new potent inhibitor of platelet aggregation. *Nishizawa, E. E., Wynalda, D. J., Suydam, D. E., Molony, B. A.* (Diabetes and Atherosclerosis Research, The Upjohn Company, Kalamazoo, Mich. 49001), p. 577

The formation of complex fibrin stabilizing factor with heparin in vitro. *Kudrjashov,*

B. A., Ulianov, A. M., Liapina, L. A. (Moscow University, Department of Physiology, Moscow, USSR), p. 589

Thrombosis Research (New York) **3** (1973) No. 6

Kinetics of platelet "populations" in the stationary state. *Boneu, B., Boneu, A., Raisson, Cl., Guiraud, R., Biermé, R.* (Laboratoire d'Hémostase, Centre Régional de Transfusion Sanguine, Toulouse Cedex F. 31052, France), p. 605

Studies on soluble fibrin in plasma IV: Isolation and characterization of the clottable proteins obtained from thrombin incubated plasma upon gelation with ethanol. *Kierulf, P.* (Hematological Research Laboratory, Department IX, University Clinic, Ullevål Hospital, Oslo, Norway), p. 613

Antithrombin III in a clinical material. *Hedner, U., Nilsson, I. M.* (Coagulation Laboratory, Allmänna Sjukhuset, Malmö, Sweden), p. 631

Improved quantitation of serum FDP after coagulation at low pH. *Arnesen, H., Ly, B., Ödegård, O. R.* (Hematological Research Laboratory, Department IX, Ullevål Hospital and Medical Department A, Oslo, Norway), p. 643

Behaviour of fibrinogen and fibrinogen degradation products (FDP) towards isolubilized fibrinogen and fibrinmonomer. *Matthias, F. R., Heene, D. L., Konradi, E.* (Department of Medicine, Justus Liebig University, Giessen, FGR), p. 657

Circulating endothelial cells isolated together with platelets and the experimental modification of their counts in rats. *Hladovec, J., Rossmann, P.* (Research Centre of Cardiovascular Disease, Institute for Clinical and Experimental Medicine, Prague, Czechoslovakia), p. 665

Macromolecular associations in dilute solutions of activated fibrinogen. *Marguerie, G., Pouit, L., Suscillon, M.* (Laboratoire d'Hématologie, D.R.F. Centre d'Etudes Nucléaires de Grenoble, 38041 Grenoble Cedex, France), p. 675

A blood fluidizing activity. *Shadid, J. N.* (Department of Surgery, Washington Hospital Center, Washington, D. C.), p. 691

Activation of prothrombin with *oxyuranus scutellatus scutellatus* (Taipan snake) venom. *Owen, W. G., Jackson, C. M.* (Department of Biological Chemistry, Washington University, St. Louis, Mo. 63110), p. 705

Collagen induced platelet aggregation: Requirement for tropocollagen multimers. *Muggli, R., Baumgartner, H. R.* (Department of Experimental Medicine, F. Hoffman-La Roche and Co., Ltd., Ch-4002 Basel, Switzerland), p. 715

The plasmin-catalyzed hydrolysis of N^{α}-CBZ-L-lysine *p*-nitrophenyl ester. *Silverstein, R. M.* (Armour Pharmaceutical Co., Kankakee, Ill. 60901), p. 729

Evidence for multiple molecular forms of autoprothrombin C (factor X_a). *Dombrose, F. A., Seegers, W. H.* (Department of Physiology, Thrombosis Specialized Center of Research, Wayne State University School of Medicine, Detroit, Mich.), p. 737

Comparative adsorption studies between fibrinogen and its degradation products and fibrinmonomer produced by reptilase and thrombin. *Matthias, F. R., Heene, D. L.* (Department of Medicine, Justus Liebig University, Giessen, FRG), p. 745

Transfusion (Philadelphia) **13** (1973) No. 3

The rhesus monkey as a model for evaluation of the preservation of stored whole blood. *Button, L. N., Garcia, F. G., Kevy, S. V.* (The Children's Hospital Medical Center, Boston, Mass. 02115), p. 119

Selected types of frozen blood for patients with multiple blood group antibodies. *Grove-Rasmussen, M., Huggins, C. E.* (Blood Bank and Transfusion Service, Massachusetts General Hospital, Boston, Mass. 02114), p. 124

In vitro analysis of platelet function during storage of platelets from plasmapheresed donors. *Moore, G. L., Mallin, W. S., Roberts, S. C., Failla, M. L., Gray, J. L.* (Blood Research Division, U. S. Army Medical Research Laboratory, Fort Knox, Ky.), p. 130

A method for preservation of papainized and Rh-sensitized red cells. *Dale, I.* (Blood Bank and Department of Immunohema-

tology, Ullevål Hospital, Oslo 7, Norway), p. 135

Paroxysmal cold hemoglobinuria (P.C.H.) following mycoplasma infection: Anti-I specificity of the biphasic hemolysin. *Bell, C. A., Zwicker, H., Rosenbaum, D. L.* (Blood Bank Orange County Medical Center, University of California, Irvine, Orange, Calif. 92668), p. 138

Gamma globulin contamination of commercial bovine albumin. *Simmons, A., Jones, J., Hendrix, D.* (Blood Transfusion Service, Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City, Iowa 52242), p. 142

Additional examples of cold autoagglutinins with M specificity. *Hysell, J. K., Beck, M. L., Gray, J. M.* (Blood Bank, St. Joseph Mercy Hospital, Ann Arbor, Mich. 48104), p. 146

Anomalous ABO grouping due to a new serum factor reactive with a reagent coloring material. *Jones, T. E., Ayrton, A. S., Blajchman, M. A.* (Department of Laboratories, Henderson General Hospital, Hamilton, Ontario, Canada), p. 150

Hemolytic disease of the newborn due to anti-Js^a. *Donovan, L. M., Tripp, K. L., Zuckerman, J. E., Konugres, A. A.* (Boston Hospital for Women, Boston, Mass. 02115), p. 153

A note on the hidden added costs of RIA adoption. *Pegels, C. C., Seagle, J. P.* (Management Science, SUNY at Buffalo, Buffalo, N. Y. 14214), p. 154

Analysis and optimization of a regional blood bank distribution process II. Derivation and use of a method for evaluating hospital management procedures. *Yahnke, D. P., Rimm, A. A., Makowski, G. G., Aster, R. H.* (Milwaukee Blood Center, Inc., Milwaukee, Wis. 53233), p. 156

Transfusion (Philadelphia) **13** (1973) No. 4

Comparison of inverted centrifugation, saline washing, and dextran sedimentation in the preparation of leukocyte-poor red cells. *Tenczar, F. J.* (Abraham Lincoln School of Medicine, University of Illinois Hospital, Chicago, Ill.), p. 183

Simple method for production of HL-A antigen poor red cells. *Miller, W. V., Wilson, M. J., Kalb, H. J.* (Central Kentucky Blood Center, 731 South Limestone, Lexington, Ky. 40508), p. 189

Leukocyte contamination of red cells in leukocyte-poor and frozen-deglycerolized units. *Perkins, H. A., Senecal, I., Howell, E.* (Irwin Memorial Blood Bank of the San Francisco Medical Society, San Francisco, Calif. 94118), p. 194

Uptake and retention of adenine moiety by stored human red blood cells. *DeVenuto, F., Wilson, S. M., Shields, C. E.* (Blood Research Division, U. S. Army Medical Research Laboratory, Fort Knox, Ky. 40121), p. 200

Nonspecific warm hemolysins of papain-treated cells: Serologic characterization and transfusion risk. *Bell, C. A., Zwicker, H., Nevius, D. B.* (Department of Pathology, University of California, Irvine, Orange County Medical Center, Orange, Calif.), p. 207

Autoimmune hemolytic anemia caused by anti-D. *Adams, J., Moore, V. K., Issitt, P. D.* (University of Cincinnati Blood Transfusion Service, Cincinnati, Ohio 45229), p. 214

Autologous transfusion in cardiac surgery: A case report of a patient with a rare antibody. *Verska, J. J., Larson, N. L.* (White Memorial Medical Center, Los Angeles, Calif. 90033), p. 219

Post-Konyne hepatitis: The ineffectiveness of screening for the hepatitis B antigen (HBAg). *Sandler, S. G., Rath, C. E., Wickerhauser, M., Dodd, R. Y., Greenwalt, T. J.* (Blood Bank, Hadassah University Hospital, P.O.B. 499, Jerusalem, Israel), p. 221

Six additional examples of anti-At^a. *Gellerman, M. M., McGreary, J., Yedinak, E., Stroup, M.* (Levine Laboratories, Ortho Research Foundation, Raritan, N. J. 08869), p. 225

Another pitfall in blood group testing for nonpaternity. *Sussman, L. N., Solomon, R.* (Blood Bank, Beth Israel Medical Center, New York, N. Y. 10003), p. 231

Determination of costs and charges for laboratory tests. A computer approach for the hospital blood bank. *Klionsky, B., Boccella, I. M., Sheth, U. M.* (Department of Pathology, Magee-Womens Hospital, Pittsburgh, Pa.), p. 233

Transfusion (Philadelphia) **13** (1973) No. 5

Blood collection and use by AABB institutional members (1971). *Hemphill, B. M.* (Irwin Memorial Blood Bank, San Francisco Medical Society, San Francisco, Calif.), p. 255

Comparison of the sensitivities of the newer detection systems for hepatitis B antigen. *Roche, J. K., Stengle, J. M.* (Blood Resource Branch, National Institutes of Health, Bethesda, Md. 20014), p. 258

Detection and quantitation of bacteria in platelet products stored at ambient temperature. *Buchholz, D. H., Young, V. M., Friedman, N. R., Reilly, J. A., Mardiney, M. J.* (Section of Immunology and Cell Biology, Baltimore Cancer Research Center, National Cancer Institute, Baltimore, Md.), p. 268

Improved granulocyte procurement with the continuous flow centrifuge. *Clift, R. A., Buckner, C. D., Williams, B. M., Hickman, R. O., Thomas, E. D.* (Department of Medicine, University School of Medicine, Seattle, Washington), p. 276

Prophylactic platelet transfusions in children with acute leukemia: A dose response study. *Roy, A. J., Jaffe, N., Djerassi, I.* (Blood Cell Research Laboratories, The Children's Cancer Research Foundation, The Children's Hospital Medical Center, Boston, Mass. 02115), p. 283

Identification and clinical implications of isoantibodies in patients with idiopathic dysgammaglobulinemia. *Ablin, R. J.* (Immunobiology Section, Department of Urology, Cook County Hospital and Graduate School of Medicine, Chicago Medical School, Chicago, Ill. 60612), p. 291

Comparison of commercial blood bank antisera. *Greendyke, R. M., Banzhaf, J. C.* (Department of Pathology, University of Rochester School of Medicine, and Dentistry, Rochester, N. Y. 14642), p. 297

Effects of ethacrynic acid on human red blood cells. *Da Costa, A. J., White, A. G.* (Southeast Regional Blood Transfusion Centre, Department of Therapeutics, Royal Infirmary, Edinburgh, Scotland), p. 305

Blood group mosaicism involving the rhesus and Duffy blood groups. *Marsh, W. L., Chaganti, R. S. K.* (Serology and Genetics Laboratory, New York Blood Center, New York, N. Y. 10021), p. 314

Three examples of Rh-positive, good responders to blood group antigens. *Issitt, P. D., McKeever, B. G., Moore, V. K., Wilkinson, S. L.* (University of Cincinnati Blood Transfusion Service, Cincinnati, Ohio 45229), p. 316

Osmotic fragility changes of ACD blood units from polycythemic donors. *Ben-David, A., Gavendo, S.* (Israel Defence Forces, Medical Corps, Blood Bank, Sheba Medical Center, Tel-Hashomer, Israel), p. 320

Distribution of fresher blood in a statewide blood program. *Katz, A. J., Morse, E. E.* (Department of Laboratory Medicine, University of Connecticut Health Center, Hartford, Conn.), p. 324

Transfusion (Philadelphia) **13** (1973) No. 6

Evaluation of methods for the preparation of HL-A antigen-poor blood. *Polesky, H. F., McCullough, J., Helgeson, M. A., Nelson, C.* (Minneapolis War Memorial Blood Bank, University of Minnesota Hospital Blood Bank, Minneapolis, Minn. 55102), p. 383

Red cell recovery and leukocyte depletion following washing of frozen-thawed red cells. *Meryman, H. T., Hornblower, M.* (Blood Research Laboratory, American National Red Cross, Bethesda, Md. 20014), p. 388

Laboratory evaluation of normal donors undergoing leukapheresis on the continuous flow centrifuge. *McCullough, J., Fortuny, I. E.* (Departments of Laboratory Medicine and Pathology, University of Minnesota Medical School, Minneapolis, Minn.), p. 394

Use of frozen cryoprecipitate for the preparation of clinical factor VIII concentrate. *Sgouris, J. T., Wickerhauser, M.* (Michigan Department of Public Health, Lansing, Mich. 48914), p. 399

Efficacy of the Latham Blood Processor to perform plateletpheresis. *Szymanski, I. O., Patti, K., Kliman, A.* (Massachusetts Red Cross Blood Program, Boston, Mass.), p. 405

The unsuitability of outdated blood for making therapeutically effective cryoprecipitate. *Burka, E. R., Puffer, T. M., Holburn, R. R., Sherwood, W. C.* (Jefferson Medical College, Thomas University Hospital, Philadelphia, Pa. 19107), p. 412

Positive antiglobulin tests in patients maintained on methadone. *Sivamurthy, S., Frankfurt, E., Levine, M. E.* (Division of Hematology, Department of Medicine, Jamaica Hospital, Jamaica, N. Y.), p. 418

Delay in the onset of immune hemolysis in vivo apparently due to heparinization. *Gray, J. M., Oberman, H. A., Beck, M. L.* (Blood Bank, St. Joseph Mercy Hospital, Ann Arbor, Mich. 48104), p. 422

Fetal cell counting as a guide to prevention of Rh sensitization. *Clayton, E. M., Jr., Birdwell, E. D., Gregory, M. G.* (St. Thomas Hospital, Nashville, Tenn.), p. 425

The second example of anti-Be^a causing hemolytic disease of the newborn. *McCreary, J., MacIlroy, M., Courtenay, D. G., Ohmart, D. L.* (Philip Levine Laboratories, Ortho Research Foundation, Raritan, N. J. 08869), p. 428

The incidence of antibodies to leukocytes and gammaglobulin IgG and IgA in a population of multitransfused Southern African Negroes. *Vos, G. H., Downing, H. J., Vos, D.* (Natal Institute of Immunology, Durban, South Africa), p. 432

Influence of ACD and CPD anticoagulants on white cell aggregation. *Lycette, R. M.* (Blood Products, Research and Development Division, Parke, Davis and Company, Rochester, Mich. 48063), p. 433

Bacteriological study of platelet concentrates stored at 22 C and 4 C. *Mallin, W. S., Reuss, D. T., Bracke, J. W., Roberts, S. C., Moore, G. L.* (U.S. Army Medical Research Laboratory, Fort Knox, Ky.), p. 439

Blood donor recruitment in a municipal hospital in a low socioeconomic community. *Bisserup, R., Rosner, F., McBarnette, L.* (Queens Hospital Center, Long Island Jewish-Hillside Medical Center, Jamaica, N. Y.), p. 443

Vox Sanguinis (Basel) **25** (1973) No. 3

An inherited blood group A variant in the Finnish population. I. Basic characteristics. *Mohn, J. F., Cunningham, R. K., Pirkola, A., Furuhjelm, U., Nevanlinna, H. R.* (Blood Group Research Unit Department of Microbiology, School of Medicine, State University of New York at Buffalo, Buffalo, N. Y. 14214), p. 193

New determinants of hepatitis B antigen. (Au or HB antigen). *Soulier, J. P., Couroucé-Pauty, A. M.* (Centre National de Transfusion Sanguine, F-75015 Paris, France), p. 212

Australia antibody production elicited by heat-treated human plasma protein solution. *Mori, Y., Momose, M., Nakano, Y., Ata, S.* (Virus Research Institute, Toyohashi City Hospital, Toyohashi, Aichi, Japan), p. 235

The selection of plasma for the preparation of antitetanus immunoglobulin. *Entwistle, C. C., Eldridge, P. L.* (Regional Transfusion and Immunohaematology Centre, Cambridge, CB2 2PT England), p. 240

The production in the pregnant cow of anti-human immunoglobulin to be used for the antiglobulin test. *Fey, H., Bütler, R., Marti, F.* (The Veterinary Bacteriological Institute, University of Berne, CH-3000 Switzerland), p. 245

Antibody response in Hodgkin's disease and other lymphomas related to HL-A antigens, immunoglobulin levels and therapy. *Sybesma, J. P. H. B., Holtzer, J. D., Borst-Eilers, E., Moes, M., Zegers, B. J. M.* (Blood Bank and Department of Haematology, University Hospital, Utrecht, The Netherlands), p. 254

The α-galactose specifity of anti-p^k. *Voak, D., Anstees, D., Pardoe, G.* (Regional Blood Transfusion and Immuno-Haematology Centre, Cambridge CB2 2PT, England), p. 263

Transfusion in the presence of anti-Sp_1. *Bell, C. A., Zwicker, H., Spira, S., Fischer, M. L.* (University of California, Irvine, Blood Bank, Orange County Medical Center, Orange, Calif. 92668), p. 271

The occurrence of Ag determinants in different lipoproteins. *Ehnholm, C., Bütler, R., Brunner, E.* (Department of Serology and Bacteriology, University of Helsinki, Helsinki, Finland), p. 281

Evidence for the existence of the rhesus complex *Cde (r')* in a Chinese. *Hawkins, B., Simons, M. J.* (Department of Human

Biology, The John Curtin School of Medical Research, The Australian National University, Canberra, A.C.T., 2601 Australia), p. 286

Vox Sanguinis (Basel) **25** (1973) No. 4

A papain-bromelin-polybrene four-channel autoanalyzer system for blood group antibody screening. Analysis of 22, 912 sera. *Habibi, B., Gerbal, A., Salmon, C.* (Centre Départemental de Transfusion Sanguine, F-75012 Paris, France), p. 289

The relative contributions of different salivary glands to the blood group activity of whole saliva in humans. *Milne, R. W., Dawes, C.* (Department of Oral Biology, Faculty of Dentistry, University of Manitoba, Winnipeg, Manitoba R3E OW3, Canada), p. 298

Prevention of Rh-immunization. Modified production of IgG anti-Rh for intravenous application by ion exchange chromatography (IEC)[1]. *Hoppe, H. H., Mester, T., Hennig, W., Krebs, H. J.* (Zentralinstitut für das Bluttransfusionswesen, D-2 Hamburg, BRD), p. 308

Haptenic relationship between bovine J, human A, and porcine A blood group systems tested with lipids and nonlipid fractions of blood. *Thiele, O. W., Koch, J.* (Physiologisch-Chemisches Institut, D-34 Göttingen, BRD), p. 317

The possibility of influencing histocompatibility antigens by proteolytic enzymes. *Bube, F. W., Siebel, E., Heumann, H.* (Blutspendezentrale der Universitätskliniken Köln, D-5 Köln, BRD), p. 327

A family with the rare red cell antigens Wr^a and 'super' Sd^a. *Lewis, M., Kaita, H., Chown, B., Tippett, P., Gavin, J., Sanger, R., Giblett, E., Steinberg, A.* (MRC Blood Group Unit, The Lister Institute, London SW 1W 8RH, England), p. 336

B^H_m: a weak B antigen variant. *Marsh, W. L., Ferrari, M., Nichols, M. E., Fernandez, G., Cooper, K.* (Serology and Genetics Laboratory, New York Blood Center, New York, N. Y. 10021), p. 341

Agglutinins from fish ova defining blood groups B and P. *Anstee, D. J., Holt, P. D. J., Pardoe, G. I.* (South-West Regional Blood Transfusion Centre, Bristol BS10, England), p. 347

Japanese families with group O and B red cells agglutinable by *Dolichos biflorus* extract. *Yamaguchi, H., Okubo, Y., Ogawa, Y., Tanaka, M.* (Research Laboratory, Osaka Red Cross Hospital, Tenniji-ku, Osaka, Japan), p. 361

Production of antibodies against hepatitis-associated antigen in donkeys. *Hirshfeld, T., Alkan, W. J., Lefler, E., Eshchar, J.* (Miles-Yeda Ltd., Rehovot, Israel), p. 370

The non-identity of anti-N and anti-N in the serum of an MN person. *Booth, P. B., Moores, Ph.* (Immunohaematology Department, Christchurch Hospital, Christchurch, New Zealand), p. 374

A dominant suppressor of A and B. *Rubinstein, P., Allen, F. H., Rosenfield, R.* (Serology and Genetics Division, New York Blood Center, New York, N.Y. 10021), p. 377

Vox Sanguinis (Basel) **25** (1973) No. 5

A possible $D(C^W)$ (e) gene complex of the Rh system. *Kornstad, L., Heier-Larsen, A. M.* (National Institute of Public Health, Postuttak, Oslo 1, Norway), p. 385

Anti-s and anti-U cold-reacting antibodies. *Lalezari, P., Malamut, D. C., Dreisiger, M. E., Sanders, C.* (Division of Immunohematology, Department of Medicine, Montefiore Hospital, New York, N. Y.), p. 390

Blood group O(H)-like activity in extracts from some invertebrates. A study with catfish and eel sera and three anti-H lectins. *Baldo, B. A., Uhlenbruck, G., Steinhausen, G.* (Clinical Immunology Unit, Princess Margaret Hospital, Perth, W. A., 6008 Australia), p. 398

Anti-A_1 Le^b in serum of a person of a blood group A_1h. *Gundolf, F.* (Blood Bank and Blood Grouping Department, University Hospital, Rigshospitalet, DK-2100 Copenhagen Ø, Denmark), p. 411

ABO blood grouping of human hair using radioactively-labelled antibodies. *Boettcher, B., Kay, D. J.* (Department of Biological Sciences, University of Newcastle, Newcastle, NSW 2308 Australia), p. 420

Small scale preparation and clinical use of factor IX-prothrombin complex. *Barrowcliffe, T. W., Stableforth, P.,*

Dormandy, K. M. (Haemophilia Centre, Royal Free Hospital, North Western Branch, London NW3 2XJ, England), p. 426

The specificity of leukocyte and platelet alloantibodies in sera of patients with nonhemolytic transfusion reactions. Absorption and elution studies. *Heinrich, D., Mueller-Eckhardt, C., Stier, W.* (Department of Internal Medicine, Section of Clinical Immunology and Blood Transfusion, D-6300 Giessen, FGR), p. 442

Automated screening test for high titre tetanus antibody in donor plasma. *Nelson, M.* (Red Cross Blood Transfusion Service, Sydney, N.S.W. 2000, Australia), p. 457

Plastic blood transfusion equipment. *Øie, S. H., D'Antoni, L.* (National Institute of Public Health, Control and Media Department, Postuttak, Oslo 1, Norway), p. 461

The role of rheumatoid factor and related human antiglobulins in the radioimmunoassay (Ausria system) for the detection of hepatitis B antigen. *Bütler, R., Brunner, E.* (Zentrallaboratorium, Blutspendedienst SRK, CH-3000 Bern 22, Switzerland), p. 466

Removal of buffy coat from stored ACD blood by dextran agglomeration and subsequent filtration. *Goldmann, S. F., Heiss, F., Scheinert, I.* (Tissue Typing Laboratory, Department of Clinical Physiology, University of Ulm, D-7900 Ulm, FRG), p. 470

A second example of anti-Ge^1, and some observations on Gerbich subgroups. *Macgregor, A., Booth, P. B.* (Institute of Human Biology, Goroka, Papua, New Guinea), p. 474

Vox Sanguinis (Basel) **25** (1973) No. 6

Permanent mixed-field polyagglutinability (PMFP). I. Serological observations. *Sturgeon, Ph., McQuiston, D. T., Taswell, H. F., Allan, Ch. J.* (The Gwynne Hazen Cherry Memorial Laboratories, Department of Pediatrics, Hematology Division, UCLA School of Medicine, Los Angeles, CA 90024), p. 481

Permanent mixed-field polyagglutinability (PMFP). II. Hematological, biophysical and biochemical observations. *Sturgeon, Ph., Luner, S. J., McQuiston, D. T.* (The Gwynne Hazen Cherry Memorial Laboratories, Department of Pediatrics, Hematology Division, UCLA School of Medicine, Los Angeles, CA 90024), p. 498

Selective serum IgA deficiency. Frequency among 15,200 French blood donors. *Frommel, D., Moullec, J., Lambin, P., Fine, J. M.* (Laboratoire d'Immunochimie, Centre National de Transfusion Sanguine, F-75739 Paris Cedex 15, France), p. 513

Neuraminidase and anti-neuraminidase serum: Effect on the cell surface properties. *Sachtleben, P., Gsell, R., Mehrishi, J. N.* (Kinderklinik St. Elizabet, 8858 Neuburg/Donau, BRD), p. 519

Quantitative variation in the G antigen of the Rh blood group system. *Case, J.* (WHO National Blood Group Reference Laboratory, Commonwealth Serum Laboratories, Parkville, Vic. 3052, Australia), p. 529

Independence of the Colton and Yt blood group systems. *Lewis, M., Kaita, H., Giblett, E. R., Steinberg, A. G.* (Rh Laboratory, Winnipeg 3, Canada), p. 540

A further observation of a recombination within HL-A system in an Austrian family. *Speiser, P., Pausch, V., Pacher, M.* (Institute for Blood Group Serology, University of Vienna, A-1090 Vienna, Austria), p. 543

A study of maternal-fetal anti-HL-A immunization. Extension of immunization. *Mayer, S., Tongio, M.-M.* (Centre de Transfusion Sanguine, 67 Strasbourg, France), p. 546

A simple inexpensive method for demonstrating *in vitro* leukocyte migration. *Ibrahim, A. B., Vyas, G. N.* (Department of Clinical Pathology and Laboratory of Medicine, University of California, San Francisco, Calif. 94143), p. 552

Enzyme anti-human-globulin test. A technique to detect enzyme autoantibody. *Ssebabi, E. C. T.* (Department of Pathology, Makerere University, P.O. Box 7072, Kampala, Uganda), p. 557

Vox Sanguinis (Basel) **26** (1974) No. 1

Surface proteins of the erythrocyte membrane effect of aging. *Conrad, M. J., Penniston, J. T.* (University of North Carolina,

Department of Chemistry, Chapel Hill, N.C. 27514), p. 1

The electrophoretic properties of some human blood cells. Effect of pH, ionic strength and antilymphocyte globulin. *Zerial, A., Wilkins, D. J.* (Battelle, Centre de Recherche de Genève, 1227 Carouge Genève, Switzerland), p. 14

Rh prophylactic treatment during pregnancy. An attempt to select for treatment those at possible risk. *Pollock, J., Lewis, M., Kaita, H., Chown, B., Bowman, J. M.* (Rh Laboratory, Winnipeg R3E OL8, Canada), p. 26

Anti-K13 and the K:13 phenotype. A blood-group variant related to the kell system. *Marsh, W. L., Jensen, L., Oyen, R., Stroup, M., Gellerman, M., Mcmahon, F. J., Tsitsera, H.* (Serology and Genetics Laboratory, New York Blood Center, New York, N.Y. 10021), p. 34

A new "private" antigen: Hey. *Yvart, J., Gerbal, A., Salmon, C.* (Centre Départemental de Transfusion Sanguine, 75012 Paris, France), p. 41

Anti-IgA antibodies in childhood. *Frommel, D., Geny, B., Griscelli, C.* (Centre National de Transfusion Sanguine, 75739 Paris Cedex 15, France), p. 45

Antiglobulin test in low-ionic strength salt solution for rapid antibody screening and cross-matching. *Löw, B., Messeter, L.* (Blood Bank, University Hospital, 221 85 Lund, Sweden), p. 53

The faggot method for separating blood lymphocytes. *Kerry, P. J., Greenwood, B.* (ARC Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England), p. 62

A five-bag system for washing fresh and frozen erythrocytes and their preservation. *Gänshirt, K. H., Seidl, S.* (Biotest Serum Institut GmbH, D-6072 Dreieichenhain, BRD), p. 66

Distribution of ABO and Rh(D) phenotypes in Uganda. *Ssebabi, E. C. T., Nzaro, E.* (Department of Pathology, Makerere University, P.O. Box 7072, Kampala, Uganda), p. 74

Anti-T agglutinin in cirrhosis of the liver. *Boccardi, V., Attinà, D., Bigliocchi, S., Girelli, G.* (Istituto di Patologia Medica I, Università di Roma, Roma, Italy), p. 83

Studies on human antiglobulins. Some properties of a "new" type. *Wiebecke, D.* (Abteilung für Transfusionsmedizin und Immunhaematologie der Universitätskliniken, D 87 Würzburg, BRD), p. 86

Reactivity of monkey erythrocytes in immune adherence. *Schwartz, J., Vardinon, N.* (Department of Human Microbiology, Medical School, Tel-Aviv University, Tel-Aviv, Israel), p. 91

Weak Lu9 antigen in one Lu: −6 member of a family. *Dybkjaer, E., Lylloff, K., Tippett, P.* (MRC Blood Group Unit, The Lister Institute, London SW 1W 8RH, England), p. 94

Vox Sanguinis (Basel) **26** (1974) No. 2

Association between HL-A and red cell antigens. An autoanalyzer study. *Nordhagen, R., Orjasaeter, H.* (National Institute of Public Health, Postuttak, Oslo 1, Norway), p. 97

HL-A typing of kidney cells and lymphocytes. *Sybesma, J. P. H. B., De Planque, B. A., Van Soelen, T., Borst-Eilers, E.* (Bloodbank, University Hospital, Utrecht, The Netherlands), p. 107

Contributions to the optimal use of human blood. III. Large-scale preparation of human C1 esterase inhibitor concentrate for clinical use. *Vogelaar, E. F., Brummelhuis, H. G. J., Krijnen, H. W.* (Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, The Netherlands), p. 118

An international proficiency survey for the detection of hepatitis B antigen and antibody in blood donations by counter-immunoelectrophoresis. *Moore, B. P. L., Meade, D., Taylor, P. E., Kelen, A. E.* (National Reference Laboratory, Canadian Red Cross Blood Transfusion Service, Toronto M4 YIH6, Canada), p. 128

Gm (Ray), a new allotypic marker on human IgG_3. *Schanfield, M. S., Fudenberg, H. H.* (Section of Immunology, University of California School of Medicine, San Francisco, Calif. 94143), p. 133

Presence of chronic lymphoid leukaemia associated antigen in other malignant haematological diseases. *Phan, D. T., Petrányi, Gy. G., Hollán, S. R.* (National Institute of Haematology and Blood

Transfusion, 1113 Budapest, Hungary), p. 141

Immunodiffusion studies of blood group A antigen. *Milgrom, F., Mohn, J. F., Loza, U.* (Department of Microbiology, School of Medicine, State University of New York at Buffalo, Buffalo N.Y. 14214), p. 147

Gc Opava: A variant of the group-specific component (Gc) system with an electrophoretic mobility intermediate between Gc 1—1 and Gc 2—2. *Vavrusa, B., Cleve, H.* (Division of Hematology and Blood Transfusion, Institute of National Health, Opava, Czechoslovakia), p. 157

Haemagglutinins from *Salvia. Bird, G. W. G., Wingham, J.* (Regional Blood Transfusion Service, Birmingham B15 2SG, England), p. 163

A new source of anti-N lectin: Leaves of the Korean *Vicia unijuga. Moon, G. J., Wiener, A. S.* (Reprint requests: A. S. Wiener, Office of the Chief Medical Examiner of New York City, New York, N.Y. 10016), p. 167

The M_1 N and Nv_g receptors of Tn-erythrocytes. *Bird, G. W. G., Wingham, J.* (Regional Blood Transfusion Service, Birmingham B15 2SG, England), p. 171

A study of the serological behaviour and nature of the anti-$B(P)P^k$ activity of *Salmonidae* roe protectins. *Voak, D., Todd, G. M., Pardoe, G. I.* (Regional Blood Transfusion and Immuno-Haematology Centre, Cambridge CB2 2PT, England), p. 176

A new variant of blood group B. *Zelenski, S. K., Litsenberger, B., Aster, R. H.* (American National Red Cross, Buffalo Regional Blood Program, Buffalo, N.Y. 14209), p. 189

A new rare blood group antigen, 'FAR', probably lined to the MNSs system. *Cregut, R., Liberge, G., Yvart, J., Brocteur, J., Salmon, C.* (Centre Départemental de Transfusion Sanguine, F-75012 Paris, France), p. 194

An automatic technique for erythrocyte antigen dosage. Preliminary results. *Marcelli-Barge, A., Benajam, A., Poirier, J. C., Dausset, J.* (Institut de Recherches sur les Maladies du Sang, Hôpital Saint-Louis, F-75475 Paris-Cedex 10, France), p. 199

Vox Sanguinis (Basel) **26** (1974) No. 3

Kinetic studies on the direct solid phase radioimmunoassay for hepatitis B antigen. *Prince, A. M., Jass, D.* (Laboratory of Virology, The New York Blood Center, New York, N.Y. 10021), p. 209

Complement-mediated changes in morphology of hepatitis B antigen-antibody complexes. *Hirschman, S. Z., Kochwa, S., Rosenfield, R., Schwartz, J.* (Division of Infectious Diseases, Department of Medicine, Mount Sinai School of Medicine, New York, N.Y. 10029), p. 222

I-active antigen of human erythrocyte membrane. *Gardas, A., Koscielak, J.* (Department of Biochemistry, Institute of Hematology, 00-957 Warsaw, Poland), p. 227

Automation of quantitative methods in immunohematology. Application to ABO system. *Monnet, A., Cabadi, Y.* (Laboratoire d'Immunologie Quantitative, Centre d'Hémotypologie du CNRS, CHU Purpan, F-31300 Toulouse, France), p. 238

Absence of B antibody in a blood group A_1 person. *Springer, G. F., Tegtmeyer, H.* (Department of Immunochemistry Research, Evanston Hospital, Evanston, Ill. 60201), p. 247

The recessive Lu(a-b-) phenotype. A family study. *Brown, F., Simpson, Sh., Cornwall, S., Moore, B. P. L., Oyen, R., Marsh, W. L.* (Halifax and Toronto Laboratories, Canadian Red Cross Blood Transfusion Service, Halifax, Canada), p. 259

The alanin aminotransferase activity as screening test for blood donors. *Nordby, G., Foss, O. P.* (Blood Bank, and Department of Immunohaematology, Ullevål Hospital, Oslo 1, Norway), p. 265

Differences between Bombay and Rh_{null} phenotypes. *Bhatia, H. M., Sathe, M., Gandhi, Sh., Mehta, B. C., Levine, P.* (Blood Group Reference Centre, Seth GS Medical College, Parel, Bombay 4000 12, India), p. 272

Time-related changes in reaction determining hepatitis B antigen in viral hepatitis patients. *Koza, J., Rampas, J.* (Institute of Hygiene and Epidemiology, 100 42 Praha 10, Czechoslovakia), p. 276

Third example of the blood group antigen To^a. *Crossland, J. D., Kornstad, L., Giles, C. M.* (Regional Transfusion Centre, Bridle Path, Leeds LS15 7TW, England), p. 280

Antigens Au^a, i and P_1 of cells of the dominant type of Lu(a-b-). *Crawford, M. N., Tippett, P., Sanger, R.* (MRC Blood Group Unit, The Lister Institute, London SW1W 8RH, England), p. 283

News Item

International Symposium on Fluorescein Angiography ISFA

President: Prof. Dr. J. François
Secretary: Dr. J. J. De Laey

Ghent, 28 March – 1 April, 1976

From 28 March till 1 April 1976 outstanding ophthalmologists from all parts of the world will convene in Ghent, Belgium, to attend the International Symposium on Fluorescein Angiography.

Main topics of this scientific medical symposium will be fluorescein angiography of pigment-epithelium, choroid and retinal periphery.

Some sessions will be devoted to instrumentation and techniques, to ocular hemodynamics – including retinal vein thrombosis – and diabetes. Each session will be introduced by invited lecturers. Moreover, some 120 papers will be read.

During the Symposium, which is expected to be attended by approximately 300 specialists, scientific and technical exhibitions will be held.

Preparations for the Symposium have been entrusted to an Organizing Committee, wich is presided by Professors Dr. J. François, Professor of Ophthalmology at the University of Ghent, Secretary of the Committee is Dr. J. J. De Laey of the University of Ghent.

Additional information will gladly be given by the Secretariat of the Organizing Committee, c/o Holland Organizing Centre, 16 Lange Voorhout, The Hague, the Netherlands.

MEDICAL PERIODICALS OF THE HUNGARIAN ACADEMY OF SCIENCES

ACTA CHIRURGICA

ACTA MEDICA

ACTA MICROBIOLOGICA

ACTA MORPHOLOGICA

ACTA PAEDIATRICA

ACTA PHYSIOLOGICA

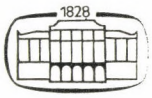
HAEMATOLOGIA

INTERNATIONAL UROLOGY AND NEPHROLOGY

These periodicals of the Hungarian Academy of Sciences publish original scientific treatises in English, German, French or Russian. The papers are written by outstanding scientists from Hungary and other countries. The editorial board of each periodica consists of professors of international reputation.
The volumes published so far have had a favourable reception in the international scientific world: the treatises are reviewed by the corresponding international reference papers.

Our periodicals are, as a rule, quarterlies: four issues make up a volume of some 400 to 500 pages.

Subscription rate per volume: US $32.00



AKADÉMIAI KIADÓ
Publishing House of the Hungarian Academy of Sciences
BUDAPEST

Distributor: KULTURA H-1389 Budapest, P.O.B. 149

Ask for the quarterly lists of our forthcoming books!

Address: AKADÉMIAI KIADÓ H-1361 Budapest, P.O.B. 36

Card Indexes

D. C. Cress, W. K. Metcalf

Platelet inhibition of human lymphocyte PHA-induced blastoid transformation. Haematologia 9, 3—13 (1975).

The reduced PHA responsiveness of human lymphocytes obtained from heparinized as compared to defibrinated blood has been shown to be due to platelet contamination in the former. Inhibition of blastoid transformation and lymphocyte death is directly related to the number of platelets added to a culture. Divalent ions partially reduce this platelet inhibitor phenomenon but do not block it completely. The "toxic" platelet components appear to be localized in the membranes and particulate matter after homogenization and hard centrifugation. Comparative studies of PHA transformation must control platelet contamination of the cultures in order to avoid severe difficulties of interpretation.

V. Kutas, E. Elekes, K. Merétey, L. Kocsár

Effect of phytohaemagglutinin on primary immune response in the rat. Haematologia 9, 15—20 (1975).

PHA pretreatment if given as a single stimulus exerted a stimulatory effect on SRBC haemolysin production in rats. If administered repeatedly, it proved to be immunosuppressive.

G. Astaldi, G. C. B. Astaldi, Ü. Topuz, L. Guarina

Lymphocyte immunological patters in leukaemia. A review. Haematologia 9, 21–33 (1975).

Investigation of the cell S-Ig in acute lymphocytic leukaemia (ALL), at the onset or relapse of the disease, shows quite marked differences from patient to patient according to the extent of the immunofluorescent-positive cells. They may vary from 0.5 to 25% or more. When these Ig-positive cells are treated with trypsin and then incubated "in vitro" for six hours, many of them are no longer Ig-positive, i.e. they do not synthesize Ig. It might be possible, that the membrane-Ig observed before trypsinization does not represent true Ig-determinants of mature B-cells (antibodies attached to leukaemia-specific determinants?). The extent of these features decrease in remission until their disappearance. Relationship between the cell immunological patterns and the treatment response in ALL could exist. In a group of ALL-patients under the same treatment, that is, vincristine and prednisone, the correlation between the course of the disease after the above-mentioned therapy showed quick and complete remission in patients with low percentage of Ig-positive cells (below 10%) and poor improvement (often without complete remission) in patients with higher percentage of Ig-positive cells. Among the most important B-lymphocyte abnormalities in chronic lymphocytic leukaemia (CLL) are the following: (a) fluorescence intensity may vary not only from patient to patient, but also from cell to cell in the same patient; (b) the Fc-receptor can be lacking; (c) the C3b-receptor is not always present or it is from 2 to 20-folds less frequent than the C3d-receptor, whereas normal human lymphocytes do not show any outstanding differences between the number of EAC rosette-forming cells either when tested with mouse complement (C3d-receptor or with human complement C3b-receptor); (d) the traffic capacity of peripheral-blood B-lymphocytes in CLL is quite defective. Results of the observations in lymphocytes in CLL, taken as a whole, suggest that CLL is in general given by the expansion of an abnormal clone of cells of B origin, arrested in their maturative development, non-responsive to the mitogen stimulation, accumulating in the peripheral-blood for a traffic deficiency. On the contrary, the T-cell class is apparently normal, and the T-cell extent in CLL-peripheral blood can be even greater than normal when taken as absolute value.

T. Révész, R. Szigeti, D. Schuler

Rosette formation in acute lymphoid leukaemia.
Haematologia *9*, 35–38 (1975).

The capacity of leukaemic lymphoblasts and remission lymphocytes, obtained from 40 children with acute lymphoid leukaemia, to form sheep red blood cell rosettes was investigated. Lymphoblasts isolated from the peripheral blood of the patients prior to antileukaemic treatment showed greatly reduced numbers of rosette-forming cells as compared to controls (4.6% *vs.* 27.5%). The ratio of rosette-forming cells during intensive induction chemotherapy was still significantly lower than the control value (15.7%), while after the achievement of complete remission the number of RFC approximated the normal value (22.5%). The presence of leukaemic serum had no significant effect on the number of RFC.

A. Leövey, B. Fekete, Gy. Szegedi

Detection in serum of antilymphocyte-globulin administered in form of eye-drops. Haematologia *9*, 39–41 (1975).

Rosette inhibition tests indicated that similarly as in previous animal experiments, anti-human lymphocytes horse globulin (AHLG) administered in the form of eye-drops entered the systemic blood circulation in man. In the eye into which the AHLG is administered, it is expected to exert a local immunosuppressive effect.

J. Brocteur, C. François-Gérard, A. André, M. Radermecker, M. Bruwier, J. Salmon

Immunization against avian proteins. Haematologia *9*, 43–47 (1975).

A study of sera of pigeon breeders showed a higher ratio of antibodies with an anti-P_1 specificity in those who show clinical signs of allergic origin. By absorption of anti-P_1 antibodies it was revealed that there exist in the cells, serum and excrement of pigeons, substances with antigenic properties similar to those of human P_1 antigen. Pigeon breeders, and particularly those who show clinical signs of allergy, possess also other antibodies which precipitate specific antigens of pigeon serum.

R. Ben Dawson, W. F. Kocholaty, R. Camp, D. Crater, T. J. Ellis, W. Spurlock, T. A. Billings, E. B. Ledford

Hemoglobin function in stored blood. XIII. A citrate-adenine preservative with optimal pH to maintain red cell 2,3-DPG (function) and ATP (viability). Haematologia *9*, 49—57 (1975).

Increasing pH by a 0.5 increment over the commonly used preservative, acid-citrate-dextrose with adenine (ACD-Ad), results in a significant improvement in 2,3-DPG, with no significant loss in concentrations which equaled those of the low pH preservatives, 5.0 and 5.5, from the 21st to the 42nd day of storage. A citrate-adenine preservative, with pH between 5.5 and 6.0, would seem to be optimal for maintenance of hemoglobin function and red cell viability, as determined by measurements of 2,3-DPG and ATP concentrations.

M. Łazewska, B. Saganek, Z. Wojtowicz, M. Józwik, M. Bielecki

Erythropoiesis inhibitor in a patient with hereditary spherocytosis. Haematologia *9*, 59—63 (1975).

The studies dealt with the effect of plasma of a patient with congenital hemolytic anaemia on the erythropoiesis in mice. The materials included the plasma from the patient before and after splenectomy and the spleen homogenate and the spleen subcellular fractions. The effect of the materials was evaluated with the amount of the ^{59}Fe taken up by the erythrocytes of the mice. The erythropoiesis was found to be inhibited by the plasma before splenectomy and by the spleen homogenate and its subcellular fractions. The inhibition was the highest in cases when the mice were given the spleen homogenates previously incubated with plasma of healthy persons.

M. Djaldetti, P. Fishman, H. Bessler, E. van der Lijn

Corticosteroid effect of eosinophils in vitro: Ultrastructural studies. Haematologia *9*, 65—72 (1975).

The effect of corticosteroid, ultracortene and ACTH, on the eosinophilic cells of a patient with hypereosinophilic syndrome was studied *in vitro*. Both drugs caused marked decrease of the number of the specific granules, disappearance of their surrounding membrane and almost complete destruction of their crystals. In addition, vacuolisation of the cytoplasm, swelling of the mitochondria and distortion of their cristae were found. Incubation of the eosinophils with the antihistaminic drug mepyramine, did not produce ultrastructural alterations.

B. Leszko, S. Pawelski

Renal function in polycythaemia. Haematologia *9*, 73—78 (1975).

In 23 patients with polycythaemia vera and symptomatic erythrocytosis, glomerular filtration rate and ruine concentration ability $\left(\max U_{osm},\ C_{osm},\ Tc_{H_2O},\ \frac{Tc_{H_2O} \times 100}{GFR},\ \frac{C_{osm} \times 100}{GFR}\right)$ were determined under conditions of antidiuresis. The restriction of fluid intake caused a significant reduction of GFR and modified the osmotic function of the kidneys. The results were similar in both types of polycythaemia.

G. Nagy, I. Dezső, M. Varsányi

Iron metabolism in polycythaemia rubra vera and secondary polycythaemia. Haematologia *9*, 79—84 (1975).

Serum iron concentration, serum iron binding capacity and saturation coefficient were assayed in polycythaemia rubra vera and secondary polyglobulia. In the exacerbation stage of polycythaemia rubra, significantly lower Se Fe and SC values were found while in the remission stage and in secondary polyglobulias these values did not differ from those of the normal controls.

B. I. Kuznik, Ja. D. Krasik, P. D. Pradun

Effects of erythrocytes on fibrinolysis. Haematologia *9*, 85—96 (1975).

The effect of destroyed and washed intact erythrocytes of normal subjects and patients with various haematological diseases was studied on the fibrinolytic activity of whole blood and plasma. Intact erythrocytes of normal and sick subjects inhibited dissolution of the clot; haemolyzed erythrocytes accelerated lysis of the euglobulin clot. Studies on fibrin films revealed in the erythrocytes of normal subjects the presence of a plasminogen activator in the fluid fraction and an inhibitor of activation in the stroma. Correlation analysis allowed to establish connections between the number of erythrocytes and the fibrinolytic activity of blood. The erythrocytes thus are affecting the process of fibrinolysis.

V. Brabec, V. Šebestík

Blood volume changes in "hypersplenic" rats.
Haematologia *9*, 97—102 (1975).

Blood volume in "hypersplenic" and normal rats was assessed by a simultaneous measurement of erythrocyte and plasma volumes by means of ^{59}Fe-labelled erythrocytes and ^{131}I-labelled human serum albumin, respectively. The "hypersplenic" condition was induced by prolonged intraperitoneal application of methylcellulose. Mean blood volume in normal rats was 6.3 ml/100 g body weight, the venous haematocrit being 48%. Mean blood volume in "hypersplenic" rats was 7.5 ml/100 g body weight, and the venous haematocrit lower by 22% than in normal animals. Compared with normal animals, the erythrocyte volume in "hypersplenic" rats was lower by 15% only. Plasma volume in "hypersplenic" rats exceeded the compensation in response to the reduction in erythrocyte mass. In addition to haemolysis, haemodilution due to plasma expansion seemed to be responsible for the anaemia in "hypersplenic" rats.

W. L. LaBaw

Auto-hypnosis in haemophilia. Haematologia *9*, 103—110 (1975).

A pilot study to determine the use of adjunctive trance therapy in the treatment of haemophiliacs has been carried out. Over a period of forty months, twenty randomly selected males were assigned to a control and an experimental group. All received due haematologic care. The ten patients in the experimental group utilized medical hypnosis as well, in group suggestive sessions to train and sustain them, but primarily in self-induced trance states. Results were compared at intervals on the basis of the amount of transfused blood and blood products. This provided an objective measure of the efficacy of trance therapy. Statistical analysis of the data confirmed the clinical observation of a greater improvement among patients in the experimental group.

NOTICE TO CONTRIBUTORS

HAEMATOLOGIA is designed for the publication of original papers, preliminary reports and reviews which contribute to the advancement in all fields related to haematology and blood transfusion. Papers in English, French, German and Russian are accepted on the condition that they have not been previously published or accepted for publication.

Manuscripts with a clear carbon copy should be sent to the Editor-in-Chief

Susan R. Hollán, M. D.
Central Research Institute of the
National Blood Service
Daróczi út 24
1113 Budapest, Hungary.

If in addition to the original typewritten copy, a duplicate copy, complete with figures, tables and references, is submitted, this will speed publication. Although every effort will be made to guard against loss, it is advised that authors retain copies of all material which they submit. The editorial board reserves the right to make literary corrections.

Manuscripts should be typed double-spaced on one side of good quality paper with proper margins and bear the title of the paper, name, address and degrees of the author together with the name of the hospital, laboratory or institute where the work has been carried out. The name and full postal address of the author who will be responsible for reading proofs should also be given. An abstract of 50 to 100 words should precede the text of the paper. The paper should not exceed 15 pages including tables and references. The approximate location of tables and figures should be indicated in the margin.

References. Only papers closely related to the author's work should be referred to. The citations should include the name of the author and/or the reference number in parenthesis. A list of numbered references should follow the end of the manuscript.

References to periodicals should mention: (1) name(s) and initials of the author(s); (2) title of paper; (3) international abbreviation of the periodical; (4) volume; (5) number of the first page; (6) year of publication in parenthesis. Thus: 14. Bean, W., Mills, A.: Coronary occlusion, heart failure and environmental temperature. *Amer. Heart J. 16*, 701 (1938).

References to books should include: (1) author(s)' name; (2) title; (3) publisher; (4) place and year of publication. Thus: 8. Alsted, G.: The incidence of peptic ulcer in Denmark. Danish Science Press Ltd., Copenhagen 1953.

Illustrations should be selected carefully and only up to a quantity required. Black-and-white photographs should be in the form of glossy prints. The author's name and the title of the paper together with the serial number of the figure should be written on the back of each print. Coloured illustrations should be given only if indispensable. Legends should be brief and attached on a separate sheet. Tables, each bearing a title, should be self-explanatory and numbered consecutively.

Authors will receive page proofs which must be sent back by return mail.

Authors are entitled to 50 reprints free of charge.

Reviews of the Hungarian Academy of Sciences are obtainable at the following addresses:

AUSTRALIA

C.B.D. Library and Subscription Service
Box 4886, G.P.O.
Sydney, N.S.W. 2001

Cosmos Book and Record Shop
145 Acland Street,
St. Kilda, 3182

Read and Co.
694—696 George Street,
Sydney, N.S.W.

AUSTRIA

Globus,
Vertrieb Ausländischer Zeitschr.
Höchstädtplatz 3,
A—1200 Wien XX.

BELGIUM

Du Monde Entier S.A.
Rue du Midi 162
1000 Bruxelles

Office International de Librairie S.A.,
Avenue Marnix 30,
1050 Bruxelles

BULGARIA

Direkzia R.E.P.
11 pl. Slaveikov,
Sofia

CANADA

Pannonia Books,
P.O. Box 1017, Postal Station „B",
Toronto, Ont. M5T 2T8

CHINA

Beijing Waiwen Shudian,
Periodical Division,
P.O. Box 50.
Peking

Peking Post Office,
Branch No. 106,
Peking

CZECHOSLOVAKIA

Mad'arská Kultura,
Václavské nám 2.
11000 Praha 1.

Poštova Novinova Služba — dovoz tisku
Vinohradská 46.
Praha 2.

Poštova Novinova Služba — dovoz tlace
Leningrádská 14.
Bratislava

DENMARK

Munksgaard's Boghandel,
Norregade 6.
DK—1165 København K.

FINLAND

Akateeminen Kirjakauppa,
Keskuskatu 2.
SF—00100 Helsinki 10.

FRANCE

Agence Litteraire et Artistique Parisienne
25 rue Royale,
Paris 8.

Office International de Documentation et Librairie
48, rue Gay-Lussac
Paris 5.

GERMAN DEMOCRATIC REPUBLIC

Zeitungsvertriebsamt
Strasse der Pariser Kommune 3—4.
1004 Berlin

GERMAN FEDERAL REPUBLIC

Kunst und Wissen,
7000 Stuttgart 1
Postfach 46,
Wilhelmstrasse 4.

GREAT BRITAIN

Blackwell's Periodicals
P.O. Box 40
Hythe Bridge Street,
Oxford OX1 2EU

Collet's Holdings Limited
Denington Estate,
Wellingborough, Northants NN8 2QT

Wm. Dawson and Sons Ltd.,
Cannon House, 10/14 Macklin Street,
London WC2B 5NG

Robert Maxwell and Co. Ltd.
4—5 Fitzroy Square,
London, W.1.

HOLLAND

Martinus Nijhoff,
P.O. Box 269,
Den Haag

Pegasus Import,
Leidsestraat 25,
Amsterdam

Swets and Zeitlinger,
Keizersgracht 487,
Amsterdam C.

ITALY

Libreria Commissionaria Sansoni
Via Lamarmora 45,
Casella Postale 552.
50121 Firenze

So. co. Lib. Ri.
Export-Import
Piazza Margana 33,
00186 Roma

JAPAN

Maruzen Co. Ltd.
P.O. Box 5050
5050 Tokyo International, 100—13 Japan

Nauka Ltd.
2—30—19 Minami-Ikebukuro,
Toshima-ku,
Tokyo 171 Japan

NORWAY

A/S Narvesens Litteraturtjeneste,
Bertrand Narvesensvei 2.
Box 6140,
Oslo 6.

POLAND

B.K.W.Z. Ruch,
ul. Wronia 23.
00—840 Warszawa

ROUMANIA

D.E.P.
Bucureşti
D.E.P.
Arad

SOVIET UNION

Pochtamt-Import
Moscow
Pochtamt-Import
Leningrad

SWEDEN

Nordiska Bokhandeln,
Fack,
10110 Stockholm 1.

SWITZERLAND

Karger Libri,
Arnold-Böcklin-Strasse 25.
4000 Basel 11.

USA

Fam Book Service,
69 Fifth Avenue,
New York, N.Y. 10003

Hungarian Books and Records,
11802 Buckeye Road,
Cleveland, Ohio 44120

Intercontinental Medical Book Corporation
381 Park Avenue South
New York, N.Y. 10016

Medical Market Research
East Washington Square,
Philadelphia, Penn. 19105

Stechert-Hafner, Inc.
31 East 10th Street,
New York, N.Y. 10003

YUGOSLAVIA

Jugoslovenska Knjiga,
Terazije 27
Beograd

Prosveta Export-Import
P.O.B. 555,
Terazije 16/1.
11001 Beograd

Index: 826861

VOLUME 9 · NUMBER 3—4 · 1975

HAEMATOLOGIA

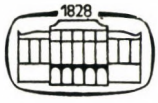
International Quarterly of Haematology

AKADÉMIAI KIADÓ
PUBLISHING HOUSE
OF THE
HUNGARIAN ACADEMY
OF SCIENCES
BUDAPEST

VOLUME 9 · NUMBER 3–4

HAEMATOLOGIA

INTERNATIONAL QUARTERLY OF HAEMATOLOGY



AKADÉMIAI KIADÓ
PUBLISHING HOUSE OF THE HUNGARIAN ACADEMY OF SCIENCES
BUDAPEST 1975

Printed in Hungary

A kiadásért felel az Akadémiai Kiadó igazgatója
Műszaki szerkesztő: Zacsik Annamária
A kézirat nyomdába érkezett: 1975. V. 30. Terjedelem: 15,95 (A/5) ív
75. Akadémiai Nyomda, Budapest — Felelős vezető: Bernát György

Contents

Haematologia 9 (3—4), pp. 179—193 (1975)

The Fine Structure of Haemopoiesis in the Human Fetal Liver

II. Origin and Differentiation of the Megakaryocyte

A. D. HOYES, D. J. RICHES, B. G. H. MARTIN

Department of Anatomy, St. Mary's Hospital Medical School, London, England

(Received May 14, 1974)

The differentiation of the megakaryocyte was studied at the ultrastructural level in the liver of human fetuses of between 49 and 134 mm crown-rump length. The development of the cells was traced from lymphoid elements with the features of haemopoietic stem cells and was divided on the basis of nuclear morphology into three stages. Granule formation commenced during the first stage and demarcation membranes could be demonstrated in the perinuclear cytoplasm early in the second stage. Late stage 2 cells often contained more than one nucleus, and the possibility that this was due to cellular fusion is discussed. The third stage was characterized by the appearance of cytoplasmic zoning and by the gradual extension of the demarcation system throughout the cytoplasm. There was evidence that the demarcation membranes were initially formed directly from the Golgi apparatus, but that their further development was due to the incorporation of elements of the agranular endoplasmic reticulum. The surface projections associated with platelet release were observed only in fully developed cells, and the formation of a zone of clear cytoplasm at the periphery was related to events occurring during the later stages of platelet release.

Introduction

Although previous ultrastructural studies of the human megakaryocyte [3, 8, 9, 10, 19, 20, 33, 37, 43, 44] have confirmed its close morphological similarity to the cells formed in the haemopoietic tissues of other mammals, there is only a limited amount of information on the changes in the fine structure of this cell during the various stages in its differentiation. The ultrastructure of the immature cell has not been clearly established, and the identity of its immediate precursor is open to question. Many of the cells previously identified as precursors of the megakaryocyte are indistinguishable from haemocytoblasts, and the dense cored vesicles which occur near the Golgi apparatus of such cells have been equated with the specific granules of the megakaryocyte [43]. There are, however, significant differences between these vesicles and megakaryocyte granules, and their occurrence in considerable numbers in the proerythroblast [18, 36] indicates that they are a normal component of the developing red cell. Specific granules and elements of the platelet demarcation system have also been demonstrated in cells which are otherwise much less mature than the typical haemocytoblast [28, 44], and there is recent experimental evidence for the formation of the various types of

blood cell from mononuclear elements which are essentially lymphoid in appearance [7, 23, 32, 39]. Cells similar to those defined by van Bekkum et al. [39] and Rubinstein and Trobaugh [32] as haemopoietic stem cells are not uncommon in the human fetal liver, and our recent observations on the formation and contribution of such cells to the production of the hepatic red cells [18] have now been extended to include a further study of the origin and early development of the megakaryocytes formed in this organ.

Materials and Methods

Twelve human fetuses with crown-rump lengths of between 49 and 134 mm were perfused through the umbilical vessels with 2% glutaraldehyde in cacodylate buffer [15] approximately 30 minutes after their removal from the uterus at therapeutic abortion. Thin slices of liver were then removed and immersed in fresh fixative. After a total period of fixation of one hour, small blocks cut from the slices were post-fixed in buffered osmium tetroxide [25], dehydrated in ethyl alcohol and embedded in TAAB resin. Ultrathin sections cut on a Porter-Blum ultramicrotome were mounted on uncoated grids and stained with lead citrate [31] before being examined in a Siemens Elmiskop 1 or Philips EM 300 electron microscope.

Buffy coat cells from the centrifuged blood of a 120 mm fetus were fixed for 15 minutes in glutaraldehyde and then processed in the same way as the other specimens.

Results

Although mature cells are more common in the material from the older fetuses, megakaryocytes in various stages of development are present in all of the specimens. Extrasinusoidal cells are also occasionally present in the older fetuses, but the majority are situated in the lumen of small sinusoids. Although the quality of preservation of the megakaryocytes is less satisfactory than that of the other cells in the liver, the changes attributable to fixation consist mainly of dilatation of the mitochondria (Fig. 3). There is also occasionally dilatation of the cisternae of the Golgi apparatus (Fig. 1), but no evidence of the presence of the chains of vesicles described by De Marsh et al. [6] and Yamada [42] and considered by Behnke [1] to be derived from fragmentation of elements of the platelet demarcation system. The differentiation of the megakaryocytes is accompanied by a progressive increase in the number of dense cored vesicles in the cytoplasm, and can be divided on the basis of the associated changes in nuclear morphology into three stages. In the first stage, the nuclei resemble those of the lymphoid elements recently categorized as haemopoietic stem cells [18]; during the second stage, they assume the features associated with active protein synthesis, and in the third stage the nuclei become irregular and there is a progressive increase in the degree of condensation of the chromatin.

Stem cells

These cells are often situated in the lumen of small sinusoids. Their nucleo-cytoplasmic ratio is high, and their slightly indented nuclei contain large amounts of condensed chromatin (Fig. 1). Small villous or club-like processes often project from the plasma membrane and centrioles can be seen near the small Golgi

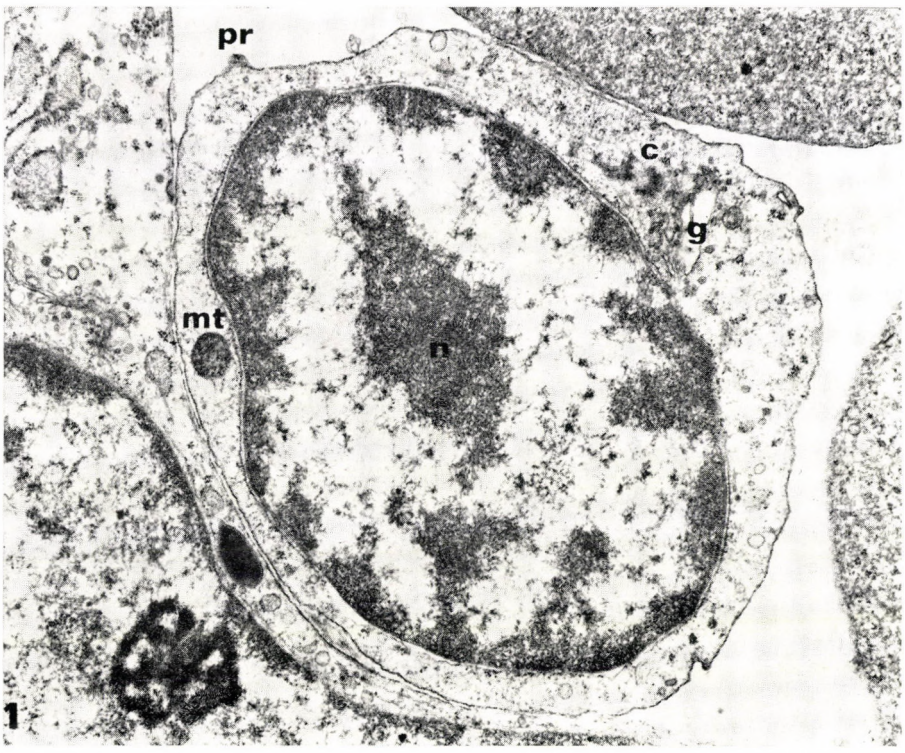


Fig. 1. Intrahepatic stem cell. n, nucleus; pr, process from surface; c, centriole; g, Golgi apparatus; mt, mitochondria. Fetus CR 55 mm. ×18,000

apparatus (Fig. 1). Other organelles are few, and include only occasional clear vesicles and scattered ribosomes and small mitochondria.

Megakaryocytes

Stage 1 cells are little larger than stem cells (Fig. 2). Their nuclei are also indented and contain large amounts of condensed chromatin (Fig. 2). The plasma membrane is less regular than that of the stem cell, and the villous projections from the surface are more prominent (Fig. 2). The projections are occupied by fine filamentous material and a thin layer of similar material is present immediately

beneath the plasma membrane. Centrioles are still frequently present in the cytoplasm, but the Golgi apparatus is larger than that of the stem cell. Cytoplasmic vesicles are also more numerous, and some contain a dense core. This is generally of uniform electron density, but differs from that of the haemocytoblast vesicle in that it is separated from the bounding membrane by a distinct interval (Fig. 2). Polysomes are fairly common and accumulations of ribosomes are often evident near the nuclear membrane (Fig. 2). The cells are also characterized by occasional elongated sacs of granular endoplasmic reticulum and small groups of large mitochondria (Fig. 2).

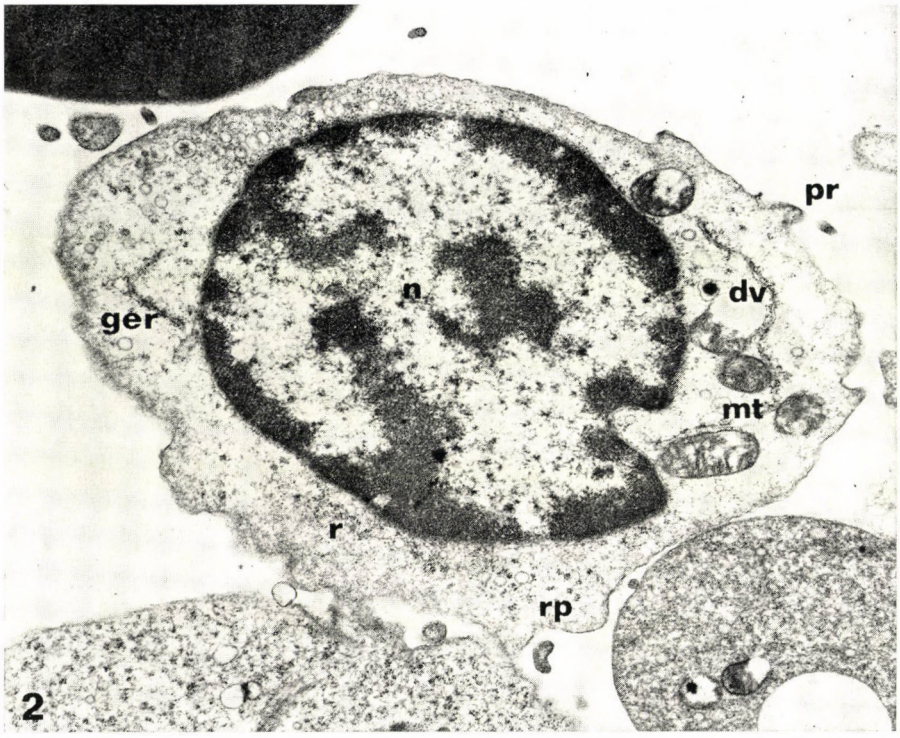


Fig. 2. Stage 1 megakaryocyte. n, nucleus; pr, projection from surface; dv, dense cored vesicle; rp, polysomes; r, single ribosomes; ger, granular endoplasmic reticulum; mt, mitochondria. Fetus CR 110 mm. ×13,000

The nuclei of *stage 2* cells are ovoid or round in section and there is only slight peripheral condensation of the chromatin (Fig. 3). The nucleolus is larger and better developed than that of the stage 1 cell and centrioles are no longer apparent in the cytoplasm. Early stage 2 cells are mononuclear and the villous projections from the surface are numerous. The projections often form elongated folds not unlike those described in the immature rat megakaryocyte [22], but are

typically distributed at random over the surface of the cell (Fig. 3). Filamentous material is still evident in these structures, but is no longer visible as a continuous layer beneath the plasma membrane. The Golgi apparatus is large and numerous small coated and uncoated vesicles now occur in the region of this structure (Fig. 4). Many of the vesicles contain material of low electron density and there is often evidence of their fusion with one another. Coated vesicles and somewhat larger clear vesicles and small vacuoles are distributed throughout the cytoplasm. The dense cored vesicles are also widely dispersed in the cells (Fig. 3): most of the

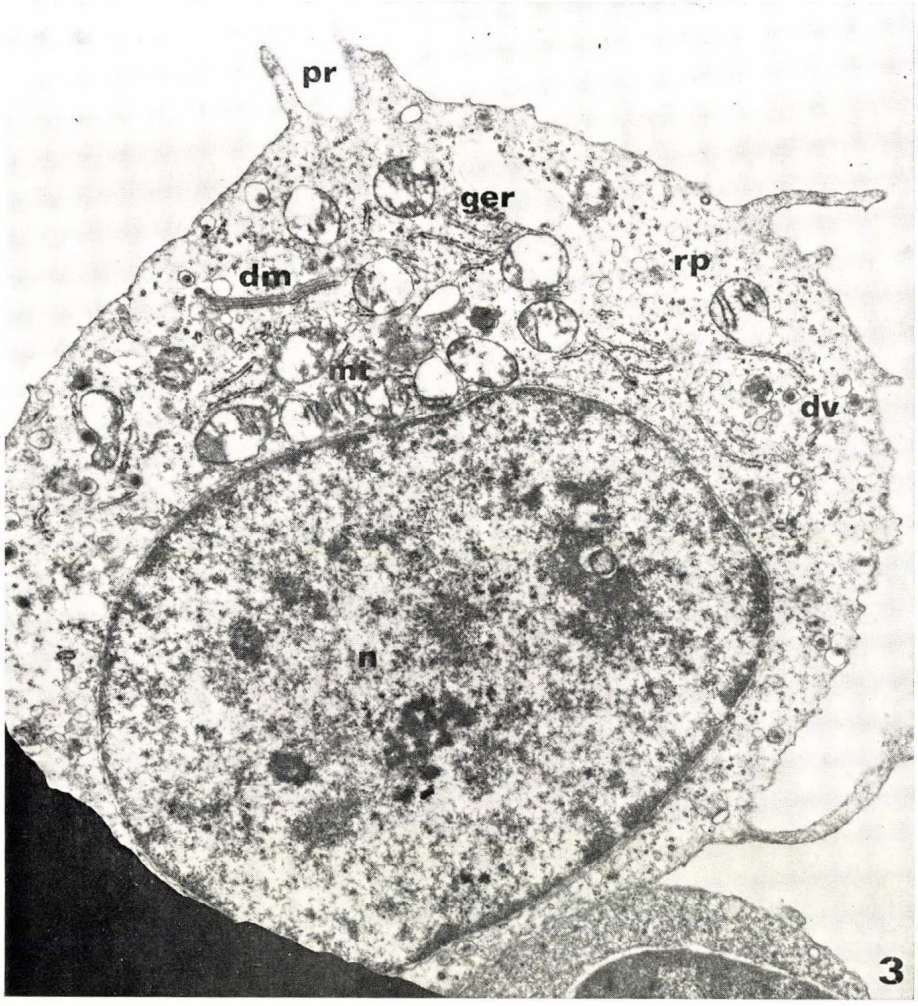


Fig. 3. Early stage 2 megakaryocyte. n, nucleus; pr, villous projections from surface; dv, dense cored vesicles; rp, polysomes; ger, granular endoplasmic reticulum; mt, mitochondria; dm, demarcation membranes. Fetus CR 55 mm. ×11,000

vesicles still contain a peripheral clear area (Figs 4–6), and many now possess the highly electron dense nucleoid of the mature megakaryocyte granule (Figs 5, 6).

Stage 2 cells also contain numerous polysomes and considerable amounts of granular endoplasmic reticulum (Fig. 3). The sacs of the reticulum typically occur in groups (Fig. 3) and often communicate with short sacs of agranular endoplasmic reticulum. The mitochondria are much more numerous than in the stage

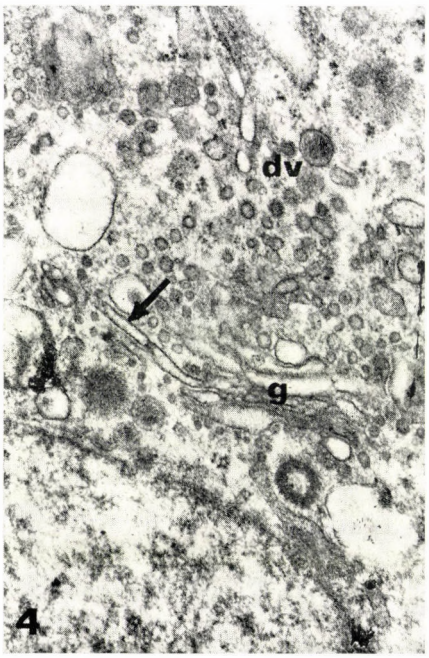


Fig. 4. Golgi region of a stage 2 cell. A membranous structure resembling a demarcation membrane (arrow) is in communication with the apparatus (g). dv, dense cored vesicle. Fetus CR 49 mm. ×30,000

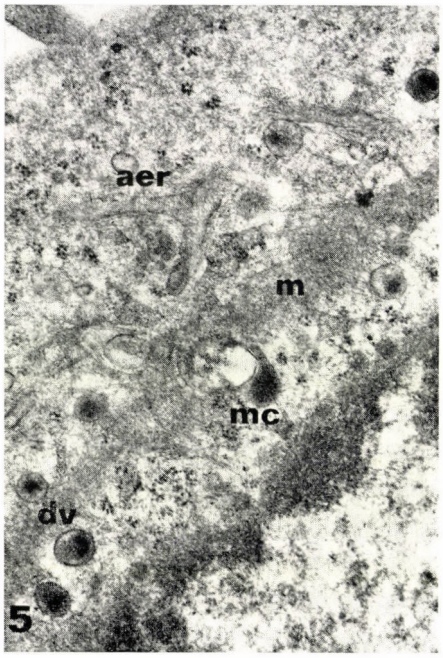


Fig. 5. Fibrillar material (m) in the perinuclear cytoplasm of an early stage 2 cell. dv, dense cored vesicles; mc, microtubule; aer, agranular endoplasmic reticulum. Fetus CR 49 mm. ×26,500

1 cell and form the groups demonstrated in the immature rat megakaryocyte [11] (Fig. 3). Deposits of dense fibrillar material are frequently evident in the perinuclear cytoplasm, and both microtubules and sacs of agranular endoplasmic reticulum are closely associated with these structures (Fig. 5).

Platelet demarcation membranes are also evident in the cytoplasm of the early stage 2 cell (Fig. 3). Some are situated near the Golgi apparatus, and structures which closely resemble the membranes can occasionally be seen in communication with the Golgi cisternae (Fig. 4). There is, however, no evidence of the communication of the membranes with the plasma membrane and the majority

are embedded in the perinuclear deposits of fibrillar material (Fig. 6). The sacs of agranular endoplasmic reticulum which are present in these regions of the cell are often closely related to the membranes (Fig. 6) and sometimes appear to be in the process of fusing with them. At this stage in the development of the cells, clear and coated vesicles occur in close proximity to the membranes only in the region of the Golgi apparatus. Dense-cored vesicles are, however, often visible near the mem-

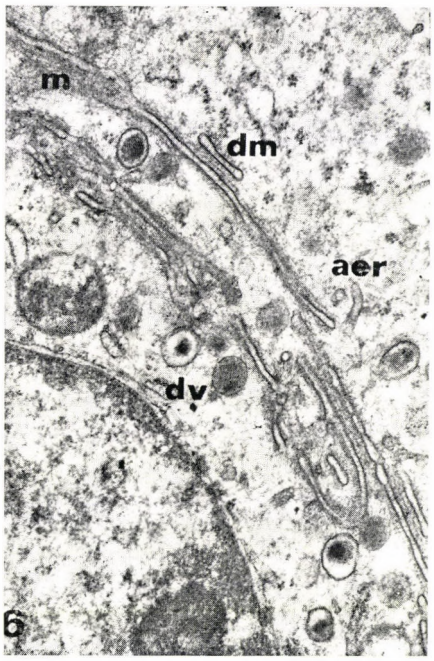


Fig. 6. Demarcation membranes (dm) embedded in fibrillar material (m) in the perinuclear cytoplasm of an early stage 2 cell. dv, dense cored vesicles; aer, agranular endoplasmic reticulum. Fetus CR 49 mm

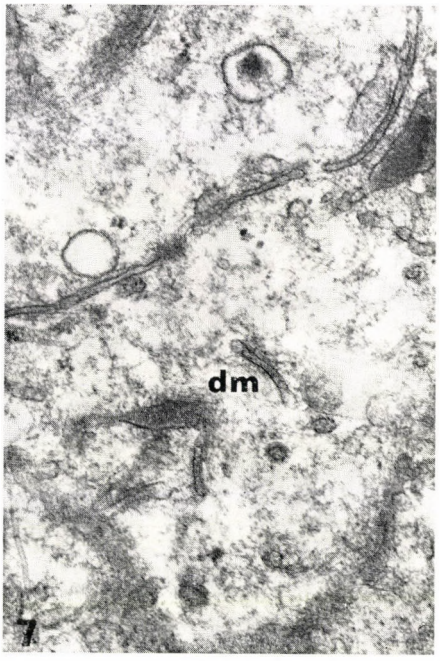


Fig. 7. Dilated demarcation membranes (dm) containing dense material in an extrasinusoidal megakaryocyte. Fetus CR 115 mm. ×39,000

branes, and in the occasional extrasinusoidal cells present in the older fetuses the membranes often contain material not unlike that present in the vesicles (Fig. 7).

Late stage 2 cells often contain two nuclei (Fig. 8), and in occasional cells three nuclei are present. The cells are often highly irregular in shape (Fig. 8) and there is a tendency for the individual organelles to be concentrated in focal areas of the cytoplasm.

The changes in nuclear morphology which occur in the *stage 3* cell are accompanied by a marked reduction in the prominence and degree of development of the nucleolus. Early stage 3 cells are characterized by the cytoplasmic zoning

which has been described in most other ultrastructural studies of the megakaryocyte. The peripheral zone is initially extensive and contains numerous polysomes. The intermediate zone is occupied by the demarcation membranes and their associated deposits of fibrillar material, microtubules and agranular endoplasmic reticulum, and the central zone contains the much enlarged and skein-like Golgi

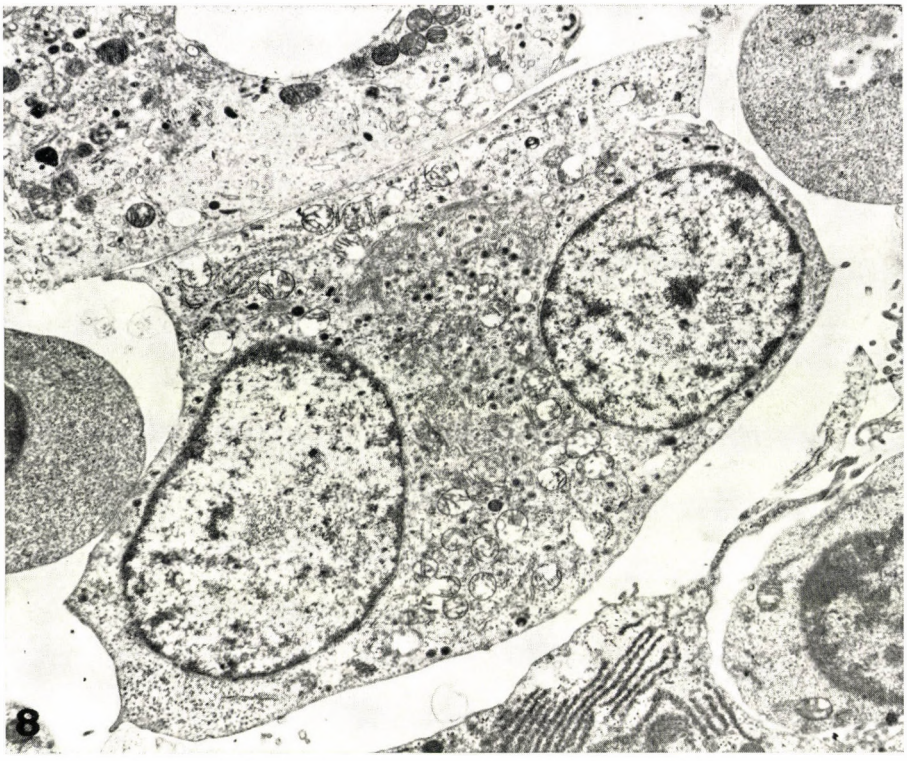


Fig. 8. Late stage 2 megakaryocyte with two nuclei. Fetus CR 55 mm. × 5,500

apparatus and numerous small vesicles. Much of the granular endoplasmic reticulum is situated in the perinuclear cytoplasm and the mitochondria and dense cored vesicles are distributed throughout the central and intermediate zones.

The establishment of cytoplasmic zoning in the cells is followed by a progressive increase in the degree of development of the demarcation membranes, and in the proportion of the cytoplasm occupied by the intermediate zone. The extension of the membranes towards the surface of the cell is generally preceded by the appearance of deposits of fibrillar material in the marginal cytoplasm (Fig. 9). There is at the same time a marked increase in the degree of irregularity of the membranes and branching is common. The membranes gradually become separated from one another and the ribosomes and small coated and uncoated

vesicles are dispersed between them (Fig. 9). The coated vesicles can often be seen attached to sacs of endoplasmic reticulum, but the frequent communication of the vesicles with the demarcation membranes which was described by Behnke [1] has not been observed. The close relationship between the agranular endoplasmic reticulum and the membranes established in the stage 2 cell is, however, main-

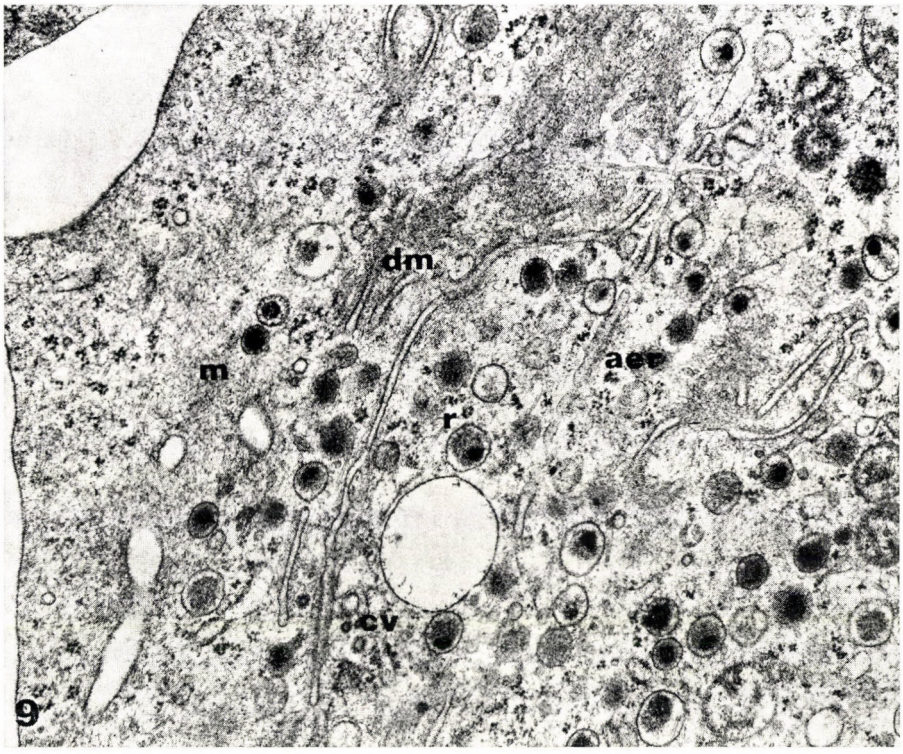


Fig. 9. Peripheral cytoplasm of a stage 3 cell. m, fibrillar material; dm, demarcation membranes; r, ribosomes; cv, coated vesicles; aer, agranular endoplasmic reticulum. Fetus CR 49 mm. ×27,500

tained throughout this period of development (Fig. 9), and especially in the region of the Golgi apparatus, the sacs of the reticulum still frequently communicate with the membranes.

In the mature stage 3 cell, the demarcation membranes form an anastomosing network which occupies almost the whole of the cytoplasm. The membranes can often be seen to communicate with the plasma membrane, and large pseudopodial processes project from at least part of the surface of the cell. Considerable amounts of fibrillar material and numerous microtubules are interspersed between the demarcation membranes, and the various types of vesicle present in the cells

are also fairly evenly distributed between these structures. A distinct central zone is no longer evident and the Golgi apparatus is often difficult to demonstrate. There is also a considerable reduction in the number of ribosomes in the cells, and the sacs of both the granular and agranular endoplasmic reticulum are dilated.

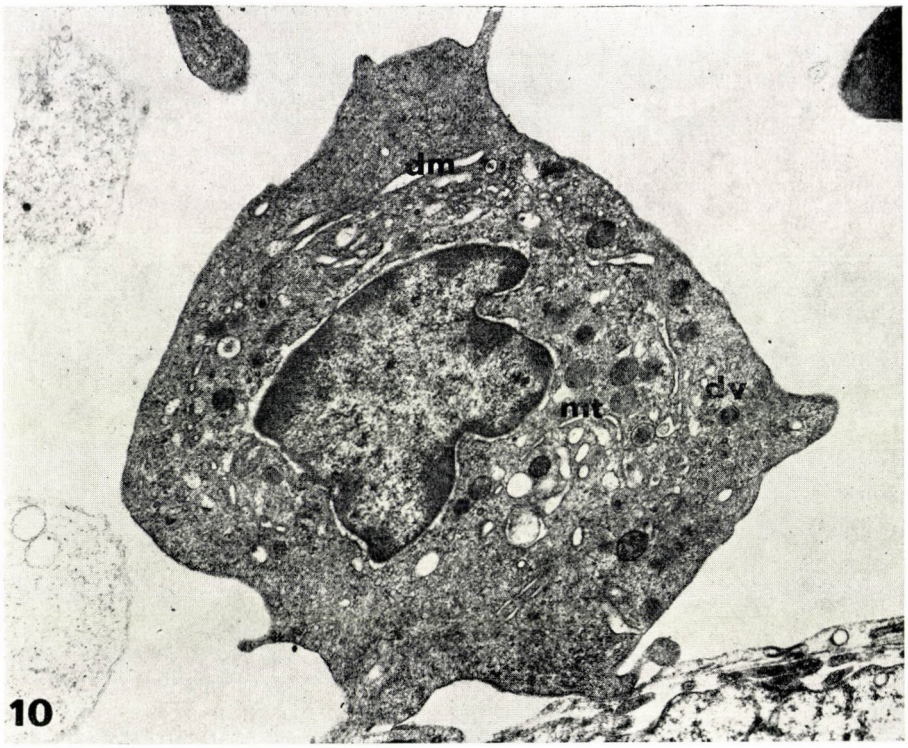


Fig. 10. Nucleated residuum of an effete megakaryocyte. mt, mitochondria; dv, dense cored vesicle; dm, dilated demarcation membranes. Fetus CR 55 mm. × 15,000

In some of the cells with pseudopodial projections, a thick zone of finely fibrillar cytoplasm is present at the periphery and the organelles are concentrated in an area of dense cytoplasm around the nucleus. The nucleated residua of exhausted megakaryocytes are also characterized by a dense cytoplasm and contain few organelles other than scattered mitochondria, occasional dense cored vesicles and dilated demarcation membranes (Fig. 10).

Platelets

The platelets present in the liver and the buffy coat of the one specimen in which it was prepared for electron microscopy are irregular in shape, but are otherwise similar to adult platelets. They contain dense cored vesicles and clear

vesicles and vacuoles, small mitochondria and aggregates of filaments and microtubules. Small amounts of glycogen are often present and although components of the dense tubular system are rarely visible, the membrane infoldings which form the open canalicular system can often be seen.

Discussion

Although a lymphocytic origin of the megakaryocyte was proposed by Howell [17] and is consistent with recent opinion on the nature of the haemopoietic stem cell, small mononuclear cells similar to those classified as stage 1 megakaryocytes have not been previously demonstrated at the ultrastructural level. Such cells already contain dense cored vesicles and are characterized by the incipient development of many of the other distinctive features of the stage 2 cell, but are much less mature than the cells identified as early precursors of the megakaryocyte in previous ultrastructural studies of the bone marrow, spleen and fetal liver [1, 11, 22, 38, 43, 44]. They are also clearly distinguishable from haemocytoblasts, but possess the nuclear and other features of the cells categorized as haemopoietic stem cells, and probably share with at least some of the red cells formed in the liver [18] a common origin from these elements.

The changes in nuclear morphology which characterize the second stage in the differentiation of the cells can be correlated with a marked increase in the number of cytoplasmic polysomes. Mononuclear stage 2 cells can sometimes be confused with early haemocytoblasts, but contain the large groups of mitochondria recently observed in the splenic megakaryocyte [11] and much larger amounts of granular endoplasmic reticulum. There are also significant differences in the fine structure and distribution of the dense cored vesicles in the two types of cell, and many of the megakaryocytes already contain platelet demarcation membranes.

Although the findings of most previous ultrastructural studies of the mammalian megakaryocyte are consistent with the intracellular development of the demarcation membranes, there is evidence from a recent study in the rat that, in this species, the membranes are formed from foci of surface membrane folding which gradually become incorporated into the cytoplasm [22]. The elongated folds which project from the developing human megakaryocyte probably correspond to those observed in the rat, but are typically distributed at random over the surface of the cell. The demarcation membranes are also initially concentrated in the perinuclear cytoplasm, and there is evidence of their frequent communication with the plasma membrane only at a much later stage in the differentiation of the cells.

The classic hypothesis of the formation of the demarcation membranes from aggregates of cytoplasmic vesicles has recently been questioned [1, 11], and our failure to demonstrate the chains of vesicles described by Yamada [42] is in accord with the view that such appearances are due to the fragmentation of preexisting membranes during processing. The frequent communication of coated

vesicles with the demarcation membranes reported by Behnke [1] has not been observed in our material, and there is a close and consistent relationship only between the dense cored vesicles and the membranes. There is, however, no direct evidence of the fusion of the vesicles with these structures, and although the occurrence of dense material in the membranes of the occasional extrasinusoidal cells present in the older specimens is suggestive of such a process, this is clearly an atypical phenomenon, and is almost certainly related to the development in the cells of the degeneration which has been observed in somewhat older fetuses with the light microscope [14]. Small vesicles similar to those associated with the Golgi apparatus have also been implicated in the transport of materials from the apparatus to the demarcation membranes [11], but have been seen to communicate only with one another, and are probably mainly involved in the formation of the dense cored vesicles [12, 16, 20, 42, 43]. Demarcation membranes are, nevertheless, often closely related to the Golgi apparatus, and the occasional occurrence of membranous structures in communication with the Golgi cisternae which has been observed during the second stage in the development of the cells is suggestive of their initial formation from this structure.

The deposits of fibrillar material which appear in the perinuclear cytoplasm in the early stage 2 cell probably correspond to those recently demonstrated in the immature myeloid megakaryocyte [28, 44]. In the fetal cell, microtubules are consistently related to the deposits, and it is possible that, as in the platelet [40], and cells such as the neuron [30], the material contributes to the formation of these structures. The demarcation membranes rapidly become embedded in the fibrillar material, and the development of this association is accompanied by the appearance of a close relationship between the membranes and sacs of agranular endoplasmic reticulum. A role of the reticulum in the formation of the demarcation membranes has been proposed on a number of occasions [4, 16, 26, 34] and the not infrequent occurrence of communications between the sacs and the membranes suggests that the further development of the demarcation system in the human fetal cell is mainly due to the progressive incorporation of elements of the reticulum into the membranes.

The condensation of the nuclear chromatin which occurs during the third stage in the differentiation of the cells is preceded by the appearance in at least a proportion of more than one nucleus. Although previous studies of the number of nuclei and the amount of DNA in the myeloid cell [5, 13, 24, 27, 28] have supported the hypothesis that the development of polyploidy in the megakaryocyte is due to the repeated synchronous endomitosis, there is evidence from a recent study of the splenic cell [35] that it also derives, at least in part, from cellular fusion. The ploidy of the fetal hepatic megakaryocyte and its capacity for mitotic activity have still to be established, but the differentiation of at least the majority of the cells in the lumen of small sinusoids clearly provides them with a suitable environment within which fusion can occur. The early development of a thin layer of fibrillar material beneath the plasma membrane and of elongated folds from the surface may also be related to their acquisition by the cells of a limited

capacity for amoeboid movement, and the marked irregularity and focal aggregation of the organelles of the late stage 2 cell is possibly an indication of recent cellular fusion. The limitation in the number of cells available for fusion imposed by the partition of the available stem cells between the large number of sinusoids formed in the liver during its period of hemopoietic activity and by the early release of many of the cells into the circulation may also be partly responsible for the occurrence of no more than three nuclei in the hepatic megakaryocyte [14].

The morphology of the stage 3 cell is similar to that of the megakaryocytes described in most previous ultrastructural studies of the bone marrow, spleen and fetal liver, and the changes in the fine structure of the cells during this period correspond to those reported by Jean et al. [19] in the human myeloid cell. The exact stage in their development at which the cells assume a capacity for platelet production is still open to doubt [44] but it is significant that the surface projections associated with platelet release [2, 4, 21, 41] are normally apparent only in cells in which the demarcation system fills the cytoplasm and there is a marked reduction in the number of ribosomes. The formation of the thick zone of clear cytoplasm which can be seen at the periphery of some of the cells with such projections has been regarded as a degenerative phenomenon [29, 38] or an artefact of fixation [2], but the occurrence of a similar degree of cytoplasmic condensation in the effete cell to that observed in the perinuclear area of cells possessing such a zone suggests that its formation is due to a major alteration in cytoplasmic organisation during the later stages of platelet release.

*

The authors are indebted to Professor K. A. Porter of the Department of Histopathology and Experimental Pathology, St. Mary's Hospital Medical School, for the use, during part of this investigation, of the Philips electron microscope provided by the Wates Foundation.

References

1. Behnke, O.: An electron microscope study of the megacaryocyte of the rat bone marrow. I. The development of the demarcation membrane system and the platelet surface coat. *J. Ultrastruct. Res. 24*, 412 (1968).
2. Behnke, O.: An electron microscope study of the rat megacaryocyte. II. Some aspects of platelet release and microtubules. *J. Ultrastruct. Res. 26*, 111 (1969).
3. Bussi, L., Jean, G., Le Coultre, L.: Ultrastructural aspects of platelets and megakaryocytes in a case of 'primary' thrombocythaemia. *Acta haemat. (Basel) 35*, 113 (1966).
4. De Bruyn, P. P. H.: The fine structure of the megakaryocyte of the bone marrow of the guinea pig. *Z. Zellforsch. 64*, 111 (1964).
5. De Leval, L.: Dosages cytophotométriques d'ADN dans des mégakaryoctes normaux de Cobaye. *C. R. Soc. Biol. (Paris) 158*, 2198 (1964).
6. De Marsh, Q. B., Kautz, J., Motulsky, A. G.: An electron microscope study of sectioned platelets and megakaryocytes. *J. clin. Invest. 34*, 929 (1955).
7. Dicke, K. A., van Noord, M. J., Maat, B., Schaefer, U. W., van Bekkum, D. W.: Identification of cells in primate bone marrow resembling the hemopoietic stem cell in the mouse. *Blood 42*, 195 (1973).

8. Falcão, L.: La démarcation des plaquettes sanguines dans les mégakaryocytes de la moelle osseuse humaine (Etude au microscope électronique). *Coagulation 1*, 229 (1968).
9. Falcão, L., Gautier, A.: Recherches ultrastructurales sur la libération des plaquettes par les mégakaryocytes humains. *Blut 16*, 57 (1967).
10. Falcão, L., Caen, J., Gautier, A.: Étude évolutive de l'ultrastructure des mégakaryocytes dans un cas de purpura thrombopénique idiopathique avant 12 jours et 5 mois après splénectomie. *Blut 19*, 156 (1969).
11. Faragó, S., Oláh, I.: Electron microscopic investigation of the developing forms of megakaryocytes. *Haematologia 4*, 103 (1970).
12. Gautier, A., Jean, G., Probst, M., Falcão, L.: Ultrastructure du mégakaryocyte et problèmes de plaquettogénèse. *Arch. ital. Anat. Istol. pat. 37*, 503 (1963).
13. Garcia, A. M.: Feulgen-DNA values in megakaryocytes. *J. Cell Biol. 20*, 342 (1964).
14. Gilmour, J. R.: Normal haemopoiesis in intra-uterine and neonatal life. *J. Path. Bact. 52*, 25 (1941).
15. Gordon, G. B., Miller, L. R., Bensch, K. G.: Fixation of tissue culture cells for ultrastructural cytochemistry. *Exp. Cell Res. 31*, 440 (1963).
16. Han, S. S., Baker, B. L.: The ultrastructure of megakaryocytes and blood platelets in the rat spleen. *Anat. Rec. 149*, 251 (1964).
17. Howell, W. H.: Observations upon the occurrence, structure and function of the giant cells of the marrow. *J. Morphol. 4*, 117 (1894).
18. Hoyes, A. D., Riches, D. J., Martin, B. G. H.: The fine structure of haemopoiesis in the human fetal liver. I. The haemopoietic precursor cells. *J. Anat. 115*, 99 (1973).
19. Jean, G., Lambertenghi-Deliliers, G., Ranzi, T., Poirier-Bassetti, M.: The human bone marrow megakaryocyte. An ultrastructural study. *Haematologia 5*, 253 (1971).
20. Jones, O. P.: Origin of megakaryocyte granules from Golgi vesicles. *Anat. Rec. 138*, 105 (1960).
21. Keyserlingk, D. Graf, Albrecht, M.: Über die Pseudopodien von Megakaryocyten und ihre Bedeutung für die Freisetzung von Thrombozyten. *Z. Zellforsch. 89*, 320 (1968).
22. MacPherson, G. G.: Origin and development of the demarcation system in megakaryocytes of rat bone marrow. *J. Ultrastruct. Res. 40*, 167 (1972).
23. Murphy, M. J., Jr., Bertles, J. F., Gordon, A. S.: Identifying characteristics of the haematopoietic precursor cell. *J. Cell Sci. 9*, 23 (1971).
24. Odell, T. T., Jr., Jackson, C. W., Gosslee, D. G.: Maturation of rat megakaryocyte studied by microspectrophotometric measurement of DNA. *Proc. Soc. exp. Biol. (N.Y.) 119*, 1194 (1965).
25. Palade, G. E.: A study of fixation for electron microscopy. *J. exp. Med. 95*, 285 (1952).
26. Paulus, J. M.: Multiple differentiation of megakaryocytes and platelets. *Blood 29*, 407 (1967).
27. Paulus, J. M.: Cytophotometric measurements of DNA in thrombopoietic megakaryocytes. *Exp. Cell Res. 53*, 310 (1968).
28. Paulus, J. M.: DNA metabolism and development of organelles in guinea-pig megakaryocytes: A combined ultrastructural, autoradiographic and cytophotometric study. *Blood 35*, 298 (1970).
29. Paulus, J. M., Mel, H. C.: Viability studies on megakaryocytes in mechanically and enzymatically suspended rat bone marrow. *Exp. Cell Res. 48*, 27 (1967).
30. Peters, A., Palay, S. L., Webster, H. de F.: The fine structure of the nervous system. The cells and their processes. Harper and Row, New York 1970.
31. Reynolds, E. S.: The use of lead citrate at high pH as an electron opaque stain in electron microscopy. *J. Cell Biol. 17*, 208 (1963).
32. Rubinstein, A. S. and Trobaugh, F. E., Jr.: The ultrastructure of presumptive hematopoietic stem cells. *Blood 42*, 61 (1973).
33. Schulz, H.: Die Erneuerung der Thrombocyten im elektronenmikroskopischen Bild. *Verh. dtsch. Ges. Path. 50*, 239 (1966).

34. Schulz, H.: Thrombocyten und Thrombose im electronenmikroskopischen Bild. Springer-Verlag, Berlin 1968.
35. Sklarew, R. J., Pachter, B., Hoffman, J., Post, J.: Formation of splenic megakaryocytes in young rat. *Exp. Cell Res. 64*, 195 (1971).
36. Sorenson, G. D.: An electron microscopic study of hematopoiesis in the yolk sac. *Lab. Invest. 10*, 178 (1961).
37. Spicer, S. S., Greene, W. B., Hardin, J. H.: Ultrastructural localisation of acid muco-substance and antimonate-precipitable cation in human and rabbit platelets and megakaryocytes. *J. Histochem. Cytochem. 17*, 781 (1969).
38. Thiéry, J.-P., Bessis, M.: Méchanisme de la plaquettogénèse. Etude "in vitro" par la microcinématographie. *Rev. Hémat. 11*, 162 (1956).
39. Van Bekkum, D. W., Van Noord, M. J., Maat, B., Dicke, K. A.: Attempts at identification of hemopoietic stem cell in mouse. *Blood 38*, 547 (1971).
40. White, J. G.: The submembrane filaments of blood platelets. *Amer. J. Path. 56*, 267 (1969).
41. Wright, J. H.: Die Entstehung der Blutplättchen. *Virchows Arch. path. Anat. 186*, 55 (1906).
42. Yamada, E.: The fine structure of the megakaryocyte in the mouse spleen. *Acta anat. (Basel) 29*, 267 (1957).
43. Zamboni, L.: Electron microscope studies of blood embryogenesis in humans. I. The ultrastructure of the fetal liver. *J. Ultrastruct. Res. 12*, 509 (1965).
44. Zucker-Franklin, D.: The ultrastructure of megakaryocytes and platelets. In Gordon, A. S. (Ed.): Regulation of Hematopoiesis. Vol. II. Appleton-Century-Crofts, New York, 1970, p. 1553.

Correspondence: Dr. A. D. Hoyes, Department of Anatomy, St. Mary's Hospital Medical School, London W2 1PG, England

Haematologia 9 (3—4), pp. 195—204 (1975)

Synchronization of Rabbit Bone-Marrow Cells in Vivo

CH. COUTELLE,* H. H. REINEKE, E. STEINDAMM,
W. MEURER, M. GRIEGER, S. ROSENTHAL*

Institute of Physiological and Biological Chemistry, Humboldt University, Berlin, GDR

(Received March 29, 1973)

The recovery of the rabbit bone-marrow from anaemia was investigated during an eight-day period of daily punctures of the tibiae after six days of phenylhydrazine treatment. A maximum of erythroid (range, 37.1 to 44.0%) and a minimum of leukoid cells (range, 8.4 to 13.4%) was observed on the fifth day of recovery. The rest, about 50% cells were reticulum cells. Signs of recovery were observed in peripheral blood as soon as on the first day after phenylhydrazine treatment. This led to the assumption that the tibiae became repopulated with active erythropoietic cells during anaemia, and that the reticulum cells might play a role as erythroid precursors in this process.

Investigation of the metabolic and physiological characteristics of bone-marrow cells is limited by the fact that the population obtained under normal conditions is heterogeneous, consisting of cells at different stages of maturation. Therefore, several investigators have attempted to induce a predominance of a certain cell form by pretreatment of the animals used as source of the haemopoietic tissue [1—3].

A simple way to obtain a high percentage of erythroid cells is to induce erythropoiesis by anaemia. This induction is caused by the increase of the endogenous e ythropoietin level as an answer to hypoxia. Lingrel [1] reported an enrichment to about 85% of erythroid cells, more than half of them late erythroid forms, in the bone-marrow of rabbits on the third day of recovery from anaemia induced by phenylhydrazine. Hershko et al. [3, 4] subjected rabbits to blood loss combined with actinomycin D treatment to obtain a predominance of early erythroid cells.

In the present work, we have investigated the different cell lines of the bone-marrow of 5 rabbits during an eight-day recovery period after phenylhydrazine induced anaemia.

* Central Institute of Molecular Biology of the Academy of Sciences of the GDR, Department of Bioregulation.

Abbreviations: PCV Packed cell volume; MCHC Mean corpuscular haemoglobin concentration; RNA Ribonucleic acid.

Material and methods

Rabbits of both sexes and of no definite breed, with a body weight between 2.5 and 3.2 kg were injected with phenylhydrazine hydrochloride on six consecutive days starting with 10 mg per kg body weight on the first day and with reduced doses, according to the effect of treatment on packed cell volume (PCV) in peripheral blood on the following days. PCVs between 10 and 20% as estimated in capillaries centrifuged in a Janetzky centrifuge (TH 11) at 18,500 *g*/2 min are shown in Table 1 together with the total dose of phenylhydrazine. The haemo-

Table 1

PCV in 5 rabbits during six-day phenylhydrazine treatment and recovery period (Symbols above columns represent the same animals as in Fig. 4)

	Body weight (kg)	△ 2.5	○ 2.6	□ 2.6	● 3.1	▲ 3.0	
	Total dose of phenylhydrazine (mg/kg)	39.5	45.5	41.3	41.3	29.1	
Day of experiment	Phenylhydrazine treatment						
1.	1	40.0	41.0	30.0	37.0	30.0	
2.	2	32.0	36.0	27.0	31.5	28.0	
3.	3	20.0	31.5	17.0	22.0	19.5	
4.	4	17.0	27.0	17.5	19.5	11.5	
5.	5	14.0	20.0	17.0	14.5	10.0	
6.	6	15.0	22.0	16.5	14.5	12.5	
	Recovery period						Packed
7.	1R	16.6	21.0	16.0	12.0	13.6	cell volumes
8.	2R	21.0	27.5	18.6	14.0	14.3	(PCV) [%]
9.	3R	25.0	28.5	19.3	22.0	22.0	
10.	4R	32.0	31.0	23.0	23.0	30.0	
11.	5R	33.0	29.4	26.0	27.5	28.0	
12.	6R	34.0	28.0	22.8		30.0	
13.	7R	31.0	34.0			31.0	
14.	8R	39.0	32.0			32.0	
15.	9R	39.5	34.0			26.0	

globin content in the peripheral blood was determined by a modification of the cyanmethaemoglobin method of Drabkin [5]. Reticulocytes were stained with brilliantcresyl blue and counted per 1000 cells. Bone-marrow was obtained from each animal on the first 5 to 8 days of the recovery period from the proximal third of the tibia. After local procaine anaesthesia and incising the skin and connective tissue covering the inner anterior part of the tibia a hole was bored by means of a dentist drill and the bone-marrow was aspirated by a S1 syringe. Every day a new hole was bored alternating the legs from day to day. This method is essentially the

same as used by Fleischer [6] with the exception that we applied local instead of general anaesthesia.

In a separate experiment, bone-marrow from the tibia, femur and humerus of 4 animals treated with phenylhydrazine in the above described manner and killed on the 5th day of recovery was flushed from the bones with BSG solution (buffered saline glucose: 37.4 mM Na_2HPO_4/KH_2PO_4-buffer pH 7.4, 117 mM NaCl, 11.2 mM glucose) containing 5 I.U. heparin/ml. All procedures were performed at 4°C. To obtain a single cell suspension, the pooled marrow of each animal was passed separately through two stainless steel sieves, the first with a mesh diameter of 0.2 mm, the second with one of 0.16 mm. Bone-marrow smears were obtained from the middle of the tibia of each animal immediately after opening this bone and from the pooled bone-marrow single cell suspension of each animal after pelleting their cells at 3000 *g* for 10 min.

The bone-marrow smears after drying for 24 hrs were stained with May–Grünwald–Giemsa.

Results

Packed cell volume, MCHC and reticulocyte count in the peripheral blood

The initial value for PCV of the 5 animals varied between 40 and 30% (Table 1). Phenylhydrazine treatment caused its decrease to between 10 and 20% on the 5th to 7th day after starting the experiment. The older animals Nos. 4 and 5 showed a poorer erythroid regeneration, as shown by the low PCV in animal 5

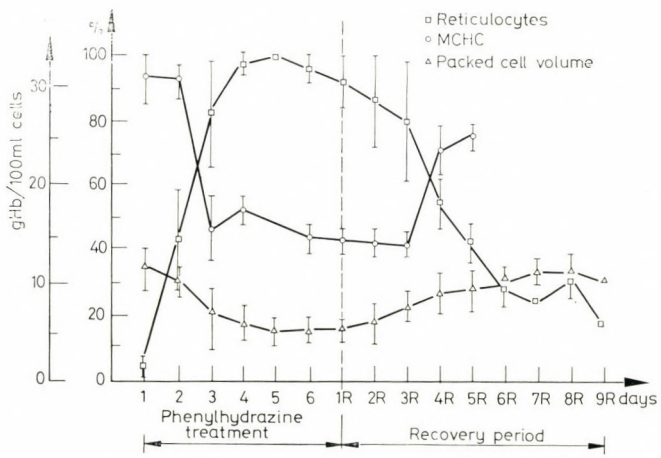


Fig. 1. PCV, MCHC and reticulocyte count of 5 rabbits during phenylhydrazine injection and recovery period. (Mean values and standard deviations)

between the 4th and 6th day in spite of the minimum doses applied, and by the slow increase of PCV in animal 4 during the first two days of the recovery period (days 7 and 8 of the experiment).

In spite of these individual differences the main tendency of the reaction was clear-cut as shown in Fig. 1. There was a drop in the PCV up to the 5th day of the experiment and a steady increase from day 7, the first day of the recovery period. A similar behaviour was observed for MCHC, with the difference that between the 1st and 3rd day of the recovery period no substantial change was detectable and that a steep increase occurred on the 4th day.

It can be seen in Fig. 1 that on the 5th day practically all circulating red blood cells were reticulocytes. Thereafter their number declined but did not reach the original value even at the end of the experiment.

Bone-marrow

In each bone-marrow smear, thousand nucleated cells were differentiated. Reticulum cells were predominant in most smears. These cells are characterized by a large nucleus with disperse chromatin sometimes containing vacuoles, and a slightly basophilic cytoplasm with ill-defined borders (Fig. 2). Some of the cells were damaged indicating their fragility. According to the pictures of similar cells given by Fleischer [6] we classified them as reticulum cells. This population was probably inhomogeneous, containing morphologically non-differentiable cells probably committed to different cell lines. The erythroid cells were further subdivided into basophilic and polychromatic erythroblasts and normoblasts.

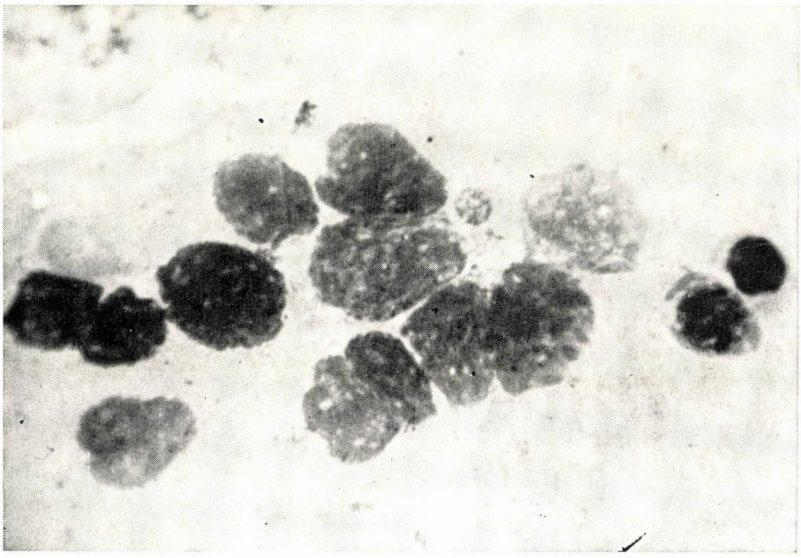


Fig. 2. Reticulum cells in the recovery period. Extreme right, erythroblasts

The percentage of erythroid cells in 3 untreated control animals differed considerably, but no significant change of the number of erythroid cells in response to the biopsies was detectable (Fig. 3). The mean leukoid and reticulum cell counts showed the same individual differences. The increase in the mean reticulum cell count up to the 6th day could have resulted from a non-specific reaction to the

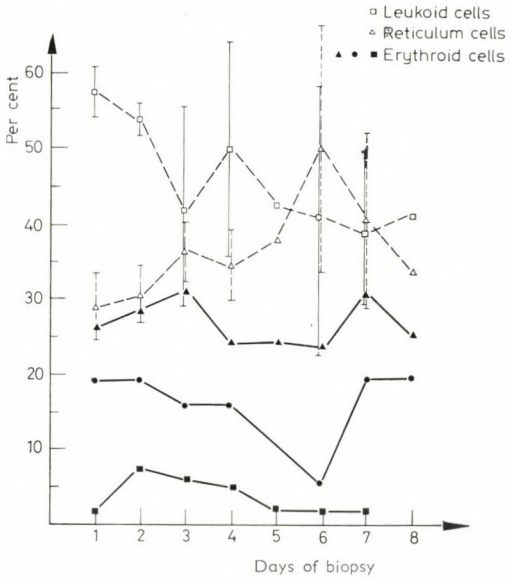


Fig. 3. Erythroid cell counts of 3 control animals during an 8-day period of bone-marrow biopsy. Mean values and standard deviation of the leukoid and reticulum cell counts

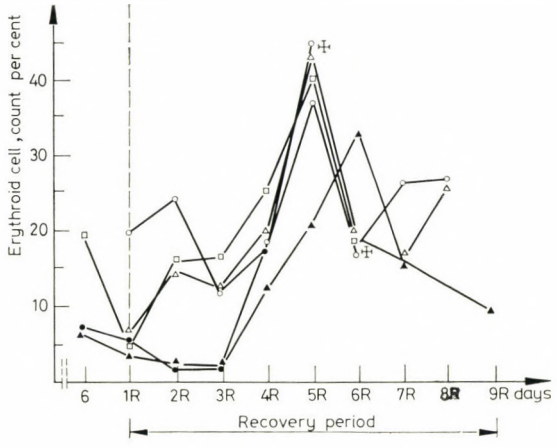


Fig. 4. Erythroid cell counts of 5 animals during the recovery period. (Symbols for different animals are the same as used in Table 2)

injury, but as seen from the standard deviation this was not statistically significant. The superimposed curves, reflecting the behaviour of the erythroid cells of all 5 rabbits during the period of recovery (Fig. 4) show that the animals reacted synchronously with a pronounced increase of the erythroid count on the 4th day. The peak of this count was reached on the 5th day in 4 rabbits with little differences

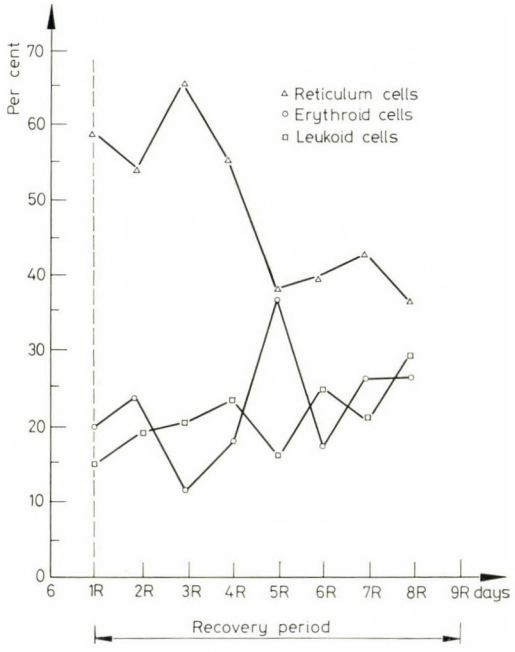


Fig. 5. Reticulum, leukoid and erythroid cells in one representative animal during the recovery period

among themselves (range, 37.1 to 44.0%). The peak erythroid count in animal 5 was retarded by 2 days and was lower than in the other animals. This seemed to be due to the poor ability of this animal to regenerate, which it had in common with animal 4 as seen from the low erythroid cell count on the first 3 days of the regeneration period and from the already mentioned weak reaction of the PCV.

A more detailed analysis of the cells of the 4 synchronously reacting animals is given in Table 2. As it can be seen, basophilic cells were predominant even on the first day. Their percentage nearly doubled until the 5th day, while the total erythroid content nearly quadruplicated by this time. The behaviour of all the three cell groups in the bone-marrow of a representative example of the 4 synchronously reacting animals is shown in Fig. 5, while Fig. 6 demonstrates the mean values for these animals. The 3rd and the 5th day of recovery are remarkable because of the abrupt changes in the cell mixture. On the 3rd day reticulum cells

Table 2

Erythroid cell count (%) on the first and fifth day of the recovery period ($\bar{x} \pm S$, n = 4)

		Day of investigation	
		1R	5R
	Total erythroid cell count	9.3 ± 2.9	41 ± 2.9
Type of cell	basophilic erythroblasts	9.5 ± 6.0	27.3 ± 8.0
	polychromatic erythroblasts	0 — 3.0	11.6 ± 5.5

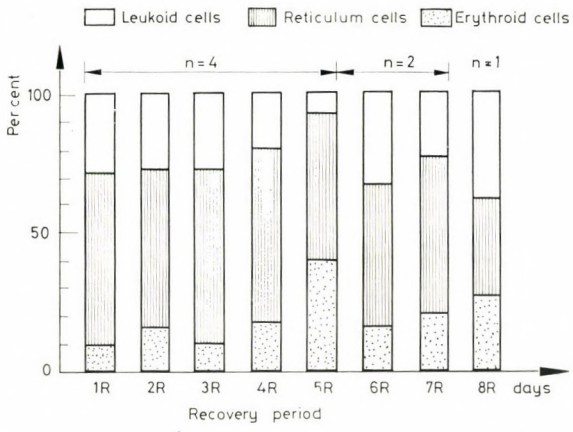


Fig. 6. Mean reticulum, leukoid and erythroid cell counts of the 4 animals reacting synchronously during the recovery period

Table 3

Erythroid, leukoid and reticulum cell counts in the tibia and in pooled cell suspensions from tibia, humerus and femur

Animal	Erythroid cells		Reticulum cells		Leucoid cells	
	tibia	suspension	tibia	suspension	tibia	suspension
1	43.9	63.7	53.1	38.8	3.0	1.5
2	33.8	74.0	63.6	24.0	2.6	2.0
3	46.5	60.0	52.3	39.0	1.2	1.0
4	40.1	62.4	57.5	34.0	2.2	3.6
$\bar{X}$	40.08	65.03	56.63	32.95	2.25	2.05
± S	5.52	6.18	5.18	6.36	0.77	1.13

were predominant. On the 5th day, a minimum of leukoid (range, 8.4 to 13.4%) and a maximum of erythroid cells (range, 37.1 to 44.0%) was seen while the reticulum count had declined. The peak erythroid cell count obtained differed substantially from that observed by Hershko et al. [3] in a single cell suspension from the pooled marrow of the humerus, tibia and femur on the 7th day of recovery from a moderate haemorrhagic anaemia followed by a single dose of actinomycin D (2 animals, 50.7 and 66.2%). Since we observed no significant difference in the erythroid cell count in the tibia, humerus and femur on the 5th day of recovery, the influence of the procedure to obtain a single cell suspension was investigated. As indicated by the high fragility of the reticulum cells, this cell type was significantly reduced during bone-marrow processing (Table 3).

Discussion

The normal erythroid cell count in bone-marrow smears of the rabbit varies between 8 and 47% [4, 6, 7, 9, 10]. The differences in the normal values of our 3 control animals probably reflect scattering. This may have been caused by the different involvement of the tibia in the production of red cells in the non-stimulated animals. On the other hand, the constancy of the individual values during the 8 days of bone-marrow biopsy showed that this procedure itself had no influence on the erythroid count. On the 3rd day of recovery from phenylhydrazine anaemia, Lingrel [1] observed in a suspension of the pooled bone-marrow from the humerus, femur and tibia of 2 rabbits about 85% erythroid cells, 58% of them late erythroid precursor cells. After a moderate haemorrhagic anaemia (haemoglobin, 6.3 g per 100 ml; reticulocytes, 29%), Hershko et al. [3] found 74% mostly late erythroid cells in the pooled bone-marrow suspension from 2 rabbits. The data of both papers are in contrast to the low erythroid counts during the first 3 days of the recovery period in our experiment, with maximum values between 15 and 25% in 3, and less than 5% in 2, of the 5 rabbits. This divergence may have been due to differences in the involvement of the tibia in erythroid cell production during the first days of recovery after anaemic stress in comparison to the erythropoietic activity of the other tubular bones used in the investigations of the above quoted authors. On the other hand, the high count of late erythroid precursor cells in their studies was somewhat surprising, since the anaemic stress is known to provoke a precipitate maturation and release of these cells into peripheral blood and an enhanced development of young cell forms. Reticulocytes most likely originating from polychromatic erythroblasts or even earlier erythroid precursor cells as a result of skipped divisions or premature enucleations were found at the maximum of haemorrhagic anaemia in the peripheral blood of rabbits [11]. The peak erythroid cell count was reached on the 5th day of the recovery period in the present study. More than half of these cells were basophilic erythroblasts. Since it takes at least 2 further days until the cells derived from these erythroblasts appear in the peripheral circulation, the early signs of

recovery seen at the periphery, like the drop of the reticulocyte count, the increase of the MCHC as early as the 4th day of the recovery period, and the steady increase of the PCV beginning with the day of the last phenylhydrazine injection, are in contrast to the rather late erythroid reaction in the bone-marrow of the tibia. The most likely explanation for this difference is the assumption of distinct sites of erythropoiesis with different erythropoietic activity in the bone-marrow of the flat and of the tubular bones. The formei sites, containing mainly red bone-marrow, might play the main role in the immediate reaction to haemopoietic stress and be responsible for the early peripheral reactions, while the latter are originally less active in erythropoiesis and become activated by repopulation from resting stem cells in these bones or by invasion from the active erythropoietic sites. An increase of undifferentiated cells 2 days prior to the maximum erythroid cell count was observed by Rosse et al. [12] after haemorrhagic stimulation of the erythropoiesis of polycythaemic guinea pigs, and by Hershko et al. [3] after a slight haemorrhagic anaemia of rabbits followed by a single dose of actinomycin D. The morphology of these precursor cells is by no means clear. Haas et al. [8] distinguished four types of "resting cells" in the bone-marrow as possible "stem cells" (two forms of reticular cells, endothelial cells and bone-marrow lymphocytes). The same authors found an increase of blast cells, that they regard as precursor cells for erythroid and myeloid repopulation of the bone-marrow on the 4th and 5th days after treatment with hydroxyurea [13]. The undifferentiated blast cells of Hershko et al. [3] and of Bohne et al. [13] are similar to our reticulum cells in their morphological appearance. In comparison to the percentage of undifferentiated cells given by Hershko et al. [3, 4] our figures for the reticulum cells of the control animals were considerably, and of the anaemic animals on the 3rd day of recovery somewhat, higher. The high fragility of these cells causing their reduction during the suspension procedure as shown in Table 3 could be responsible for these differences. Borsook et al. [14] have reported on a dramatic increase of basophilic erythroblasts during incubation for one hour of normal bone-marrow cells with peripheral leucocytes. Since during this time at most one mitosis could have occurred, a large amount of erythroid precursor cells must be present in the normal bone-marrow. In the light of these considerations at least part of the reticulum cells observed in the early recovery period could be precursor cells of the erythroid cell line. The percentage of erythroid cells obtained at this maximum differs substantially from those observed by Hershko et al. [3] (2 animals, 50.7 and 66.2%, respectively).

Our study of the procedure to obtain a single cell suspension showed that the reticulum cells become significantly reduced during the bone-marrow processing, increasing the relative number of erythroid cells (Table 3) up to values corresponding to those of Hershko et al. [3]. The similarity of the bone-marrow reaction observed in our experiment and in those of Rosse et al. [12] and Hershko et al. [3] suggests that the main synchronizing effector is the endogenous erythropoietin level that is increased by phenylhydrazine or a blood loss. Actinomycin D as used by Hershko et al. [3] might therefore not be necessary.

References

1. Lingrel, J. B.: Studies on the rapidly labeled RNA of rabbit bone marrow cells. *Biochem. biophys. Acta (Amst.) 142*, 75 (1967).
2. Gazeryan, K. G., Kiranov, G. J., Kulminskaya, A. S.: The properties of 30—60s DNA like RNA in animal cells. *Biochimija (USSR) 6*, 1238 (1970).
3. Hershko, Ch., Schwartz, R., Izak, G.: Morphologic and biochemical changes in rabbit bone marrow induced by actinomycin D. *Brit. J. Haemat. 17*, 569 (1969).
4. Hershko, Ch., Izak, G., Schwartz, R.: The effect of erythropoietin and erythroid hyperplasia on the response of rabbit bone marrow to actinomycin D. *Israel J. med. Sci. 7*, 910 (1971).
5. Zijista, W. G., van Kampen, E. J.: Standardization of hemoglobinometry. *Clin. chim. Acta 5*, 719 (1960).
6. Fleischer, J.: Das normale Knochenmarkbild des Kaninchens. *Folia haemat. (Lpz.) 79*, 89 (1962).
7. Friederici, L.: Der Einfluß von Sulfonamiden, Stickstoff-Lost, TEM und Aminopterin auf das Blut und die blutbildende Organe des Kaninchens. *Folia haemat. (Lpz.) 73*, 49 (1956).
8. Haas, R. J., Bohne, F., Fliedner, T. M.: On the development of slowly-turning-over cell types in neonatal rat bone marrow. (Studies utilizing the complete tritiated thymidine labeling method complemented by ^{14}C thymidine administration.) *Blood 34*, 791 (1969).
9. Curletto, R.: Cit. by Ferrara, A.: Vergleichende Morphologie des Blutes der Laboratoriumstiere. In: Handbuch der gesamten Hämatologie. Heilmeyer, L., Hittmair, A. (eds.). Vol. I. Urban u. Schwarzenberg, München 1957.
10. Duma, J.: Les animaux de laboratoire. Flammarion, Paris. Cit. Fleischer (6).
11. Coutelle, Ch., Rosenthal, S., Gross, J., David, H., Uerlings, I.: Leitkriterien der Retikulozytenreifung: Das Verhalten der RNS- und Retikulozytenwerte in erythroiden Zellpopulationen verschiedener Dichte im Verlauf einer Entblutungsanämie beim Kaninchen. *Acta biol. med. germ. 31*, 781 (1973).
12. Rosse, C., Griffiths, D. A., Edwards, A., Gadies, C. G. C., Long, A. H. L., Wright, J. L. W., Yoffey, J. M.: Identity of the erythroblast precursors in the bone marrow. *Acta haemat. (Lpz.) 43*, 80 (1970).
13. Bohne, F., Haas, R. J., Fliedner, T. M., Fache, J.: The role of slowly proliferating cells in rat bone marrow during regeneration following hydroxyurea. *Brit. J. Haemat. 19*, 533 (1970).
14. Borsook, H., Jiggins, S., Wilson, R. T.: Stimulation of rabbit erythroblast multiplication *in vitro* by blood leucocytes: Cytological observations. *J. Cell comp. Physiol. 79*, 267 (1972).

Correspondence: Dr. Ch. Coutelle, Institut für Physiologische und Biologische Chemie der Humboldt Universität, Hessische Straße 3/4, 104 Berlin, DDR

Haematologia 9 (3—4), pp. 205—208 (1975)

Histamine Fluorescence in Group Forming Peritoneal Cells of the Rat Embryo

G. CSABA, T. RICHTER

Department of Biology, Semmelweis University Medical School, Budapest

(Received September 26, 1973)

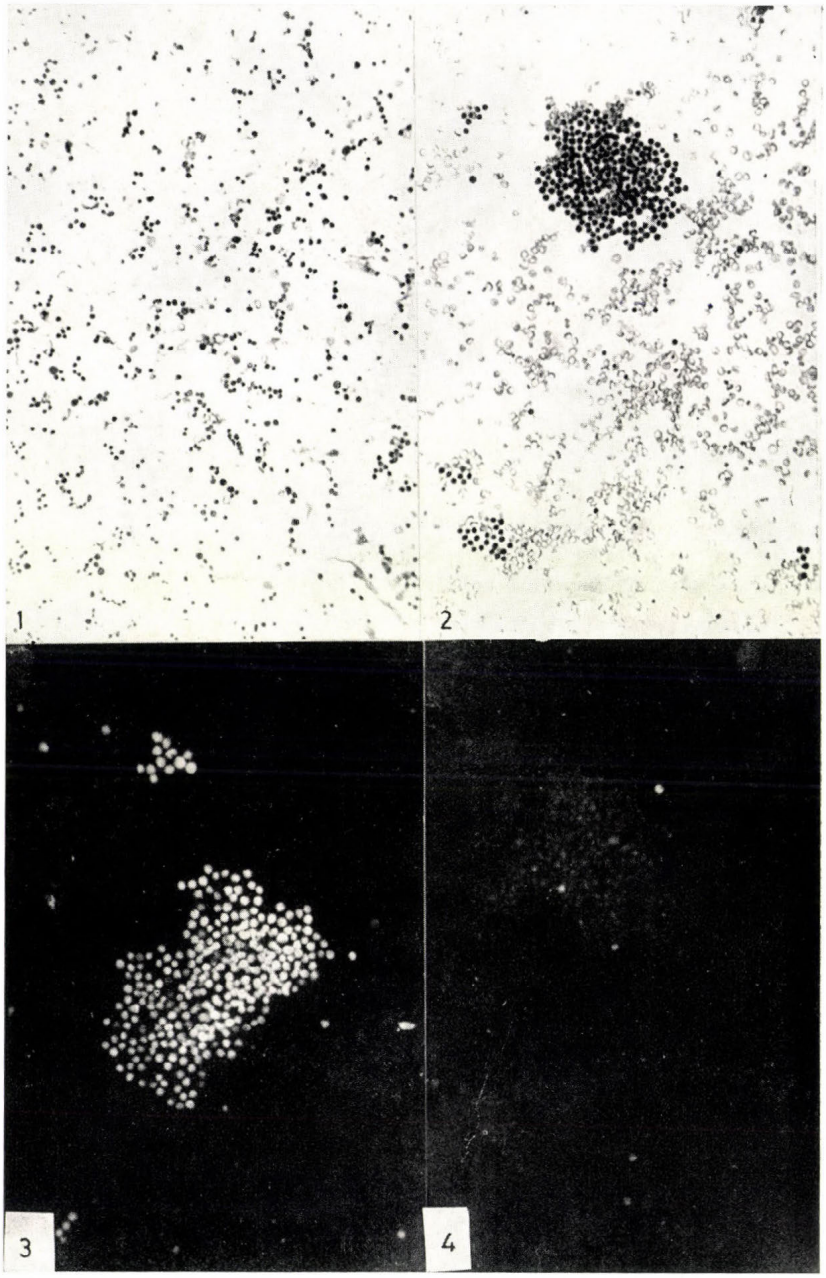
In the peritoneal fluid of 18—21-day-old rat embryos the lymphocytes form groups and give an intensive yellow — histamine — fluorescence. The groups contain myeloid elements, too. After birth the fluorescence disappears.

Introduction

Young forms of the mast cells are of lymphoid character [2, 3]. These young cells cannot be found in every part of the organism, but the peritoneal fluid contains all forms of developing mast cells and a great number of lymphoid forms [3]. The lymphoid mast cells show only alcian blue positivity or alcian blue–safranin staining [2, 3]. Their cytoplasm contains serotonin and histamine [3—5]. Our earlier experiments demonstrated the occurrence of biogenic amines also in alcian blue negative cells [5], and we therefore assumed that the presence of biogenic amines was not restricted to the mast cells.

Material and methods

The peritoneal fluid of 15—21-day Wistar CB rat embryos, a total of 50 animals, that of two-day-old new-borns and a total of 30 adult animals was studied in thick drop preparations. After injecting and withdrawing of isotonic sodium citrate solution, the drops prepared were dried above Kieselgel and then induced for two hours with formaldehyde vapour according to Falck's [6] method and with o-phthalaldehyde (OPT) as in the method of Juhlin and Shelley [7]. A Zeiss (Jena) fluorescence microscope was used for the examinations. The same procedure was performed for examining the sections made from the thymus of the embryos after fixation in cold absolute alcohol. These methods allowed to detect the histamine and 5-HT content of cells qualitatively. Falck's method demonstrates the amines in general, after two hours' exposition to formaldehyde vapour the arising yellow fluorescence points to the presence of 5-HT. The OPT method is specific for histamine. The parallel preparations were stained with alcian blue–safranin, Giemsa's solution and with haematoxylin-eosin (HE).



Figs 1—2. Thick drop preparation from the peritoneal fluid of a 17-day-old and a 19-day-old rat embryo. On the 17th day (Fig. 1), the nucleated cells are still dispersed, whilst on the 19th day (Fig. 2) they are assembled in groups. HE, ×80

Figs 3—4. Thick drop preparation from the peritoneal fluid of a 19-day-old rat embryo treated with OPT (Fig. 3) and by Falck's method (Fig. 4). The intense histamine fluorescence and the negativity of serotonin fluorescence can be seen in the cells forming groups. Falck's method demonstrates fluorescence only in the mast cells. ×80

Results

In the peritoneal fiuid of 15, 16 and 17-day-old embryos there are few alcian blue positive mast cells; they give a weak histamine fluorescence. In addition, there are some dispersed leukocytes and nucleated erythrocytes (Fig. 1). From the 18th day this picture changes. The leucocytes form groups and single nucleated cells can hardly be found (Fig. 2). The cells forming groups give an intense yellow

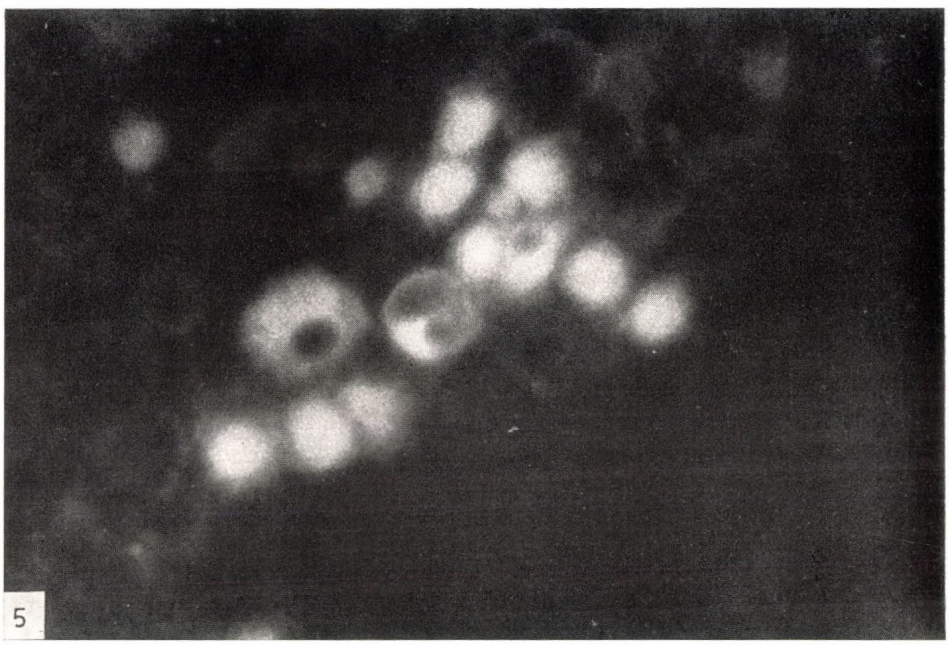


Fig. 5. Thick drop preparation from the peritoneal fluid of an 18-day-old rat embryo. Cells giving yellow OPT fluorescence are mostly of mononuclear lymphoid character. The negative picture of the nuclei shows that among the cells of the fluorescent groups, granulocytes also occur. ×640

OPT fluorescence (Fig. 3), whilst serotonin cannot be demonstrated in them (Fig. 4), and they give no alcian blue-safranin staining and show no autofluorescence. Single mast cells also occur. The cell groups contain lymphoid and myeloid elements as well as macrophages (Fig. 5). Cell groups giving fluorescence are observed up to birth, the fluorescence being most intense on the 18th and 19th days. On the first days after birth the tendency of the cells to form groups persists, but the fluorescence disappears. At this time only the mast cells show fluorescence. In the preparations made from adult animals no group-formation can be seen.

Discussion

According to the findings, the lymphoid cells found in the peritoneal fluid contain histamine at a certain period of embryonic development. Later on, histamine can be detected only in lymphoid cells transforming into mast cells. It seems, however, that during embryonic life the granulocytes also contain histamine. The importance of this fact is not known, although a lymphocyte transforming factor was demonstrated in the granulocytes [10]. This would explain the group-formation and the similar histochemical features. As for group-formation, the present findings failed to reveal whether it was a physiological phenomenon or an artifact. The fact that it could not be observed before the 17th intrauterine day or in the adult animal points to the physiological nature of the process in the same way as the property of the lymphocytes to form groups also with myeloid elements [1, 8]. The fluorescence of the lymphoid cells in itself indicates that amine synthesis represents a common capacity of the peritoneal lymphoid cells; but regarding group-formation as a physiological phenomenon, one may ascribe to that the appearance of histamine may have some importance in relation to immunobiological development. This is all the more so because the peak of certain immunological processes seems to be on the 18th intrauterine day [9]. Should this be the case, the peritoneal lymphoid cells might represent a special case since in the same period similar fluorescent lymphoid cells could not be demonstrated in either the thymus or the spleen.

References

1. Burnet, F. M.: Cellular immunology. Melbourne Univ. Press, Melbourne 1969.
2. Combs, J. W., Lagunoff, D., Benditt, E. P.: Differentiation and proliferation of embryonic mast cells of the rat. *J. Cell Biol. 25*, 577 (1965).
3. Csaba, G., Surján, L. jr., Fischer, J., Törő, I. jr.: On the mechanism of mast cell formation. Effect of glucocorticoids on the mast cells of normal and thymectomized rats. *Acta biol. Acad. Sci. hung. 20*, 57 (1969).
4. Csaba, G.: Mechanism of the formation of mast cell granules. VII. Participation of amines and basic proteins in the formation of the mast cell granule. Analysis of the heterogeneity of mast cells. *Acta biol. Acad. Sci. hung. 22*, 155 (1971).
5. Csaba, G.: Regulation of mast cell formation. Academic Press, Budapest 1972.
6. Falck, B.: Observations on the possibilities of the cellular localization of monoamines by a fluorescence method. *Acta physiol. scand. 16* (Suppl.) *197* (1962).
7. Juhlin, L., Shelley, W. B.: Detection of histamine by a new fluorescent o-phthalaldehyde stain. *J. Histochem. 14*, 525 (1966).
8. McFarland, W., Heilman, D. H.: Lymphocyte foot appendage: its role in lymphocyte function and in immunological reactions. *Nature (Lond.) 205*, 887 (1965).
9. Moisier, D. E.: Transient appearance of PHA-reactive thymocytes in the fetal mouse. *Nature new Biol. 242*, 184 (1973).
10. Tchorzewsky, M., Sulowska, Z., Denys, A.: A new lymphocyte transforming factor derived from the lysosomes of polymorphonuclear leucocytes. *Experientia (Basel) 29*, 481 (1973).

Correspondence: Prof. G. Csaba, Department of Biology, Semmelweis University Medical School, Tűzoltó u. 58. 1450 Budapest, Hungary

Haematologia 9 (3—4), pp. 209—217 (1975)

Ультраструктурная цитохимия пероксидазы и кислой фосфатазы в созревающих эозинофилах мышей

Р. А. МУРАВЬЕВ, В. В. РОГОВИН, В. М. ФРОЛОВА, Н. Г. ГЕРАНИНА, Л. А. ПИРУЗЯН

Отдел медицинской биофизики, Институт химической физики, Академия Наук СССР, Москва

(Поступила 15-го января 1973 г.)

Электронно-цитохимически исследовали распределение пероксидазы и кислой фосфатазы в созревающих эозинофилах костного мозга мышей. Пероксидазная активность обнаружена в перинуклеарном пространстве, эндоплазматической сети, комплексе Гольджи, незрелых и специфических кристаллосодержащих гранулах. По мере созревания клеток пероксидаза последовательно исчезает из вышеперечисленных органелл, и в зрелых эозинофилах хранится в специфических гранулах. Некоторые зрелые специфические гранулы не проявляют пероксидазной активности. Выдвигается гипотеза о полной конденсации фермента в кристалл. Клетки, инкубируемые в среде без перекиси водорода, показывают слабую пероксидазную активность в некоторых гранулах. Вероятно, эта активность связана с присутствием в них эндогенных неорганических перекисей. В созревающих эозинофилах кислая фосфатаза локализуется в комплексе Гольджи и в незрелых специфических гранулах. По мере созревания последних кислая фосфатаза исчезает из гранул.

В доступной нам литературе нет сведений об электронно-цитохимическом исследовании пероксидазы в эозинофилах мышей. Поэтому целью нашей работы явилось изучение транспорта и упаковки в гранулы пероксидазы в созревающих эозинофилах мышей и одновременное выявление локализации кислой фосфатазы и пероксидазы (дубль-реакция) в эозинофилах.

Материал и методы

Наблюдения производили на эозинофилах из костного мозга беспородных белых мышей и мышей линии C_3На обоего пола весом 18—20 г. Костный мозг брали из бедренной кости животных.

Кусочки ткани фиксировали в 4% глутаральдегиде на 0,1 М какодилатном буфере (pH 7,4) в течение 5 часов при 0—4°. Затем отмывали в 0,1 М какодилатном буфере (pH 7,4) с 7% сахарозой 18—20 часов на холоду и инкубировали на пероксидазу в модифицированной среде Грехема-Карновского (9) в течение 10 мин. при 37 °С. Инкубационная среда содержала 0,01% перекиси водорода, 7% сахарозы и 20 мг 3,3-диаминобензидина тетрахлорида в 10 мл 0,1 М Трис-буфере (pH 7,6). После инкубации кусочки

ткани отмывали 5—7 мин. в 7% сахарозе и дофиксировали в 2%OSO_4 в течение 20 часов. Затем клетки обезвоживали в ацетоне возрастающей концентрации и заключали в Дуркупан.

Контроль на активность пероксидазы

1. Опущение из среды 3,3′-диаминобензидина.
2. Опущение из среды перекиси водорода (в этом случае время инкубации было 10 мин. и 1 час).
3. Преинкубация в абсолютном ацетоне от 40 мин. до 24 часов с последующей инкубацией в полной или неполной среде (опущение перекиси водорода).
4. 30-ти минутная преинкубация в растворах ингибиторов: 0,01 M KCN 0,1 M KCN, 0,01 MNa_3N, 0,1 MNa_3N, 0,01 M гидроксиламина и последующая инкубация в полных средах, содержащих вышеприведенные ингибиторы в тех же концентрациях.

Методика одновременного выявления пероксидазы и кислой фосфатазы (дубль-реакция) изложена ранее (1). Тонкие срезы готовили на ультрамикротоме LKB. Неконтрастированные и контрастированные цитратом свинца (13) срезы изучали в электронном микроскопе HU-11 B.

Результаты

Пероксидазная активность в эозинофилах линейных животных ниже, чем в эозинофилах беспородных мышей. Поэтому основные результаты получены на костном мозге беспородных мышей.

Увеличение концентрации 3,3-диаминобензидина в среде до 20 мг на 10 мл раствора позволило сократить время инкубации до 10 мин., причем плотность продукта реакции оказалась достаточной для наблюдения в электронный микроскоп. При инкубации более 10 мин. гранулы эозинофилов становились слишком плотными и вырывались при резке. Увеличение времени фиксации в 2% OSO_4 повышает контрастность, не приводя к артефактам.

Созревающие эозинофилы можно условно разделить на три группы по степени зрелости: промиэлоциты, миэлоциты и сегменто-ядерные клетки. Первые характеризуются хорошо развитой эндоплазматической сетью с широкими каналами, выраженным комплексом Гольджи и овальным или бобовидным ядром. В миэлоците эндоплазматическая сеть представлена более узкими каналами, комплекс Гольджи меньше, ядро сильно изогнуто. В сегменто-ядерной клетке эндоплазматическая сеть и комплекс Гольджи сильно редуцированы.

Эозинофилы, находящиеся на разных стадиях развития, показали пероксидазную активность. В промиэлоцитах (рис. 1) продукт реакции ло-

кализован в каналах и цистернах эндоплазматической сети, включая перинуклеарное пространство, в цистернах, колбовидных расширениях цистерн, пузырьках и вакуолях комплекса Гольджи и в незрелых гранулах. Плотность осадка возрастает от эндоплазматической сети к гранулам.

По мере созревания клеток пероксидаза исчезает из эндоплазматической сети и остается лишь в элементах комплекса Гольджи и в гранулах (рис. 2). В цистернах Гольджи продукт реакции часто локализован в области,

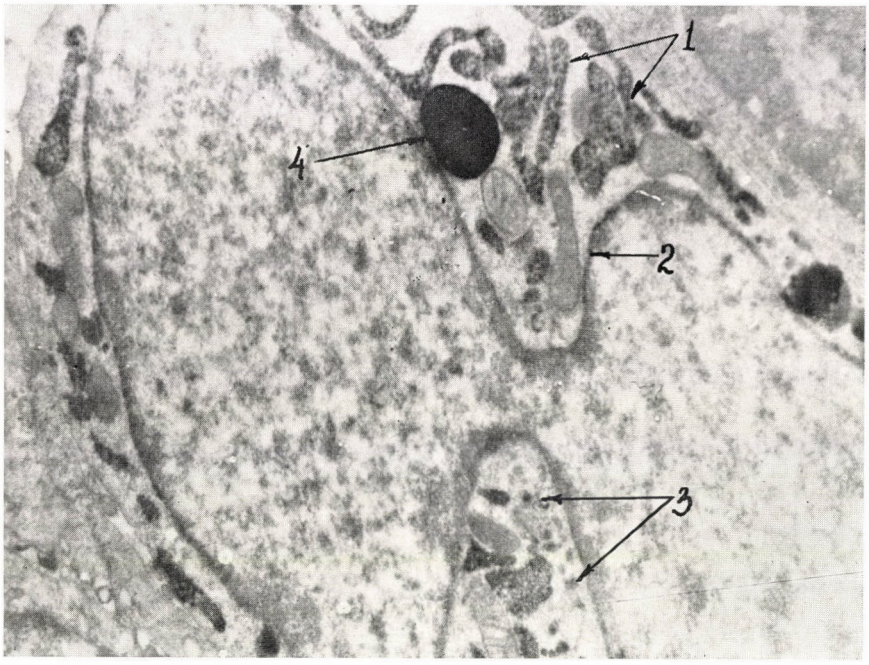


Рис. 1. Эозинофильный промиэлоцит. Электронно-цитохимическая реакция на пероксидазу. Продукт реакции виден в широких каналах и цистернах эндоплазматической сети (1), в перинуклеарном пространстве (2), в комплексе Гольджи (3), в незрелых специфических гранулах (4). × 25000

прилегающей к мембранам, центр на вид остается пустым. Только колбовидные расширения на концах цистерн Гольджи полностью заполнены продуктом реакции. От них отшнуровываются мелкие пузырьки с гомогенным содержимым средней плотности. При их слиянии образуются незрелые гранулы.

В миэлоците появляются кристаллосодержащие зрелые гранулы. Они содержат продукт реакции только в матриксе, кристалл остается светлым.

В зрелых клетках (рис. 3) реакция отрицательна в эндоплазматической сети и комплексе Гольджи и положительна в матриксе зрелых специфических

гранул. Некоторые из этих гранул пероксидазной реакции не проявили, другие заполнены продуктом реакции лишь наполовину (рис. 3). Пероксидазоотрицательные гранулы лежат как в центре клетки, так и на периферии. В зрелых клетках иногда встречаются незрелые гранулы.

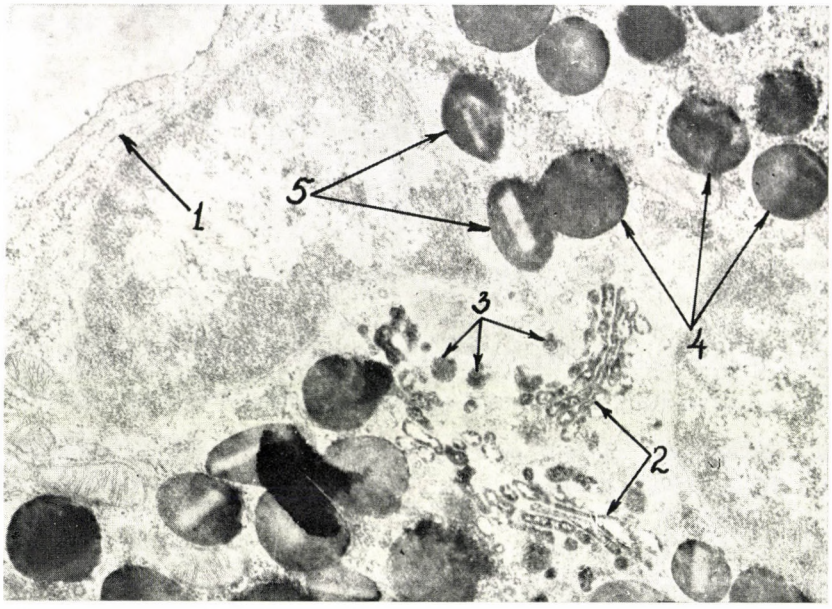


Рис. 2. Эозинофильный миэлоцит. Электронно-цитохимическая реакция на пероксидазу. Каналы эндоплазматической сети без продукта реакции (1). Цистерны (2), мелкие пузырьки (3) комплекса Гольджи, содержащие продукт реакции на пероксидазу. Незрелые специфические гранулы (4) равномерно заполнены продуктом реакции. В зрелых гранулах (5) продукт реакции локализован только в матриксе, кристалл светлый. ×11300

Клетки, инкубируемые в среде без 3,3′-диаминобензидина, пероксидазной активности не проявляли. Опущение из среды перекиси водорода приводит к интересным результатам: в некоторых гранулах сохраняется слабая реакция. Интенсивность ее увеличивается при удлинении инкубации до 1 часа, а также при 40-минутном воздействии абсолютного ацетона перед инкубацией в среде. При более длительной преинкубации в ацетоне разрушаются клеточные структуры, и продукт реакции диффузно распределяется в клетке. 0,01 M KCN и 0,1 M KCN лишь частично снижает активность пероксидазы. 0,01 M Na_3N снижает активность значительно сильнее, но не до конца, только 0,1 M Na_3N полностью ингибирует активность пероксидазы. Действие 0,1 M гидроксиламина также приводит к полному подавлению реакции.

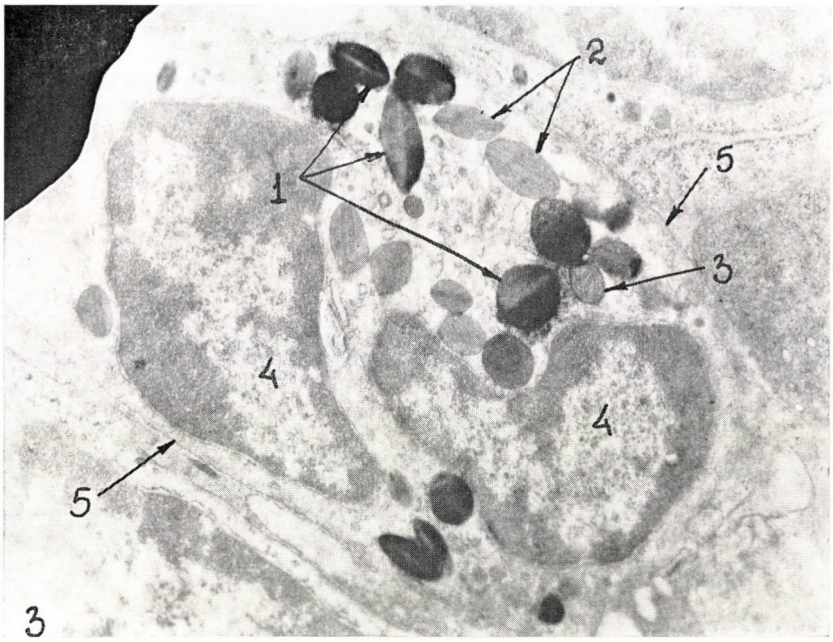


Рис 3. Фрагменг сегментоядерного эозинофила. Электронно-цитохимическая реакция на пероксидазу. Видны зрелые гранулы, содержащие продукт реакции (1). Рядом лежат пероксидазоотрицательные гранулы (2). ×26000

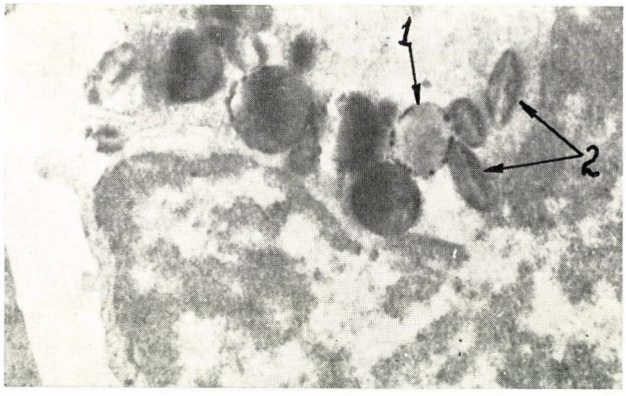


Рис. 4. Фрагмент эозинофильного миэлоцита. Дубль-реакция на пероксидазу и кислую фосфатазу. Видна незрелая гранула (1), где на фоне менее плотного осадка продукта реакции на пероксидазу по периферии органеллы лежат значительно более плотные отложения продукта реакции на кислую фосфатазу. Зрелые эозинофильные гранулы (2) содержат гомогенный продукт реакции на пероксидазу. Кристалл остается неокрашенным. × 27000

При проведении дубль-реакции в цитоплазме миэлоцита активность пероксидазы локализуется в специфических гранулах (рис. 4). В незрелых гранулах пероксидазная активность обнаружена по всему матриксу гранулы. В зрелых гранулах пероксидазная активность локализована в матриксе, кристалл остается неокрашенным, кислая фосфатаза присутствует в матриксе некоторых незрелых специфических гранул (рис. 4), а также в комплексе Гольджи. В незрелой грануле на фоне менее плотного осадка продукта реакции на пероксидазу значительно более плотные отложения продукта реакции на кислую фосфатазу располагаются по периферии гранулы у мембраны. Зрелые эозинофильные гранулы, которые можно легко узнать по присутствию кристалла, не содержат кислой фосфатазы. В зрелом эозинофиле, где комплекс Гольджи сильно редуцирован, кислая фосфатаза не определялась ни в комплексе Гольджи, ни в зрелых гранулах. Продукт реакции на кислую фосфатазу — мелкокристаллический и очень плотный. Продукт реакции на пероксидазу — гомогенный, умеренной плотности. Поэтому продукты реакции на оба фермента легко различимы.

Обсуждение

В эозинофилах костного мозга мышей пероксидазная активность найдена в перинуклеарном пространстве, эндоплазматической сети, элементах комплекса Гольджи, незрелых и специфических гранулах. При созревании эозинофилов пероксидаза последовательно исчезает из перинуклеарного пространства, эндоплазматической сети, комплекса Гольджи, и в зрелых клетках остается только в гранулах. Видимо, в процессе вызревания клетки элементы аппарата синтеза секреторного белка редуцируются, а фермент накапливается и хранится в гранулах. Это соответствует общей схеме Джемиесона и Паладе (10, 11), а также авторадиографическим исследованиям путей образования зернистости гранулоцитов [8]. Наши результаты по локализации пероксидазы в эозинофилах мышей совпадают с данными других авторов, полученными на кроликах и крысах [2, 3, 12], кроликах [6] и крысах [4, 15, 16].

В эозинофилах обнаруживаются два вида гранул: незрелые и специфические, кристаллосодержащие. Миллер и Герцог [12] писали об уменьшении числа незрелых гранул в созревающих эозинофилах и об увеличении числа специфических гранул. Вопрос о судьбе незрелых гранул является спорным. Дискутируются две возможности:

1. Незрелые гранулы в зрелых эозинофилах не образуются и элиминируются из развивающихся клеток [2, 3].

2. Незрелые гранулы превращаются в специфические через гипотетический процесс созревания [6, 14]. Ветцель с соавт. [14] описал ряд переходных форм между незрелыми и зрелыми гранулами в эозинофилах кролика. Но тем не менее превращение гомогенных гранул в кристаллосодержащие не доказано. У крыс промежуточные формы не найдены. Вообще, этих

форм может и не быть, так как кристаллизация возможно проходит очень быстро под влиянием некоторого инициирующего фактора. Мы придерживаемся точки зрения Дэна с сотр. [6].

Мы наблюдали неоднородную реактивность специфических гранул на пероксидазу. Возможно, это связано с отсутствием проницаемости для 3,3-диаминобензидина и перекиси водорода в гранулу, либо с полной конденсацией фермента в кристалл.

Котран и Литт [5] обнаружили реактивность некоторых гранул при инкубации эозинофилов морских свинок в среде без перекиси водорода. Это противоречит результатам, полученным Бэйнтон и Фаркухар [3] на эозинофилах кроликов и крыс. Мы наблюдали слабую реакцию в некоторых гранулах при опущении из среды перекиси водорода, 0,1 M Na_3N снимает эту активность. Вероятно, в этом случае в качестве окислителя в реакции принимают участие эндогенные перекиси, но это не перекиси лицидов, так как 40-минутная преинкубация в абсолютном ацетоне не снимает реакцию, а, наоборот, усиливает ее, очевидно, за счет незначительного разрушения мембран и увеличения проницаемости для субстрата. Более длительная преинкубация в ацетоне приводит к значительному разрушению мембран в клетке и утечке фермента.

Таким образом, гранулы эозинофилов неоднородны относительно присутствия в них эндогенных перекисей. Те гранулы, в которых есть эндогенные перекиси, более реактивны и, возможно, играют большую роль в процессе жизнедеятельности клетки.

Возможно, инкубация в неполной среде (без перекиси водорода) позволит охарактеризовать гранулы не только по активности фермента, когда, как отмечалось выше, была найдена определенная гетерогенность активности матрикса, но и по уровню концентрации эндогенных перекисей. Гетерогенность по присутствию эндогенных перекисей может отражать суммарный уровень активности метаболических систем, образующих перекись водорода в грануле.

Ранее мы сообщали [1] о результатах проведения двойной цитохимической реакции на созревающих нейтрофилах мышей. Оказалось, что кислая фосфатаза локализуется главным образом в комплексе Гольджи, а пероксидаза — в азурофильных гранулах. Результаты, полученные на эозинофилах, еще раз подтверждают наше предположение о том, что гранулы, содержащие пероксидазу, не являются лизосомами. Содержащаяся в незрелых гранулах кислая фосфатаза исчезает из них по мере созревания. Отсутствие кислой фосфатазы в зрелых специфических гранулах соответствует данным Бэйнтон и Фаркухар [3] и Эномото и Китани [7].

Литература

1. Роговин В. В., Муравьев Р. А., Геранина Н. Г., Фролова В. М., Пирузян Л. А.: Дубль-реакция (кислая фосфатаза и пероксидаза) в созревающих нейтрофилах мышей. Электронно-цитохимическое исследование. *Изв. АН СССР, сер. биол.* 1, 135 (1972).
2. Bainton, D. F., Farquhar, M. G.: Segregation and packing of granule enzymes in eosinophils. *J. Cell Biol. 35*, 6A (1967).
3. Bainton, D. F., Farquhar, M. G.: Segregation and packing of granule enzymes in eosinophilic leucocytes. *J. Cell Biol. 45*, 54 (1970).
4. Behnke, O.: Demonstration of endogenous peroxidase activity in the electron microscope. *J. Histochem. Cytochem. 17*, 62 (1969).
5. Cotran, R. S., Litt, M.: The entry of granule-associated peroxidase into the phagocytic vacuoles of eosinophils. *J. exp. Med. 129*, 1291 (1969).
6. Dunn, W. B., Hardin, J. H., Spicer, S. S.: Ultrastructural localization of myeloperoxidase in human neutrophil and rabbit heterophil and eosinophil leucocytes. *Blood 32*, 395 (1968).
7. Enomoto, T., Kitani, T.: Electron microscopic studies on peroxidase and acid phosphatase reaction in human leucocytes. *Acta haemat. Jap. 29*, 554 (1966).
8. Fedorko, M. E., Hirsch, J. G.: Cytoplasmic granule formation in myelocytes. *J. Cell Biol. 29*, 307 (1966).
9. Graham, R. C. Jr., Karnovsky, M. S.: The early stages of absorption of injected horseradish peroxidase in the proximal tubules of mouse kidney. Ultrastructural cytochemistry by a new technique. *J. Histochem. Cytochem. 14*, 291 (1966).
10. Jamieson, J. D., Palade, G. E.: Intracellular transport of secretory proteins on the pancreatic exocrine cell. I. Role of the peripheral elements of Golgi complex. *J. Cell Biol. 34*, 577 (1967).
11. Jamieson, J. D., Palade, G. E.: Intracellular transport of secretory proteins on the pancreatic exocrine cell. II. Transport to condensing vacuoles and zymogen granule *J. Cell Biol. 34*, 597 (1967).
12. Miller, F., Herzog, V.: Die Lokalisation von Peroxidase und saurer Phosphatase in eosinophilen Leucocyten während der Reifung. Elektronenmikroskopische Untersuchungen am Knochenmark von Ratte und Kaninchen. *Z. Zellforsch. 97*, 84 (1969).
13. Reynolds, E. S.: The use of lead citrate at high pH as an electronopaque stain in electron microscopy. *J. Cell Biol. 17*, 208 (1963).
14. Wetzel, B. K., Spicer, S. S., Horn, R. G.: Fine structural localization of acid and alkaline phosphatases in cell of rabbit blood and bone marrow. *J. Histochem. Cytochem. 15*, 311 (1967).
15. Yamada, E.: Electron microscopy of the peroxidase in granula leucocytes of rat bone marrow. *Arch. Histol. Jap. 27*, 131 (1966).
16. Yamada, E., Yamauchi, R.: Some observations on the cytochemistry and morphogenesis of the granulocytes in the rat bone marrow as revealed by electron microscopy. *Acta haemat. Jap. 24*, 530 (1966).

Ultrastructural Cytochemistry of Peroxidase and Acid Phosphates in Mouse Eosinophils

The distribution of peroxidase and acid phosphatase activity in the bone marrow of mouse eosinophils was investigated by electron microscopy. Peroxidase activity was found in the perinuclear space, the endoplasmic reticulum, the Golgi complex, non-mature and mature specific crystal-containing granules. In the course of development peroxidase activity disappears from the cisternal system. In mature eosinophils the enzyme is stored in specific granules, but some of these failed to reveal peroxidase activity. A hypothesis is offered concerning the complete condensation into crystal of the enzyme. In cells incubated in peroxide-free media some granular components stained weakly. Their activity probably depended on the presence of endogenous non-organic peroxidase. In developing eosinophils acid phosphatase was found in the Golgi complex and in non-mature specific granules. In the course of development, acid phosphatase disappears from the granules.

Correspondence: Dr. V. V. Rogovin, Academy of Sciences, Institute of Chemical Physics, Department of Medical Biophysics, Moscow V-334, Soviet Union

Haematologia 9 (3—4), pp. 219—225 (1975)

Ультраструктурная цитохимия пероксидазы в созревающих нейтрофилах мышей

Р. А. МУРАВЬЕВ, В. В. РОГОВИН, В. М. ФРОЛОВА, Н. Г. ГЕРАНИНА, Л. А. ПИРУЗЯН

Отдел медицинской биофизики, Институт химической физики, Академия Наук СССР, Москва

(Поступила 15-го января 1973 г.)

Электронно-цитохимически исследовали распределение пероксидазной активности в созревающих нейтрофилах мышей. Активность фермента обнаружена в шероховатой эндоплазматической сети, комплексе Гольджи и азурофильных гранулах. Обсуждается предположение о гетерогенности азурофильных гранул относительно присутствия в них эндогенных неорганических перекисей.

Ранее мы сообщали о результатах исследования дубль-реакции (кислая фосфатаза и пероксидаза) в нейтрофилах мышей [1]. В настоящей работе будет более подробно рассмотрено распределение активности пероксидазы в созревающих нейтрофилах из костного мозга мышей.

Материал и методы

Наблюдения производили на нейтрофилах из костного мозга беспородных белых мышей и мышей линии C_3Ha, весом 18—20 г. Костный мозг брали из бедренной кости животных.

Кусочки ткани фиксировали в 4% глутаральдегиде на 0,1 М какодилатном бифере (pH 7,4) в течение 5 часов при 0—4°С. Затем отмывали в 0,1 М какодилатном буфере (pH 7,4) с 7% сахарозой 18—20 часов на холоду и инкубировали на пероксидазу в модифицированной среде Грехема-Карновского [13] в течение 10 мин. при 37 °С. Инкубационная среда содержала 0,01% перекиси водорода, 7% сахарозы и 20 мг 3,3′-диаминобензидина в 10 мл 0,1 М Трис-буфере (pH 7,6). После инкубации кусочки ткани отмывали 5—7 мин. в 7% сахарозе и дофиксировали в 2% OSO_4 в течение 20 часов. Затем клетки обезвоживали в ацетоне возрастающей концентрации и заключали в Дуркупан.

Контроли на активность пероксидазы:

1. Опущение из среды 3,3′-диаминобензидина;

2. Опущение из среды перекиси водорода (в этом случае время инкубации было 10 мин. и 1 час);

3. Преинкубация в абсолютном ацетоне от 40 мин. до 24 часов с последующей инкубацией в полной или неполной среде (опущение перекиси водорода);

4. 30-ти минутная преинкубация в растворах ингибиторов: 0,01 М, 0,1 М KCN, 0,01 М Na_3N, 0,1 М Na_3N, 0,1 М гидроксиламина — и последующая инкубация в полных средах, содержащих вышеприведенные ингибиторы в тех же концентрациях.

Результаты

Несколько опытов было поставлено на костном мозге мышей C_3Ha. Пероксидазная активность в них заметно ниже, чем в нейтрофилах беспородных мышей. Поэтому исследование проводилось на костном мозге последних.

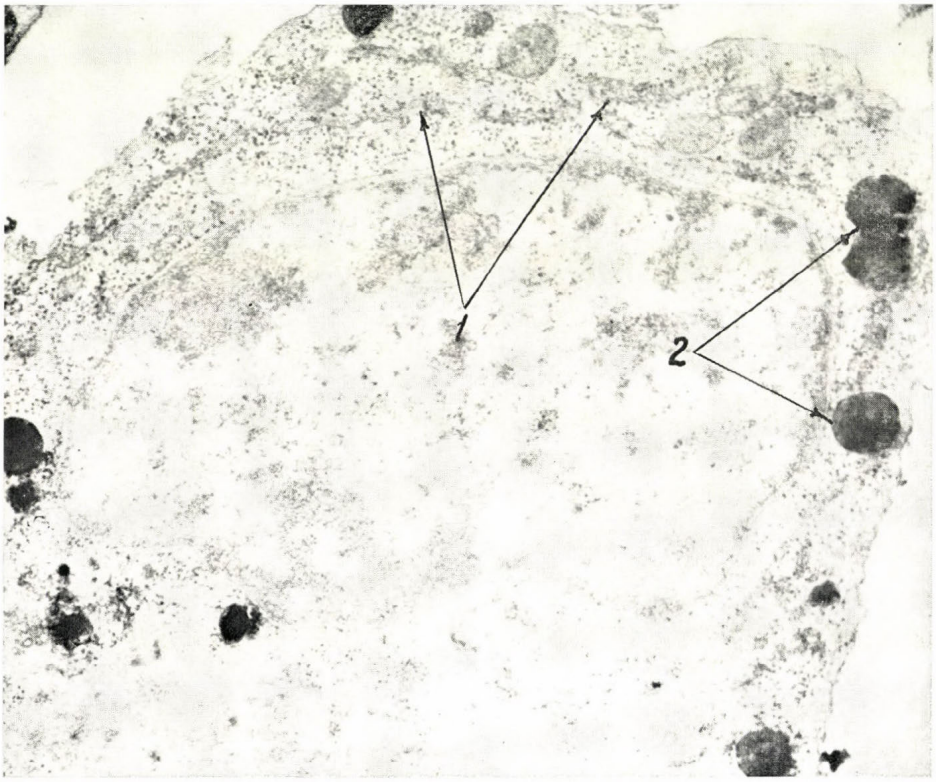


Рис. 1. Фрагмент нейтрофильного промиэлоцита. Электронно-цитохимическая реакция на пероксидазу. Продукт реакции содержится в эндоплазматической сети (1) и в азурофильных гранулах (2). ×33000

Созревающие нейтрофилы можно условно разделить на три группы по степени зрелости: промиэлоциты, миэлоциты и сегменто-ядерные клетки. Промиэлоциты характеризуются хорошо развитой эндоплазматической сетью, комплекс Гольджи у них хорошо выражен, ядро почти овальное или бобовидное. В миэлоците эндоплазматическая сеть представлена более узкими каналами, комплекс Гольджи, по сравнению с промиэлоцитом, имеет меньше цистерн, ядро сильно изогнуто. В сегменто-ядерной клетке эндоплазматическая сеть и комплекс Гольджи сильно редуцированы.

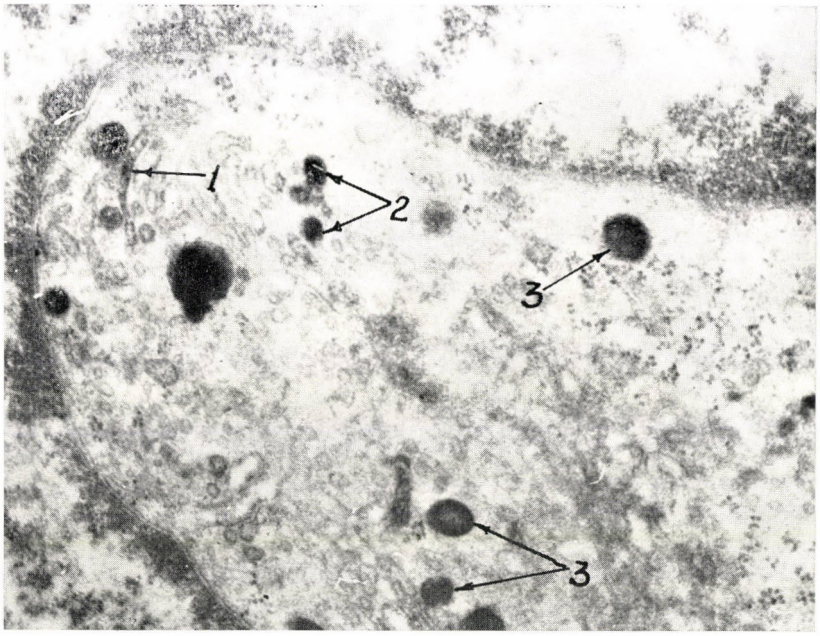


Рис. 2. Фрагмент нейтрофильного миэлоцита. Электронно-цитохимическая реакция на пероксидазу. Комплекс Гольджи с плотным продуктом реакции в цистернах (1) и в мелких пузырьках (2). Азурофильные гранулы (3). × 35000

В промиэлоцитах пероксидазная активность обнаружена в шероховатой эндоплазматической сети (рис. 1), в комплексе Гольджи и в овальных гранулах, соответствующих азурофильным [9, 15]. В цистернах Гольджи продукт реакции локализован у ограничивающей мембраны и полностью заполняет концевые расширения, от которых отшнуровываются мелкие пузырьки, образующие при слиянии азурофильные гранулы. Плотность продукта реакции возрастает от эндоплазматической сети к гранулам.

Миэлоциты уже не содержат пероксидазу в эндоплазматической сети. Продукт реакции виден только в комплексе Гольджи и в азурофильных гранулах (рис. 2). Некоторые из них имеют кристалл. Рядом с азурофиль-

ными гранулами в миэлоците лежат светлые (без продукта реакции) гранулы. Они несколько мельче азурофильных и соответствуют специфическим, содержащим щелочную фосфатазу [5, 6, 9].

В сегменто-ядерных нейтрофилах положительными на пероксидазу являются только азурофильные гранулы. Эндоплазматическая сеть и комплекс Гольджи, а также специфические гранулы не содержат продукта реакции (рис. 3).

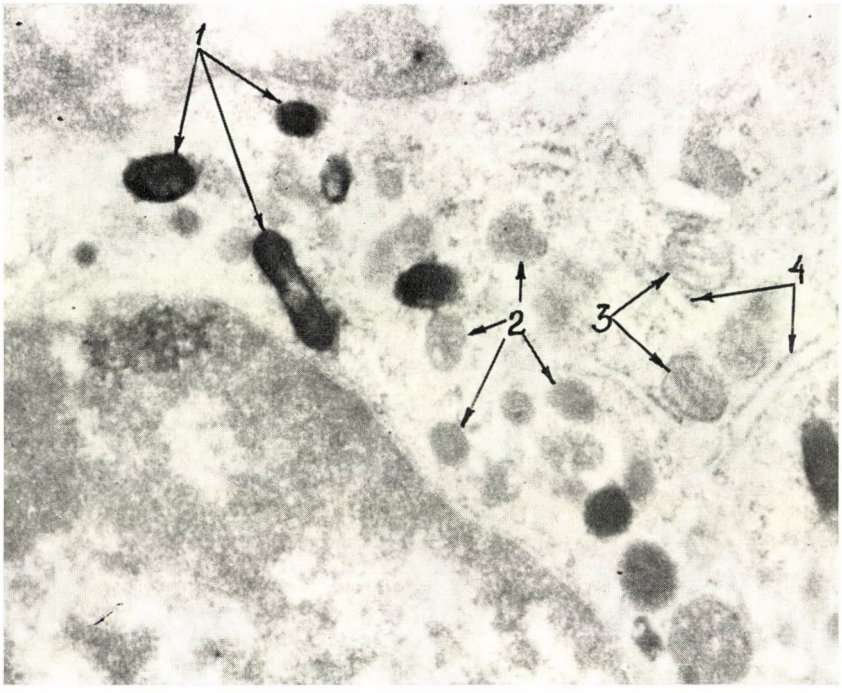


Рис. 3. Фрагмент зрелого нейтрофила мышей. Электронно-цитохимическая реакция на пероксидазу. Азурофильные гранулы с продуктом реакции (1). Специфические гранулы (2), митохондрии (3), каналы эндоплазматической сети (4) лишены продукта реакции. ×38000

Контроль специфичности реакции на пероксидазу.

Активность пероксидазы нейтрофилов полностью ингибируется 0,01 М Na_3N и 0,1 М гидроксиламина, но не до конца 0,01 М Na_3N, а 0,01 М и 0,1 М KCN незначительно снижают пероксидазную активность. Реакция отрицательна в отсутствие 3,3′-диаминобензидина. При опушении из среды перекиси водорода в некоторых азурофильных гранулах нейтрофилов остается слабая реакция. 40-минутное воздействие абсолютного ацетона перед инкубацией в неполной среде (без перекиси водорода) приводит к не-

которому усилению реакции. При увеличении времени преинкубации в ацетоне до 24 часов происходит разрушение клеточных структур и продукт реакции диффузно распределяется по клетке.

Обсуждение

В созревающих эозинофилах конвейер транспорта и упаковки в гранулы пероксидазы довольно хорошо изучен. Этот фермент обнаружен в перинуклеарном пространстве, шероховатой эндоплазматической сети, комплексе Гольджи, в незрелых гранулах и зрелых гранулах эозинофилов кроликов и крыс [8, 10, 14], кроликов [11], крыс [7, 18, 19]. Биохимически найдено, что пероксидаза нейтрофилов отличается от пероксидазы эозинофилов [4]. Возможно, распределение ее в созревающих нейтрофилах другое, отличное от распределения в эозинофилах.

Шимада [17], исследуя нейтрофилы из костного мозга человека, отметил положительную реакцию на пероксидазу в азурофильных гранулах, комплексе Гольджи, шероховатой эндоплазматической сети и в перинуклеарном пространстве. Он объяснил это поступлением в цистерны Гольджи пероксидазы, синтезированной в эндоплазматической сети. Такая интерпретация подтверждается данными Аккермана, полученными при исследовании нейтрофилов кошки [2] и человека [3]. Он наблюдал последовательное исчезновение пероксидазы из перинуклеарного пространства, эндоплазматической сети и комплекса Гольджи по мере созревания нейтрофилов. В зрелых клетках фермент оставался только в азурофильных гранулах. Наши наблюдения подтверждают это. Нам удалось проследить конвейер транспорта и упаковки в гранулы пероксидазы в созревающих нейтрофилах из костного мозга мышей: фермент, видимо, образуется в эндоплазматической сети, поступает в цистерны комплекса Гольджи, от концевых расширений которых отшнуровываются мелкие пузырьки, образующие при слиянии азурофильные гранулы. Эти результаты соответствуют данным авторадиографических исследований Паладе [16] на экзокринных клетках поджелудочной железы и Федорко и Хирша [12] на гранулоцитах.

Некоторые авторы, исследуя нейтрофилы кроликов [9], крыс [7], человека и кроликов [11], человека [15], нашли пероксидазную активнотсь только в азурофильных гранулах. МакКолл с соавт. [15] изучал зрелые клетки из периферической крови. Наши исследования и данные других авторов [3, 17] показали, что зрелые клетки не содержат пероксидазы в эндоплазматической сети и комплексе Гольджи. Возможно, другие авторы, изучая нейтрофилы костного мозга не обнаружили фермент нигде, кроме гранул, вследствие высокой чувствительности пероксидазы нейтрофилов к фиксации.

В наших опытах некоторые азурофильные гранулы в миэлоците содержали кристалл. Вероятно, кристаллизация фермента отражает процесс

созревания гранул, так как на стадии промиэлицита не было замечено ни одной азурофильной гранулы с кристаллом.

Бэйнтон и Фаркухар [9] писали об отложении продукта реакции на периферии азурофильных гранул в отсутствие перекиси водорода. Мы также наблюдали слабую реакцию в некоторых гранулах при опущении из среды перекиси водорода. Продукт реакции полностью заполнял гранулу. Возможно, в данном случае роль окислителя в реакции играют эндогенные неорганические перекиси, так как 40-минутное действие абсолютного ацетона перед инкубацией в неполной среде (без перекиси водорода) не снимало рекцию, а усиливало ее, вероятно, за счет некоторого разрушения мембраны и увеличения проницаемости для субстрата. При более длительной преинкубации в ацетоне мембраны настолько разрушались, что происходила утечка фермента, и продукт реакции диффузно распределялся по клетке. Вероятно, азурофильные гранулы нейтрофилов гетерогенны относительно присутствия в них эндогенных перекисей. Гранулы, в которых перекисей больше, реактивнее и, возможно, играют более значительную роль в бактерицидной функции нейтрофилов.

Литература

1. Роговин В. В., Муравьев Р. А., Геранина Н. Г., Фролова В. М., Пирузян Л. А.: Дубль-реакция (кислая фосфатаза и пероксидаза) в созревающих нейтрофилах мышей. Электронно-цитохимическое исследование. *Изв. АН СССР, сер. биол. 1*, 135 (1972).
2. Ackermann, G. A.: Ultrastructure and cytochemistry of developing neutrophil. *Lab. Invest. 19*, 290 (1968).
3. Ackermann, G. A.: Azurophil and specific granule formation in developing neutrophils of normal human bone marrow. *Anat. Rec. 169*, 265 (1971).
4. Archer, G. T., Aair, G., Jackas, M., Morell, D. B.: Studies on rat eosinophil peroxidase. *Biochim. biophys. Acta 99*, 96 (1965).
5. Baggiolini, M., Hirch, J. G., de Duve, C.: Resolution of granules from rabbit heterophil leucocytes into distinctive populations by zonal sedimentation. *J. Cell Biol. 40*, 529 (1969).
6. Baggiolini, M., Hirch, J. G., de Duve, C.: Future biochemical and morphological studies of granule fractions from rabbit heterophil leucocytes. *J. Cell Biol. 70*, 586 (1970).
7. Behnke, O.: Demonstration of endogenous peroxidase activity in the electron microscope. *J. Histochem. Cytochem. 17*, 62 (1969).
8. Bainton, D. F., Farquhar, M. G.: Segregation and packing of granule enzymes in eosinophils. *J. Cell Biol. 35*, 6A (1967).
9. Bainton, D. F., Farquhar, M. G.: Differences in enzyme content of azurophil and specific granules of polymorphonuclear leucocytes. II. Cytochemistry and electron microscopy of bone marrow cells. *J. Cell Biol. 39*, 299 (1968).
10. Bainton, D. F., Farquhar, M. G.: Segregation and packing of granule enzymes in eosinophilic leuococytes. *J. Cell Biol. 45*, 54 (1970).
11. Dunn, W. B., Hardin, J. H., Spicer, S. S.: Ultrastructural localization of myeloperoxidase in human neutrophil and rabbit heterophil and eosinophil leucocytes. *Blood 32*, 395 (1968).
12. Fedorko, M. E., Hirsch, J. G.: Cytoplasmic granule formation in myelocytes. *J. Cell Biol. 29*, 307 (1966).

13. Graham, R. C. Jr., Karnovsky, M. S.: The early stages of absorption of injected horseradish peroxidase in the proximal tubules of mouse kidney. Ultrastructural cytochemistry by a new technique. *J. Histochem. 14*, 291 (1966).
14. Miller, F., Herzog, V.: Die Lokalisation von Peroxidase und saurer Phosphatase in eosinophilen Leucocyten während der Reifung. Elektronenmikroskopisch-cytochemische Untersuchungen am Knochenmark von Ratte und Kaninchen. *Z. Zellforsch. 97*, 84 (1969).
15. McCall, C. E., Katayama, J., Cotran, R. S., Finland, M.: Lysosomal and ultrastructural changes in human "toxic" neutrophils during bacterial infection. *J. exp. Med. 129*, 267 (1969).
16. Palade, G. E.: Structure and function at the cellular level. *J. Amer. med. Ass. 198*, 815 (1966).
17. Shimada, Y.: Ultrastructural cytochemical studies on human blood cells. *Nagoya Med. J. 15*, 239 (1969).
18. Yamada, E.: Electron microscopy of the peroxidase in granular leucocytes of rat bone marrow. *Arch. Histol. Jap. 27*, 131 (1966).
19. Yamada, E., Yamauchi, R.: Some observations on the cytochemistry and morphogenesis of the granulocytes in the rat bone marrow as revealed by electron microscopy. *Acta haemat. Jap. 24*, 530 (1966).

Ultrastructural Cytochemistry of Peroxidase in Mouse Neutrophils

The distribution of peroxidase activity of developing neutrophils in mice was investigated by electron microscopy. The enzyme was found in the rough endoplasmic reticulum, the Golgi complex and azurophilic granules. The heterogeneity of azurophilic granules and their endogenous non-organic peroxide content are discussed.

Correspondence: Dr. V. V. Rogovin, Academy of Sciences, Institute of Chemical Physics, Department of Medical Biophysics, Moscow V-334, Soviet Union

Haematologia 9 (3—4), pp. 227—233 (1975)

Кинетическая модель экспериментального лейкоза. Закономерности развития ретикулосаркоматоза мышей

Н. М. ЭМАНУЭЛЬ, Л. М. ДРОНОВА, В. Н. ЕРОХИН, Е. И. БЕЛИЧ

Сектор кинетики химических и биологических процессов Института химической физики, АН СССР, Москва, СССР

(Поступило 27-го декабря 1973 г.)

Изучена кинетика развития нового перевиваемого штамма — ретикулосаркоматоза мышей линии CC57 Br. Развитие ретикулосаркоматоза количественно оценивалось по изменению веса метаплазированных органов. По экспериментальным данным строились соответствующие кинетические графики. Для описания кинетических кривых изменения всех показателей развития ретикулосаркоматоза использованы экспоненциальная ($\phi = \phi_0 + \phi_1 e^{\phi t}$) и степенная ($\phi = \phi_0 + at^b$) функции. В этих уравнениях ϕ — значение рассматриваемого показателя ко времени t; ϕ_0 — значение этого показателя в норме; a, b, ϕ, ϕ_1 — кинетические константы, определяющие форму кривой. Кинетическая модель ретикулосаркоматоза мышей может быть использована для количественных исследований в экспериментальной онкологии.

Благодаря своеобразному развитию лейкозов как системных заболеваний, решающее значение в их лечении имеют лекарственные методы. Поэтому одной из важных проблем экспериментальной гематологии является как задача отыскания новых противолейкозных препаратов, так и оптимизация их применения. Для этих исследований желательно иметь экспериментальные модели, которые по возможности приближались бы к соответствующим заболеваниям человека, и располагать критериями оценки противоопухолевой активности изучаемых химических соединений [9, 10].

Лейкозный процесс, как и всякий патологический процесс, развивается во времени и, следовательно, может быть охарактеризован определенными кинетическими закономерностями. Воздействие различных противоопухолевых агентов на лейкозный процесс сказывается на величине кинетических констант, характеризующих течение этого процесса. Это позволяет применить кинетические параметры для количественной оценки эффективности противолейкозных воздействий.

Настоящая работа является одной из серии работ, которые проводятся в Секторе кинетики химических и биологических процессов Института химической физики с 1958 года и посвящены исследованию кинетических закономерностей развития экспериментальных опухолей различного происхождения и локализации. Был создан ряд кинетических моделей перевиваемых лейкозов: гемоцитобластоз La [7], лимфолейкоз L—1210 [8], эритромиелоз Швеца [2], солидная и асцитная форма лимфолейкоза NKLy [5].

В данной статье приводятся результаты изучения кинетики развития ретикулосаркоматоза мышей. Этот штамм был получен В. М. Бергольцем [1, 6] при введении мышам пассированной в переживающей культуре ткани суспензии селезенки и костного мозга человека, умершего от острого гемоцитобластоза.

Ретикулосаркоматоз перевивается внутрибрюшинно на взрослых мышей линии СС57 Br [4] клеточной взвесью и бесклеточным фильтратом лейкозных тканей. Развитие ретикулосаркоматоза характеризуется бластоматозным поражением лимфатического аппарата и внутренних органов. У животных увеличивается печень, селезенка и почки, разрастаются опухолевые узлы в петлях кишечника. При микроскопическом исследовании отпечатков метаплазированных органов наблюдаются довольно крупные молодые клеточные формы, относящиеся к ретикулярным клеткам гемопоэтической системы [1].

Для трансплантации ретикулосаркоматоза в нашем исследовании использовались опухолевые узлы и селезенка, взятые на 20-е сутки после очередной перевивки штамма. Гомогенную массу, полученную при продавливании сквозь ситечко мельчителя, разбавляли физиологическим раствором NaCl и вводили мышам внутрибрюшинно по 0,3 мл суспензии, содержащей 15—20 млн. клеток.

Развитие ретикулосаркоматоза количественно оценивалось по изменению веса печени, почек, селезенки и брыжейки с разрастающимися опу-

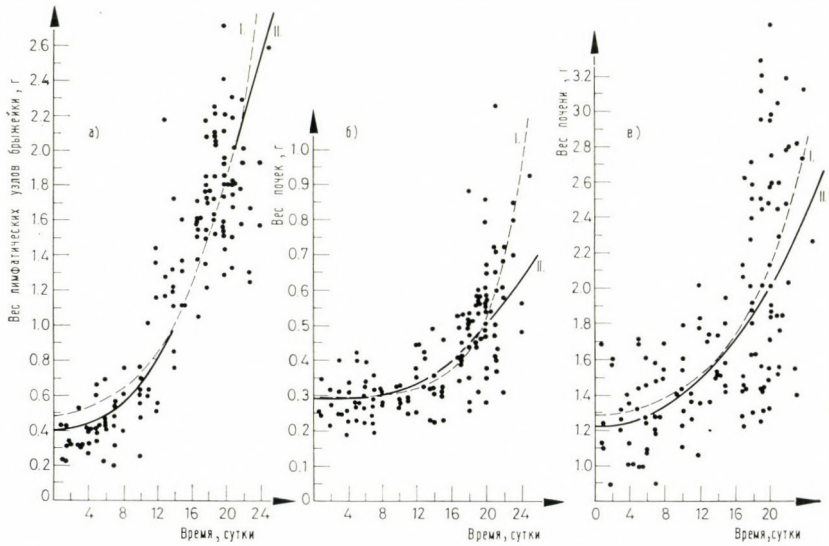


Рис. 1. Кинетика изменения веса отдельных органов, аппроксимированная экспоненциальной (I) и степенной (II) функциями: а) лимфатические узлы брыжейки; б) почки; в) печень

холевыми узлами, а также по гематологическим показателям: числу лейкоцитов в 1 мм^3 крови и процентному соотношению форменных элементов крови. Для этого у мышей один раз в сутки брали кровь для подсчета числа лейкоцитов и лейкоцитарной формулы. Затем мышей забивали и извлекали указанные органы. По экспериментальным данным строились соответствующие кинетические графики. Каждая точка, нанесенная на сеть координат, относится к отдельному животному. Для того, чтобы выяснить, насколько адекватно вес печени и селезенки отражает развитие лейкозного процесса именно за счет увеличения количества патологических клеток в них, подсчитывалось общее количество клеток и число лейкозных клеток в этих органах. После взвешивания печень (селезенку) продавливали сквозь мельчитель и добавляли 5-процентный раствор уксусной кислоты. Для получения гомогенной суспензии взвесь клеток в уксусной кислоте в течение трех минут пропускали через шприц, постепенно заменяя иглы большого диаметра на более тонкие [3].

Концентрация клеток определялась в камере Горяева. Зная объем взвеси, нетрудно определить общее число клеток в органе. По мазкам, приготовленным из измельченной ткани органа, подсчитывали процентное соотношение патологических и нормальных клеток.

На рис. 1 показаны кинетические данные по изменению веса лимфатических узлов брыжейки у мышей при развитии ретикулосаркоматоза. Чтобы получить необходимые количественные характеристики, наблюдаемые в опыте кинетические кривые аппроксимированы экспоненциальной (I) и степенной (II) функциями:

$$\phi = \phi_0 + \phi_1 e^{\phi t} \qquad \text{(I)}$$

$$\phi = \phi_0 + at^b \qquad \text{(II)}$$

Таблица 1

Уравнения кинетических кривых изменения различных показателей развития ретикулосаркоматоза

Показатели	Экспоненциальная функция	Степенная функция
1	2	3
Вес лимфатических узлов брыжейки	$\phi = 0{,}40 + 7{,}9 \cdot 10^{-3} e^{0{,}14t}$	$\phi = 0{,}40 + 1{,}36 \cdot 10^{-3} t^{2{,}31}$
Вес почек	$\phi = 0{,}29 + 0{,}1 \cdot 10^{-3} e^{0{,}26t}$	$\phi = 0{,}29 + 0{,}03 \cdot 10^{-3} t^{2{,}99}$
Вес печени	$\phi = 1{,}22 + 5{,}4 \cdot 10^{-3} e^{0{,}13t}$	$\phi = 1{,}22 + 3{,}30 \cdot 10^{-3} t^{1{,}80}$
Вес селезенки		$\phi = 0{,}14 + 13{,}40 \cdot 10^{-3} t^{0{,}99}$
Число лейкозных клеток в печени (млн.)	$\phi = 0{,}28 e^{0{,}29t}$	
Суммарный вес органов	$\phi = 2{,}05 + 9{,}4 \cdot 10^{-3} e^{0{,}17t}$	$\phi = 2{,}05 + 1{,}82 \cdot 10^{-3} t^{2{,}46}$

где ϕ — значение рассматриваемого показателя ко времени t, ϕ_0 — значение этого показателя в норме, a, b, ϕ_1, ϕ_1 — кинетические константы, определяющие форму кривой.

Указанные простые зависимости были использованы также для описания кинетических кривых изменения и всех других изученных позателей развития ретикулосаркоматоза. Рисунок 1 иллюстрирует также увеличение веса почек (*б*) и печени (*в*) в процессе развития болезни. Соответствующие кинетические уравнения приведены в таблице 1.

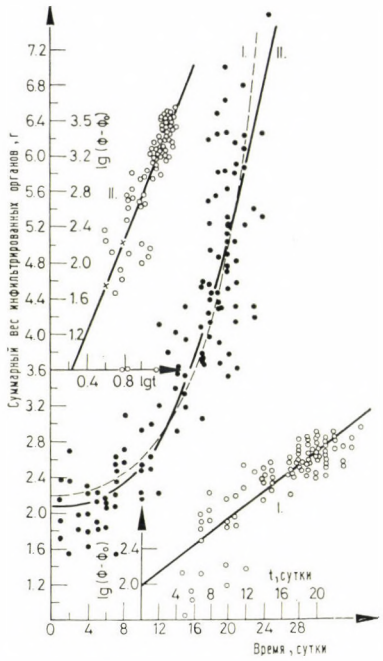


Рис. 2. Кинетика изменения суммарного веса инфильтрированных органов: I — экспоненциальная апроксимация; II — степенная апроксимация

Поскольку конечной целью химиотерапии лейкозов является ликвидация по возможности всех лейкозных клеток во всех органах, инфильтрированных этими клетками, то за развитием ретикулосаркоматоза можно следить по изменению суммарного веса упомянутых выше органов: печени, почек и др. Действительно, такая кинетическая кривая описывается теми же математическими законами, что и соответствующие кинетические кривые изменения отдельных органов (рис. 2, таблица 1). Следовательно, при использовании ретикулосаркоматоза как модели для количественных химиотерапевтических опытов можно ограничиться измерением суммарного веса печени, почек, селезенки, лимфатических узлов брыжейки.

При изучении общего количества лейкоцитов в периферической крови не удалось выявить четкой закономерности при развитии ретикулосаркоматоза. Можно лишь отметить, что значительного лейкоцитоза не наблюдается, и в мазках крови отмечаются только единичные патологические

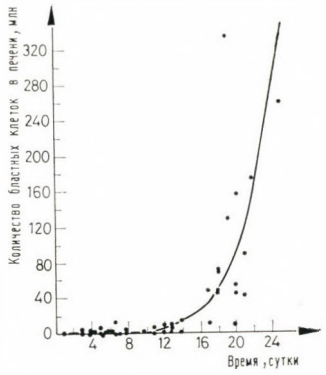


Рис. 3. Кинетическая кривая нарастания количества патологических клеток в печени больных мышей

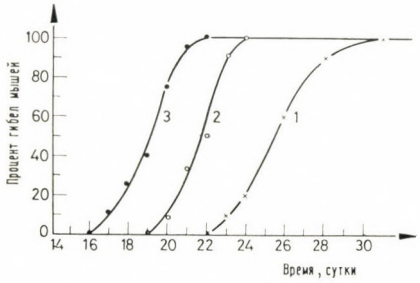


Рис. 4. Кривые гибели мышей с ретикулосаркоматозом: апрель 1969 г.; ноябрь 1969 г.; февраль 1970 г.

клетки. При подсчете процентного соотношения форменных элементов крови было обнаружено, что к концу заболевания у мышей наблюдается увеличение количества нейтрофильных лейкоцитов, а количество лимфоцитов оставалось в пределах нормы.

Опыты по изучению количества патологических клеток в печени и селезенке показали, что при развитии ретикулосаркоматоза в этих органах наблюдается экспоненциальное увеличение количества лейкозных клеток, что хорошо видно из рисунка 3. Кинетическое уравнение увеличения количества лейкозных клеток приведено в таблице 1. При этом общее число клеток печени практически не изменяется. Это говорит о том, что нарастание

веса органа происходит в основном за счет увеличения количества опухолевых клеток.

Кинетическое изучение ретикулосаркоматоза было начато в апреле 1969 года. За время, прошедшее с этого момента до февраля 1970 года, произошло некоторое сокращение продолжительности жизни мышей с ретикулосаркоматозом. Эти данные приведены в таблице 2 и графически изображены на рисунке 4. Разница в продолжительности жизни животных статистически достоверна. В настоящее время эта величина практически не изменяется от опыта к опыту. Очевидно, формирование ретикулосаркоматоза как стабильного перевиваемого штамма закончилось.

Таблица 2

Средняя продолжительность жизни мышей с ретикулосаркоматозом

Апрель 1969 г.	Ноябрь 1969 г.	Февраль 1970 г.
$26{,}6 \pm 1{,}9$	$22{,}2 \pm 0{,}8$	$19{,}6 \pm 0{,}7$

Уменьшение средней продолжительности жизни подопытных живогных привело к увеличению константы скорости процесса ϕ (формула 1) примерно на 70%, то есть к уменьшению времени удвоения количества опухолевых клеток, если при расчетах пользоваться экспоненциальной аппроксимацией.

Как следует из приведенных данных, изученный штамм ретикулосаркоматоза мышей может быть использован для количественных исследований в экспериментальной онкологии, в первую очередь для количественной характеристики активности противоопухолевых препаратов. Показатели лейкозного процесса легко измеряются, а их изменение во времени описывается простыми математическими зависимостями. В случае экспоненциальной аппроксимации кинетических кривых роста злокачественных новообразований может быть использован кинетический критерий торможения [7, 10].

Опыты с сарколизином и эндоксаном показали, что ретикулосаркоматоз обладает определенной чувствительностью к алкилирующим агентам.

Авторы выражают благодарность профессору В. М. Бергольцу за предоставление штамма и обсуждение результатов.

Литература

1. Бергольц, В. М.: Вирусный лейкоз (ретикулосаркоматоз) мышей, индуцированный лейкозным материалом человека. *Бюлл. экспериментальной биологии и медицины* 9, 78 (1968).
2. Дронова Л. М., Белич Е. И., Ерохин В. Н., Эмануэль Н. М.: Кинетические закономерности развития эритромиелоза у крыс. *Изв. АН СССР, сер. биол.* 5, 743 (1966).

3. Зимин,Ю. И.: Изменение кроветворения у крыс при реакции стресс. *Цюлл. экспериментальной биологии и медицины 7*, 19 (1969).
4. Медведев Н. Н.: Линейные мыши. «*Медицина*», *Москва*, 1964.
5. Пелевина И. И., Афанасьев Г. Г., Липчина Л. П., Андреев В. М., Эмануэль Н. М.: Кинетика роста перевиваемой лимфосаркомы NKLy в асцитной и солидной формах. *Изв. АН СССР, сер. биол.* 6, 841 (1966).
6. Франк Г. А., Бергольц, В. М.: Морфология и морфогенез вирусного ретикулоза у мышей линии СС57 Br. *Пробл. гематологии и переливания крови* 6, 27 (1970).
7. Эмануэль Н. М., Коновалова Н. П., Дронова Л. М.: Кинетическая характеристика противоопухолевой активности химических соединений различных классов. *Докл. АН СССР* 143, 3, 737 (1962).
8. Эмануэль Н. М., Коновалова Н. П., Богданов Г. Н., Васильева Л. С.: Кинетика развития асцитной лейкемии L-1210. *Докл. АН СССР* 106, 6, 1421 (1965).
9. Эмануэль Н. М.: Кинетические закономерности действия химиотерапевтических соединений на опухолевые процессы. *В кн.* «*Пути синтеза и изыскания противоопухолевых препаратов*». «*Медицина*». *Москва*, (1970).
10. Эмануэль Н. М., Евсеенко Л. С.: Количественные основы клинической онкологии. «*Медицина*», *Москва*, (1970).
11. Эмануэль, Н. М., Кухаренко Ю. А., Дронова, Л. М., Ерохин В. Н.: Статистическое обоснование кинетического критерия оценки эффективности противоопухолевых воздействий в эксперименте. *Изв. АН СССР, сер. биол.* 2, 224 (1970).

A Kinetic Model of Experimental Leukosis

Regularities in the Development of Reticulosarcomatosis in Mice

The kinetics of development of a new transplantable reticulosarcomatosis was studied in CC_{57}Br mice. Tumour development was estimated from changes in the weight of metaplastic organs by means of kinetic curves constructed on the basis of changes of all parameters characterized by exponential and power functions. The kinetic model of reticulosarcomatosis is recommended for use in quantitative research in experimental oncology.

Correspondence: Dr. V. N. Erokhin, Institute of Chemical Physics
Academy of Sciences. Vorobjovskoje 2b, Moscow, V-334, USSR

Haematologia 9 (3—4), pp. 235—241 (1975)

A "New" Blood Factor, Cl, Demonstrated with Extracts of Seeds of the Korean *Clerodendron trichotomum* Thunberg*

A. S. WIENER, G. J. MOON

Office of the Chief Medical Examiner of New York City
and the Department of Forensic Medicine and the Laboratory for Experimental Medicine and Surgery in Primates (LEMSIP) of the New York University School of Medicine, New York City and the Korean Medical School, Seoul, Korea

(Received October 12, 1973)

By absorbing extracts of seeds of the Korean *Clerodendron trichotomum* Thunberg with selected human group O red cells, a lectin has been prepared, which defines a hitherto undescribed specificity, designated **Cl**, defining individual differences in human red cells. The specificity **Cl** appears to characterize a structure associated with the A–B–H–Le marcomolecule, both of red cells and of saliva, which is distinct from the combining groups for A, B, H and Le. Moreover, the reactivity of red cells with anti-**Cl** lectin is destroyed by treatment of the red cells with proteolytic enzymes, unlike the reactions for A, B, H and Le.

The use of seed extracts (lectins) as diagnostic reagents for blood grouping and for biochemical studies has become general [1]. One of the supposed advantages of such reagents is their presumed chemical simplicity, *viz.* it has been tacitly assumed that seed extracts consist of a homogeneous population of lectin molecules as contrasted with blood serum antibodies which have been shown to consist of an entire spectrum of molecules of related structure. However, as Wiener et al. [2] have demonstrated, seed extracts like serum antibodies can be fractionated into lectins of more than one specificity by absorption with properly selected red cells. Applying this principle to extracts of leaves of the Korean *Vicia unijuga*, Moon and Wiener [3] succeeded in fractionating a potent anti-**N** lectin, useful as a diagnostic reagent for laboratory tests as well as for blood group research. The purpose of the present report is to describe the application of this principle to extracts of the seeds of the Korean tree, *Clerodendron trichotomum* Thunberg, for the preparation of a lectin defining a new blood group specificity, **Cl.**

Extracts of ground seeds of *Clerodendron trichotomum* Thunberg were prepared in the usual manner and tested against a series of more than 50 specimens of human blood; all were strongly agglutinated. However, when the extract was titrated against the same red cells, differences in titre were observed. Red cells reacting in lowest titre were then used for absorbing the lectin, and when the absorption was complete, a reagent resulted which gave marked agglutination with

* This article is dedicated to Dr. Susan R. Hollán for her magnificent contribution to medicine in the field of haematology, on the occasion of the 25th anniversary of the National Institute of Haematology and Blood Transfusion which she helped to found.

certain red cells, while it failed to agglutinate or only weakly agglutinated other red cells (Table 1). Since such differences in reactivity were observed also among red cells of group O, it was apparent that the blood factor (specificity) being detected by the lectin, designated anti-**Cl** after the seed from which it was prepared, was distinct from the known A–B–H blood factors. Tests with the absorbed seed extract (anti-**Cl** lectin) were therefore carried out against 20 blood specimens from commercial panels of cells of known blood groups, and blood factor **Cl** was shown to be different not only from A, B and H, but also from the blood factors **M**, **N**, **S**, **s**, **P**, **Lu**^{a}, **K**, **k**, **Jk**^{a}, **Jk**^{b}, **Fy**^{a}, **Fy**^{b}, **Le**^{a}, **Le**^{b}, **Xg**^{a}, **Rh**$_{0}$, **rh′**, **rh″**, **hr′**, **hr″** and **hr**. Tests were therefore carried out against a larger series of blood specimens in an attempt to define the nature of the newly found specificity **Cl**.

Table 1

Fractionation of anti-**Cl** lectin from extracts of seeds of *Clerodendron trichototomum* Thunberg by absorption with selected group O red cells

Tested against red cells of	Reaction with seed extract					
	Undiluted	diluted				
		1 : 2	1 : 4	1 : 8	1 : 16	1 : 32
Unabsorbed seed extract						
1. P. C., group A_1	+±	±	−	−	−	−
2. H. Y. Y., group O	+++	+++	+++	++	+	−
3. Dr. K., group O	++	+±	+	−	−	−
4. Y. H. W., group B	+++	++±	++	+±	−	−
5. C. L., group A_1	++	+±	+±	+	−	−
6. Chimpanzee, group A	+++	+++	++	+±	−	−
Seed extract, after absorption with group O red blood cells No. 3						
1. P. C., group A_1	−	−	−	−	−	−
2. H. Y. Y., group O	++±	++	++	+	−	−
3. Dr. K., group O	−	−	−	−	−	−
4. Y. H. W., group B	++	+±	−	−	−	−
5. C. L., group A_1	−	−	−	−	−	−
6. Chimpanzee, group A	++±	++	+±	±	−	−

To simplify analysis of the results of tests with anti-**Cl** lectin, the reactions were classified into four categories according to the intensity of the agglutination observed, ++ representing the most intense agglutination, + moderate agglutination, ± weak or doubtful agglutination, and − absence of agglutination. In the first experiments on a series of 133 blood specimens (Table 2), the findings were classified also according to the race of subject being tested. As shown in Table 2, no striking differences were observed in the distribution of the blood factor **Cl**

Table 2

Reactions of anti-**Cl** with red cells from Whites, Negroes and Chinese

Racial derivation of blood specimens	Number of blood specimens giving reactions of intensity				
	++	+	±	−	Total
Whites	20	26	6	7	59
Blacks	16	21	11	3	51
Chinese	9	6	0	8	23
Total	45	53	17	18	133

Table 3

Relationship of **Cl** factor to the A–B–O Blood Groups

A-B-0 blood group of specimen tested	Number of specimens agglutinated by anti-**Cl** lectin at intensity				
	++	+	±	−	Total
First Series					
O	26	6	8	0	40
A	2	7	7	7	23
B	2	5	2	1	10
AB	1	1	0	1	3
Total	31	19	17	9	76
Second Series					
O	29	6	5	7	47
A_1	2	5	3	18	28
A_2	3	2	0	2	7
B	4	2	2	9	17
A_1B	0	1	2	3	6
Total	38	16	12	39	105

among Whites, Negroes and Chinese. A second series of 76 blood specimens was then tested, and this time more attention was paid to the A-B-O blood groups. It was then noticed that most of the strong reactions occurred with blood specimens of group O, while most of the negative reactions occurred with blood specimens of group A. Since this was reminiscent of the behaviour of anti-**H** reagents, a further series of 105 blood specimens was tested, this time paying attention also to the subgroups of A. As shown in Table 3, the strongest reactions occurred most often

in blood groups O and A_2, the weakest reactions occurred most often in subgroups A_1 and A_1B, while blood specimens of group B had an intermediate position. Despite this resemblance to the specificity **H**, anti-**Cl** was clearly not identical with specificity anti-**H**, because 7 blood specimens out of 47 of group O and 2 out of 7 subgroups A_2 failed to agglutinate, while 2 out of 28 blood specimens of group A_1 gave intense agglutination. Furthermore, tests with the absorbed anti-**Cl** lectin on blood specimens from more than 10 group A chimpanzees uniformly gave strong agglutination (cf. Table 1), while none of these blood specimens was agglutinated by anti-**H** lectin.

The findings up to this point indicated a probable association between the newly found blood factor **Cl** and the blood factor **H** detected by saline extracts of *Ulex europeus* seeds. Therefore, Table 4 was prepared which compares the reactions of a random series of 94 blood specimens with the two lectins anti-**Cl** and anti-**H**. Simple inspection of Table 4 confirms the anticipated presence of an association between blood factors **Cl** and **H**. In fact, Table 4 can readily be converted into a 2×2 contingency factor by combining into a single category blood

Table 4

Relationship between the **H** and **Cl** Blood Factors

Intensity of reactions with anti-**Cl** lectin	Number of blood specimens reacting with anti-**H** lectin *(Ulex europeus)* at intensity				
	++	+	±	−	Total
++	31	11	1	6	49
+	3	8	1	2	14
±	0	3	4	6	13
−	0	3	1	14	18
Total	34	25	7	28	94

specimens reacting in strengths ++ or + and into a second category those giving ± or − reactions. The value of χ proved to be 31.7 for one degree of freedom, and by taking $r = \chi/\sqrt{N}$, where N is the number of blood specimens tested, it is found that $r = 0.58$, confirming the presence of a strong correlation between the reactions for **H** and **Cl**.

Thus, the findings indicated that anti-**Cl** was detecting another specificity of the A–B–H macromolecule, but due to a combining group distinct from A, B and H, or else due to a structure closely connected with the A–B–H macromolecule. If this idea was correct it would be expected to hold also for the blood group substances in saliva, i.e., anti-**Cl** serum should be inhibitable by saliva from A–B–H secretors but not by non-secretor saliva. Therefore, a series of samples of boiled saliva was tested by the standard inhibition method [4] with anti-H and anti-**Cl** reagents. For the tests, indicator red cells of group O were used which were **Cl**-

positive, and the anti-**H** and anti-**Cl** lectins were diluted so as to have a 6 units titre for the indicator cells. Moreover, to obtain clear-cut reactions the extracts of *Clerodendron* seeds were used directly, without prior absorption with **Cl**-negative red cells. The results of the tests are shown in Table 5. As predicted, saliva indeed proved capable of inhibiting anti-**Cl** lectin, and the saliva from non-

Table 5

Comparison of the saliva inhibition titers for anti-**H** lectin *(Ulex europeus)* and anti-**Cl** lectin (*Clerodendron* Thunberg)

Saliva of	Inhibition titers for		Saliva of	Inhibition titers for	
	Anti-Cl	Anti-H		Anti-Cl	Anti-H
Human			*Chimpanzee*		
No. 1	4	16	No. 1	4	4
No. 2	2	4	No. 2	8	64
No. 3	1	1	No. 3	8	16
No. 4	1/2	0	*Stump-tail macaques*		
No. 5	16	4			
No. 6	16	64	No. 1	4	32
No. 7	4	4	No. 2	256	256
No. 8	4	8	*Baboons*		
No. 9	1/2	1/2	No. 1	16	64
No. 10	1	0	No. 2	16	256
No. 11	0	0	No. 3	8	128
No. 12	1	16	No. 4	4	16
			No. 5	4	64

secretors gave the lowest inhibition titres, *viz.* only 0 to 1 units, while the salivas having the highest inhibition titres for H, e.g., stumptail macaque saliva No. 2, also had the highest inhibition titres for **Cl**.

As a further test of the theory, blood samples from individuals of the Bombay type were tested. Since Bombay red cells are non-reactive for A, B and H, they should also be non-reactive for **Cl**, and as Table 6 demonstrates, the absorbed *Clerodendron* seed extracts (anti-**Cl**) indeed failed to agglutinate unmodified Bombay red cells, of which three specimens were tested. To gain further insight into the nature of the **Cl** specificity, titrations were carried out against a series of blood specimens of human and non-human primate origin, the red cells being tested not only unmodified but also after treatment with a proteolytic enzyme (ficinated red cells). Those results are also shown in Table 6. The findings not only showed the previously noted correlation between the reactions with anti-**H** and anti-**Cl**, but also helped to crystallize further the nature of the differences between them. Firstly, it will be noticed that Bombay red cells are strongly agglutinated by crude extracts of the *Clerodendron* seeds; it is only the absorbed extract or purified anti-**Cl** reagent which does not agglutinate the unmodified Bombay red cells. This confirms the presence of at least two major fractions of

Table 6

Comparative titers of anti-**H** lectin (extracts of seeds of *Ulex europeus*), and extracts of *Clerodendron* seeds unabsorbed and absorbed, for untreated and ficinated red cells from a variety of blood samples of human and non-human primate orgin

Blood specimen tested	Titers of anti-H vs.		Titers of extracts of Clerodendron seeds			
			Unabsorbed vs.		Absorbed with red cells No. 11 vs.	
	Untreated RBC	Ficinated RBC	Untreated RBC'	Ficinated RBC'	Untreated RBC	Ficinated RBC
Bombay type						
1. D. P.	0	0	14	80	0	2
2. L. E.	0	0	12	96	0	3
3. S. A.	0	0	12	48	0	2
Cord blood						
4. M. A., group O	16	160	14	80	2	16
5. G. T., group O	12	160	12	80	0	3
Adult blood						
6. R. H., group A_1	16	128	5	64	0	3
7. D. S., group A_1	1/2	100	12	64	0	2
8. R. A., group O	40	350	40	80	16	6
9. B. F., group O	32	300	48	96	14	6
10. Lot 1226, group O	48	350	56	96	12	6
11. *CK 4029, group O	48	350	10	128	1	3
12. W. L., group B	12	80	40	56	14	2
Chimpanzee						
13. Hep, group A	0	0	64	24	12	0
14. Mary, group A	0	0	32	8	24	0
Gibbon						
15. Whitey, group A_1B	0	4	1	16	0	3
16. Penny, group A_1B	0	4	2	40	0	3
Baboon						
17. No. 84, Cerelle	0	0	64	24	12	0
18. No. 660	0	0	10	12	0	1

* Red cells used for absorbing extract of Clerodendron seeds

lectins in the extracts of *Clerodendron* seeds; one of the fractions is a panagglutinin (except, perhaps, for gibbon red cells), i.e., the fraction removed by absorbing with **Cl**-negative red cells, and the other fraction is the anti-**Cl** lectin which is the subject of this report. Secondly, it is to be noticed that while ficin treatment of the red cells increases their activity with anti-**H** lectin, it appears to destroy their reactivity with anti-**Cl** lectin, leaving behind in the latter case only a feeble non-specific reaction, presumably due to remnants of the panagglutinin not removed by the absorbing red cells.

In conclusion, therefore, a type-specific lectin of a specificity not previously described, designated anti-**Cl**, has been separated from extracts of seeds of the Korean *Clerodendron trichotomum* Thunberg, by absorption of the seed extracts with selected human red cells. The specificity detected by this anti-**Cl** reagent appears to be due to a structure on or closely connected with the A–B–H–Le macromolecule, but distinct from the combining groups for H, A, B and Le. Moreover, treatment of red cells with a proteolytic enzyme like ficin destroys their reactivity with anti-**Cl** lectin, even though such treatment leaves unaffected or increases the reactivity for A, B, H and Le. This suggests that sialic acid may play an important role in this newly found specificity, just as it does for the specificities M and N.

*

The authors thank Dr. A W. Rowe of the Cryobiology Laboratory of the New York Blood Center for samples of Bombay blood; and Dr. A. F. Cioffi of Eastern Blood Bank for blood specimens from blood donors. Misses Pat Ryan and Sally Tangonan assisted in carrying out the tests. This investigation was aided, in part, by U.S. Public Health N.I.H. grant GM-12074.

References

1. Tobiska, J.: Die Phytohämagglutinine. Akademie Verlag, Berlin 1964.
2. Wiener, A. S., Moor-Jankowski, J., Gordon, E. B.: The specificity of hemagglutinating bean and seed extracts (lectins). *Int. Arch. Allergy 36*, 582 (1969).
3. Moon, G. J., Wiener, A. S.: A new source of anti-N lectin; leaves of the Korean *Vicia unijuga*. *Vox Sang. 26*, 167 (1974).
4. Erskine, A. G.: Principles and Practice of Blood Grouping. C. V. Mosby, St. Louis 1973.

Correspondence: Prof. Dr. A. S. Wiener, 64 Rutland Road, Brooklyn, N. Y. 11225, U.S.A.

Haematologia 9 (3—4), pp. 243—251 (1975)

Rh_0 or D, -D- and the Blocking Patterns
A GENETIC (TEMPLATE) EXPLANATION

T. R. TOVELL

Montreal, Quebec, Canada

(Received March 7, 1973)

By the use of the gene template it will be shown that D appears at two different sites on the Rh locus, and that the locus cannot simply be DCE — or a similar one. Further, -D- does not appear to be a super Rh_0 as described by Wiener. Finally, a simp le explanation is offered for the action of incomplete (blocking) and agglutinating antibodies.

Introduction

A feature of the recently proposed gene template [1] is that, unlike previous theories, it presents a structure to explain both antigens and antibodies. It indicates that the antigens may have a structure that is monomeric, dimeric and trimeric, which also appears to be the type of structure that has now been reported for the antibodies (for pentamers see discussion). This feature seems to be a necessary one if the idea of antigen/antibody reactions being — "mortise and tenon" — "keyed" — "fitting into depressions" — is valid, or if the antibody is a "mirror image of the antigen".

As a result, it is proposed that genetic theories that do not allow the antigen structure to appear as monomers, dimers and trimers are likely to prove incorrect.

In support of this contention and in favour of the lapped or complex structure of the template it will be shown that D in the Rh blood system may not be a single allele on the Rh locus as the Fisher—Race [3] scheme proposes, but may be located at two positions.

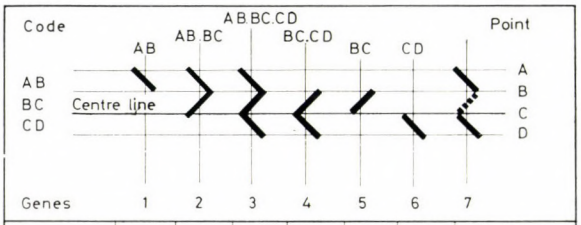
As a result, no arrangement of the C, D, E, c, e, receptors on a single locus can be valid unless at least some of the identifications are repeated.

It will also be shown that Wiener's [2] explanation of -D-, or D--, or Super Rh^0 (a strong Rh^0 factor occupying the missing sites) is not likely to be correct because, if such were the case, the basic species template could not produce the full range of antibodies — C, c, E, e, f, Ce, Ee and C^w — that have been reported [4] from these carriers.

Finally, an explanation of blocking or incomplete antibodies will be given which suggests that difficulty in understanding these reactions may be due to ineffective genetic concepts.

Method

The gene template (Fig. 1), used previously to explain the systems listed [1, 5] will be used to explain the possible genetic structure of Rh_0 or D, -D-, etc., and will also be used to illustrate blocking or incomplete antibodies.



System						
ABO	A_1	A_2	A_3	B	O	O_1
Rh	r	R_1	R_Z	R_2	R_0	R_0
CDe	ce	CDe	CDE	cDE	cDe	cDe
MNSs	NS	MS	MS_1	Ms	Ns	Ns
Gm (zafy)	z	za	zafy	afy	a(y)	f(y)
Hp	IF	2	3	2M	IS	IM(?)

Fig. 1. Gene template. For explanation of identifications see Ref. 1

Material

Hughes-Jones [6] has reported that IgG anti D binds to antigen by one site and IgM anti D binds by two sites. Also see Holburn (27).

He has also reported that, "If IgM and IgG anti D are added at the same time to red cells, one IgM molecule prevents the uptake of two IgG molecules" and he remarks, "(this suggests) that D- antigen sites *occur in groups* and that the large IgM molecule attached to one D- antigen site prevents the binding of an IgG molecule to a neighbouring site by steric hindrance".

The gene template, divided in detail for the Rh system (Fig. 2) shows that each of the lowest two units (monomers) of the template has one D site. Thus there are two monomer antigens (cDe or R_0) that carry a single D site, a dimer antigen (cDE or R_2) that carries two sites, a trimer antigen (CDE or R_z) that also carries two sites – and finally another dimer antigen (CDe or R_1) that carries a single D site.

The antibody pattern that results from this template (see Ref. 1 for full details) for anti D only is:

1. Monomer anti D, i.e. IgG – two types – (each monomer with one D site).
2. A dimer and trimer with two sites each of anti D which may be IgA or IgM.
3. A dimer with a single site which may also be IgA or IgM.

The observations of Hughes-Jones are therefore interpreted by the template as meaning that anti D can appear as one site on a monomer, or as either one or two sites on multiple units, which may correspond to IgA or IgM. There is evidence that IgM consists of IgG monomer units in combination [7].

The second observation of Hughes-Jones "one IgM molecule prevents the uptake of two IgG molecules" corresponds exactly with this template explanation because the D sites on most IgM molecules will be twice as many as those on IgG.

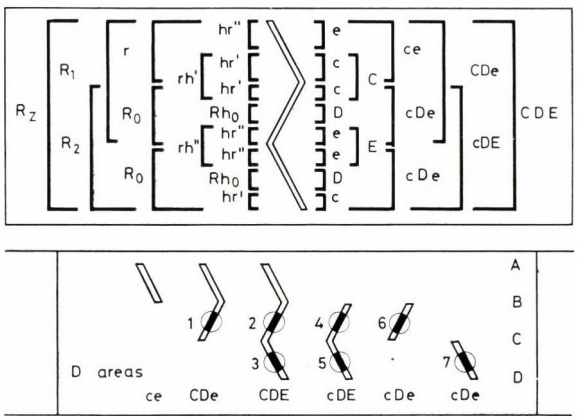


Fig. 2. Rh identifications on gene template. *Note:* D occurs on centre and lower units, i.e. code BC and CD, and occurs seven times on five different genes (antigens)

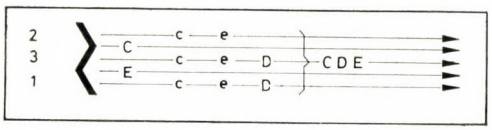


Fig. 3. Rh identifications on IgG sub-groups Ig2, Ig3 and Ig1. Template predicts that D is not on Ig2, C is not on Ig1 and E is not on Ig2. These units may, however, be combined with the units showing C, D, E identifications. C and E, being a bond identification will always be on parts (at least) of two units

Equally, since IgM anti D blocks two of the antigen monomers, this may be a "steric hindrance" – but it might be equally correct to propose that IgM anti D is a more complex molecule and therefore it must block two single (monomer) IgG molecules.

Apart from agreement with the template, the observations of Hughes-Jones appear to be further supported by the fact that anti D IgG is found on the sub-types yG1 and yG3 but not yG2 (yG4 will be discussed later).

The significance of this is shown in Fig. 3 where the template units are noted as yG2, yG3 and yG1 in that order, as proposed by Kunkel et al. [8].

The template (Fig. 3) shows the IgG subclass of some of the Rh antibodies reported by Abramson and Schur [9]. In this study D was also reported to be on Ig2 in three of seven examples, mixed with normal anti D IgG molecules.

The possible significance of this scheme based on the template is as follows: (a) D will be found on yG3 and yG1 but not yG2; (b) C will be on yG2 and yG3 but not yG1; (c) E will be on yG3 and yG1 but not yG2; (d) c and e will be on all three units; (e) CDE will consist of three units; (f) CD will be on either yG2 and yG3 or all three units.

Anti D was also identified on Ig4. Abramson and Schur found it once in 27 samples when testing anti CD and Morell et al. [10] have identified it, twice with reasonable titre, in two unboosted examples and in all of 22 boosted samples.

These inconsistencies seem to make it uncertain as to how Ig4 is related to the Rh system. The rarity in unboosted samples suggests that it may be part of fragments of Ig1, Ig2, or Ig3 mixed with Ig4 – or that Ig4 is attached because it is adjacent (i. e. a spacer between adjacent systems). Compare the IgA subdivisions IgAa and IgAb.

-D-

It has been assumed [11] that -D- or D-- may be a support for the DCE arrangement in that it represents an allele where the C and E loci are not occupied – whereas Wiener [2] considers that it is due to chemical structural change in which a strong Rh_0 factor occupies the sites of the other anti Rh sera.

This last explanation cannot be correct if the basic template structure directs the production of both antigen and antibody as has been proposed previously. If -D- or D-- was, in fact, DDD, it is clear from the Rh template (Fig. 2) that some at least of the antibodies that have been produced [5] could not be produced. This particularly applies to either anti C or anti E.

That C and E have been deleted, appears to be correct as far as this gene with its three receptor loci is concerned, but this does not appear to support an overall three allele theory because, as has been shown, D appears to be at two sites – and this double appearance of D may coincide with the greater complexity shown in Fig. 2 which shows the CDE locus to be in the order ecCcDeEeDc.

D^u

The possible existence of two sites for D on the template monomers then leads to the proposal that an individual may express one D gene as an antigen and the other D gene as an antibody.

However, as explained in a previous paper [1] this would be a rarity and what is far more likely is that the qualities of one D antigen will lead to a production of D antibodies that are reciprocal, i.e. it will not react with the carrier. This suggests that an incomplete D will produce a reciprocal anti D comparable to the anti B_w produced by A_1B_w type blood. Such an incomplete D antigen has been termed D^u and it appears to range in strength from normal D to zero.

It also seems likely that the hr^s identification of Shapiro (discussed in 1) may be on one of the D genes and not the other – and this also appears to have some meaning for the factors termed Rh^A, Rh^B, Rh^C, etc. which may be present or missing from D antigens.

Miscellaneous

The following observations are offered as additional evidence of template structure – particularly as it applies to D.

1. If Rh positive cells are exposed to a mixture of agglutinating or incomplete anti D, the incomplete antibody seems to win the race for antigen [12, 13].

Because a natural unbroken antigen must normally be a total single (monomer) unit at least, this means that cDe, for example, is in fact a "complete" antigen (which equals the antigen R_0 of Wiener).

Also since c, D or e, alone, appear to be parts of a complete antigen they may validly be termed "partial" or "incomplete" antigens.

D alone may be attached to a basic monomer template or it may be paired only with part of the monomer (Fig. 4). The total monomer with D on it would logically be a naturally produced antibody – but D attached to only part of the monomer may be due to refined or specific D inoculation, i.e. it may be equivalent to an immune antibody.

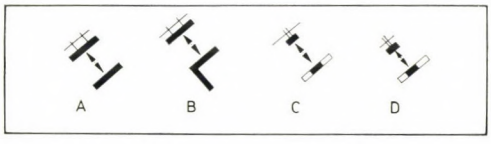


Fig. 4. Initial diagram of antibody reaction. A. Normal agglutination. *Example* – anti A with A_1; B. Agglutination (partial). *Example* — anti A with A_2, (H remainder, vacant); C. Partial antibody on monomer combining with part of an antigen. *Example* — anti D with -D-; D. Partial antibody (fragment) combining with part of an antigen. *Example* – incomplete anti -D- with -D-. In the case of Fig. 4D the equal size of antibody and antigen should form the strongest (ring force) combination

Also, since the monomer with anti D identification on it may be larger than incomplete anti -D-, it seems likely that the smaller, less complex, antibody will be able to combine more rapidly (see Fig. 4).

2. Higher pressure is needed to inactivate incomplete anti Rh than agglutinating anti Rh [14]. Incomplete anti Rh appears to be smaller and therefore there may be less to breakdown. It should, for example, be simpler to breakdown a chain of say sixty amino acids than a chain of say, ten.

3. Heat inactivates anti Rh agglutinins [15, 16]. The reasons appear to be similar to the last item.

4. If Rh positive cells are exposed to trypsin [17] or a filtrate of a broth of cholera vibrio [18], they become agglutinable by incomplete anti Rh.

Again it appears that the larger structure is broken down (or sections of it are isolated) so that a smaller antibody – incomplete anti Rh – can combine directly with a partial (or same sized) antigen.

5. Anti D blocking antibodies are resistant to washing off the red cells but agglutinating anti D antibodies are washed off easily [19–21].

This appears to indicate that the blocking antibodies (small units) combine totally with the corresponding part of the antigen – but that agglutinating anti D does not do so because the monomer to which it is attached has vacant antibody sites that cannot combine with antigen (Fig. 4C).

Blocking or incomplete antibody/antigen reactions

At about the same time, Race [13] and Wiener [12] carried out experiments that can be summarized as follows. If Rh positive cells are suspended in a serum containing incomplete anti-D, then the mixture is centrifuged and the cells are washed and re-suspended in saline, these cells will no longer be agglutinated by agglutinating anti D although they will be as agglutinable as before by anti-c, anti-C and anti-E. This particular behaviour is shown in Fig. 5, where it will be

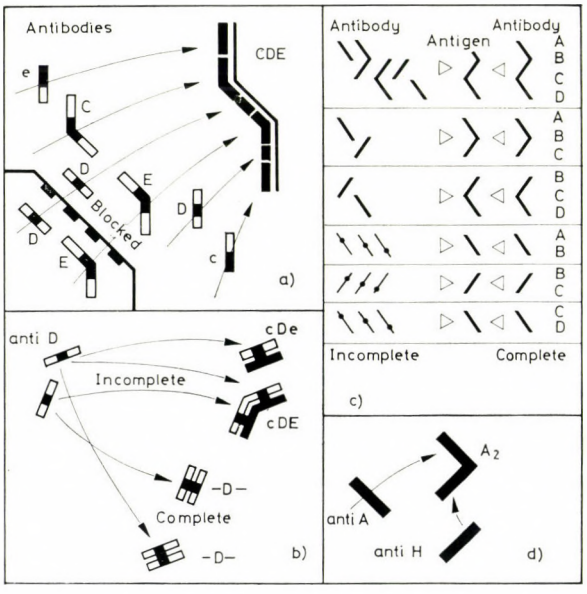


Fig. 5. Antibody reactions. A. Incomplete or blocking. B. Action of anti D. C. Patterns showing that the action is complete or incomplete – and not necessarily the antigens or antibodies. D. Showing action of both anti A and anti H with A_2

seen that such behaviour coincides with the proposed gene template structure. It would also appear to support Wiener's opinion that the CDE identifications are simply parts of antigens.

Finally, the action illustrated would also appear to support the Fisher–Race theory but cannot if, as indicated here, D has two sites – and will be even less applicable if the C and e sites repeat as is also proposed.

Figure 5B illustrates and may explain a query of Kabat [26]: "The ability of blocking antibodies to agglutinate enzyme treated erythrocytes of -D-/-D- erythrocytes in saline is very hard to understand unless these antibodies have more than one antibody group per molecule." The explanation illustrated means that incomplete antibody agglutinates the -D-/-D- antigen because it is also incomplete, i.e. both are of approximately equal size. However, blocking (or incomplete) anti D should not theoretically agglutinate D/D cells in saline because its combination may be blocked by additional parts of the total monomer to which is attached.

The implication of this last observation is that antibodies appear to combine completely with antigens of equal size, but will not agglutinate completely if the antigen is of a different size. As a result, an incomplete antibody may be complete in its action with an incomplete antigen – but be incomplete with a complete antigen – and a proposed scheme of this nature is shown in Fig. 5.

Discussion

If the antibodies combine directly with the antigen on the cell membrane, as is indicated by this genetic scheme, it appears to follow that the antigens on the cell membrane are simply identifications on parts of or the whole chromosome. This would suggest that the cell membrane is simply a chromosome mesh which may be in helical form, or in a form that was duplicated as a helical.

The structure of the membrane – as proposed by Danielli and Dawson [22] and Robertson [23] and illustrated by Hollán [24] would fit this scheme, viz. protein chromosome layers externally and internally, with a lipid layer in between or a similar scheme where the helicals appear externally and internally but also wind through the lipid layer. The carbohydrate percentage (7% to 10%) also appears to be significant because IgG (a monomer) is reported to have about 2% carbohydrate whereas IgA or IgM have about 12%.

Since IgA and IgM appear to be bonded monomers, the greater amount of carbohydrate may point to carbohydrate formation due to bond action. Therefore, the 7% to 10% of carbohydrate in the cell membrane may point to the proteins of the surface being bonded proteins that form a chromosome mesh.

The capacity of incomplete anti D to combine with similarly sized (?) incomplete D (-D-) antigens contrasted to its inability to agglutinate complete D antigens also appears to suggest that the method of attraction and combination is not due simply to direct (repulsive, attractive) forces. Firstly, because there is no

evidence that the total charges in each unit are opposite – and some evidence to say that antigens and antibodies repel each other – and secondly, because even if they were attracted to combine it should mean that incomplete anti D would combine equally strongly whether with -D- cells or D cells.

The manner of combination proposed, which may be at variance with present schemes, is as follows. The chromosome (or gene units) may have an UP-DOWN sequence as on DNA [25]. This UP-DOWN sequence may allow a ring force to operate in the chromosome strands, especially at division – causing the helicals to compress. So it is proposed here that the antibody combines with the antigen by a 'ring' force that operates when the antigen/antibodies combine.

It follows that when antibodies can combine with equally limited antigens that complete 'ring' force may operate and draw the units tightly together. This action would enable incomplete antibodies to combine better with antigens that have been subject to forms of bond destruction such as enzymes, pressure and heat, for in such cases these destructive processes would create incomplete antigens that would be more equal in length to the antibodies. On the other hand, if there is a difference in size, the 'ring' force may be hindered in its operation.

IgM now classed as a pentamer may according to the template be Ig2, Ig3, Ig1, plus two spacer units (without antigen sites) Ig4a and Ig4b.

References

1. Tovell, T. R., Vos, G. H.: A genetic scheme for the blood systems ABO, Rh and MNSs, and an explanation of antigen/antibody patterns. *Haematologia 7*, 35 (1973).
2. Wiener, A. S., Wexler, I. B.: Die Vererburg der Blutgruppen. George Thieme Verlag, Stuttgart 1960, p. 204. (Discussed by Prokop, O. and Uhlenbruck, G. In: Human Blood and Serum Groups, McLaren, London 1969).
3. Fisher, R. A.: cited by Race, R. R.: An "incomplete" antibody in human serum. *Nature (Lond.) 153*, 771 (1944).
4. Hackel, E.: Rh antibodies in the serum of two -D-/-D- people. *Vox Sang. 2*, 331 (1957).
5. Tovell, T.: A possible genetic explanation of the hepatitis B subtypes. *J. Immunogenet. 2*, 101 (1975).
6. Hughes-Jones, N. C.: The attachment of IgG molecules on the red cell surface. *Haematologia 6*, 269 (1972).
7. Tomasi, T. B., Kunkel, H. G.: Dissociation and reassociation studies of an IgS macroglobulin with rheumatoid factor properties. *Arthr. and Rheum. 4*, 125 (1961).
8. Kunkel, H. G., Natvig, J. B., Joslin, F. C.: "Lepore" type of hybrid globulin. *Proc. nat. Acad. Sci. (Wash.), 62*, 144 (1969).
9. Abramson, N., Schur, P. H.: The IgG subclasses of red cell antibodies and relationship to monocyte binding. *Blood 40*, 500 (1972).
10. Morell, A., Skvaril, F., Rufener, J. L.: Characterization of Rh antibodies formed after incompatible pregnancies and after repeated booster injections. *Vox Sang. 24*, 323 (1973).
11. Prokop, P., Uhlenbruck, G.: Human Blood and Serum Groups. McLaren, London 1969, p. 204.
12. Wiener, A. S.: A new test (blocking test) for Rh sensitisation. *Proc. soc. exp. Biol. (N. Y) 56*, 173 (1944).

13. Race, R. R.: An "incomplete" antibody in human serum. *Nature (Lond.) 153*, 771 (1944).
14. Boyd, W. C.: The effect of high pressure on hemagglutinating antibodies. *J. exp. Med. 83*, 401 (1946).
15. Kleczkowski, A.: Effect of heat on flocculating antibodies of rabbit anti-sera. *Brit. J. exp. Path. 22*, 192 (1941).
16. Coombs, R. R. A., Race, R. R.: Further observations on the "incomplete" or "blocking" Rh antibody. *Nature (Lond.) 156*, 233 (1945).
17. Morton, J. A., Pickles, M. M.: Use of trypsin in the detection of incomplete anti-Rh antibodies. *Nature (Lond.) 159*, 779 (1947).
18. Pickles, M. M.: Effects of cholera filtrate on red cells as demonstrated by incomplete Rh antibodies. *Nature (Lond.) 158*, 880 (1946).
19. Witebsky, E., Mohn, J. F.: Studies on Rh antibodies. I. Analysis of a zone phenomenon in an Rh antiserum by splitting the serum into two fractions by means of dialysis. *J. Lab. clin. Med. 33*, 1353 (1948).
20. Mohn, J. F., Witebsky, E.: Studies on Rh antibodies. II. The demonstration of a third type of Rh antibody with blocking properties. *J. Lab. clin. Med. 33*, 1361 (1948).
21. Mohn, J. F., Witebsky, E.: Studies on Rh antibodies. III. Analysis of a zone phenomenon in an Rh antiserum split by dialysis into four fractions. *J. Lab. clin. Med. 33*, 1369 (1948).
22. Danielli, J. F., Dawson, H.: A contribution to the theory of permeability of thin films. *J. Cell comp. Physiol. 5*, (1935).
23. Robertson, J. D.: The molecular structure and contact relationships of cell membranes. *Progr. Biophys. 10*, 344 (1960).
24. Hollán, S. R., Breuer, J. H., Szelényi, J. G.: On the red cell membrane. *Haematologia 6*, 217 (1972).
25. Watson, J. D., Crick, F. H. C.: Genetical implications of structure of deoxyribonucleic acid. *Nature (Lond.) 171*, 964 (1953).
26. Kabat, E. A.: Blood Group Substances. Academic Press, New York, 1956, p. 258.
27. Holburn, A. M., Carton, J. P., Economidou, J., Gardner, B., Hughes-Jones, N. C.: Observations on the reactions between D-positive red cells and ^{125}I-labelled anti-D molecules and subunits. *Immunology 21*, 499 (1971).

Correspondence: Mr. T. R. Tovell, 3605 Ridgewood 307, Montreal, Quebec, Canada

Haematologia 9 (3—4), pp. 253—255 (1975)

Lack of Immune Tolerance to Hepatitis B Antigen in Offsprings of Guinea Pigs Injected with HB Ag during Pregnancy

D. VALLÓ, G. HALMOSDI, J. PERKEDI

Postgraduate School of Medicine, Budapest

(Received April 12, 1974)

Immune tolerance to hepatitis B antigen has been examined in the guinea pig. The offsprings of guinea pigs injected with purified HB Ag during pregnancy were found capable of producing HB antibodies. Purified HB Ag is suitable for producing immune serum for the systemic screening of blood donors for HB Ag.

Systematic examinations on the occurrence of hepatitis B antigen (HB Ag) have shown that HB Ag can be detected for years in the blood of otherwise healthy individuals. The phenomenon has been termed hepatitis-associated antigen carrier state [1], and many examinations have been performed to decide whether it was due to immune tolerance [3]. In humans, controversial results were obtained. According to some authors [2—4], HB Ag is transmitted transplacentally, others [5—9] found evidence to the opposite.

Sera of high titre and high specificity for HB antibodies (HB Ab) can be produced in the guinea pig [10], thus this species is suitable for studies on immune tolerance.

Methods

Purified HB Ag

Mixed plasma of donors was used for producing purified HB Ag [11]. The serum was purified by hydrolysis for 16 hours with a small amount of pepsin, reversible precipitation with polyethylene glycol (PEG), and electrogel-filtration according to Bundschuh [12], using a Pharmacia K 50/100 column and Sephadex G 200 gel.

Immunization

Two female and 8 male adult guinea pigs of 300 to 350 g weight were treated with 0.2 ml of the purified 1 mg/ml HB Ag preparation on 5 occasions in 2 weeks. The first dose contained besides the HB Ag an equivalent amount of complete Freund adjuvant, and was given subcutaneously. The further doses consisted of purified HB Ag + incomplete Freund adjuvant in equal proportion and were

given subcutaneously; 0.1 ml HB Ag was injected intravenously without adjuvant. Two weeks after the fifth injection the male animals were bled and the sera were stored at −20°C. After the first injection the 2 females were mated with the males. Five guinea pigs were born; these were brought up and then treated with HB Ag as described above followed by bleeding. The mother animals were bled 2 weeks after reinjection.

Ouchterlony's method

1% agarose (Serva, reinst), 0.1 M NaCl, 0.01 M Tris buffer and 0.001 M EDTA pH 7.6 were mixed and 2 mm thick plates were poured in Petri dishes. HB Ag serum was put into the central well 6 mm in diameter, the immune sera were distributed into 3 mm wells situated 3 mm apart. The plates were incubated at 25°C for 48 hours and at 4°C for 24 hrs. The reaction was evaluated against a dark background in transmitted light.

Immune electroosmophoresis

HB Ag was detected by modified electroosmophoresis [13, 14] on plates of 0.05 M veronal-acetate buffer pH 8.6 and 0.8% agarose. The sera to be examined were put into wells 6 mm in diameter and the specified immune sera into 2 mm wells situated 3 mm apart. 6 V/cm current was applied for 90 minutes. Reactions were evaluated against a dark background in transmitted light.

The sensitivity of the method was controlled by using serum containing a known quantity of HB Ag (15); the method was found to detect HB Ag at a concentration of 0.045 mg/ml.

Results

After the first dose of HB Ag, the sera of the 8 male guinea pigs proved negative with human HB Ag-negative sera, and positive with human HB Ag-positive sera. These positive reactions were identical with that of human HB Ag immune serum. Examination of the guinea pig sera revealed a high-anti-a titre and a low anti-d and anti-x specificity as stated by G. L. Le Bouvier.

The sera of the 5 offsprings with HB Ag-positive blood samples gave a positive reaction identical with that of the 2 mother animals, of the 8 males and of the human immune serum.

Next, 1000 blood donors were tested for HB Ag with the sera of the 8 male guinea pigs, 5 offsprings and the human immune serum. HB Ag positivity was confirmed in 16 cases (1.6%) with all the three kinds of immune serum.

Discussion

The results allowed to conclude that the offsprings of guinea pigs immunized with purified HB Ag during pregnancy are capable of producing HB Ab, HB Ag being assumed not to pass across the placenta, therefore, no immune tolerance to HB Ag can develop in the offsprings. It must, however, be considered that the HB virus does not multiply in the guinea pig, so this model should be compared to human infection with certain reservations.

As the HB Ag used for immunization was produced from mixed donor plasma, the obtained immune serum contained anti-d but no anti-y specific antibodies. It was therefore expected that D type will be in excess among HB Ag carriers. The distribution pattern of subtypes remains to be determined by experiments still in progress.

*

We wish to thank Dr. G. L. Le Bouvier (Yale University School of Medicine) for typing the sera; Dr. K. Madalinski (State Institute of Hygiene, Warsaw) for kind supply of serum with known HB Ag content; and the National Institute of Haematology and Blood Transfusion, Budapest, for human HB Ab-positive serum.

References

1. WHO Scientific Group: Viral Hepatitis. Technical Report Series No. 512, Geneva 1973.
2. Krech, U., Sonnabend, W.: Australia antigen in newborn babies. *Lancet 1*, 779 (1970).
3. Merrill, D. A., Dubois, R. S., Kohler, P. F.: Neonatal onset of the hepatitis-associated antigen carrier state. *New Engl. J. Med. 287*, 1280 (1972).
4. Schweitzer, I. L., Mosley, J. W., Ashcaval, M., Edwards, M., Overby, L. B.: Factors influencing neonatal infection by hepatitis B virus. *Gastroenterology 65*, 277 (1973).
5. London, W. T., Di Figlia, M., Rodgers, J.: Failure of transplacental transmission of Australia antigen. *Lancet 2*, 900 (1969).
6. Moroni, G. A., Constantino, D., Zampieri, G., Gianotti, G. A., Doglia, M., Del Prete, S.: Do the hepatitis antigens cross the placenta? *Lancet 2*, 376 (1971).
7. Holzbach, T.: Australia antigen hepatitis in pregnancy. Evidence against transplacental transmission of Australia antigen in early and late pregnancy. *Arch. intern. Med. 130*, 234 (1972).
8. Skinhoj, P., Olesen, H., Cohn, J., Mikkelsen, M.: Hepatitis-associated antigen in pregnant women. *Acta path. microbiol. scand. Section B 80*, 362 (1972).
9. Kukowski, K., London, W. T., Sutnick, A. I., Kahn, M., Blumberg, B. S.: Comparison of progeny of mothers with and without Australia antigen. *Hum. Biol. 44*, 489 (1972).
10. Tassi, G. C., Mistretta, A. P., De Barbieri, A.: Purification of Australia antigen (hepatitis-associated antigen, H.A.A.) and preparation of the specific antiserum. *Boll. Ist. Sieroter. Milan. 49*, 337 (1970).
11. Halmosdi, G., Perkedi, J., Valló, D.: Hepatitis B antigen (Australia antigen) tisztitásának egyszerűsitett módszere. *Kísérl. Orvostud. 26*, 285 (1974).
12. Bundschuh, G.: Präparative Trennung von Proteingemischen durch Sephadex gelfiltration bei gleichzeitiger Einwirkung von Gleichstrom (Retardationsfiltration). *J. Chromatogr. 56*, 241 (1971).

13. Halmosdi, G., Perkedi, J., Valló, D.: Módositott immunelectroosmophoresis eljárás a HAA kimutatás biztonságának fokozására. *Kíserl. Orvostud. 25*, 457 (1973).
14. Halmosdi, G., Perkedi, J., Valló, D.: Serumhepatitis átvitel megakadályozására irányuló vizsgálatok véradóknál. *Transfusio 7*, 46 (1973).
15. Madalinski, K., Brozosko, W. J., Budkowska, A., Mikulska, B.: Quantitative determination of hepatitis B antigen by means of radial immunodiffusion. *Clin. exp. Immunol. 15*, 549 (1973).

Correspondence: Dr. D. Valló, Postgraduate School of Medicine, Blood Centre, Szabolcs u.35, 1135 Budapest, Hungary

Haematologia 9 (3–4), pp. 257–260 (1975)

Blastic Crisis in Previously Clinically Silent Chronic Myelogenous Leukemia

U. MINTZ, S. BAR-MEIR, M. SHAKLAI, J. PINKHAS, A. DE VRIES

Department of Internal Medicine D, Beilinson Medical Center,
Tel-Aviv University Medical School, Petah Tiqva, Israel

(Received November 12, 1974)

A patient is described in whom CML first presented as blastic crisis. The diagnosis of CML was based upon the findings of Ph^1 chromosome in the bone marrow, basophilia in the peripheral blood, absence of NAP activity in the leukocytes, elevated serum vitamin B_{12} and an enlarged firm spleen. CML with blastic crisis as its first expression is relatively rare, as compared to CML in which blastic crisis appears as a phase of prolonged clinically manifest disease.

The Philadelphia (Ph^1) chromosome is found mainly in patients with chronic myelogenous leukemia (CML) [9] but, more rarely, it may be present also in patients with other myeloproliferative disorders such as myeloid metaplasia [3], thrombocythemia [2], polycythemia vera [6], and eosinophilic leukemia [8]. In recent years the Ph^1 chromosome has also been described in 14 patients with acute myelogenous leukemia (AML) [1, 4–8, 10]. Because of the relative rarity of the Ph^1 chromosome in AML, it has been suggested [1] that such patients have in fact CML which had been clinically silent prior to the blastic crisis, the appearance of which mimicked AML. We wish to report on an additional patient with a similar course.

Case report

A 32-year-old Israeli-born taxi driver was referred to our department with the diagnosis of AML. Two weeks prior to admission he started to complain of bone pains and a white blood cell count of 180,000 with 20% blasts was found.

Physical examination showed the patient in a fair general condition with a normal body temperature and blood pressure. Generalized lymphadenopathy was found, the edge of the liver was palpated and a firm and non-tender spleen was felt 3 cm below the costal margin. The eyegrounds showed engorged veins and numerous whitish infiltrates.

Laboratory data were as follows. The urine was normal, the hemoglobin 12.8 g per 100 ml, hematocrit 35%, white blood cell count 200,000 with 20% blasts, 10% promyelocytes, 8% metamyelocytes, 6% myelocytes, 22% band forms, 27% neutrophil polymorphonuclears, 5% basophils, 1% monocytes and

1% lymphocytes. The platelet count was 150,000. No neutrophil alkaline phosphatase (NAP) activity was detected. A bone marrow aspiration biopsy disclosed marked hyperplasia of the white blood cell series with 78% blasts; karyotype examination revealed the presence of Ph^1 chromosome (Fig. 1). The serum vitamin B_{12} was 2184 pg/ml. There were no other abnormal findings in the blood, specifically there was no evidence of hemolysis, coagulation disturbances or paraproteins.

Treatment was given with intravenous rubidomycin, 40 to 80 mg per day, a total of 600 mg in 13 days; and allopurinol, 300 mg per day. Within 2 weeks the bone pains, the lymphadenopathy and the retinal changes disappeared, and the spleen and liver became unpalpable; the white blood cell count dropped to 6000 with 2% blasts. After an additional 2 weeks the lymphadenopathy and hepatosplenomegaly reappeared and rubidomycin was reinstituted but had to be dis-

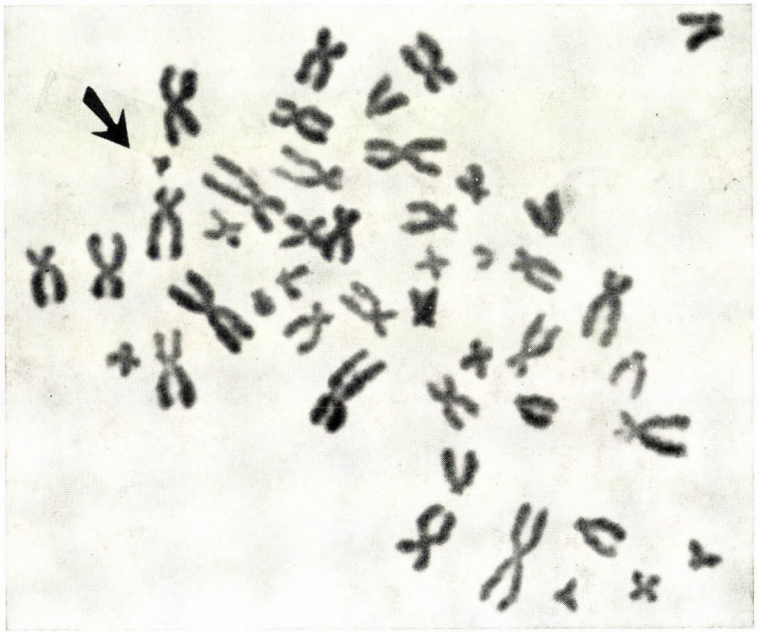


Fig. 1. Philadelphia chromosome (arrow)

continued because of an ischemic pattern in the electrocardiogram. Instead, combined therapy with cytosine-arabinoside and steroids, and subsequently hydroxyurea and later 6-mercaptopurine were given, as well as transfusions of blood, white blood cells and platelets, antibiotics and allopurinol. However, the patient's condition worsened and he developed hypoproteinemia and edema, muscle wasting, melena and hematemesis, and subsequently oral and pulmonary moniliasis with the appearance of a "fungus ball" in the chest X-ray (Fig. 2). Further treat-

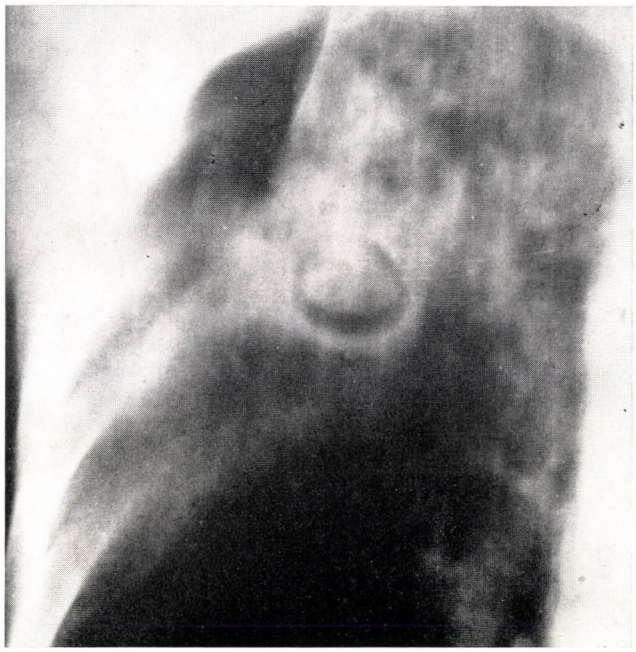


Fig. 2. Fungus ball in chest X-ray tomography

ment with amphotericin and fluorocytosine was of no avail and the patient died of respiratory failure, 5 months after the diagnosis of leukemia had been established. Postmortem examination revealed widespread leukemic infiltrations and moniliasis, with severe involvement of the lungs.

Discussion

Two concepts have been forwarded concerning this specific form of leukemia which is "acute" in its clinical and laboratory manifestations but exhibits the Ph^1 chromosome. Bornstein et al. [1] suppose that such patients present an abortive form of CML which is clinically silent until the appearance of a blastic crisis. In support of the pre-existence of CML as the background of the acute picture, these authors as well as Hammouda [4] mention the presence of Ph^1 chromosome, peripheral blood basophilia and splenomegaly. In contrast, Hossfeld et al. [5] are of the opinion that these patients have "true" AML.

In the patient described here evidence of CML was found in the presence of Ph^1 chromosome, splenomegaly, basophilia, elevated serum vitamin B_{12} level and absence of NAP activity in the granulocytes. On the other hand, the presence of a high percentage of blasts in his peripheral blood and bone marrow and the stormy clinical course seemed characteristic of AML. The combination of these

features in the patient led us to classify him with that relatively rare form of CML in which a blastic crisis is the presenting manifestation. The diagnosis of a blastic crisis in the background of preexisting CML has prognostic importance, in that the disease in such patients is more resistant to chemotherapy than true AML [1].

References

1. Bornstein, R. S., Nesbit, M., Kennedy, B. J.: Chronic myelogenous leukemia presenting in blastic crisis. *Cancer 30*, 939 (1972).
2. Dougan, L., Woodliff, H. J., Questi, P.: Cytogenic studies in megakaryocytic myelosis. *Med. J. Aust. 1*, 62 (1967).
3. Forrester, R. H., Louro, J. M.: Philadelphia chromosome abnormality in agnogenic myeloid metaplasia. *Ann. intern. Med. 64*, 622 (1966).
4. Hammouda, F.: Chromosome abnormality in acute leukemia. *Lancet 2*, 410 (1963).
5. Hossfeld, K. K., Han, T., Holdsworth, R. N., Sandberg, A. A.: Chromosomes and causation of human cancer and leukemia. VII. The significance of the Ph^1 chromosome in conditions other than C.M.L. *Cancer 27*, 186 (1971).
6. Khan, M. H., Martin, H.: Myeloblastenleukemie mit Philadelphia-Chromosom. *Klin. Wschr. 45*, 821 (1967).
7. Kiossoglou, K. A., Mitus, W. J., Dameshek, W.: Chromosomal aberrations in acute leukemia. *Blood 26*, 610 (1965).
8. Mastrangelo, R., Zuelzer, W. N., Thompson, R. I.: The significance of the Ph^1 chromosome in acute myeloblastic leukemia: serial cytogenetic studies in a critical case. *Pediatrics 40*, 834 (1967).
9. Nowell, P. C., Hungerford, D. A.: Chromosome studies on normal and leukemic leukocytes. *J. nat. Cancer Inst. 25*, 85 (1960).
10. Tijo, J. H., Carbone, P. P., Whang, J., Frei, E.: The Philadelphia chromosome and chronic myelogenous leukemia. *J. nat. Cancer Inst. 36*, 567 (1966).

Correspondence: Prof. A. de Vries, Beilinson Hospital, Kupat-Holim, Health Insurance Institution, Petah Tiqva, Israel

Haematologia 9 (3—4), pp. 261—278 (1975)

A Case of IgD-lambda Myeloma

J. JÁKÓ, SZ. VIRÁGH, MARIANNA BOGA, G. BROOSER, GY. DÓBIÁS, J. DOMÁN, SZ. OTTÓ, Z. RISKÓ, P. SZEMERE

First and Fourth Departments of Medicine, Departments of Pathological Anatomy, Ophthalmology, Experimental Clinical Laboratory Investigation, Postgraduate Medical School and National Institute of Oncology, Budapest, Hungary

(Received July 5, 1974)

A case of IgD myeloma is presented. The severe damage of both kidneys resulted in uraemia, and death. Fluorescein angiography failed to reveal a typical paraproteinaemic fundus. The elevated serum IgD level decreased from 1000 mg to 400 mg per 100 ml during cytostatic therapy. The effect of the antineoplastic drugs on the plasmocytes was demonstrated by microphotograms. The caryograms revealed multiple changes.

The existence of type D immunoglobulin (IgD) has been revealed in a case of myeloma [43, 44].

This Ig can be detected in 17% of the normal population; it does not appear below the age of three months. Hyper IgD-aemia is extremely rare [39]; the normal concentration of this type of immunoglobulin is about 3 mg in 100 ml of serum. Its electrophoretic mobility as well as the location of the precipitin line are very similar to IgA. The sedimentation constant was found to be around 7,4 S [46], the molecular weight approximately 180,000. The IgD is synthetized in the plasma cells and can be broken down enzymatically, like IgG [49, 51, 53] cells of the whole organism [11, 12, 45]. These cells, however, do not differ from cells producing other immunoglobulins [36] and 70% of them is located in the intravasal space. The half survival time (T 1/2) was estimated at the catabolic rate at 10 to 12% [42]. Though its antibody function, as its antinuclear-antibody property [26, 27, 55, 61], anti-thyroid [27], anti-diphthery-toxoid, anti-bovine-gammaglobulin [20], anti-penicillin [18], and anti-insulin [14] properties have been proved, its real role has not yet been established. There are no data of its skin sensitizing and complement binding effects [16, 21, 22, 35, 54]. It is assumed that IgD is bound to the membrane of the circulating lymphocytes [8], moreover, in a high percentage to the lymphocytes located in the umbilicus [48]. More recently this Ig has been supposed to be a receptor of lymphocytes [47]. In cases of nephropathy, the IgD binds to the glomerular membrane, but its pathogenic role is not likely [58].

Approximately one and a half per cent of the myeloma cases are IgD monoclonal gammopathies [23]; most of them proved to be of the lambda type. The distribution according to sex and age was similar as in other myelomas. The case at issue was also one of IgD lambda. Table 1 shows the data in the available literature.

Table 1

Type	No. of cases	Male	Female	Sex unknown	Age, years	References
Lambda	77	35	25	17	40—86	2, 5, 6, 7, 9, 10, 15, 16, 17, 24, 29, 30, 31, 32, 34, 37, 38, 40, 43, 52, 56, 59, 60, 62
Kappa	12	9	1	2	40—73	13, 16, 17, 28, 34, 54, 57, 63
Not identified	8	1	2	5	47—81	1, 3, 4, 16, 25, 33, 34
Total	97	45	28	24		

Case report

J. J., a 65-year-old female patient was admitted to the Fourth Department of Medicine on 2nd October, 1972. At 8 years of age, adenotomy, and at 14 years tonsillectomy and then appendectomy had been performed on the patient. Since her childhood she had been known to have "kidney disease"; in the last ten years she had been under continuous urological control and had treatment because of kidney stones and recurrent pyelonephritis, and local silver nitrate therapy for ulcerous cystitis for one year. In the last years her blood pressure had been elevated. Three or four months prior to admission she had lost weight, and became weak and fell faint. She had had also polydipsia as well as polyuria. A few weeks before admission she had suffered a rib fracture on the left side, caused by pressure, and felt pains in the bones. She was admitted with anaemia and a sedimentation rate of 120 mm/hr. For further findings see Tables 2, 3 and 4.

Table 2

Urine	
Specific gravity	1005—1009
Protein	positive
Bence—Jones protein	positive
Esbach	2.1%
Pus	traces
Sugar	negative
Sediment	leukocytes, hyalin casts
Culture	E. coli, Proteus, Pseudomonas aeruginosa
Endogenous creatinine clearance	22 ml

Table 3

Date	Serum creatinine, g/100 ml	BUN (normal value), 20 mg/100 ml	Total protein, g/100 ml	ESR, mm/hr	IgD in serum, mg/100 ml	Urinary culture
2. 10. 1972	2.5	60	7.0	85		
19. 10. 1972	—	—	6.9	50		E. coli, sign. bacteriuria*
30. 10. 1972	—	—	—	65	1000	E. coli, Proteus, Pseudomonas aeruginosa
12. 1. 1973	1.4	40	6.9	50		
24. 1. 1973	—	—	—	—		
12. 2. 1973	—	—	—	52	250	
20. 3. 1973	1.5	32	6.7	30		E. coli
28. 5. 1973	—	49	—	—	approx. 100	E. coli
19. 6. 1973	4.6	95	6.4	50		Sterile

* IgD concentration was detected by Hyland Immunoplate.

Renography performed with ^{131}I-Na-iodohippurate revealed severe defects in both kidneys (Fig. 1).

Histological examinations by light and electron microscopy proved the existence of serious parenchymal lesions in both kidneys. Fluorescein angiography

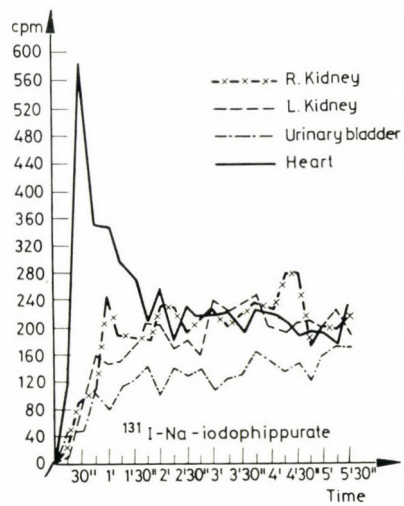


Fig. 1 Renography performed with ^{131}I-Na-iodohippurate

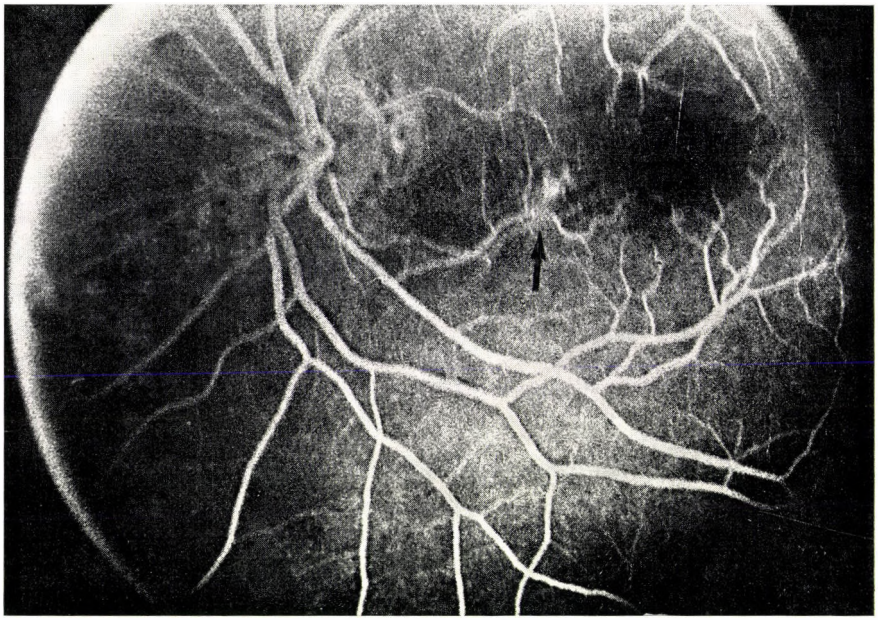


Fig. 2. The capillaries around the macula are partly obstructed. Leakage of dye at border of macular region (marked with arrow)

of the ophthalmoscopically negative eyes did not show a normal picture, but no typical paraproteinaemic fundus was found (Fig. 2).

Immunoelectrophoresis revealed a discrete plus precipitin line (↓) with no IgM and IgA precipitin bonds and the typical picture of Ig-D-lambda monoclonal gammopathy (Fig. 3).

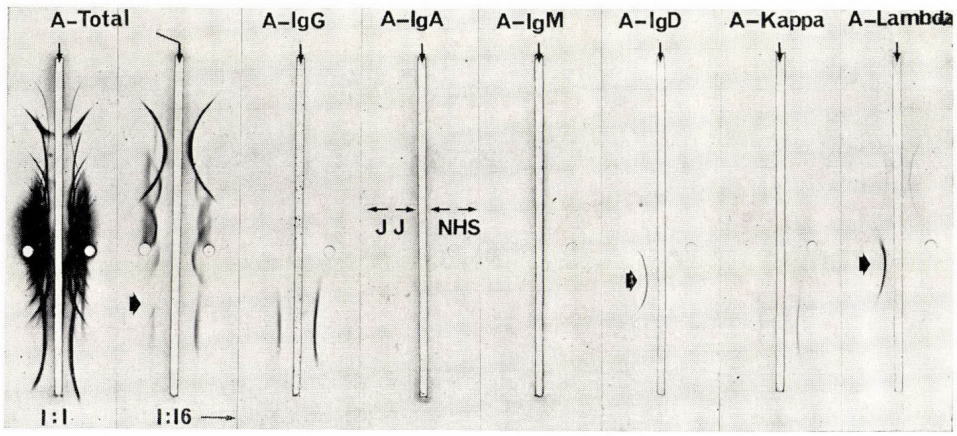


Fig. 3. Analytical examination of Ig-D-lambda monoclonal gammopathy

Table 4

Colloid lability test (thymol turbidity, etc.)	negative
Cryoglobulin and cryofibrinogen	negative
Sia test	negative
Latex test	negative
Paper electrophoresis:	
albumin	60%
alpha$_1$ globulin	3.3%
alpha$_2$ globulin	6.7%
beta globulin	10.0%
gamma globulin	20.0%
Agarose electrophoresis	visible M gradient

Table 5

Immunogram	Patient			
	Normal value	28. 10. 1972	12. 1. 1973	16. 4. 1973
Flexner 1b	24	2	2	2
Flexner 2a	14	4	2	2
Flexner 3	34	4	4	2
Sonne	28	4	4	4
Coli 26	25	ø	2	2
Coli 55	4	2	2	2
Coli 86	12	4	8	2
Coli 111	6	2	ø	2
Sheep R.B.C.	2	ø	ø	ø
Rabbit R.B.C.	105	32	—	—
AST	230 AE/ml	240 AE/ml	280 AE/ml	140 AE/ml
Staph. alpha-antitoxin	1.2 AE/ml	0.12 AE/ml	0.24 AE/ml	0.24 AE/ml
Anti A	14	16	8	4
Anti B	24	2	2	ø

Table 6

Date	Haemoglobin, g/100 ml	Leukocyte count	Platelet count
2. 10. 1972. Before cyclophosphamide therapy	7.8	6 700	—
17. 10. 1972. End of cyclophosphamide therapy	7.8	5 100	58 000
13. 10. 1972. Beginning of melphalan therapy	8.8	1 700	63 000
11. 11. 1972. End of melphalan therapy	7.8	4 500	80 000
6. 2. 1973. Discharge	8.5	5 900	—
15. 3. 1973. Readmission	8.9	4 900	150 000
21. 6. 1973. Death	8.9	2 000	46 000

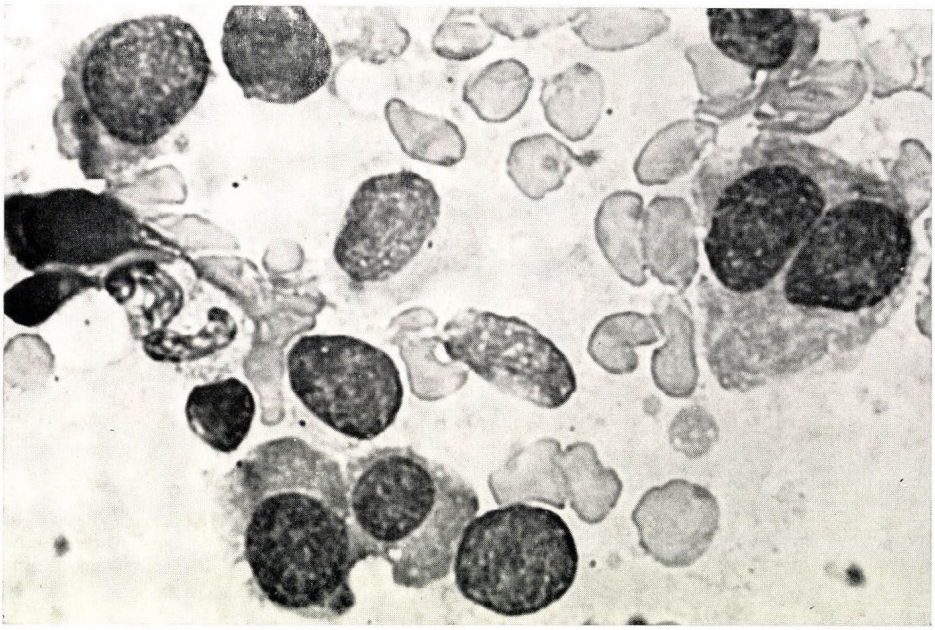


Fig. 4. Microphotogram of bone marrow

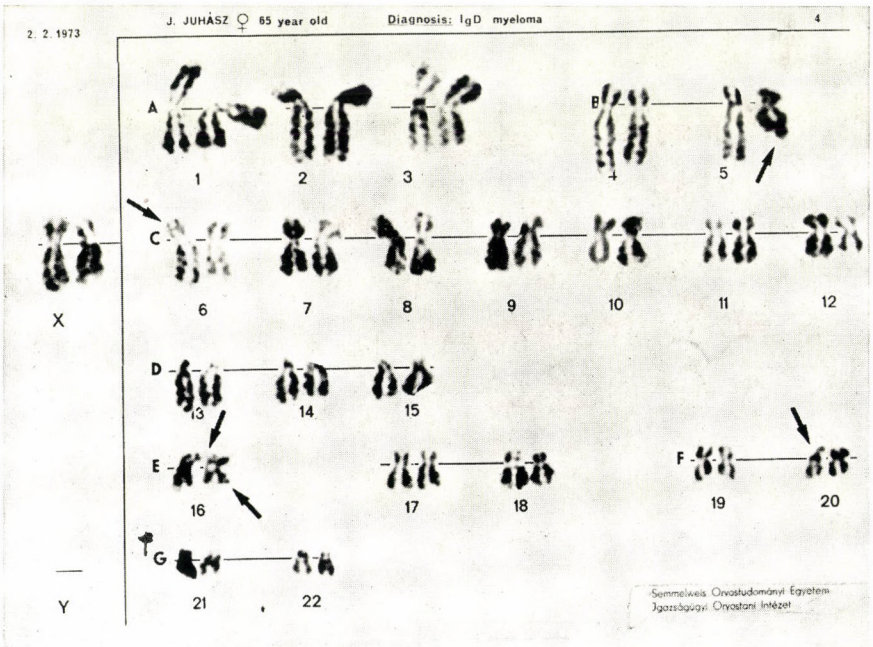
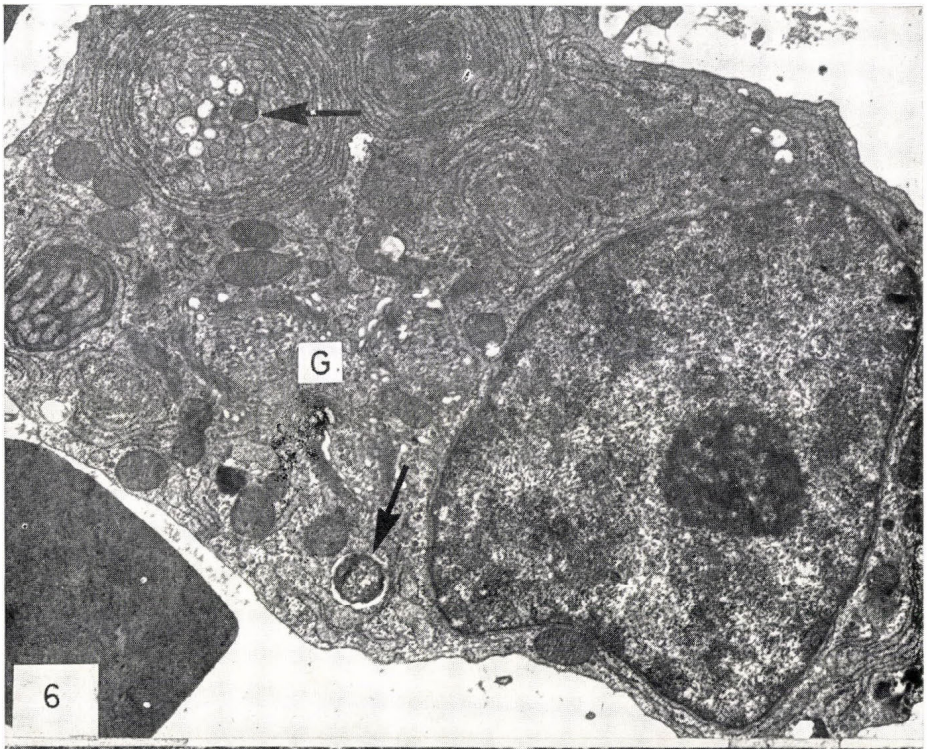
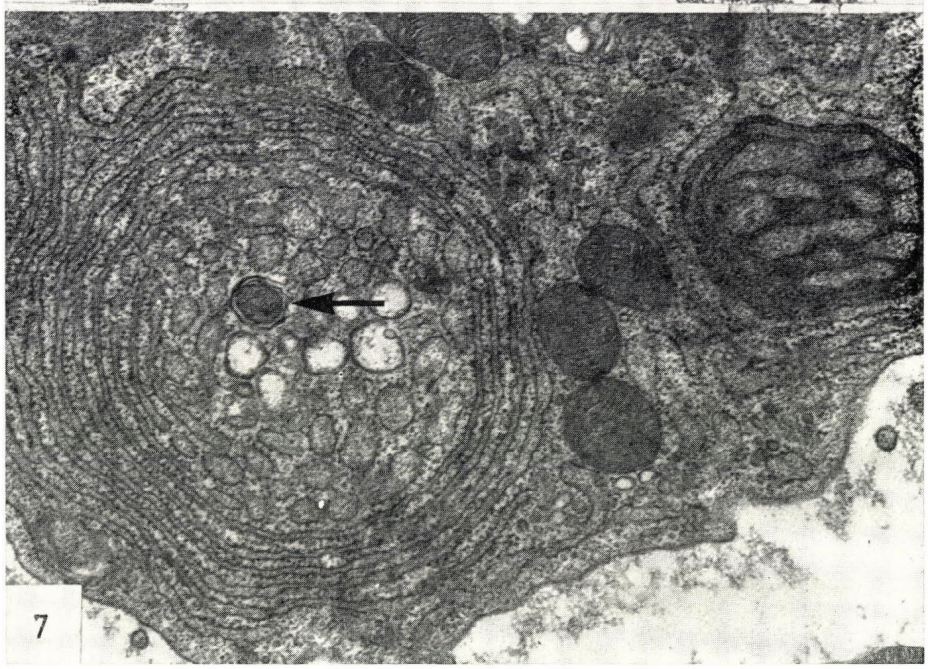


Fig. 5. The caryogram showed q- on the B_5, chromatoid bridge on one G_6, a "minute" formation resembling a ring on E_{16}. On one member of F_{20}, a secondary submedian metacentric incurvation was observed. Deletion and chromosomes without centromere were also found. In general, the cells in the culture were in poor condition; the chromosomes were despiraled





See legends on page 274

The patient's immunogram revealed a decreased resistance to bacteria (secondary antibody deficiency syndrome, Table 5).

The antibody character of the pathological IgD could not be proved by the antigens applied. Some haematological data are shown in Table 6.

X-ray findings

Skull: Erosions of bean or pea size on the left side of occipital squama.

Ribs: Erosions on dorsal arch of VIIth and VIIIth osteoporotic ribs on the left side. Fracture of VIIIth rib in posterior axillary line.

Spinal column: Erosions of bean or pea size on the lower dorsal vertebrae.

First bone marrow aspiration: 4th October 1972 (Fig. 4).

Caryograms: 4th November 1972, and 2nd February 1973 (Fig. 5).

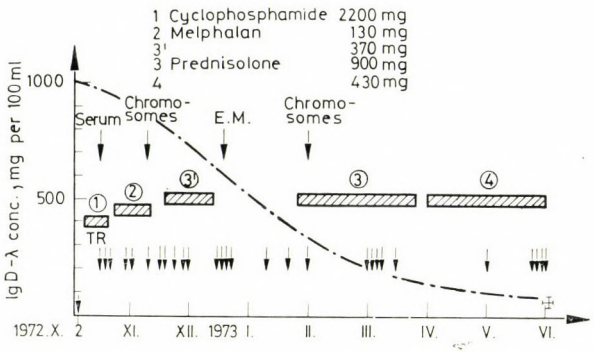
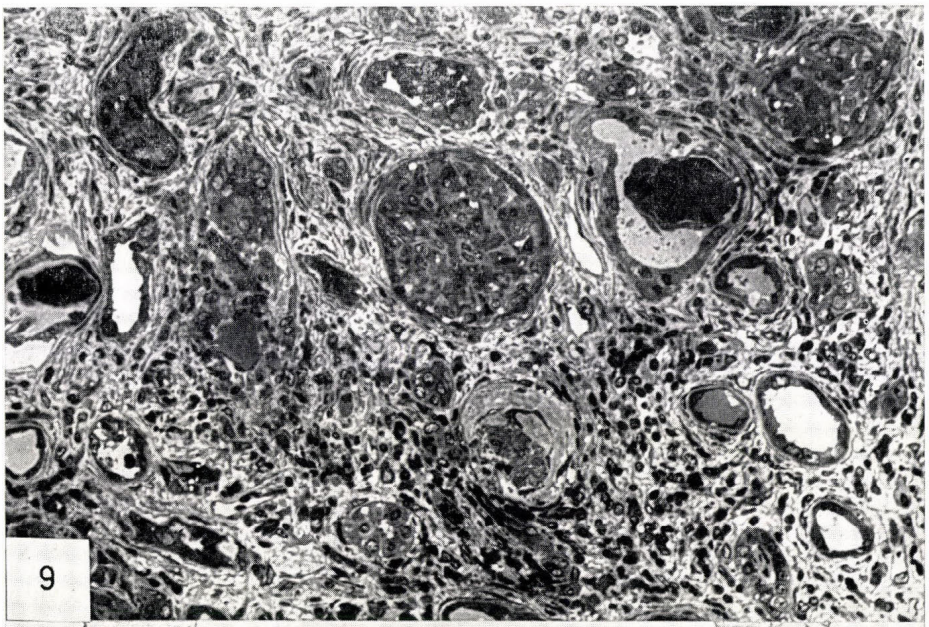


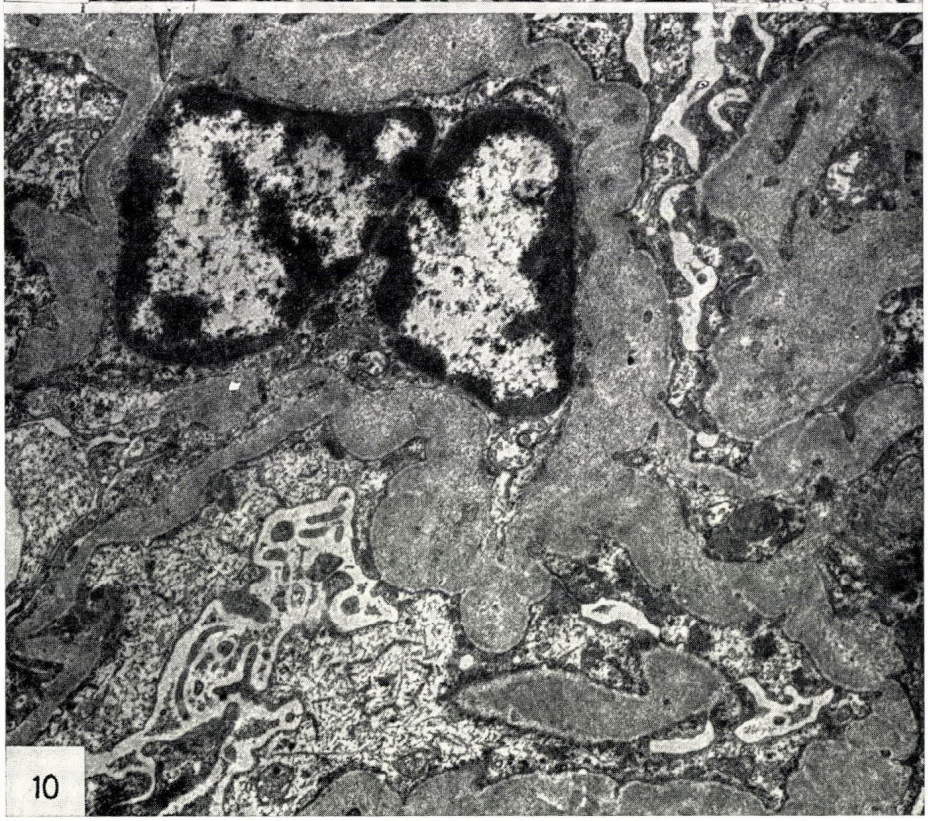
Fig. 8

Electron microscopic examination of bone marrow was performed on 12th December 1972. In the sternal marrow, many plasma cells were found. Their majority was well differentiated with an elaborated rough-surfaced endoplasmic reticulum, and a highly developed Golgi system. In many plasma cells the ergastoplasmic lamellae exhibited the focal concentric arrangement. In the focus of these membrane whorles the tubules were often distended, the density of their content diminished and the membrane surface was totally or partially deprived of ribosomes. Autophagic vacuoles and other lysosome-like bodies were frequent in the centre of the membrane whorles, and also in other parts of the cytoplasm. At some places the cytoplasmic ground substance was condensed inside the membrane whorles, and the rough-surfaced tubules were distended (Figs 6 and 7). Such structures showed a tendency toward the development of autophagic vacuoles.

In the course of therapy, the greatest problem was to influence the symptoms and the consequences of the renal failure. Obviously, the second most important task was to control the myeloma as the main cause of the disease (Fig. 8).

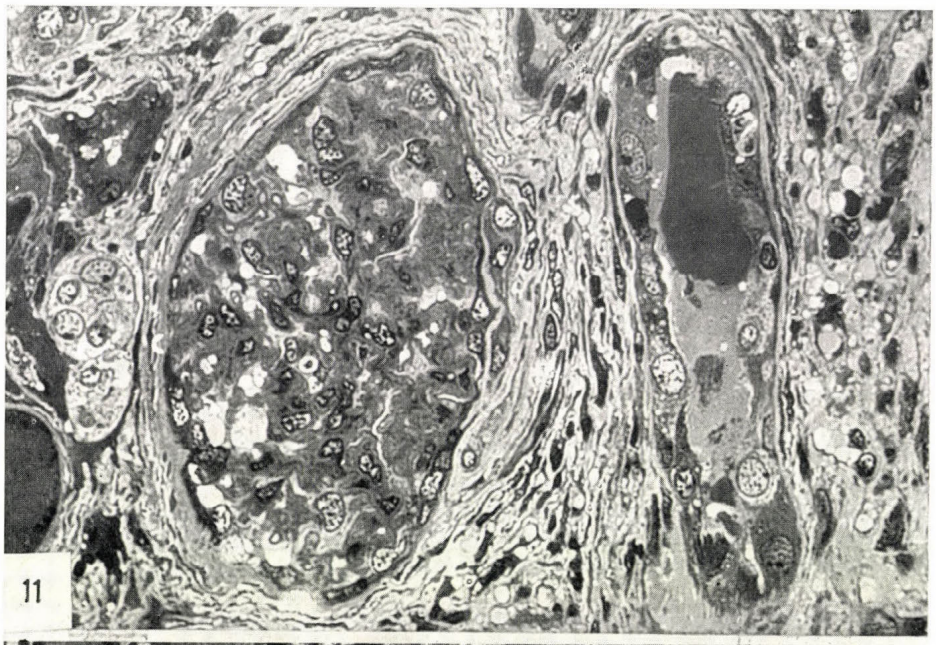


9

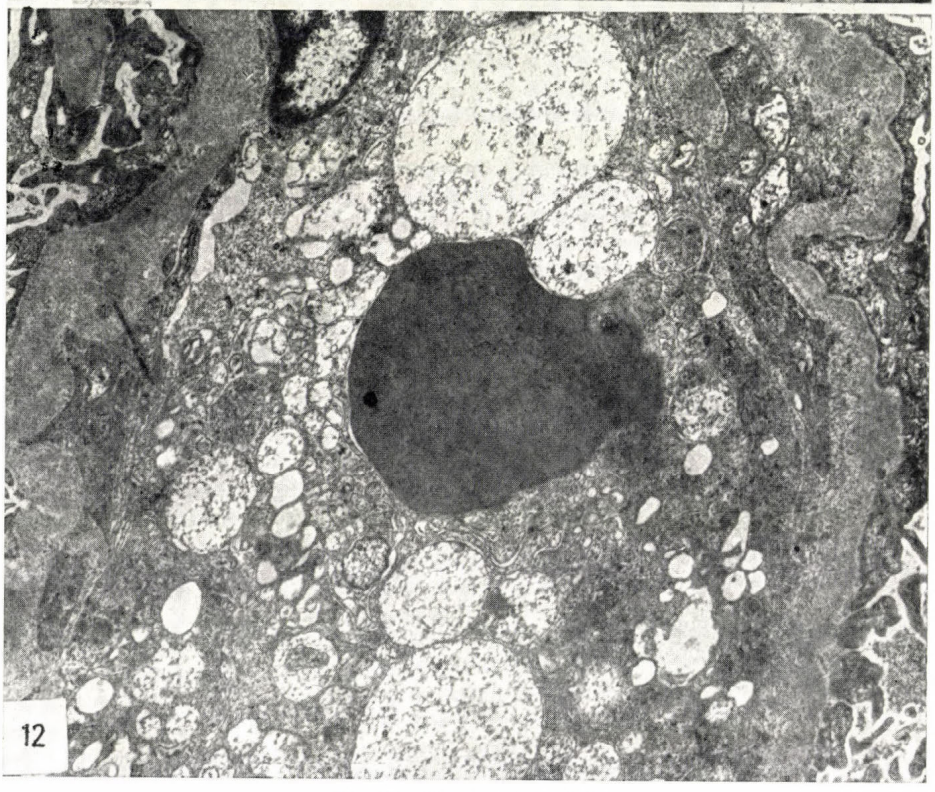


10

See legends on page 274

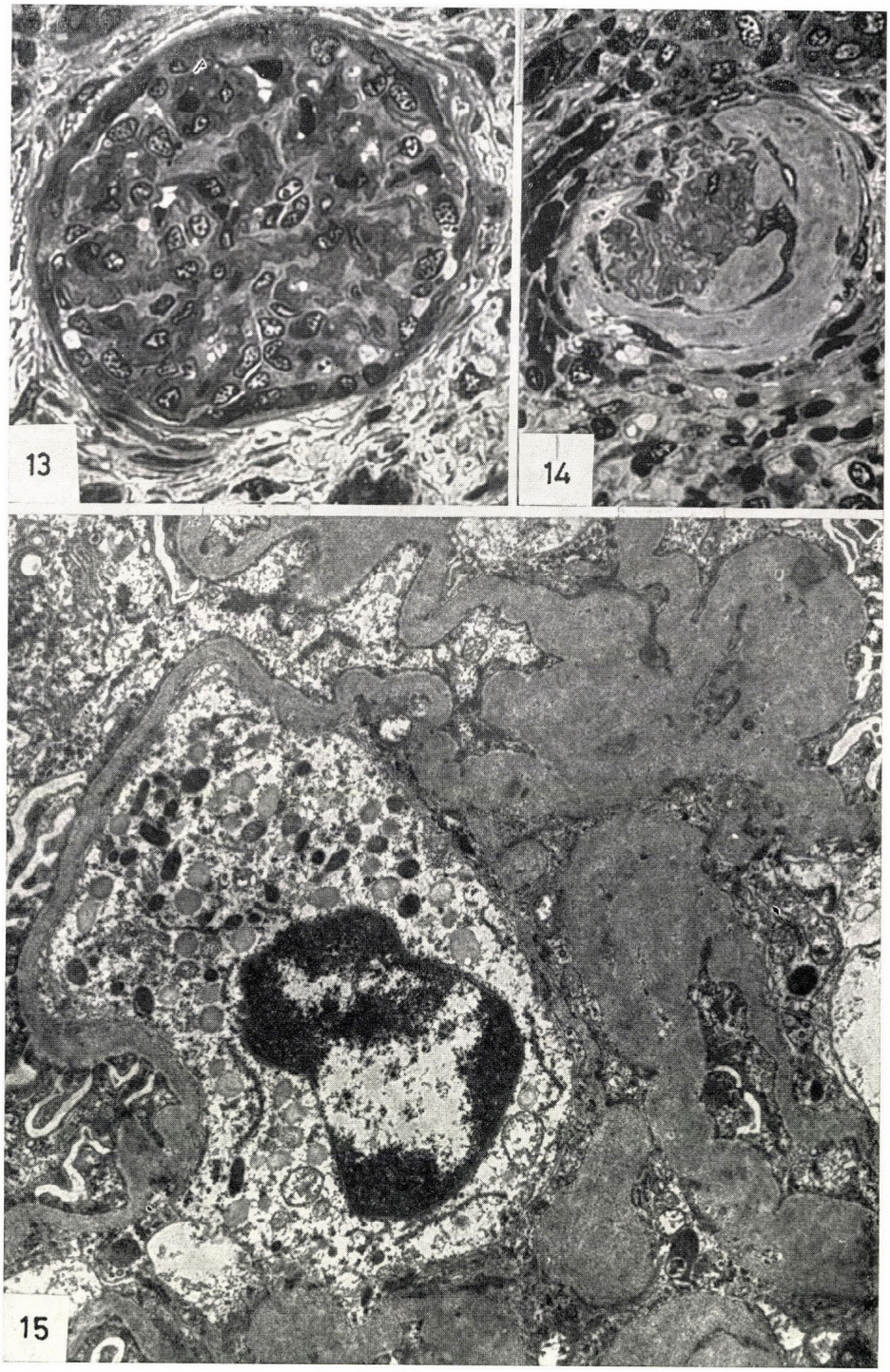


11

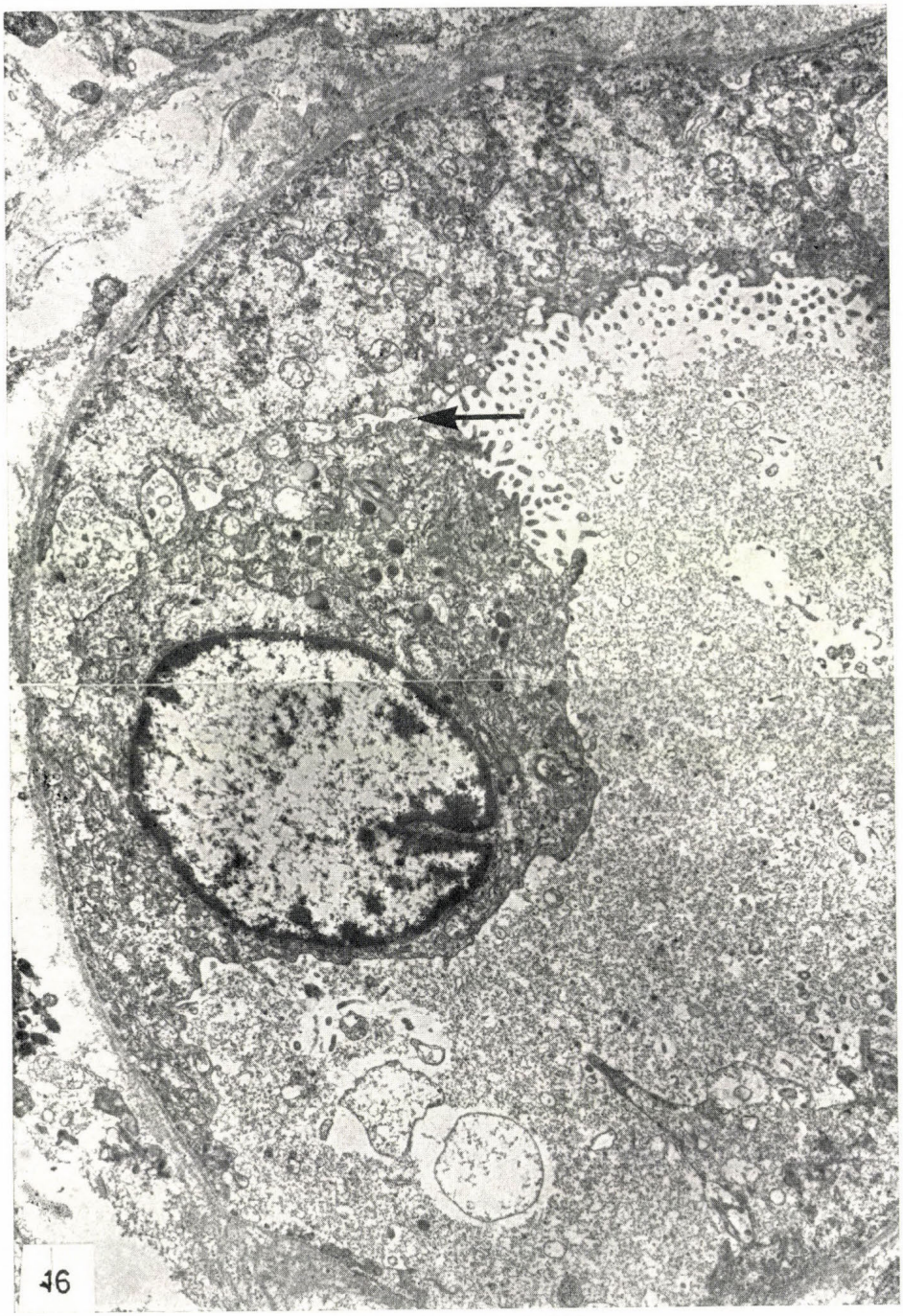


12

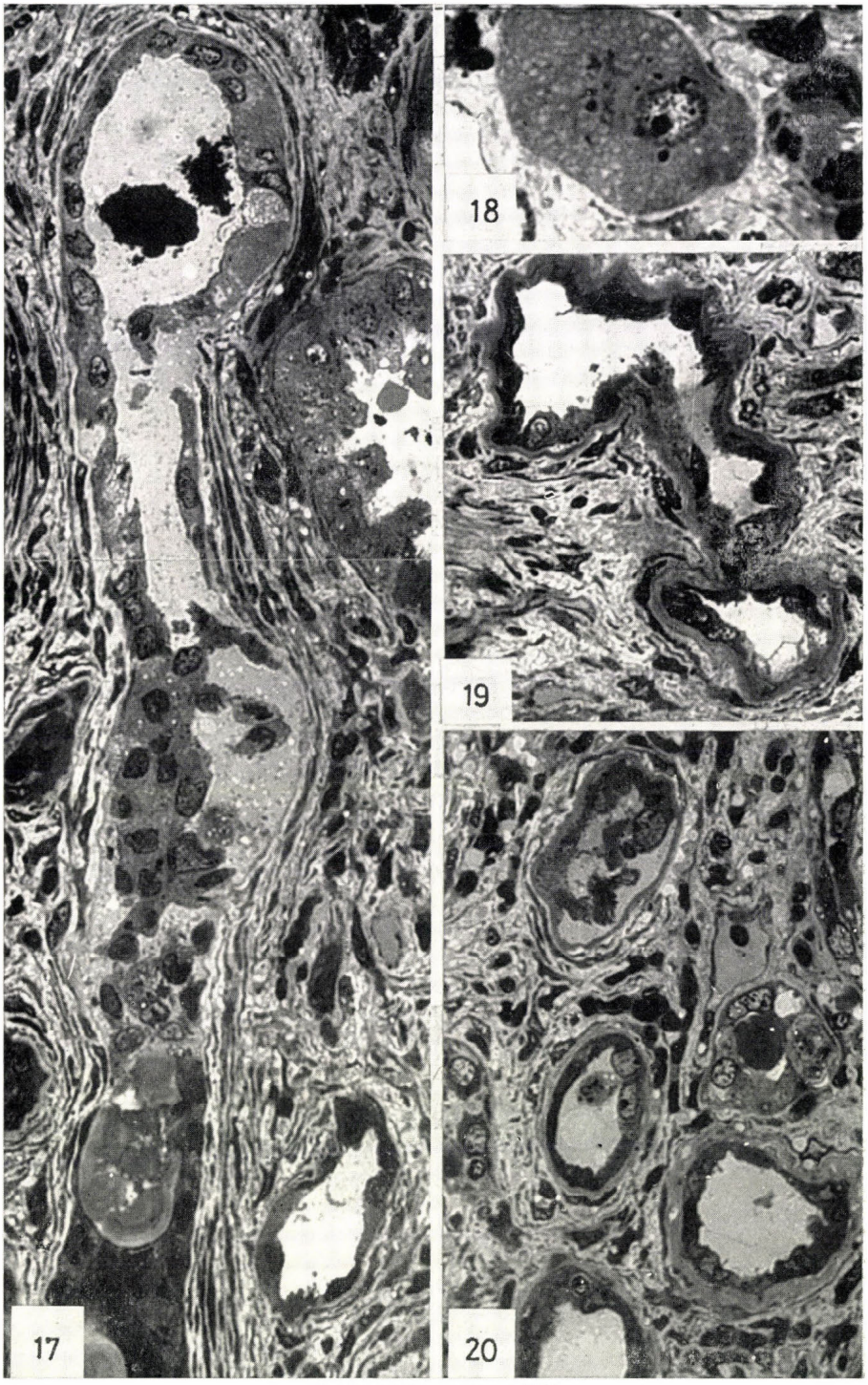
See legends on page 274



See legends on page 274



See legends on page 274



See legends on page 274

Figs 6 and 7. Electron micrographs of a sternal bone marrow plasma cell (Fig. 7 is a detail of Fig. 6). The eccentric nucleus contains a large nucleolus and clumps of peripheral heterochromatin. Most tubules of the well-developed rough-surfaced endoplasmic reticulum demonstrate a focal concentric arrangement. In the centre of the concentric lamellae the tubules are distended, partially degranulated, and some of them deprived of the semiopaque fine granular content. In other membrane whorls the cytoplasmic ground substance is condensed. Two autophagic vacuoles (arrows) are seen in the cytoplasm. The Golgi apparatus (G) is highly developed

Fig. 9. Light micrograph of renal cortex showing chronic interstitial inflammation, glomerular changes and atrophy of tubules, containing characteristic casts. Two glomeruli in the centre are seen in Figs 13 and 14 under high-power toluidin blue stained semi-thin section
Fig. 10. Thickened basement membrane of glomerular capillary. Flattened and fused foot processes of podocytes, with filaments and microtubules in their cytoplasm

Fig. 11. Marked thickening of capsular basement membrane. Hydropic swelling of some cells. Periglomerular fibrosis. The obliquely cut tubule contains a large cast
Fig. 12. Swollen glomerular cell with many large vacuoles containing fine floccular material

Fig. 13. The visceral and parietal layers of the glomerulus are fused. Basement membrane material is present in the tuft
Fig. 14. Partially scarred glomerulus
Fig. 15. Mesangial thickening and many lysosome-like bodies in the cytoplasm of a mesangial cell. Large irregular basement membrane

Fig. 16. Lumen and intercellular space (arrow) of the tubule seem to contain a similar flocculant material. Epithelial cell with imbibed cytoplasm. There is no epithelial lining cell at the lower part of the tubule. Tubular lumen and interstitial space are separated by peritubular basement membrane

Fig. 17. Plugging of a longitudinally cut tubule by precipitated protein and necrosed debris (bottom). The tubular epithelial cells are detached at some places (on the right) from the peritubular basement membrane. Vacuolated tubular cells (top right)
Fig. 18. Interstitial macrophage in vicinity of damaged renal tubules
Fig. 19. Chronic tubular atrophy with flattened cell and thickened peritubular basement membrane
Fig. 20. Different degrees of tubular atrophy with epithelial cell desquamation and basement membrane thickening

---

The patient received cytostatics, antibiotics and anabolic steroids regularly and simultaneously. Her condition improved slowly and gradually, and after approximately three months of treatment she became mobile. Another month later she was discharged and was followed-up regularly. Still later her condition deteriorated, readmission became necessary and she died of uraemia.

Postmortem examination

Necropsy was performed six hours after death. In accordance with the clinical data, a soft, gelatinous, greyish-red tumour tissue was found scattered over the whole skeletal system. Cut surfaces of the sternum, skull, femur, ilium,

ribs and spine revealed multifocal infiltration of the bone marrow and of the spongy substance of the bones. Diffuse osteoporosis was observed. Sporadically the bone marrow was completely replaced by solid tumour. Microscopically, broad sheets of closely packed cells were present in the bone marrow. The tumour cells were similar to normal plasma cells but with more abundant cytoplasm and more eccentric nuclei. Some cells contained two nuclei.

The liver (weight, 1130 g) was smaller than normal and its surfaces showed signs of chronic congestion. Microscopically, the architecture was preserved. The cell content of the sinusoids increased markedly, at some places they were slightly infiltrated by tumorous plasma cells.

The lymph nodes were normal in size.

The tertiary pulmonary arteries of the right lung were occluded by emboli originating from a parietal thrombus in the left femoral vein.

Electron microscopic appearance of the kidney

In the kidney, chronic interstitial inflammation with marked nephron injury was seen. The glomeruli demonstrated different degrees of progressive scarring, and the tubules signs of chronic atrophy (Fig. 9). Most of the convoluted tubules could not be recognized.

In the glomeruli, many endothelial cells showed hydropic swelling. Large vacuoles with floccular content were seen in the cytoplasm (Figs 11 and 12). The endothelial cells showed few fenestrae. The basement membrane of the glomerular capillaries was thickened. Mesangial thickenings were frequent and the mesangial cells contained lysosome-like electron dense bodies (Figs 13 and 15). The filtration slits between the foot processes of the podocytes were narrowed and often absent. The cytoplasm of the prodocytes contained many microfilaments and microtubules (Fig. 10). The basement membrane of Bowman's capsule was considerably thickened (Fig. 11) and in many glomeruli the capsular epithelial cells were also thicker (Fig. 13). In the partially scarred glomeruli the tuft was embedded in a basement membrane-like material (Fig. 14).

Most of the tubules exhibited signs of chronic atrophy. The epithelial cells were flattened, shrunken and/or vacuolated. Typical brush borders and the basal infoldings of the cells could not be found although some microvilli were present at places. Many tubular epithelial cells were imbibed with the protein-rich material found in the lumen of the tubules. Such material filled the distended intercellular spaces, too. Cell ruptures and cell desquamation were frequent in the tubules (Figs 16 and 17). Large macrophages showing the foreign body reaction of the interstitium were common (Fig. 18). Plugging of the tubules by precipitated protein and by necrosed debris was frequent. The peritubular basement membrane demonstrated marked thickening around the atrophic and distended tubules (Figs 19 and 20).

Discussion

The case seemed interesting in view of the rarity of IgD myeloma and also as the course of the disease supported von Baehr's theory of the kidney damaging effect of light chains [5]. The powerful effect of cytostatic therapy on the pathological immunoglobulin titre also deserves attention. The question arises why the plasmocytes, known to be resistant to therapy [19, 41], were so sensitive in this case. (Their sensitivity was shown by the decrease of the IgD titre as well as by the changed morphology revealed by electron microscopy.) Is it that the forerunners of the IgD producing plasmocytes – one group of the lymphocyte population – were originally sensitive to these drugs? The caryograms seemed to support this theory, since these alterations differ from the changes usually described in monoclonal gammopathies [50].

*

We are indebted to Dr. P. Vittay for the radiorenogram.

References

1. André, R.: Purpura de type amyloide révélateur d'une immunglobuline IgD. *Presse méd. 79*, 1021 (1971).
2. Bachmann, R.: IgD myeloma. *Nobel Symp. 3*, 605 (1967).
3. Backhausz, R.: Current problems of immunglobulin research. *Ann. Immunol. hung. 11*, 123 (1968).
4. Backhausz, R.: Az immunglobulinkutatás aktuális kérdései. *Orv. Hetil. 109*, 2241 (1968).
5. Baehr, R. von: Bericht über zwei Fälle von IgD-Plasmocytom. *Inn. Med. 9*, 406 (1972).
6. Ben-Bassat, I., Frand, U. I., Iserki, C., Ramot, B.: Plasma cell leukemia with IgD paraprotein. *Arch. intern. Med. 121*, 361 (1968).
7. Bert, G., Fontana, F.: IgD myeloma. *Brit. med. J. 2*, 117 (1968).
8. Boxel, J. A. van, Paul, W. E., Terry, W. D., Green, I.: IgD-bearing human lymphocytes. *J. Immunol. 109*, 648 (1972).
9. Braun, H. J., Aly, F. W.: Die Diagnose des gamma D-Plasmozytoms. *Dtsch. med. Wschr. 94*, 114 (1969).
10. Burtin, P., Guilbert, B., Buffe, D.: Deux cas de myélome à immunglobuline D. *Bull. Cancer (Paris) 53*, 57 (1966).
11. Crabbé, P. A., Heremans, J. F.: Presence of large numbers of plasma cells containing IgD in the rectal mucosa of a patient with ulcerative colitis. *Acta clin. belg. 21*, 73 (1966).
12. Crabbé, P. A., Heremans, J. F.: Distribution in human nasopharyngeal tonsils of plasma cells containing different types of immunglobulin polypeptide chains. *Lab. Invest. 16*, 112 (1967).
13. Dammacco, F., Bonomo, L.: IgD myelomatosis. Report of a case. *Scand. J. Haemat. 5*, 161 (1968).
14. Devey, M., Senderson, C. J., Carter, D., Coombs, R. R. A.: IgD antibody to insulin. *Lancet 2*, 1280 (1970).
15. Dugue, M., Rousselet, F., Kahn, M. F., Girard, M. L.: Études biologiques sur 559 cas de paraproteinémies. *Clin. chim. Acta 33*, 75 (1971).
16. Fahey, L. J., Carbone, P. P., Rowe, D. S., Bachmann, R.: Plasma cell myeloma with D-myeloma protein (IgD myeloma). *Amer. J. Med. 45*, 373 (1968).
17. Fishkin, B. G., Glassy, F. J., Hattersley, P. G., Hirose, F. M., Spiegelberg, H. L.: IgD multiple myeloma: a report of five cases. *Amer. J. clin. Path. 53*, 209 (1970).

18. Gleich, G. J., Bieger, R. C., Stankievic, R.: Antigen combining activity associated with immunglobulin D. *Science 165*, 666 (1969).
19. Greul, W., Huland, H., Schäfer, H. J.: Zur Frage der Langzeittherapie des Plasmozytoms. *Dtsch. med. Wschr. 98*, 496 (1973).
20. Heiner, D. C., Saha, A., Rose, B.: Antigen binding activity and physico-chemical characteristics of IgD. *Fed. Proc. 28*, 766 (1966).
21. Henney, C. S., Welscher, H. D., Terry, W. D., Rowe, D. S.: Studies on human IgD. II. The lack of skin-sensitizing and complement fixing activities of IgD. *Immunochemistry 6*, 445 (1969).
22. Hiramatsu, S., Tsuyuguchi, I., Inai, S.: Lack of binding of complement by IgD. *Biken's J. 12*, 43 (1969).
23. Hobbs, J. R.: Immunochemical classes of myelomatosis. Including data from a therapeutic trial conducted by a Medical Research Council Working Party. *Brit. J. Haemat. 16*, 599 (1969).
24. Hobbs, J. R., Slot, G. M., Campbell, C. H., Clein, G. B., Scott, J. T., Crowther, D., Swan, H. T.: Six cases of gamma-D myelomatosis. *Lancet 2*, 614 (1966).
25. H. Sárfy, E., Backhausz, R.: A zinksulfat zavarossági fehérje próba jelentősége az immunopathiák felismerésében. *Rheum. Balneol. Allerg. (Budap.) 8*, 43 (1967).
26. Ishizaka, K., Ishizaka, T., Lee, E. H.: Physicochemical properties of reaginic antibody. II. Characteristic properties of reaginic antibody different from human A-isohemagglutinin and D-globulin. *J. Allergy 37*, 336 (1967).
27. Kantor, G. L., Van Herle, A. J., Barnett, E. V.: Autoantibodies of the IgD class. *Clin. exp. Immunol. 6*, 951 (1970).
28. Kindler, U., Pietrek, G., Hüning, G.: Gamma-D-Plasmozytom. *Dtsch. med. Wschr. 95*, 2275 (1970).
29. Klemm, D., Hischubothe, H., Heimpel, H., Kasemir, H. D.: Gamma-D-Paraproteinämie bei Plasmocytom. *Klin. Wschr. 45*, 590 (1967).
30. Laurell, C. B., Snigurowich, J.: The frequency of Kappa and Lambda Chains in pathologic serum gamma-G, gamma-A, gamma-D and gamma-u immunoglobulins. *Scand. J. Haemat. 4*, 46 (1967).
31. Masaki, A., Danbara, C., Harada, H., Teramura, I., Sanada, I., Takata, T., Shinozaki, K.: A case of IgD myeloma. *Acta haemat. jap. 30*, 475 (1967).
32. Meiser, J., Huhnstock, K.: Atypische Paraproteinosen. *Verh. dtsch. Ges. inn. Med. 73*, 821 (1967).
33. Michot, F.: Gamma-D-Plasmocytom und progressive Muskeldystrophie: eine Kombination von zwei seltenen Krankheitsbildern. *Schweiz. med. Wschr. 98* 1598 (1968).
34. Oberdorfer, A., Schnauffer, K., Lange, H.-J., Neiss, A.: Zur Verteilung von Paraproteinämien nach Geschlecht und Alter der Patienten, Paraprotein-Klassen, Subklassen und Leichtketten-Typen. *Z. klin. Chem. 11*, 51 (1973).
35. Ovary, Z.: Lack of skin-sensitizing property of D myeloma protein in guinea pigs. *J. Immunol. 102*, 790 (1969).
36. Pernis, B., Chiappino, G., Rowe, D. S.: Cells producing IgD immunoglobulins in human spleen. *Nature (Lond.) 211*, 424 (1966).
37. Pruzanski, W., Rother, I.: IgD plasma cell neoplasia: clinical manifestation and characteristic features. *Canad. med. Ass. J. 102*, 1061 (1970).
38. Puskás, É., Medgyesi, Gy., Gergely, J., Brenner, F., Hindy, J., Prekop, M.: Immunkémiai módszerek alkalmazásának jelentősége az IgD myeloma felismerésében. *Orv. Hetil. 115*, 1329 (1974).
39. Rádl, J., Masopust, J., Lackové, E.: Selective hyperimmunoglobulinaemia A and D in a case of chronic generalized eczema and prolonged sepsis. *Helv. paediat. Acta 22*, 278 (1967).
40. Rentsch, I.: Gamma-D-Plasmozytom. *Med. Welt 20*, 1304 (1968).
41. Rivers, S. L., Patno, M. E.: Cyclophosphamide vs. melphalan in treatment of plasma cell myeloma. *J. Amer. med. Ass. 207*, 1328 (1969).

42. Rogentine, G. N., Rowe, D. S., Bradley, J., Waldmann, T. A., Fahey, J. L.: Metabolism of human immunoglobulin D (IgD). *J. clin. Invest. 45*, 1467 (1966).
43. Rowe, D. S., Fahey, J. L.: A new class of human immunoglobulins. I. A unique myeloma-protein. *J. exp. Med. 121*, 171 (1965).
44. Rowe, D. S., Fahey, J. L.: A new class of human immunoglobulins. II. Normal serum IgD. *J. exp. Med. 121*, 185 (1965).
45. Rowe, D. S., Crabbé, P. A., Turner, M. W.: Immunoglobulin D in serum body fluids and lymphoid tissue. *Clin. exp. Immunol. 3*, 477 (1968).
46. Rowe, D. S., Dolser, F., Welsher, H. D.: Studies on human IgD. Molecular weight and sedimentation coefficient. *Immunochemistry 6*, 437 (1969).
47. Rowe, D. S., Hug, K., Forni, L., Pernis, B.: Immunoglobulin D as a lymphocyte receptor. *J. exp. Med. 138*, 965 (1973).
48. Rowe, D. S., Hug, K., Faulk, W. P., McCornick, J. N., Gerber, H.: IgD on the surface of peripheral blood lymphocytes of human newborn. *Nature new Biol. 242*, 155 (1973).
49. Saha, A., Chowdhury, P., Samburiy, S., Behelak, Y., Heiner, D. C., Rose, B.: Studies on human IgD. II. Physico-chemical characterization of human IgD. *J. Immunol. 105*, 238 (1970).
50. Siebner, H.: Über Chromosomenuntersuchungen bei Paraproteinämien. *Fortschr. Med. 87*, 30 (1969).
51. Skvaril, F., Rádl, J.: The fragmentation of human IgD during storage. *Clin. chim. Acta 15*, 554 (1967).
52. Spengler, G. A., Bütler, R., Pflugshaupt, R., Lopez, V., Barandum, S.: Gamma-D-Paraproteinämien. Kasuistischer Beitrag an Hand von zwei Beobachtungen. *Schweiz. med. Wschr. 97*, 170 (1967).
53. Spiegelberg, H. L., Prahl, J. W., Grey, H. M.: Structural studies of human D myeloma protein. *Biochemistry 9*, 2115 (1970).
54. Spiegelberg, H. L.: Gamma D immunglobulin. In: Contemporary Topics in Immunochemistry. F. P. Inman (ed.). Plenum Press, New York 1972, p. 165.
55. Schmidt, K., Mueller-Eckhardt, Ch.: Antinuclear autoantibodies of IgD class. An analysis of 82 patients. *Z. Immun. Forsch. 145*, 384 (1973).
56. Schneider, W.: Seltene Paraproteinämien. Ein Fall von Gamma-D-Plasmozytom. *Dtsch. med. Wschr. 92*, 2172 (1967).
57. Schneider, W.: Zur Diagnostik seltener Paraproteine. *Blut 20*, 4 (1970).
58. Tarantino, A., Imbasciati, E., Limido, D., Pietrogrande, M., Pinticelli, C.: Deposits of IgD in renal disease. Immunohistological study of 180 renal biopsies. *Europ. J. clin. Invest. 4*, 175 (1974).
59. Ventruto, V., Quattrin, N.: Studio di un caso di mieloma IgD (Prima osservazione italiana). *Haematologica 51*, 545 (1966).
60. Waldenström, J.: Monoclonal and Polyclonal Hypergammaglobulinaemia. Cambridge University Press, 1968.
61. Watson, I., Heiner, D., Rose, B., Bootello, A.: The demonstration of IgD antinuclear antibody activity in systemic lupus erythematosus. *Clin. Res. 17*, 362 (1969).
62. Wiedermann, D., Wiedermann, B., Rádl, J., Skvaril, F., Vaerman, P.: Über einen Fall von Immunglobulin-D-Plasmocytom. *Schweiz. med. Wschr. 97*, 207 (1967).
63. Zawardski, Z. A., Rubini, J. R.: D myeloma. Report of two cases. *Arch. intern. Med. 11* 387 (1967).

Correspondence: Dr. J. Jákó, Postgraduate Medical School, First Department of Medicine, Szabolcs u. 35, 1135 Budapest, Hungary

Haematologia 9 (3–4), pp. 279–282 (1975)

Tissue Antigens and Cytotoxic Antibodies in Polycythaemia Rubra Vera

G. NAGY, VALÉRIA STENSZKY, IRMA TIMÁR, KATALIN MURVAY

First Department of Medicine, Debrecen University Medical School, County Hospital and County Blood Transfusion Service, Debrecen, Hungary

(Received January 30, 1974)

The distribution of tissue antigens for 22 antigens was studied in 46 patients suffering from polycythaemia rubra vera (PRV), using antibody containing sera from 80 multigravidae. The incidence of HL-A 5 was significant higher and that of HL-A 7 significant, while the frequency of HL-A 13 was remarkably lower than in the normal population. No difference was found in ABO and Rh (D) antigen distribution for erythrocytes. No antibodies against erythrocytes, thrombocytes or lymphocytotoxic ones could be demonstrated.

According to data in the literature, there is a certain relationship between the distribution of blood groups and the incidence of haematological diseases. According to examinations performed by Nersziszjan et al. [14] in more than 2000 haematological patients, within the ABO system group O occurs more frequently in acute leukaemia, groups A and AB in pernicious anaemia, group AB in Werlhof's syndrome and group B in haemophilia, as against the normal population. Differences were found also in the distribution of Rh (D) antigen inasmuch as the ratio of Rh-negative patients proved to be significantly higher in acute leukaemia, chronic myeloid leukaemia, hypoplastic anaemia and haemophilia. The investigations associated with organ transplantation and the better understanding of tissue antigens have aroused interest in the relationship between tissue antigens and the various illnesses, especially haematological diseases [6, 7, 10, 15–17, 22]. It has been attempted to find some correlation between development of the disease and the incidence of certain HL-A antigens for Hodgkin's disease [1, 6, 7, 11, 16], malignant lymphomas [10, 11, 15] and SLE [3, 5], etc. The results obtained and the conclusions drawn are not uniform.

Another field of research is centred on the appearance of lymphocytotoxic antibodies in the sera of patients with various diseases [8, 9, 12, 18–20]. According to literary data, certain tissue antigens occur more and others less frequently than in the normal population in part of the haemoblastoses. In spite of this we have found no data concerning the tissue antigens and cytotoxic antibodes in patients with polycythaemia rubra vera (PRV).

Material and Methods

The distribution of tissue antigens was analysed in 46 patients suffering from PRV. The incidence of ABO, Rh (D) and tissue antigens was studied in

respect of antigen distribution. The development of antibodies against all the three cell lines was investigated. Tissue antigens were determined by the international standard lymphocytotoxicity microtest [20]. Typing for 22 antigens was done by using antibody containing sera collected from 80 multigravidae. More than two sera with antibody were used for the determination of each antigen. The results obtained were compared with the per cent distribution and gene frequency for the normal population. The lymphocytotoxicity microtest, using lymphocytes from 50 healthy non-related blood donors was adopted to locate the antibodies in the sera of the patients. The antibodies against thrombocytes were studied by means of thrombocytes from 50 donors, by Colombani's [2] complement fixation microtechnique.

Results

No difference was found in the distribution of ABO and Rh (D) antigens as against the data for erythrocytes of several thousand healthy donors.

When examining the tissue antigens of the patients, significant differences were found for 3 antigens.

Four hundred and ninety blood donors served as normal controls. The repartition of tissue antigens is given in Table 1.

Table 1

Frequency of antigens in 46 PRV patients

	Normal	Gene frequency in normal blood donors	Gene frequency in PRV patients	p
	HL-A 1	0.1475	0.1308	
	HL-A 2	0.2989	0.2697	
	HL-A 3	0.1271	0.1308	
	HL-A 9	0.1215	0.1437	
locus 1	HL-A 10	0.0923	0.1056	
	HL-A 11	0.0701	0.0455	
	W 28	0.0388	0.0339	
	W 32	0.0315	0.0225	
	HL-A 5	0.0521	0.1567	0.0001
	HL-A 7	0.0946	0.1835	0.0111
	HL-A 8	0.1016	0.0691	
	HL-A 12	0.1135	0.1181	
	HL-A 13	0.0498	0.0112	0.0927
	W 5	0.0853	0.0572	
locus 2	W 10	0.0853	0.1181	
	W 14	0.0359	0.0225	
	W 15	0.0432	0.0225	
	W 17	0.0513	0.0225	
	W 22	0.0199	0.0225	
	W 27	0.0506	0.0455	

As it clearly appears from Table 1, a highly significant increase ($p = 0.0001$) was found in the frequency of HL-A 5, and a significant increase ($p = 0.0111$) in that of HL-A 7. On the other hand, a not significant, though remarkable diminution was observed in the appearance of antigen HL-A 13.

Considering that PRV is affecting all the three cell lines of haemopoiesis (erythropoiesis, myelopoiesis, thrombocytopoiesis), the next experiments were designed to find the respective antibodies.

Immunoantibodies against erythrocytes could not be found either on the cell itself or in the serum.

Antibodies against lymphocytes were tested by lymphocytes from 50 healthy blood donors, with incubation at room temperature and at 15°C. No lymphocytotoxic antibody was found.

Attempts were made to demonstrate antibodies against thrombocytes by thrombocytes from 50 healthy donors, adopting the complement fixation technique. The tests led to negative results in this case, too.

Discussion

Various authors found either a significant rise or fall of certain tissue antigens in haematological disease. Thus e.g. HL-A 2 and 12 occur more frequently, HL-A 1 significantly less frequently in acute lymphoid leukaemia [17, 22]; HL-A 9, W 5 antigens more frequently in chronic lymphoid leukaemia [6], HL-A 5, W 5 in Hodgkin's disease [1, 6, 7, 11, 16], HL-A 12, 13 in reticulosis [10], HL-A 7, W 17 in lymphosarcoma [10].

In the present experiments, a highly significant rise ($p = 0.0001$) was found in the frequency of HL-A 5, a significant rise ($p = 0.0111$) in that of HL-A 7 and a not significant, though remarkable fall in the incidence of HL-A 13 in 46 patients with Vaque–Osler's disease. Although significant differences calculated from the data of 46 patients in all must be interpreted with proper criticism, we have still drawn some conclusions from these 3 antigenic differences. We have attempted to establish correlations in the incidence of the 3 different antigens versus their frequency in the normal population and certain clinical parameters such as age, sex, duration and type of the disease (thrombotic, haemorrhagic forms), and their response to therapy. However, no unambiguous relationship could be demonstrated. In the second half of the experiments we searched for antibodies against peripheral haemocytes (erythrocytes, lymphocytes, thrombocytes). Immunoantibodies against erythrocytes could not be detected either on the cell itself or in the serum.

Our hypothesis that the moderate lymphopenia associated with PRV [4, 13] would be due to lymphocytotoxic antibodies could not be proved.

We attempted to detect antibodies against thrombocytes by thrombocytes from 50 healthy blood donors, adopting the complement fixation technique. These investigations too gave negative results. Accordingly, the failure or delay of the increase in the thrombocyte count, often experienced in the course of

exacerbations after treatment with radiophosphorus or cytostatics, could be accounted for by immunological factors.

References

1. Amiel, J. L.: Discussion. Symposium on the relationships between histocompatibility antigens and tumor antigens. *Transplant. Proc. 3*, 1277 (1971).
2. Colombani, J., D'Amaro, J., Gabb, B., Smith, G., Svejgaard, A.: International agreement on a microtechnique of platelet complement fixation. *Transplant. Proc. 3*, 121 (1971).
3. Dausset, J.: Correlation between histocompatibility antigens and susceptibility to illness. In: Progress in Clinical Immunology. Grune and Stratton, New York 1971.
4. Goll, K. H.: Über die Pathogenese der Polycythaemia vera. *Folia haemat. (Lpz.) 77*, 1 (1959).
5. Grumet, F. C., Coukell, A., Bodmer, J. G., Bodmer, W. F., McDevitt, H. O.: Histocompatibility (HL-A) antigens associated with systemic lupus erythematosus. A possible genetic predisposition to disease. *New Engl. J. Med. 285*, 193 (1971).
6. Jeannet, M., Magnin, C.: HL-A antigens in haematological malignant disease. *Transplant. Proc. 3*, 1301 (1971).
7. Kissmeyer-Nielsen, F., Jensen, K. G., Ferrara, G. B., Kierbye, K. E., Svejgard, A.: HL-A phenotypes in Hodgkin's disease. A preliminary report. *Transplant. Proc. 3*, 1287 (1971).
8. Kreisler, M., Naito, S., Terasaki, P. I.: Cytotoxins in disease. V. Various diseases. *Transplant. Proc. 3*, 112 (1971).
9. Mayer, S., Soussi, R., Tongio, M. M., Berrebi, A.: Recherche d'anticorps leuco-plaquettaires dans lupus erythemateux disseminé et les syndromes apparantés. *Nouv. Rev. franç. Hémat. 14*, 147 (1971).
10. Morris, P. J., Forbes, J. T.: HL-A in follicular lymphoma, reticulum cell sarcoma, lymphosarcoma and infectious mononucleosis. *Transplant. Proc. 3*, 1315 (1971).
11. Morris, P. J., Forbes, J. F.: HL-A and Hodgkin's disease. *Transplant. Proc. 3*, 1275 (1971).
12. Naito, S., Hiratu, A. A., Estrada, H. G., Terasaki, P. I.: Lymphocytotoxins in disease. IV. Cold cytotoxins in pregnancy, sore throat and rheumatic heart disease. *Tissue antigens 1*, 219 (1971).
13. Nagy, Gy.: Polycythaemia rubra vera. *Az orvostudomány aktuális problémái. 2*, 131 (1971).
14. Нерсиян В. М., Торгомян Т. Л., Елиян Л. И., Узунян Л. Х., Щербакова Л. Н., Оганджанян И. К.: Распределение групп крови системы АВ0, резус, MN и P сред9 больных с заболеваниями системы крови. *Пробл. гематол. 17*, 39 (1972).
15. Rege, W., Patel, E., Briggs, V. A.: Leukocyte antigens and disease. II. Association of HL-A 5 and lymphomas. *Amer. J. clin. Path. 58*, 14 (1972).
16. van Rood, J. J., van Leeuwen, A.: HL-A and the group five system in Hodgkin's disease. *Transplant. Proc. 3*, 1283 (1971).
17. Rogentine, G. N. Jr., Yankee, R. A., Gart, J. J., Nam, J., Frapani, R. J.: HL-A antigens and disease. Acute lymphomatic leukemia. *J. clin. Invest. 51*, 2420 (1972).
18. Stastny, P., Ziff, M.: Antibodies against cell membrane constituents in systemic lupus erythematosus and related disease. *Clin. exp. Immunol. 8*, 543 (1971).
19. Stenszky, V., Szegedi, Gy., Aszódi, L., Petrányi, Gy.: HL-A and systemic lupus erythematosus. *Haematologia 7*, 211 (1973).
20. Terasaki, P. I., McCleland, J. D.: Microdroplet assay of human serum cytotoxins. *Nature (Lond.) 204*, 998 (1964).
21. Terasaki, P. I., Mottironi, V. D., Barnett, E. V.: Cytotoxin in disease. Autocytotoxins in lupus. *New Engl. J. Med. 283*, 724 (1970).
22. Walford, R. L., Zeller, E., Coombs, L., Konrád, P.: HL-A specificities in acute and chronic lymphatic leukemia. *Transplant. Proc. 3*, 1297 (1971).

Correspondence: Dr. G. Nagy, Central Hospital, Róbert Károly krt. 44, 1134 Budapest, Hungary

Haematologia 9 (3—4), pp. 283—286 (1975)

Cytostatic Treatment of Polycythaemia Rubra Vera

Comparison of the Effects of Some Cytostatics in 100 Patients in a Period of Five Years

G. NAGY, MÁRIA LÉHI, GY. PETRÁNYI

First Department of Medicine, University Medical School, Debrecen, Hungary

(Received December 7, 1973)

Experience with cytostatic treatment performed in patients with polycythaemia rubra vera is reviewed. The effectivity and side effects of the drugs applied are evaluated. Mannosulfan and mitobromitol were the drugs most suitable for treatment. In certain special cases, 5-hydroxyurea was also satisfactory, while mitolactol was the least suitable.

Application of new cytostatics and of their combinations, a comparison of their effectivity and possible side effects are the most effective means for improving the therapeutical result in haemoblastoses [12]. Although the results ensured in these conditions by cytostatics are poorer and in many a respect more restricted than the effect of antibiotics in infectious diseases, their therapeutical role is identical until a causal therapy has been found.

Polycythaemia rubra vera (PRV) is a particular illness among the haemoblastoses [7] in that, if treated appropriately, it is relatively benign and takes a protracted course. It is therefore well- suited for investigating the pathological and clinical features in detail [9, 10]. Cytostatics effective in PRV are useful also in the other condition belonging to this group of diseases, and vice versa [11]. Our own experience also supports this: mannosulfan and 5-hydroxyurea proved effective in PRV, therefore we started giving these drugs also to patients with chronic myeloid leukaemia (CML). Mitobromitol was initially administered only to patients with CML but in PVR it also proved effective.

Materials and methods

Until 1967, all our PRV patients were treated exclusively with radiophosphorus (^{32}P). Since 1967, most of the patients receive cytostatics. ^{32}P is applied only in patients with long history of PRV; or in the presence of dangerous complications such as cerebral vascular crisis, myocardial infarction, multiple embolisms, or if the patient's condition is very serious due to some other reasons; and if the previously applied cytostatic treatment had no effect.

During 5 years 100 patients were treated with cytostatics. Thirty had mitobromitol, 40 mannosulfan, 20 5-hydroxyurea and 10 mitolactol treatment. Their mean age was 54.2 years (range 18 to 74 years). The sex distribution was 63 males,

37 females. The disease had started more than 5 years before in 52, before 3 years in 22, and before 1 year in 18 cases. In 37 cases, vascular complications occurred in the history, in 92 cases splenomegaly, and in 67 cases hepatomegaly.

Mean RBC count: 6,800,000 (5,750,000 – 7,300,000); WBC: 2600 (8600 – 17,000); platelet count 556,000 (450,000 – 745,000). Eighty-six patients displayed an increased granulocytic alkaline phosphatase activity.

The drugs were administered orally in the following doses: mitobromitol, 0.25 g; mannosulfan, 1.0 g; 5-hydroxyurea, 2.0 g; mitolactol, 0.45 g. Mean dosage was, in the same order as above, 6.75 g; 12.00 g; 16.5 g; and 6.5 g. During one course the patient was given one type of cytostatic. The time of onset of the disease was different, but no relationship was found between the sensitivity to a new drug and the length of the process. In those cases when the red blood cell count, haemoglobin and haematocrit values were very high or previously some vascular complications (thrombosis, thromboembolism or significant bleeding) occurred, repeated venesection was performed. Altogether a total of 1000 – 1600 ml of blood was withdrawn in 150 – 250 ml fractions every second day, parallel with cytostatic therapy.

Results

Complete normalization of counts in peripheral blood and bone marrow, a subsidence or significant decrease of splenomegaly and hepatomegaly and the relief of complaints connected with the disease were considered the criteria of remission. Patients in working age were able to continue their work during periods of remission. Results of cytostatic therapy and the complications arising are shown in Table 1.

At the time of exacerbation, five of the patients shown in Table 1 were treated with mitobromitol and 10 with mannosulfan, hence the difference between the number of treated and total number of patients. Treatment with 5-hydroxyurea or mitolactol was applied only once in the same patient.

Mitolactol was effective in every case, mitobromitol in 32 of 35 cases, 5-hydroxyurea in 18 of 20 cases, mitolactol in 6 of 10 cases. The mean duration of

Table 1

Cytostatic	Average dose (day/course), g	Number of treated patients	Total number of treatments	Number of effective treatments	Number of complications	Mean duration of remission, months
Mitobromitol	0.25/6.75	30	35	32	3	18.3
Mannosulfan	1.0/12.0	40	50	50	0	16.3
5-Hydroxyurea	2.0/16.5	20	20	18	3	7.5
Mitolactol	0.45/6.50	10	10	6	1	5.1
Total	—	100	115	106	7	—

remission was about identical after mitobromitol and mannosulfan; in the patients treated with 5-hydroxyurea it was significantly shorter and shortest in the cases where mitolactol was applied.

Complications due to treatment such as reversible leukocytopenia and thrombocytopenia were observed in 3 cases treated with mitobromitol, in three cases treated with 5-hydroxyurea and in one case treated with mitolactol.

Two of the three cases where leukocytopenia and thrombocytopenia developed had previously been treated with radiophosphorus, $1\frac{1}{2}-2$ years preceding mitobromitol treatment. The radiophosphorus proved effective at this time, as it ensured a complete clinical and haematological remission. In one case a recent PRV was confirmed. All three patients developed cytopenia between the 20th and 25th days of treatment, white blood cell count decreased to $1000-1500$, the platelet count to $15{,}000-21{,}000$. Two of the 5 patients treated with 5-hydroxyurea had previously been given radiophosphorus; one of them had had once radiophosphorus and once mitobromitol. In 2 of the 3 patients the cytopenia had appeared after an increased dose (30 g) of 5-hydroxyurea and in one case after 12 g of the drug, between the 20th and 30th days of treatment. White blood cell count decreased to $2000-2500$, the platelet count to $35{,}000-50{,}000$. In the case where mitolactol had been applied and cytopenia appeared the patient had already received radiophosphorus, mitobromitol and mannosulfan. In this case the cytopenia was less severe than in the cases where it had manifested itself after a dose of 4.5 g mitolactol. In all cases where complications arose a fresh platelet suspension, transfusion of blood and antibiotics completely normalized the blood picture in $2-3$ weeks.

The cytostatic most effective in the treatment of PRV thus seemed to be mannosulfan. It always ensured a remission, whether applied as a first treatment or as a treatment of relapse; the drug caused no complications and the mean duration of remission was one and a half years. Remissions after mitobromitol therapy were longer but in 3 of 35 cases the drug was ineffective and in another 3 cases complications such as leukopenia and thrombocytopenia arose. In cases when resistance had developed to the drug applied, 5-hydroxyurea seemed to be useful, although the remissions caused by it were significantly shorter and the number of ineffective cures and the frequency of complications were higher than with mitobromitol. Among the four cytostatics, mitolactol was the least suitable; in 6 of 10 patients a remission was ensured but it lasted only for a half year.

Discussion

Vascular complications are frequent in untreated or insufficiently treated PRV patients. Cserbak [2] observed 139 (63%) in a series of 219 cases. Watkins and Fairley [15] reported on 50% complications such as thrombosis, thromboembolism and bleedings, in a series of approximately 100 patients. Chievitz and Thiede [1] studying the postmortem findings of 250 PRV cases, observed that in 100 cases (40%) the cause of death was thrombosis and in 15 (6%) a haemorrhage.

The question remains whether leukaemic transformation [14] was due to the otherwise effective radiophosphorus therapy.

As to the other cytostatic drugs, Killmann and Cronkite [6], Maurice and Alberto [8] reported on their experience with Busulfan, Demidova [4] with triaziquone and Deconti and Calabresi [3] with azauridine and azaribine treatment, and Szentkláray [13] with mitobromitol. According to these reports, the first three cytostatics were frequently causing leukocytopenia and thrombocytopenia, hence they are not too suitable for therapeutic purposes. Good results were achieved with mitobromitol, azauridine and azaribine.

Considering all points, in our opinion, mannosulfan is the most cytostatic in PRV and our experience was favourable with mitobromitol. In certain cases 5-hydroxyurea was also beneficial, although the remission caused by it was significantly shorter than with the other two cytostatics. Mitolactol ensured poor results; this drug was the least suitable for the therapy of PRV.

References

1. Chievitz, E., Thiede, T.: Complication and causes of death in polycythaemia vera. *Acta med. scand. 172*, 513 (1962).
2. Черьак Е. М.: Некоторые вопросы клиники и патогенеза сосудистой патологии при эритемии. *Тер. Арх. 40*, 71 (1968).
3. Deconti, R. C., Calabresi, P.: Treatment of polycythaemia vera with Azauridine and Azaribine. *Ann. intern. Med. 73*, 575 (1970).
4. Демидова А. В.: Новые аспекты терапии эритемии. Химиотерапии эритемии. Опыт лечения Тренимоном и Маркофаном. *Тер. Арх. 38*, 64 (1966).
5. Harman, I. B., Ledlie, E. M.: Survival of polycythaemia vera patients treated with radioactive phosphorus. *Brit. med. J. 2*, 146 (1967).
6. Killmann, S. A., Cronkite, E. O.: Treatment of polycythaemia vera with Myleran. *Amer. J. med. Sci. 241*, 218 (1961).
7. Lawrence, J. H.: Polycythaemia; Physiology, Diagnosis and Treatment Based on 303 Cases. Grune and Stratton, New York 1955.
8. Maurice, P. A., Alberto, P.: Résultats à long terme du traitement de la polycythémie par le Myleran. Définition des critères pour une posologie adéquate. *Schweiz. med. Wschr. 97*, 1477 (1967).
9. Nagy, Gy.: Klinikai vizsgálatok és erythropoetin aktivitási mérések polycythaemia verás beteganyagon. Thesis, Debrecen 1968.
10. Nagy, Gy.: Polyglobuliák. *Orv. Hetil. 111*, 1743 (1970).
11. Nagy Gy.: Polycythaemia rubra vera. Klinikai kép, pathologia és therápia. In: Az orvostudomány aktuális problémái. Medicina, Budapest 1971.
12. Nagy, Gy., Balázs, Cs., Petrányi, Gy.: A chronicus myeloid leukaemia Zitostop kezelése. *Orv. Hetil. 112*, 2352 (1971).
13. Szentkláray J.: A polycythaemia vera kezelése Myelobromollal. *Orv. Hetil. 107*, 2182 (1966).
14. Szur, L., Lewis, S. M., Path, M. C.: The haematological complications of polycythaemia vera and treatment with radioactive phosphorus. *Brit. J. Radiol. 39*, 122 (1966).
15. Watkins, J., Fairley, G. H.: Treatment of polycythaemia vera. *Brit. J. med. 2*, 664 (1967).

Correspondence: Dr. G. Nagy, Central Hospital, Róbert Károly krt. 44, 1134 Budapest, Hungary

Book Reviews

Present Problems in Haematology. Proceedings of the Second Meeting of the European and African Division of the International Society of Haematology, Prague, August 27 to 29, 1973. Eds.: J. Libánsky, L. Donner. Excerpta Medica, Amsterdam and Avicenum Czechoslovak Medical Press, Prague 1974.

(The full text of 26 papers, with author and subject index, 302 pages.)

This is a very useful book for everyone interested in the new developments of haematological research and practice. The papers give a good survey of the progress in such topics which have changed most rapidly during the last few years.

In the first section 11 papers deal with the ethiopathogenesis and treatment of leukaemia. The present state of the biochemistry of oncornaviruses is discussed first. There are studies on various aspects of preleukaemic states, and on the ultrastructure of human leukaemic lymphocytes. An excellent review by J. F. Doré et al. discusses the human leukaemia-associated antigens and immune reactions. Further papers deal with chemotherapy and immunotherapy of acute leukaemia; experiments in animals as well as detailed clinical experience are presented by Mathé et al. On the classification and present state of treatment of lymphomas A. Stacher's paper is most interesting.

In the second section the immunology of leukocytes, the HL-A system and its application in clinical medicine are discussed. An interesting paper deals with the genetic factors associated with the major histocompatibility system, i.e. the structural and/or regulatory genes. Several papers are devoted to the connection between the morphology and immunological function of lymphocytes. Still in this section the nature of the transplantation reaction and the question of non-specific immunosuppressive therapy are discussed. A review by G. Mathé et al. on the present state of bone marrow transplantation is based on the authors' own clinical experience.

The third section deals with haemocoagulation and fibrinolysis. Three theoretical papers discuss the interaction of coagulation factors, the naturally occurring and synthetic thrombin inhibitors, and the fibrinolysis and fibrinogen degradation products. A brief paper by H. G. Lash gives an up-to-date description of the pathophysiological and clinical aspects of diffuse intravascular coagulation.

Anna Mód

S. Sumida: *Transfusion of Blood Preserved by Freezing*. Georg Thieme Verlag, Stuttgart 1974. 92 pages, 117 illustrations. Price: DM 58.—

The biological effects of cold have been known for centuries, but the relationship between low temperature and life remained largely unexplained until 1940, when Luyet and Gehenio published their work "Life and Death at Low Temperatures". Since that time various disciplines have become interested in the rapidly expanding field of cryobiology. The observation in 1951 by Audrey Smith that glycerol protects cells from the lethal effects of freezing has opened the possibility for the long-term preservation of cellular components of blood.

The introduction of component therapy has created an increasing demand for erythrocytes, leucocytes and platelets. Their clinical application has been the major driving force for research to preserve blood cells for transfusion at low temperatures.

In this monograph, Sumida explains the freezing damage to red cells in terms of his own observations with the cryomicroscope. This is followed by a comprehensive summary of the author's studies of frozen blood *in vitro* and *in vivo*, using both the high glycerol-slow freeze and the low glycerol-rapid freeze methods of preservation.

The monograph is not restricted to the preservation of red cells but presents a promising approach to the freezing of platelets. As this method becomes more practical, it will allow an increased use of frozen platelet preparations for the treatment of thrombocytopenias.

The advantages of frozen blood are the ready accessibility of both rare and common red blood cells, decreased occurrence of immunizing histocompatibility antigens, and a low incidence of transfusion hepatitis.

Frozen blood remains the only hope for indefinite storage. It is only a matter of time before frozen blood will become a common supply in every blood bank for supplementing fresh blood.

This beautifully illustrated and authoritative monograph will assist everybody in coping with the problems associated with the freezing of red cells and platelets.

Veronika Harsányi

Addine G. Erskine: *The Principles and Practice of Blood Grouping*. Mosby, Saint Louis 1973. 356 pages, with 84 illustrations. Price:

This book is intended to offer a classroom text to beginners in blood grouping and at the same time to present comprehensive and up-to-date information for the more advanced workers in the field. "Whereas just a short time ago blood transfusions were specialty procedures, resorted to infrequently and then only in cases of dire emergency, today they have become routine, thanks to the knowledge of the blood groups. It is therefore necessary for the modern blood bank technologist to be well versed in the fundamentals of blood grouping."

The book is divided into three parts. Parts I and II deal with principles and methods of blood grouping while part III gives a short review of blood groups in non-human primates.

Part I gives a short history of the principles of blood grouping. It does not only describe the most important blood group systems but deals with their immunological as well as genetical and chemical bases. A glossary of the terms used in blood grouping makes the book still more useful.

Part II deals with the laboratory methods of blood grouping. As these methods seem to be simpler than many other laboratory procedures it is a common belief that they can be executed reliably by persons having a minimum of training and experience. The author calls attention to this dangerous view and stresses the importance of careful attention to details and necessary controls.

Dealing with coding of blood group reactions, Erskine makes a step toward introducing computers into the medical laboratory, undoubtedly a matter of the not too distant future.

In part III the blood groups of non-human primates are discussed, a subject now attracting world-wide attention.

This book will satisfy the needs for an up-to-date general textbook as a reference source together with detailed instructions for carrying out the tests.

Ágnes Friss

Abstracts

The interaction between transferrin and rabbit reticulocyte ghosts. E. H. Morgan and E. Baker (Department of Physiology, University of Western Australia, Nedlands, Western Australia). *Biochim. biophys. Acta* (Amst.) *363*, 240 (1974).

The properties of the membrane receptors involved in iron transfer from plasma transferrin to cells were studied using rabbit reticulocyte ghosts prepared by hypotonic haemolysis and pure rabbit plasma proteins labelled with ^{125}I, ^{131}I and/or ^{59}Fe. The specificity of the transferrin-binding receptors was apparently lost during preparation of the reticulocyte ghosts. In contrast to the reaction with intact cells, transferrin uptake and reflux from ghosts were independent of the reticulocyte count, similar in quantity and kinetics to albumin uptake, and not affected by sulfhydryl reagents which inhibit transferrin uptake by intact cells. These results indicate that the structural integrity of the reticulocyte is critical for the specific uptake of transferrin and that identification and isolation of transferrin receptors after hypotonic lysis are unlikely to be successful.

A. Egyed

Energy-dependent accumulation of iron by isolated rabbit reticulocyte mitochondria. I. Romslo (Department of Biochemistry, University of Bergen, Arstadvollen, Bergen). *Biochim. biophys. Acta (Amst.) 357*, 34 (1974).

Rabbit reticulocyte mitochondria isolated in a medium of sucrose, N-2-hydroxyethyl piperazine-N'-2-ethanesulphonic acid and bovine serum albumin rapidly accumulate iron from the suspending medium when ^{59}Fe(III)-sucrose is used as a soluble and stable model complex. In liver mitochondria the accumulation occurs by two different mechanisms, i.e. by an energy-independent and an energy-dependent (uncoupler-sensitive) one. Energy-dependent accumulation is inhibited to approx. 80% by cyanide. The reticulocyte mitochondria possess high and low-affinity binding sites of iron as recently reported for rat liver mitochondria. At pH 7.4, the low-affinity sites bind about 110 nmoles of iron per mg of protein with $K'_m \approx 0.3$ mM. The high-affinity sites bind about 28 nmoles of iron per mg of protein with $K'_m \approx 50$ μM, and the binding is completely inhibited by the uncoupler carbonyl cyanide m-chlorophenylhydrazone. By comparing the energy-dependent accumulation of iron and calcium in mitochondria from reticulocytes and different organs, it is found that iron accumulation (in state 1) relative to calcium (in state 4) is favoured in reticulocytes by a factor of 5 (relative to liver) to 40 (relative to heart).

A. Egyed

Mobilization of iron from reticulocyte ghosts by cytoplasmic agents. E. F. Workman, Jr. and G. W. Bates (Department of Biochemistry and Biophysics, College of Agriculture, and Texas Agricultural Experiment Station, Texas A. and M. University, College Station, Texas). *Biochem. biophys. Res. Comm. 58*, 787 (1974).

The preparation of ghosts from rabbit reticulocytes previously incubated with ^{59}Fe-

transferrin allows to study membrane iron mobilization by cytoplasmic factors, and intracellular iron pathways in a cell-free system. Incubation of ^{59}Fe-ghosts with unlabeled reticulocyte lysate results in mobilization of the membrane bound iron and its utilization for hemoglobin and ferritin synthesis. An iron binding component migrating near the low molecular weight range on a Sephadex G-100 column was rechromatographed on G-25 and emerged with the void volume. Chromatographic behavior suggested a molecular weight near 5000. The component was subjected to gel electrophoresis; it migrated as a single TCA precipitable band that stained with Coomassie blue. The Lowry test for protein was positive. The component was found to bind ferrous ion reversibly, and to be active metabolically.

A. Egyed

Evidence that ferrihemoglobin may function as an intracellular heme carrier in reticulocytes. H. M. Schulman (Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, Quebec). *Canad. J. Biochem. 52*, 665 (1974).

Ferrihaemoglobin (1) stimulates globin synthesis in rabbit reticulocytes and in a reticulocyte cell-free protein synthesizing system, and (2) causes newly synthesized $\alpha\beta$-globin dimers to form tetramers which are indistinguishable from haemoglobin in the ultracentrifuge. These observations are consistent with the idea that a small pool of ferrihaemoglobin may act as an intracellular haem carrier in reticulocytes.

A. Egyed

The gelation of deoxyhemoglobin S in erythrocytes as detected by transverse water proton relaxation measurements. G. L. Cottam, K. M. Valentine, K. Yamaoka and M. R. Waterman (Department of Biochemistry, The University of Texas Southwestern Medical School at Dallas, Dallas, Texas). *Arch. Biochem. 162*, 487 (1974).

At 37°C, when samples of blood, washed erythrocytes, or isolated hemoglobin from individuals with sickle cell disease are deoxygenated, the transverse water proton relaxation time is sharply decreased. In similar samples from normal adults homozygous for hemoglobin A, only a slight decrease in t_2 was observed upon deoxygenation at 37°C. In samples containing deoxyhemoglobin S, the value of t_2 increases as the temperature is decreased from 37°C to 4°C, in contrast to samples containing oxyhemoglobin S, oxyhemoglobin A, or deoxyhemoglobin A, where t_2 decreases as the temperature decreases. It is suggested that the decrease in t_2 observed in samples of deoxyhemoglobin S at 37°C is the result of an increase in the amount of preferentially oriented water at macromolecular interfaces which occurs under conditions known to produce deoxyhemoglobin S gelation. Conditions which reverse deoxyhemoglobin S gelation such as lowering the temperature to 4°C, decrease the amount of preferentially oriented water which results in an increase in the value of t_2. Thus, measurement of the transverse water proton relaxation time can be used to monitor the gelation of deoxyhemoglobin S inside the erythrocyte.

B. Sarkadi

Some characteristics of a phospholipase A_2 from sheep red cell membranes. R. Kramer, B. Jungi and P. Zahler (Theodor Kocher-Institute, University of Berne, and Central Laboratories of the Swiss Blood Transfusion Service SRK, Berne, Switzerland). *Biochim. biophys. Acta* (Amst.) *373*, 404 (1974).

Red cell membranes of sheep contain a phospholipase A_2 (phosphatide 2-acyl-hydrolase, EC 3.1.1.4), which degrades exogenous phosphatidyl choline. The enzyme requires Ca^{2+} and is stimulated by detergents such as Triton X-100 or deoxycholate. Its pH optimum is 8.0. Phosphatidyl choline hydrolysis is not affected by albumin or high ionic strength. The enzyme has a broad temperature optimum between 30 and 45°C and is relatively heat stable. Phospholipase A activity is destroyed by 2-chloroethanol, but partially regained upon dialysis against an aqueous buffer. The enzyme is completely inhibited in the presence of dodecylsulphate.

After removal of the denaturant, the enzymatic activity is restored.

G. Gárdos

The interaction of concanavalin A with sheep erythrocytes. B. Shore and V. Shore (Biomedical Division, Lawrence Livermore Laboratory, University of California, Livermore, Calif.). *Biochim. biophys. Acta (Amst.) 373*, 313 (1974).

Concavalin A and ^{125}I-labeled concanavalin A were used as probes for comparison of sheep low-potassium (LK) and high potassium (HK) erythrocytes with respect to their agglutinability and membrane properties. Under conditions of equivalent concanavalln A binding, freshly isolated sheep HK cells agglutinated to a much greater extent than the LK cells at 23 or 35°C; agglutination was progressive over periods of 1—4 hrs, but the differential between LK and HK cells persisted. On additional standing overnight in the cold, both LK and HK cells were extensively agglutinated. After preincubation in a salt-buffer solution (without lectin) at 35°C for 4 hrs followed by standing overnight at 4°C, rapid and extensive agglutination but not increased binding of concanavalin A occurred in both sheep HK and LK cells. Cells preincubated in the presence of an energy source and/or bovine plasma albumin also agglutinated rapidly. The rate of agglutination of freshly isolated cells of either kind was not decreased by the presence of an energy supply. Agglutination of sheep LK and HK erythrocytes by concanavalin A appears to occur in two steps: the first, a relatively rapid and temperature-independent binding of lectin which is very similar if not identical in the LK and HK cells; and the second, agglutination of the cells, which is slow by comparison with dog and rabbit erythrocytes under the same conditions. The second step depends upon a change in the cells that occurs relatively slowly after their isolation whether or not concanavalin A or an energy supply is present. This change might occur more rapidly in HK cells and this causes the differential in agglutinability of LK and HK cells.

Ilma Szász

Blood cell abnormalities complicating the hypophosphatemia of hyperalimentation: erythrocyte and platelet ATP deficiency associated with hemolytic anemia and bleeding in hyperalimented dogs. Y. Yawata, R. P. Hebbel, S. Silvis, R. Howe and H. Jacob (Department of Medicine, University of Minnesota Medical School, the University of Minnesota Hospitals, and the Minneapolis Veterans Administration Hospital, Minneapolis). *J. Lab. clin. Med. 84*, 643 (1974).

Hemolytic anemia and hemorrhagic diathesis may occur in starved dogs infused with solutions of amino acids and hypertonic glucose ("hyperalimentation"). Dogs, as well as humans, develop profound hypophosphatemia within 24 hours of infusion. Parallel with the decrease in serum P, red cell and platelet ATP levels fall. Red cells become spheroidal, dehydrated, poorly filterable, and entrapped by the spleen; concomitantly, their survival is shortened. These abnormalities are prevented or reversed if cellular ATP is maintained by supplementation of animals with phosphate *in vivo* or by brief incubation of depleted red cells with adenosine and phosphate *in vitro*. Associated with ATP depletion in platelets, clot retraction is disturbed; thrombocytopenia also occurs, which results in a 5- to 10-fold decrease in platelet survival. Maintenance of serum P levels by phosphate supplementation of infusion solutions prevents the platelet abnormalities and the hemorrhagic diathesis. It is concluded that hypophosphatemia in hyperalimented dogs critically affects red cell and platelet function and survival through depletion of cellular ATP. By extrapolation to humans, it is suggested that serum P levels be monitored and carefully maintained in hyperalimented individuals so as to prevent the above complications.

Ilma Szász

Phosphate metabolism in intact human erythrocytes: Determination by phosphorus-31 nuclear magnetic resonance spectroscopy. T. O. Henderson, A. J. R. Costello and A. Emachi (Departments of Biological Chemistry and Physiology, University of Illinois at the Medical Center, Chicago, Ill.). *Proc. nat. Acad. Sci. (Wash.) 71*, 2487 (1974).

Whole human blood was examined by ^{31}P nuclear magnetic resonance spectroscopy.

Individual phosphates (α, β, γ) of ATP were identifiable, and two microenvironments appeared to be present for this molecule. When sequential recordings of freshly collected blood were made, 2,3-diphosphoglycerate was observed to decrease with a concomitant increase in inorganic orthophosphate. When aged cells containing little 2,3-diphosphoglycerate were incubated in the presence of inosine and pyruvate, 2,3-diphosphoglycerate formation could be demonstrated. Thus, cellular metabolism can be recorded directly in intact cells by ^{31}P nuclear magnetic resonance.

G. Gárdos

Comparison of factors regulating red cell 2,3-diphosphoglycerate (2,3-DPG) in acute and chronic hypoxemia. A. S. Keitt, Ch. Hinkes and A. J. Block (Department of Medicine, University of Florida and the Veterans Administration Hospital, Gainesville, Fla.) *J. Lab. clin. Med. 84*, 275 (1974).

In twelve hypoxemic patients with severe chronic obstructive pulmonary disease (COPD), red cell 2,3-diphosphoglycerate (2,3-DPG) correlated significantly with arterial PO_2 ($p < 0.05$), but not with arterial pH. Arterial oxygenation was increased by chronic administration of nasal oxygen by cannula for 4 to 12 months. Seven of these patients were rendered acutely hypoxemic by withdrawing their supplemental oxygen. The acute change in their red cell 2,3-DPG was highly correlated with a change in arterial pH ($p < 0.001$) but not with the change in arterial PO_2. Arterial pH seems to be the best predictor of red cell 2,3-DPG in acute hypoxemia and metabolic acid-base disorders while arterial PO_2 or a related factor is pre-eminent in stable COPD.

Ilma Szász

(Na^+-K^+)-activated ATPase in cattle erythrocytes. J. C. Ellory and S. Carleton (A.R.C. Institute of Animal Physiology, Babraham, Cambridge). *Biochim. biophys. Acta (Amst.) 363*, 397 (1974).

In the presence of 150 mM Na^+, increasing K^+ levels initially stimulated ($K^+ < 5$ mM) and then inhibited ouabain-sensitive ATPase in cattle erythrocyte ghosts. Ouabain-sensitive K^+ uptake measurements in high Na^+ medium showed that the external affinity for K^+ was about the same for high and low K^+ cells. K^+ inhibition of ATPase was greatest in ghosts derived from low K^+ cells, and least in ghosts from high K^+ cells, but a spectrum of sensitivities was found, correlating with the original red cell K^+ level. Sensitization with sheep anti-L reagent gave an increased overall ouabain-sensitive ATPase activity, with a small decrease in the apparent affinity for the K^+-inhibition component.

B. Sarkadi

Changes of membrane permeability due to extensive cholesterol depletion in mammalian erythrocytes. M. Grunze and B. Deuticke (Abteilung Physiologie, Medizinische Fakultät, Technische Hochschule Aachen, Aachen, BRD). *Biochim. biophys. Acta (Amst.) 356*, 125 (1974).

From porcine, bovine and human erythrocytes, 55% of the total membrane cholesterol could be removed by incubating the cells in suspension of lecithin liposomes. Up to 30% depletion, membrane permeability remained unaltered; more extensive depletion induced a marked increase of the transfer rates of non-electrolytes and of organic acids penetrating by nonionic diffusion. This biphasic response of permeability to cholesterol depletion, which has not been observed in artificial lipid membranes, may be related to the heterogeneity of the erythrocyte membrane lipids or to a pool of cholesterol not interacting with the phospholipids.

B. Sarkadi

Evidence for an asymmetric distribution of phospholipids in the human erythrocyte membrane. A. Kahlenberg, C. Walker and R. Rohrlick (Laboratory of Membrane Biochemistry, Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, Quebec). *Canad. J. Biochem. 52*, 803 (1974).

The changes in phospholipid composition of the inner (cytoplasmic) surface of the human erythrocyte membrane resulting from

the digestion of sealed inside-out vesicles with phospholipases A_2 and C were determined. Practically all of the phosphatidyl ethanolamine and phosphatidyl serine and 30—40% of the phosphatidyl choline and sphingomyelin of inside-out vesicles were found to be accessible to enzyme hydrolysis. In contrast, all of the above phospholipids of unsealed ghosts were susceptible to phospholipolytic digestion. These results are a direct demonstration of the asymmetric distribution of phospholipids in the human erythrocyte membrane.

Ilma Szász

Lactoperoxidase labeling of erythrocyte membranes from the inside and outside. B. C. Shin and K. L. Carraway (Department of Biochemistry, Oklahoma State University, Stillwater, Okla.). *Biochim. biophys. Acta (Amst.) 345*, 141 (1974).

Lactoperoxidase labeling of resealed erythrocyte ghosts has been performed to determine which polypeptides of erythrocyte membranes extended through the membrane. The resealed ghost was chosen because it approximates the intact cell better than does the isolated membrane. The interior surface of the membrane of the resealed ghost was labeled by sealing lactoperoxidase into the ghosts before adding ^{125}I- and H_2O_2. Labeling from the outside was carried out by standard method. Only two polypeptides were shown to be labeled from the outside. One was the 100,000 molecular weight component (Component III) and the other was the major glycoprotein. Resealed ghosts labeled from the inside show substantial labeling of spectrin and Component III. Labeling of the glycoprotein is far less extensive, particularly when compared to the labeling of Component III. These results show clearly that Component III spans the erythrocyte membrane in the resealed ghost, which is a close analogue of the intact cell. The results for the glycoprotein are not nearly so clear. The iodinable groups of the glycoprotein are relatively unreactive from the inside, suggesting that the protein conformation or the organization of the protein in the membrane prevents the ready accessibilty of these groups to the cytoplasm.

B. Sarkadi

Crosslinking of glycoproteins in human erythrocyte ghosts. T. H. Ji and Inhae Ji (Division of Biochemistry, University of Wyoming, Laramie, Wyoming). *J. molec. Biol. 86*, 129 (1974).

Membrane glycoproteins of human erythrocytes can be resolved into three major bands (GP-1, GP-2 and GP-3) by sodium dodecyl sulphate–polyacrylamide gel electrophoresis. When the ghosts or intact erythrocytes were reacted with the crosslinking reagent dimethyl malonimidate, a novel glycoprotein band (GP-A) of crosslinked product appeared on the gel electrophoretograms of the solubilized membranes. When the crosslinked glycoproteins (GP-A) were ammonolyzed to cleave the crosslinks and subjected again to electrophoresis on fresh gels, two glycoprotein bands (GP-1 and GP-2) were produced. It is concluded that GP-1 and GP-2 were crosslinked to form GP-A in the membrane. Only a small fraction of the glycoproteins was crosslinked, even after the ghosts were reacted with excess amounts of the reagent and for extended periods of time of crosslinking.

G. Gárdos

A microfluorimetric study of translational diffusion in erythrocyte membranes. R. Peters, J. Peters, K. H. Tews and W. Bähr (Max-Planck-Institut für Biophysikalische Chemie (Karl-Friedrich-Bonhoeffer-Institut), D-34 Göttingen und Abteilung für Biomathematik des Klinikums der Johann-Wolfgang-Goethe-Universität, D-6000 Frankfurt/Main, FRG). *Biochim. biophys. Acta (Amst.) 367*, 282 (1974).

A method is described which permits a quantitative study of translational diffusion in the membranes of single cells. Human erythrocytes were labelled with fluorescein isothiocyanate and then hemolyzed, which yielded ghosts of normal shape and strong fluorescence. By application of sodium dodecylsulphate–polyacrylamide gel electrophoresis it was found that a large part of the fluorescein isothiocyanate was bound to proteins of the erythrocyte membrane. In a fluorescence microscope, single ghosts were exposed to a sharply bounded intensive

beam of light in such a manner that in each case only one half of the ghost was bleached. By microscopic measurements it was studied whether fluorescent material would diffuse from the unbleached part of the membrane into the bleached part and vice versa. Within the measuring time of 20 min at room temperature no significant degree of such a diffusion could be detected. In order to evaluate the experimental data quantitatively, the diffusion equation for a spherical surface was solved, and the obtained solution was integrated over the hemispheres. A value of $3 \cdot 10^{-12}$ cm^2/s was derived from the experimental data as the upper limit of the diffusion coefficient of fluorescein isothiocyanate-labelled compounds in the erythrocyte membrane at 20°—23°C.

G. Gárdos

From the International Literature of Haematology

Acta Haematologica (Basel) **51** (1974) No. 1

Myeloid cell actinomycin binding in human myeloid leukaemia. *Pileri, A., Masera, P., Garbarino, G., Hulin, N.* (Division of Haematology, Medical Clinic, University of Torino, 10126 Torino, Italy), p. 1

Secondary anemia (XV) and reticuloendothelial uptake in cancer. *Reizenstein, P., Gheorghescu, B.* (Section of Hematology, Karolinska Sjukhuset, S-104 01 Stockholm 60, Sweden), p. 9

Synthese von Hämoglobin, RNS and DNS bei hämolytischer Anämie, Thalassämie und akuter Blutungsanämie. *Müller, D., Boll, M., Hahn, E.* (Stadtkrankenhaus Hof, Medizinische Klinik, D-8670 (Hof/Saale, BRD), p. 19

Lipid peroxidation in erythrocytes. Supravital staining of peroxidised cells by crystal violet. *Tudhope, G. R., Hopkins, J.* (Department of Pharmacology and Therapeutics, University of Dundee, Dundee DD1 4HB, Scotland), p. 29

Abnormal factor X (factor X Friuli) coagulation disorder. The heterozygote population. A study of 57 subjects. *Girolami, A., Brunetti, A., Bareggi, G., Cella, G.* (Istituto di Semeiotica Medica, Padova, Italy), p. 40

Hereditary elliptocytosis associated with pernicious anaemia. *Ghosh, M. L.* (Department of Haematology, District General Hospital, Barnsley, Yorkshire, England), p. 51

Purpura characterised by thrombasthenia associated with alterations of blood lipids. *del Principe, D., Ballati, G., Castro, M., Diglio, G., Giardini, O.* (Clinica Pediatrica dell'Università di Roma, Rome, Italy), p. 55

Acta Haematologica (Basel) **51** (1974) No. 2

Rosette-forming lymphocytes in normal and patients with malignant lymphomas. *Cohnen, G., Augener, W., Buka, A., Brittinger, G.* (Medizinische Klinik, D-43 Essen, BRD), p. 65

PHA response of blood and lymph node lymphocytes in vitro in malignant lymphomas. *Navone, R., Stramignoni, A.* (I. Istituto di Anatomia e Istologia Patologica dell'Università, I-10126 Torino, Italy), p. 76

A study of lymphocytic β-glucuronidase in various benign and malignant lymphatic processes. *Woessner, S., Millá, F., Rozman, C.* (Hospital Clinico y Provincial, Barcelona, Spain), p. 84

Anomalies immunitaires au cours des splénomégalies myéloïdes avec myélosclérose. *Boivin, P., Bernard, J.-F., Hakim, J. Wroclans, M.* (Hôpital Beaujon, F-92110 Clichy, France), p. 91

Capacity of rat haemopoietic colony-forming units to produce differentiated progeny. *Dunn, C. D. R.* (Department of Haematology, The Welsh National School of Medicine, Cardiff, CF4 4XW Wales), p. 101

Distribution of colony-forming cells in mouse bone marrow. *Svoboda, V.* (Institute of Hygiene and Epidemiology, Department of Radiation Hygiene, 10042 Prague 10, Czechoslovakia), p. 113

Concurrent infectious mononucleosis and acute myelocytic leukemia. *Langenhuysen, M. M. A. C.* (Division of Hematology, Department of Medicine, University Hospital, Groningen, The Netherlands), p. 121

Acta Haematologica (Basel) **51** (1974) No. 3

Stimulation and reactivity of leukaemic cells in acute myeloid leukaemia. *Pegrum, G. D., Evans, C. A., Middleton, V. L.* (Charing Cross Hospital, London W6, England), p. 129

Poly(A)-containing RNA molecules in electrophoretically separated fractions of rapidly labeled nuclear RNA from unstimulated and PHA-stimulated human lymphocytes. *Torelli, U., Torelli, G.* (Istituto di Patologia Speciale Medica, 41100 Modena, Italy), p. 140

Site of action of desferrioxamine in removing iron in normal and pathological conditions. *Bobeck-Rutsaert, M. M. J. C., Kelder, A. M. op Den, Wiltink, W. F., Eijk, H. G. Van, Leijnse, B.* (Medical Faculty, Erasmus University, Rotterdam 3002, The Netherlands), p. 151

Nature of the antigammaglobulin activity in cryoglobulinemic disorders. *Balestrieri, G., Invernizzi, F., Consogno, G., Di S. Secondo, V. R., Tincani, A., Zanussi, C.* (Institute of Medical Pathology II, University of Milan, I-20123 Milan, Italy), p. 159

Origin, morphologic and functional characteristics of a new lymphoid cell type in irradiated mouse bone marrow. *Haot, J., Betz, E. H., Simar, L. J., Revesz, L.* (Laboratoire d'Anatomie Pathologique, Université de Liège, B-4000 Liège, Belgium), p. 170

The γ-chain in a Ghanian adult, homozygous for hereditary persistence of foetal haemoglobin. *Kamuzora, H., Ringelhann, B., Konotey-Ahulu, F. I. D., Lehmann, H. Lorkin, P. A.* (Reprint request: Prof. H. Lehmann, MRC Abnormal Haemoglobin Unit, University Department of Biochemistry, Cambridge CB2, 2QR, England), p. 179

Homozygous $\beta\delta$-thalassaemia. Description of a case and review of the literature. *Tsistrakis, G. A., Amarantos, S. P., Konkouris, L. L.* (Department of Haematology, Medical Clinic B., University of Thessaloniki, Thessaloniki, Greece), p. 185

Acta Haematologica (Basel) **51** (1974) No. 4

Binding of folic acid to serum proteins. III. The effect of pernicious anaemia. *Markkanen, T., Himanen, P., Pajula, R.-L.* (Vanha Littoistentie 50, 20520 Turku 52, Finland), p. 193

Folate binding in animal plasma. *Mantzos, J. D., Alevizou-Terzaki, V., Gyftaki, E.* (Department of Clinical Therapeutics, University of Athens, Alexandra Hospital, Athens, Greece), p. 204

The relevance of immune reactions in acute favism. *Fiorelli, G., Podda, M., Corrias, A, Fargion, S.* (Istituto di Patologia Medica, 20122 Milano, Italy), p. 211

Turnover of lysozyme-positive monocytes in normal rat blood. *Syrén, E.* (Department of Pathology, University of Helsinki, 00290 Helsinki 29, Finland), p. 219

Einfluß der neonatalen Thymektomie auf die virale Leukämogenese der Maus. *Rudolph, M., Fey, F.* (Zentralinstitut für Krebsforschung der Akademie der Wissenschaften der DDR, Experimenteller Bereich, DDR-1115 Berlin-Buch), p. 227

Globin chain synthesis in sickle cell trait under conditions of folate antagonism. *Honig, G. R., Mason, R. G., Vida, L. N.* (Department of Pediatrics, The Abraham Lincoln School of Medicine, Chicago, Ill. 60612), p. 236

Glucose-6-phosphate dehydrogenase Toulouse. A new variant with marked instability and severe deficiency discovered in a family of Mediterranean ancestry. *Vergnes, H., Yoshida, A., Gourdin, D., Gherardi, M., Biermé, R., Ruffié, J.* (Laboratoire d'Enzymologie, Centre d'Hémotypologie, CHU Purpan, F-31300 Toulouse, France), p. 240

First report of Hb E in Italy. *Ricco, G., Gallo, E., Pugliatti, L., Pich, P. G., Mazza, U.* (Istituto di Patologia Speciale Medica, 10126 Torino, Italy), p. 250

Acta Haematologica (Basel) **51** (1974) No. 5

Thrombocythaemia. Familial occurrence and transition into blastic crisis. *Fickers, M., Speck, B.* (Department of Haematology, J. A. Cohen Institute of Radiopathology and Radiation Protection, University Medical Centre, Leiden, The Netherlands), p. 257

The influence of repeated and prolonged stimulation on the PHA-response of lymphocytes in Hodgkin's disease. *Ippoliti,*

G., Marini, G., Ascari, E., Casirola, G. (Clinica Medica Generale, Policlinico, Pavia, Italy), p. 266

Enhanced uptake of anti-Rh_0 coated red cells by cultured human monocytes. *Ohta, H., Shimizu, K.* (First Department of Internal Medicine, Nagoya University School of Medicine, Showa-ku, Nagoya, Japan), p. 270

Modification des plaquettes sanguines au cours des accidents de décompression. *Stoltz, J. F., Broussolle, B., Hyacinthe, R., Alexandre, P., Mainart, G., Larcan, A., Streiff, F.* (Centre Régional de Transfusion Sanguine, F-54000 Nancy, France), p. 275

Lysozyme-negative, peroxidase-positive mononuclear cells: A new kinetically distinct cell population in normal rat blood. *Syrén, E.* (Department of Pathology, University of Helsinki, 00290 Helsinki 29, Finland), p. 282

Splenic feedback in red cell regeneration. *Iyengar, B., Chandra, K.* (Department of Pathology, Maulana Azad Medical College, New Delhi 110003, India), p. 290

Pathogenesis of anemia associated with *Mycoplasma pneumoniae. Fiala, M., Myhre, B. A., Chinh, L. T., Territo, M., Edgington, T. S., Kattlove, H.* (Harbor General Hospital, Torrance, Calif. 90509), p. 297

'Nonsecretory' multiple myeloma. Report of a case. *Indiveri, F., Barabino, A., Santolini, M. E., Santolini, B.* (Istituto Scientifico di Medicina Interna, Genova, Italy), p. 302

Glucose-6-phosphate dehydrogenase Jackson. A new variant associated with hemolytic anemia. *Thigpen, J. T., Steinberg, M. H., Beutler, E., Gillespie, G. T., Jr., Dreiling, B. J., Morrison, F. S.* (Division of Hematology, University of Mississippi, School of Medicine, Hematology Research Laboratory, Jackson VA Center, Jackson, Miss.), p. 310

Hemoglobin S-Gα Georgia disease: A case report. *Wrightstone, R. N., Hubbard, M., Huisman, T. H. J.* (Laboratory of Protein Chemistry and Comprehensive Sickle Cell Center, Department of Medical Technology, Medical College of Georgia, Augusta, Ga. 30902), p. 315

Acta Haematologica (Basel) **51** (1974) No. 6

Fibrinogen/fibrin degradation products and factor XIII. *Miloszewski, K., Sheltawy, M. J., Losowsky, M. S.* (Department of Medicine, St. James's Hospital, Leeds LS9 7TF, Yorkshire, England), p. 321

Haemostatic defects in myelofibrosis. *Papayannis, A. G., Stathakis, N. E., Economopoulos, T. C., Arapakis, G., Gardikas, C.* (Reprint requests from: C. Gardikas, Evangelismos Hospital, Athens 140, Greece), p. 331

Red cell life span in sickle cell trait. *Barbedo, M. M., McCurdy, P. R.* (General Hospital, Washington, D. C. 20003), p. 339

Wirkung von kombinierter neonataler Thymektomie und Splenektomie auf die virale Leukamogenese der Maus. *Rudolph, M., Frey, F.* (Zentralinstitut für Krebsforschung der AdW, Bereich Experimentelle Krebsforschung, DDR-1115 Berlin-Buch), p. 344

Structure of haemoglobin Wien β130 (H8) tyrosine-aspartic acid; an unstable haemoglobin variant. *Lorkin, P. A., Pietschmann, H., Braunsteiner, H., Lehmann, H.* (Reprint requests from: H. Lehmann, MRC Abnormal Haemoglobin Unit, Department of Biochemistry, Addenbrooke's Hospital, Cambridge CB2 2QR, England), p. 351

Normal factor VIII antigen level in combined congenital deficiency of factor V and factor VIII. *Girolami, A., Bareggi, G.* (Istituto di Semeiotica Medica, Padua, Italia), p. 362

Blood (New York) **43** (1974) No. 1

Cell-mediated immunity in acute nonlymphocytic leukemia: Relationship to host factors, therapy, and prognosis. *Greene, W. H., Schimpff, S. C., Wiernik, P. H.* (Medical Oncology Section of the Baltimore Cancer Research Center, National Cancer Institute, Baltimore, Md. 21211), p. 1

Evidence for the clonal origin of chronic myeloid leukemia from a sex chromosome mosaic: Clinical, cytogenetic, and marrow culture studies. *Moore, M. A. S., Ekert, H., Fitzgerald, M. G., Carmichael, A.* (Cancer Research Unit, Walter and Eliza Hall

Institute, Royal Melbourne Hospital, Victoria, Australia), p. 15

The effect of neutropenia on the cell cycle of granulocyte precursors in an in vivo culture system. *Niskanen, E., Jr., Tyler, W. S., Symann, M., Stohlman, F., Jr. Howard, D.* (Department of Medicine, St. Elizabeth's Hospital, Boston, Mass. 02135), p. 23

Induction of sustained hemopoiesis in fatty marrow. *Tavassoli, M., Maniatis, A., Crosby, W. H.* (L. C. Jacobson Blood Center, Scripps Clinic and Research Foundation, La Jolla, Calif. 92037), p. 33

Effects of several androgens and steroid metabolites on erythropoietin production in the isolated perfused dog kidney. *Paulo, L. G., Fink, G. D., Roh, B. L., Fisher, J. W.* (Department of Pharmacology, Tulane University School of Medicine, New Orleans, La. 70112), p. 39

Oxygen transport by the red cell: Effects of chronic hemodialysis. *Miller, M. E., Zaroulis, Ch. G., Valeri, C. R., Stohlman, F., Jr.* (Department of Medicine, St. Elizabeth's Hospital, Boston, Mass. 02135), p. 49

Inhibition of hemoglobin synthesis by cyanate in vitro. *Alter, B. P., Kan, Y. W., Nathan, D. G.* (Division of Hematology of the Department of Medicine, Children's Hospital Medical Center, Boston, Mass. 02115), p. 57

Toxic effects of high-dose cyanate administration in rodents. *Alter, B. P., Kan, Y. W., Nathan, D. G.* (Division of Hematology of the Department of Medicine, Children's Hospital Medical Center, Boston, Mass. 02115), p. 69

Hemoglobin $Lepore_{Boston}$ in two Iranian families. *Rahbar, S., Golban-Moghadam, N., Saoodi, H.* (Department of Immunology, and the Department Biophysics, University of Tehran, Tehran, Iran), p. 79

Protein–quinone interaction: In vitro induction of indirect antiglobulin reactions with methyldopa. *Gottlieb, A. J., Wurzel, H. A.* (Department of Medicine, Section of Hematology, Pepper Laboratories of the University of Pennsylvania School of Medicine, Philadelphia, Pa. 19104), p. 85

Regulatory mechanism of glutathione reductase activity in human red cells. *Yawata, Y., Tanaka, K. R.* (Department of Medicine, University of Minnesota Medical School, Minneapolis, Minn. 55455), p. 99

Megakaryocytopoiesis in experimental iron deficiency anemia. *Choi, S. I., Simone, J. V., Jackson, C. W.* (Laboratory of Hematology, St. Jude Children's Research Hospital, Memphis, Tenn. 38101), p. 111

Effect of storage on sulfhydryl and disulfide groups of human platelets. *Ando, Y., Steiner, M., Baldini, M. G.* (Division of Hematologic Research, The Memorial Hospital, Pawtucket, R. I. 02860), p. 121

A simple method for freezing human platelets using 6% dimethylsulfoxide and storage at −80°C. *Valeri, C. R., Feingold, H., Marchionni, L. D.* (Naval Blood Research Laboratory, Chelsea, Mass. 02150), p. 131

Detection of myeloma cells in the urine sediment. *Pringle, J. P., Graham, R. C., Bernier, G. M.* (Department of Medicine, University Hospitals of Cleveland, Cleveland, Ohio 44106), p. 137

Blood (New York) **43** (1974) No. 2

Allogeneic marrow grafting for treatment of aplastic anemia. *Storb, R., Thomas, E. D., Buckner, C. D., Clift, R. A., Johnson F. L., Fefer, A., Glucksberg, H., Giblett, E. R., Lerner, K. G., Neiman, P.* (Division of Oncology, Department of Medicine, University of Washington School of Medicine, Seattle, Wash. 98195), p. 157

Potential for prolonged disease-free survival following combination chemotherapy of non-Hodgkin's lymphoma. *Schein, Ph. S., Chabner, B. A., Canellos, G. P., Young, R. C., Berard, C., DeVita, V. T.* (Medicine Branch and Laboratory of Pathology, National Cancer Institute, Bethesda, Md. 20014), p. 181

Macroglobulinemia in a child with acute leukemia. *Čejka, J., Bollinger, R. O., Schuit, H. R. E., Lusher, J. M., Chang, Ch. H., Zuelzer, W. W.* (The Children's Hospital, The Child Research Center of Michigan, Detroit, Mich. 48201), p. 191

Granulocyte function in the Chediak-Higashi syndrome of mice. *Gallin, J. I., Bujak, J. S., Patten, E., Wolff, Sh. M.* (Laboratory of Clinical Investigation,

National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Md. 20014), p. 201

Effects of anticoagulants and storage on granulocyte function in bank blood. *McCullough, J., Carter, S. J., Quie, P. G.* (Departments of Laboratory Medicine and Pediatrics, University of Minnesota Medical School, Minneapolis, Minn. 55455), p. 207

Familial thrombosis due to antithrombin III deficiency. *Marciniak, E., Farley, C. H., DeSimone, Ph.* (Department of Medicine, University of Kentucky Medical Center, Lexington, Ky. 40506), p. 219

Paroxysmal nocturnal hemoglobinuria with elevated fetal hemoglobin. *Rassiga-Pidot, A. L., Cornwell, G. G. III, McIntyre, O. R.* (Department of Internal Medicine, Dartmouth-Hitchcock Medical Center, Hanover, N. H. 03755), p. 233

An elution procedure for visualization of adult hemoglobins in human blood smears. *Kabat, D.* (Department of Biochemistry, University of Oregon Medical School, Portland, Ore. 97201), p. 239

Intranuclear hemoglobin in erythroblasts of β-thalassemia. *Yataganas, X., Gahrton, G., Thorell, B.* (Institute for Medical Cell Research and Genetics, Medical Nobel Institute, Karolinska Institutet, Stockholm, Sweden), p. 243

Homozygous state for Hb Constant Spring (Slow-moving Hb X components). *Luan Eng Lie-Injo, Ganesan, J., Clegg, J. B., Weatherall, D. J.* (University of California International Center for Medical Research (UC ICMR), San Francisco, Calif. 94143), p. 251

Hemoglobin Rush [β 101 (G3) glutamine]: A new unstable hemoglobin causing mild hemolytic anemia. *Adams, J. G. III., Winter, W. P., Tausk, K., Heller, P.* (Veterans Administration West Side Hospital, Chicago, Ill. 60680), p. 261

G-6-PD Manchester: A new variant associated with chronic nonspherocytic hemolytic anemia. *Milner, G., Delamore, I. W., Yoshida, A.* (Department of Clinical Haematology, Manchester Royal Infirmary, Manchester, England), p. 271

Effect of cyanate on erythrocyte deformability. *Durocher, J. R., Glader, B. E., Gaines, L. T., Conrad, M. E.* (Department of Hematology, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D. C. 20012), p. 277

Decreased glutathione peroxidase activity secondary to severe iron deficiency: A possible mechanism responsible for the shortened life span of the iron-deficient red cell. *Rodvien, R., Gillum, A., Weintraub, L. R.* (Hematology Research Laboratory, University Hospital, Boston University Medical Center, Boston, Mass. 02118), p. 281

Erythrocyte coproporphyrin and protoporphyrin in ethanol-induced sideroblastic erythropoiesis. *Ali, M. A. M., Sweeney, G.* (Department of Pathology and Medicine, McMaster University, Hamilton Civic Hospitals, Hamilton, Ontario, Canada), p. 291

Hypothesis: Changes in the O_2 dissociation curve and sickling; A general formulation and therapeutic strategy. *Beutler, E.* (Division of Medicine, City of Hope Center, Duarte, Calif. 91010), p. 297

Blood (New York) **43** (1974) No. 3

The plasminogen activator of vampire bat saliva. *Cartwright, T.* (Nuffield Institute of Comparative Medicine, Zoological Society of London, London N.W.1, England), p. 317

Factor XIII deficiency: A genetic study of two affected kindreds in Finland. *McDonagh, J., McDonagh, R. P., Myllylä, G., Ikkala, E.* (University of North Carolina School of Medicine, Chapel Hill, N. C. 27514), p. 327

Chronic granulocytic leukemia (CGL) during the course of chronic lymphocytic leukemia (CLL): Correlation of blood, marrow, and spleen morphology and cytogenetics. *Whang-Peng, J., Gralnick, H. R., Johnson, R. E., Lee, E. C., Lear, A.* (National Cancer Institute, National Institutes of Health, Bethesda, Md. 20014), p. 333

Juvenile "chronic granulocytic" leukemia: A panmyelopathy with prominent monocytic involvement and circulating monocyte colony-forming cells. *Altman, A. J., Palmer, C. G., Baehner, R. L.* (Division of Pediatric Hematology, James Whitcomb Riley Hospital for Children, Indiana

University School of Medicine, Indianapolis, Ind. 46202), p. 341

Androgenic hormones and human granulopoiesis in vitro. *Rosenblum, A. L., Carbone, P. P.* (Medical Oncology Area, National Cancer Institute, Bethesda, Md. 20014), p. 351

In vitro growth of granulocytic colonies from circulating cells in human cord blood. *Knudtzon, S.* (Department of Medicine, Finsen Institute, Copenhagen, Denmark), p. 357

Effect of chloramphenicol and thiamphenicol on the in vitro colony-forming cell. *Ratzan, J. R., Moore, M. A. S., Yunis, A. A.* (Department of Medicine, University of Miami School of Medicine, Miami, Fla. 33152), p. 363

The intravascular survival of neutrophils labeled in vivo. *Vincent, P. C., Chanana, A. D., Cronkite, E. P., Joel, D. D.* (Medical Research Center, Brookhaven National Laboratory, Upton, N. Y. 11973), p. 371

Cyclical granulopoiesis in chronic granulocytic leukemia: A simulation study. *Wheldon, T. E., Kirk, J., Finlay, H. M.* (Western Regional Hospital Board, Department of Clinical Physics, and Bio-Engineering, Glasgow, Scotland), p. 379

Lymphoid nodules of bone marrow: Normal and abnormal. *Rywlin, A. M., Ortega, R. S., Dominguez, C. J.* (Department of Pathology and Laboratory Medicine, Mount Sinai Medical Center, Miami Beach, Fla. 33140), p. 389

The effect of methotrexate on transformation and mitosis of normal human blood lymphocytes in vitro. *Rozenszajn, L. A., Radnay, J.* (Clinical Laboratories, Meir Hospital, Kfar Saba, Israel), p. 401

Concentration of fetal red blood cells from a mixture of maternal and fetal blood by anti-i serum. An aid to prenatal diagnosis of hemoglobinopathies. *Kan, Y. W., Nathan, D. G., Cividalli, G., Crookston, M. C.* (Division of Hematology of the Department of Medicine, Children's Hospital Medical Center, Department of Pediatrics, Harvard Medical School, Boston, Mass. 02115), p. 411

Hemoglobin affinity for oxygen in chronic renal disease: The effect of hemodialysis. *Lichtman, M. A., Murphy, M. S., Byer, B. J., Freeman, R. B.* (University of Rochester School of Medicine and Dentistry, Rochester, N. Y. 14642), p. 417

Hepatic erythropoietin production in the lead-poisoned rat. *Schooley, J. C., Mahlmann, L. J.* (Lawrence Berkeley Laboratory, Donner Laboratory, University of California, Berkeley, Calif. 94720), p. 425

Fetal rat utilization of ^{55}Fe absorbed by fetal intestine from swallowed amniotic fluid. *Orlic, D., Lev, R., Rosenthal, W. S.* (Departments of Anatomy, Pathology and Medicine, New York Medical College, Valhalla, N. Y. 10595), p. 429

The determination of erythrocyte folate concentration using a two-phase ligand-binding radioassay. *Rothenberg, S. P., da Costa, M., Lawson, J., Rosenberg, Z.* (Division of Hematology, Department of Medicine, New York Medical College, Metropolitan Hospital Medical Center, New York, N. Y. 10029), p. 437

N-acetylneuraminic acid deficiency in erythrocyte membranes: Biophysical and biochemical correlates. *Chien, S., Cooper, G. W., Jr., Jan, K., Miller, L. H., Howe, C., Usami, Sh., Lalezari, P.* (Departments of Physiology, Anatomy, and Microbiology, Columbia University, New York, N. Y. 10031), p. 445

Blood (New York) **43** (1974) No. 4

Posthepatitic severe aplastic anemia. An indication for early bone marrow transplantation. *Camitta, B. M., Nathan, D. G., Forman, E. N., Parkman, R., Rappeport, J. M., Orellana, T. D.* (Department of Medicine, Division of Hematology, Children's Hospital Medical Center, Harvard Medical School, Boston, Mass. 02115), p. 473

MU-chain disease in an African patient. *Bonhomme, J., Seligmann, M., Mihaesco, C., Clauvel, J. P., Danon, F., Brouet, J. C., Bouvry, P., Martine, J., Clerc, M.* (Hôpital Saint-Louis, Paris, France), p. 485

A monoclonal IgM with antibodylike specificity for phospholipids in a patient with lymphoma. *Cooper, M. R., Cohen, H. J., Huntley, C. C., Waite, B. M., Spees, L., Spurr, C. L.* (Departments of Medicine, Pediatrics and Biochemistry, Bowman Gray School of Medicine, Wake

Forest University, Winston-Salem, N. C. 27103), p. 493

Plasma cell dyscrasia associated with the production of incomplete (? deleted) IgG molecules, gamma heavy chains, and free lambda chains containing carbohydrate: Description of the first case. *Isobe, T., Osserman, E. F.* (Department of Medicine and Institute of Cancer Research, College of Physicians and Surgeons, Columbia University, New York, N. Y. 10032), p. 505

Hemoglobin Duarte: ($\alpha_2\beta_2^{62(E6)Ala\rightarrow Pro}$): A new unstable hemoglobin with increased oxygen affinity. *Beutler, E., Lang, A., Lehmann, H.* (Division of Hope Medical Center, Duarte, Calif. 91010), p. 527

Electrophoretic and kinetic studies of mutant erythrocyte pyruvate kinases. *Nakashma, K., Miwa, Sh., Oda, S., Tanaka, T. Imamura, K., Nishina, T.* (Department of Internal Medicine, Yamaguchi University School of Medicine, Ube, Yamaguchi 755, Japan), p. 537

The use of ^{125}I as a membrane protein label for erythrocyte survival studies. *Weintraub, M., Gerson, K., Silber, R.* (Department of Medicine, New York University Medical Center, New York, N. Y. 10016), p. 549

Trisomy 8 in acute myeloblastic leukemia and sideroachrestic anemia. *Jonasson, J., Gahrton, G., Lindsten, J., Simonsson-Lindemalm, C., Zech, L.* (Department of Clinical Genetics, Karolinska Hospital, Stockholm, Sweden), p. 557

Neutrophil and monocyte kinetics in a case of cyclic neutropenia. *Meuret, G., Fliedner, T. M.* (Department of Hematology and Oncology, Kantonsspital, CH-9006 St. Gallen, Switzerland), p. 565

Some properties of the circulating hemopoietic stem cells. *Gidáli, J., Fehér, I., Antal, S.* (Frédéric Joliot-Curie National Research Institute for Radiobiology and Radiohygiene, H-1221 Budapest, Hungary), p. 573

Ferritin in serum: Diagnosis of iron deficiency and iron overload in infants and children. *Siimes, M. A., Addiego, J. E., Jr., Dallman, P. R.* (Department of Pediatrics, University of California-San Francisco, San Francisco, Calif. 94143), p. 581

Separation of megakaryocytes from mouse bone marrow by velocity sedimentation. *Nakeff, A., Maat, B.* (Section of Cancer Biology, Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, Mo. 63110), p. 591

Platelet coagulant activities and hemostasis: A hypothesis. *Walsh, P. N.* (Specialized Center for Thrombosis Research, Department of Medicine, Temple University Health Sciences Center, Philadelphia, Pa. 19140), p. 597

Sickle hemoglobin: A specific radioimmunoassay. *Rowley, P. T., Doherty, R. A., Rosecrans, Ch., Cernichiari, E.* (University of Rochester School of Medicine, and Dentistry, Rochester, N. Y.), p. 607

Blood (New York) **43** (1974) No. 5

Degradation of bovine factor VIII by plasmin and trypsin. *Kirby, E. P., Martin, N., Marder, V. J.* (Department of Biochemistry, Temple University Health Sciences Center, Philadelphia, Pa. 19140), p. 629

Fletcher factor deficiency: Family study and detection. *Abildgaard, Ch. F., Harrison, J.* (University of California at Davis, Calif. 95616), p. 641

Hydrogen peroxide and platelet function. *Canaso, R. T., Rodvien, R., Scoon, K., Levine, P. H.* (New England Medical Center Hospital, Boston, Mass. 02111), p. 645

Synthesis of hemoglobin Abraham Lincoln (β32 Leu → Pro). *Honig, G. R., Mason, R. G., Vida, L. N., Shamsuddin, M.* (Department of Pediatrics, Abraham Lincoln School of Medicine, Chicago, Ill. 60612), p. 657

A scanning electron microscopic study of the spleen. *Weiss, L.* (Johns Hopkins University School of Medicine, Baltimore, Md. 21205), p. 665

The metabolism of transferrin-bound ^{111}In and ^{59}Fe in the rat. *Beamish, M. R., Brown, E. B.* (Washington, University, St. Louis, Mo. 63110), p. 693

A comparison of the behavior of ^{111}In and ^{59}Fe-labeled transferrin on incubation with human and rat reticulocytes. *Beamish, M. R., Brown, E. B.* (Washington University, St. Louis, Mo. 63110), p. 703

A new case of Mu heavy chain disease: Clinical and immunochemical studies. *Dammacco, F., Bonomo, L., Franklin, E. C.* (Clinica Medica II, University of Bari Medical School, Bari, Italy), p. 713

Acute leukemia following localized irradiation for carcinoma of the larynx. *Karchmer, R. K., Caldwell, G. G., Chin, T. D. Y.* (University of Utah Medical Center, Salt Lake City, Utah 84112), p. 721

The role of peroxidase in the bactericidal activity of human blood eosinophils. *Bujak, J. S., Root, R. K.* (University of Washington, Seattle, Wash. 98105), p. 727

The ingestion of IgG-sensitized erythrocytes by abnormal neutrophils. *Zipursky, A., Brown, E. J.* (Department of Pediatrics, McMaster University, Hamilton, Ontario, Canada), p. 737

Restrained adenyl cyclase in human neutrophils: Stimulation of cyclic adenosine 3':5'-monophosphate formation and adenyl cyclase activity by phagocytosis and prostaglandins. *Stolc, V.* (University of Pittsburgh School of Medicine, Department of Pathology, Pittsburgh, Pa. 15261), p. 743

Production of colony-stimulating factor by malignant leukocytes. *Golde, D. W., Rothman, B., Cline, M. J.* (Division of Hematology/Oncology, UCLA Center for the Health Sciences, Los Angeles, Calif. 90024), p. 749

Granulocyte transfusions in leukopenic dogs: In vivo and in vitro function of granulocytes obtained by continuous-flow filtration leukopheresis. *Debelak, K. M., Epstein, R. B., Andersen, B. R.* (Departments of Medicine and Microbiology, Abraham Lincoln School of Medicine, University of Illinois, Chicago, Ill. 60612), p. 757

Evidence against transferrin as a binder of either vitamin B_{12} or folic acid. *Jacob, E., Herbert, V.* (Columbia University College of Physicians and Surgeons, New York, N. Y. 10032), p. 767

Blood (New York) **43** (1974) No. 6

The effect of autologous serum on lymphocyte response to human leukemia cells. *Bryan, J. H., Johnson, G. E., Leventhal, B. G.* (University of North Carolina Chapel Hill, N. C.), p. 781

Comparison of normal and CLL lymphocyte surface Ig determinants using peroxidase-labeled antibodies. I. Detection and quantitation of light chain determinants. *Ternynck, T., Dighiero, G., Follezou, J., Binet, J.-L.* (Unité d'Immunocytochimie, Département de Biologie Moléculaire, Institut Pasteur, Paris, France), p. 789

Dysplastic platelets and circulating megakaryocytes in chronic myeloproliferative diseases. I. The platelets: Ultrastructure and peroxidase reaction. *Maldonado, J. E., Pintado, T., Pierre, R. V.* (Mayo Medical School, Mayo Clinic and Mayo Foundation, Rochester, Minn. 55901), p. 797

Dysplastic platelets and circulating megakaryocytes in chronic myeloproliferative diseases. II. Ultrastructure of circulating megakaryocytes. *Maldonado, J. E.* (Mayo Medical School, Mayo Clinic and Mayo Foundation, Rochester, Minn. 55901), p. 811

A syndrome of platelet-release abnormality and mild hemophilia. *Chesney, C., Colman, R.-W., Pechet, L.* (Harvard Medical School, Boston, Mass. 02115), p. 821

Platelet satellitism. *Kjeldsberg, C. R., Swanson, J.* (Division of Clinical Pathology, University of Utah Medical Center, Salt Lake City, Utah 84132), p. 831

Clonal origin of the Philadelphia chromosome from either the paternal or the maternal chromosome number 22. *Gahrton, G., Lindsten, J., Zech, L.* (Department of Internal Medicine, Huddinge Sjukhus, Karolinska Institutet, Stockholm, Sweden), p. 837

Parameters of marrow proliferative capacity *in vitro:* Detection of a sex difference in normal human granulopoiesis. *Rosenblum, A. L., Bull, J. M., Carbone, P. P.* (Division of Cancer Therapy, National Cancer Institute, Bethesda, Md. 20014), p. 841

Responsiveness of human granulocytic leukemic cells to colony-stimulating factor. *Metcalf, D., Moore, M. A. S., Sheridan, J. W., Spitzer, G.* (Cancer Research Unit, Walter and Eliza Hall Institute, Melbourne, Australia), p. 847

Sodium and potassium concentration and transmembrane fluxes in leukocytes. *Cividalli, G., Nathan, D. G.* (Reprint

requests: D. G. Nathan, Children's Hospital Medical Center, Boston, Mass. 02115), p. 861

Recurrent attacks of abdominal pain and fever with familial segmentation arrest of granulocytes. *Murros, J., Konttinen, A.* (First Department of Internal Medicine, University Hospital of Helsinki, Helsinki, Finland), p. 871

Interaction between rabbit erythroblast ferritin and normal plasma proteins. *Yamada, H., Gabuzda, T. G.* (First Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, Japan), p. 875

Cytochemical and radioautographic identification of cells induced to synthesize hemoglobin. *Rosse, C., Trotter, J. A.* (Department of Biological Structure, University of Washington School of Medicine, Seattle, Wash. 98195), p. 885

Ultrastructure of sickled deer erythrocytes. I. The typical crescent and holly leaf forms. *Simpson, C. F., Taylor, W. J.* (Department of Veterinary Sciences, University of Florida, Gainsville, Fla. 32611), p. 899

Ultrastructure of sickled deer erythrocytes. II. The matchstick cell. *Taylor, W. J., Simpson, C. F.* (Department of Medicine, College of Medicine, University of Florida, Gainsville, Fla. 32611), p. 907

The value of the serum vitamin B_{12} level in diagnosing B_{12} deficiency. *Pierce, H. I., Hillman, R. S.* (Department of Medicine, Division of Hematology, University of Washington School of Medicine, Seattle, Wash. 98195), p. 915

Blut (München) **29** (1974) No. 1

Blood component preparation in single plastic bags. *Schneider, W., Fröhlich, C., McCarty, L. J.* (German Red Cross Blood Transfusion Service, Hagen Institute, D-5800 Hagen, FRG), p. 1

Antikörper der Spezifitäten Anti-C^w/Anti-D. *Finke, M., Sachs, V., Mühlfeld, J.* (Blutspendezentrale, D-23 Kiel, BRD), p. 12

Isolierung, Charakterisierung und quantitative immunologische Bestimmung des Steroid-bindenden β-Globulins. *Bohn, H.* (Behringwerke AG, D-355 Marburg/Lahn, BRD), p. 17

Immunofluorescent identification of a human thymic specific antigen. *Ablin, R. J., Morris, A. J.* (Cook County Hospital, Chicago, Ill.), p. 32

Characteristics of macrophages in vitro derived from peripheral blood cells. *von Heyden, H. W., von Heyden, D.* (Department of Internal Medicine II, University of Tübingen, D-74 Tübingen, FRG), p. 37

Enterogene Methämoglobinämie bei heterozygoter NADH-Methämoglobin-Reduktase-Defizienz der Erythrozyten. *Schmidt, K., Faber, K., Heni, F.* (Medizinische Poliklinik der Universität Tübingen, 7400 Tübingen, BRD), p. 43

Fehlendes Chromosom Nr. 7 in der präleukämischen Phase einer Myeloblastenleukose bei einem Kind. *Kaufmann, U., Löffler, H., Foerster, W., Desaga, J. F., Koch, F.* (Zentrum für Kinderheilkunde, D-6300 Gießen, BRD), p. 50

Blut (München) **29** (1974) No. 2

Haemostatic defects in polycythaemia vera. *Stathakis, N. E., Papayannis, A. G., Arapakis, G., Gardikas, C.* (Professorial Medical Unit, Evangelismos Hospital, Athens 140, Greece), p. 77

Acute lymphocytic leukemia. Cytochemistry and ultrastructure. *Schmalzl, F., Huhn, D., Abbrederis, K., Braunsteiner, H.* (Department of Medicine, University of Innsbruck, A-6020 Innsbruck, Austria), p. 87

Die Wirkung von Tritium-Wasser auf die Entwicklung der fetalen Hämopoese der Ratte. *Haas, R. J., Schreml, W.* (Zentrum für Innere Medizin und Kinderheilkunde, Department für Pädiatrie, Universität Ulm, D-7900 Ulm/Donau, BRD), p. 96

Scanning electron microscopy of erythrocyte ghosts prepared with and without ATP addition. *Mirčevová, L.* (Institute of Hematology and Blood Transfusion, Prague 2, Czechoslovakia), p. 108

Occurrence of adenyl cyclase activity in human erythrocytes. *Kaiser, G., Quiring, K., Gauger, D., Palm, D., Becker, H. Schoeppe, W.* (Zentrum der Pharmakologie, Klinikum der Universität, D-6 Frankfurt/Main, BRD), p. 115

Osmotic behaviour of human red blood cells. Effect of non-ionic detergents.

Gaehtgens, P., Benner, K.-U. (Institute for Normal and Pathological Physiology, University of Cologne, D-5000 Cologne, FRG), p. 123

Dilution curve studies in prothrombin complex factors, deficiencies and abnormalities. *Girolami, A., Brunetti, A., De Marco, L., Fioretti, D.* (University of Padua Medical School, Institute of Semeiotica Medica, Padua, Italy), p. 134

On the diagnosis of rare paraproteins. *Schneider, W., Fröhlich, C., Glaßner, K., McCarty, L. J.* (German Red Cross Blood Transfusion Service, Hagen Institute, D-58 Hagen, FRG), p. 144

Blut (München) **29** (1974) No. 3

Some approaches to deciding HB Ag (Australia antigen) positivity by counter-immunoelectrophoresis. *Pintera, J., Vacl, J., Holland, P. V., Alter, H. J.* (Institute of Blood Transfusion and Hematology, 657 20 Brno, Czechoslovakia), p. 165

Die Wärmelysiszeit, eine neue in-vivo-Methode zur Beurteilung der Hämostase. *Sutor, H.* (Universitäts-Kinderklinik, D-78 Freiburg, BRD), p. 172

Die fortlaufende Messung der Plättchenaggregation ohne Zugabe von Aggregationsauslösern. *Jäger, W., Kutschera, J., Wendeberg, H., Kauschmann, R., Riese,, W., Pietsch, U., Berger, E., Bennert, C.* (Zentrum der Inneren Medizin der Johann-Wolfgang-Goethe-Universität, 6 Frankfurt/Main, BRD), p. 184

Akute medikamentös-allergische Thrombozytopenie durch Antazolin. *Gassel, W.-D., Schneider, D.* (Medizinische Universitäts-Poliklinik, D-355 Marburg/Lahn, BRD), p. 195

Red cell, plasma and whole blood volumes in organs of normal and hypersplenic rats. *Sebestik, V., Brabec, V.* (Institute of Hematology and Blood Transfusion, 128 20 Prague, 2 Czechoslovakia), p. 203

Electron microscopic study of lymphosarcoma cell leukemia. *Djaldetti, M., Landau, M., Mandel, E. M., Har-Zaav, L., Lewinski, U.* (Department of Medicine "B" and Hematology Clinic, Hasharon Hospital, Petah-Tiqva, Israel), p. 210

G/G translocation and chronic myelocytic leukaemia. *Bottura, C., Coutinho, V.* (Medical School of Ribeirao Preto, S. Paulo, Brasil), p. 216

The in-vitro inhibition of erythrocyte sickling by Biuret. *Photiades, D. P., Khalil, S. A. H., Osamo, N. O., Obi, J. O.* (Department of Physiology, Faculty of Medicine and Pharmacy, University of Benin, Benin City, Nigeria), p. 219

Blut (München) **29** (1974) No. 4

Schwangerschaft und Entbindung bei familiärem Morbus Glanzmann-Naegeli. *Vinazzer, H., Bergmann, H., Wolf, F.* (Blutgerinnungslaboratorium, Linz a. D., Österreich), p. 233

Factor VIII-related antigen in tissues detected by the indirect immunofluorescence technique. *Gruson, R., Rizza, Ch. R.* (I. Medizinische Abteilung, Marienkrankenhaus, 2000 Hamburg 76, BRD), p. 241

Die fortlaufende Messung der Plättchenaggregation ohne Zugabe von Aggregationsauslösern. II. Experimentelle Befunde und Prüfung von Aggregationshemmern. *Jäger, W., Kutschera, J., Wendeberg, H., Kauschmann, R., Riese, W., Pietsch, U., Berger, E., Bennert, Ch.* (Zentrum der Inneren Medizin, Johann-Wolfgang-Goethe-Universität Frankfurt/Main, Abteilung für Angiologie, 6 Frankfurt/Main 70, BRD), p. 251

Relationship between Ristocetin-induced platelet aggregation and factor VIII (activity and antigen) in v. Willebrand's disease. *Barbui, T., Battista, R., Dini, E.* (Division of Hematology, Regional Civil Hospital, Vicenza, Italy), p. 260

Normal granulocyte collection with a modified repetitive cycle filtration leukapheresis. *de Fliedner, V., Meuret, G., Senn, H.* (Medizinische Klinik C, Kantonsspital, CH-9006 St. Gallen, Switzerland), p. 265

Hemoglobin content and projection area of erythrocytes as indication of cell age. *Morselt, A. F. W., Tijmes, N. T.* (Histological Laboratory, University of Amsterdam, Amsterdam, The Netherlands), p. 277

Blut (München) **29** (1974) No. 5

Untersuchungen zur Frage der Aktivierung des Gerinnungssystem in Blutkonserven. *Barthels, M., Stangel, W., Poliwoda, H., Trobisch, H.* (Abteilung für Hämatologie, Department Innere Medizin, Medizinische Hochschule Hannover, D-3 Hannover, BRD), p. 289

Dichtergradienten-Zentrifugation menschlicher Blutplättchen. Enzymmuster und osmotische Resistenz einzelner Fraktionen. *Petschow, D., Friedel, R., Trautschold, I.* (Institut für Klinische Biochemie der Medizinischen Hochschule Hannover, D-3 Hannover, BRD), p. 297

Factor VIII immunological assay. An evaluation of several methods using whole plasma. *Girolami, A., Sticchi, A., Barbui, T., Bareggi, G.* (University of Padua Medical School, Institute of "Semeiotica Medica", Padova, Italy), p. 309

Untersuchungen zur Bedeutung des Peroxidase-Nachweises bei akuter myeloischer Leukämie. *Hennekeuser, H. H., Möbius, W.* (Medizinische Universitätsklinik, D-7800 Freiburg/Brsg., BRD), p. 317

Criteria for the differentiation of lymphoid cell lines. *v. Heyden, H. W., v. Heyden, D.* (Medical University Clinic, Section II, D-74 Tübingen, FRG), p. 323

Immunhistochemische Untersuchungen an Lymphozyten der Maus. Markierung mit Anti-B-Zell- und Anti-T-Zell-Globulin, *Huhn, D., Rodt, H., Thierfelder, S.* (I. Medizinische Klinik, Universität München, 8 München 2, BRD), p. 332

Die Zyklusabhängigkeit der zirkulierenden Zahl menschlicher Blutmastzellen (Blutbasophiler). Ein Beitrag zur Bestimmung des Ovulationszeitpunktes. *Mettler, L., Schirwani, D., Endreß, M., Parwaresch, M. R. R.* (Frauenklinik u. Hebammenanstalt der Universität Kiel, D-2300 Kiel, BRD), p. 344

Strontium-85 profile counting of spine in multiple myeloma. *Puranen, J., Salokannel, J., Timonen, T.* (Department of Surgery, University of Oulu, Oulu, Finland), p. 351

Das atypische Allel Fy^x: Untersuchungen einer Familie. *Sorgo, G.* (Institut für Gerichtliche Medizin der Universität Salzburg, A-5020 Salzburg, Austria), p. 357

Blut (München) **29** (1974) No. 6

Zum Verhalten des Erythropoetins bei aregeneratorischen Blutbildungsstörungen unter Therapie mit anabolen Steroiden. *Neumann, E., Honetz, N., Wurm, B.* (I. Medizinische Universitäts-Klinik Wien. A-1095 Wien, Austria), p. 373

Unterschiedliche Sauerstoffaffinität des Hämoglobins bei Anämien verschiedener Ätiologie. *Humpeler, E., Amor, H., Braunsteiner, H.* (Physiologisches Institut der Universität Innsbruck, A-6020 Inns, bruck Austria), p. 382

Congenital dyserythropoietic anemia, type II (Hempas). First five reported cases in Italy. *Barbui, T., Cazzavillan, M., Chisesi, T., Battista, R., Cartei, G., Dini, E.* (Regional Civil Hospital, Division of Hematology, Vicenza, Italy), p. 391

Calcium and potassium disturbances in acute leukemia. *Höcker, P., Reizenstein, P.* (Reprint requests: Dr. P. Reisenstein, Department of Medicine, Section of Hematology, Karolinska Hospital, Stockholm 60, Sweden), p. 398

Untersuchungen über die Möglichkeit der Übertragung von Toxoplasmen durch Bluttransfusionen. *Janitschke, K., Werner, H., Hasse, W.* (Robert-Koch-Institut, Laboratoriumsgruppe Medizinische Parasitologie, D-1 Berlin, BRD), p. 407

Production of antibodies specific for human thymus derived lymphocytes purified from antibodies crossreacting with colony-forming cells. *Rodt, H., Betzel, B., Brehm, G., Thierfelder, S.* (Abteilung Immunologie, Institut für Hämatologie, D-8000 München, BRD), p. 416

Standardmethoden für die Bestimmung des Erythrozyten- und Plasmavolumens. Bericht des Internationalen Komitees für Standardisierung in der Hämatologie (ICSH), p. 422

British Journal of Haematology (Oxford) **26** (1974) No. 1

Apti-haemophilic factor, normal and abnormal. *Bennett, B.* (Department of Medicine, University of Aberdeen, Foresterhill, Aberdeen AB9 2ZD, Scotland), p. 1

Leukaemic reticuloendotheliosis ('hairy' cell leukaemia): A distinct clinico-pathological entity. *Catovsky, D., Pettit, J. E., Galton, D. A. G., Spiers, A. S. D., Harrison, C. V.* (M. R. C. Leukaemia Unit, Royal Postgraduate Medical School, London, W12 0HS, England), p. 9

The B-lymphocyte nature of the hairy cell of leukaemic reticuloendotheliosis. *Catovsky, D., Pettit, J. E., Galetto, J., Okos, A., Galton, D. A. G.* (M. R. C. Leukaemia Unit, Royal Postgraduate Medical School, London W12 0HS, England), p. 29

Studies of the role of red cell membrane peroxidation in paroxysmal nocturnal haemoglobinuria (PNH). *Paniker, N. V., Arnold, A. B., Hartmann, R. C.* (Division of Hematology, Department of Medicine, Vanderbilt University School of Medicine and Hospital, Nashville, Tenn. 37232), p. 39

Production of paroxysmal nocturnal haemoglobinuria-like red cells by reducing and oxidizing agents. *Goldstein, B. D.* (Department of Medicine, New York University School of Medicine, New York, N. Y.), p. 49

Erythrocyte membrane vacuole formation in hereditary spherocytosis. *Schrier, S. L., Ben-Bassat, I., Bensch, K., Seeger, M., Junga, I.* (Stanford University School of Medicine, Stanford, Calif. 94305), p. 59

Metabolic studies on red cells from patients with chronic renal disease on haemodialysis. *Wallas, Ch. H.* (Division of Hematology, George Washington University Medical Center, Washington, D. C. 20037), p. 71

Effect of chloramphenicol on reticulocyte Δ-aminolaevulinic acid synthetase in rabbits. *Rosenberg, A., Marcus, O.* (Department of Medicine, Division of Hematology, Jewish General Hospital, Montreal 249, Quebec, Canada), p. 79

Red cell survival studies in patients with unstable haemoglobin disorders. *Bentley, S. A., Lewis, S. M., White, J. M.* (Department of Haematology, Royal Postgraduate Medical School Hammersmith Hospital, London W12 0HS, England), p. 85

The effect of elution on the reactivity of antibodies of the ABO system, including cross-reacting antibodies, as demonstrated by use of red cells of various subgroups of A, and group B. *Dodd, B. E., Lincoln, P. J.* (Department of Forensic Medicine, London Hospital Medical College, London EI 2AD, England), p. 93

Changes in megakaryocyte development following thrombocytopenia. *MacPherson, G. G.* (Sir William Dunn School of Pathology, University of Oxford, Oxford, England), p. 105

May-Hegglin anomaly: A defect in megakaryocyte fragmentation? *Godwin, H. A., Ginsburg, A. D.* (Department of Medicine, Baylor College of Medicine, Texas Medical Center, Houston, Texas 77025), p. 117

Acquired factor-IX inhibitor in a non-haemophilic patient with autoimmune disease. *Largo, R., Sigg, P., von Felten, A., Straub, P. W.* (Department of Medicine, Kantonsspital, University of Zürich, Zürich, Switzerland), p. 129

'Autosomal haemophilia': A variant of von Willebrand's disease. *Veltkamp, J. J., van Tilburg, N. H.* (Hemostasis and Thrombosis Research Unit, Academisch Ziekenhuis, Leiden, The Netherlands), p. 141

Bleeding time from incisions standardized by protruding skin fold method. *Stavem, P.* (Section of Haematology, Medical Department A, Rikshospitalet, Oslo, Norway), p. 153

British Journal of Haematology (Oxford) **26** (1974) No. 2

The role of transferrin in iron transport. *Aisen, P.* (Departments of Biophysics and Medicine, Albert Einstein College of Medicine, Bronx, N. Y. 10461), p. 159

In vitro modifications of red cell acetylcholinesterase activity. *Herz, F., Kaplan, E.* (Department of Pathology, Montefiore Hospital and Medical Center, Bronx, N. Y. 10467), p. 165

Elution correction in ^{51}Cr red cell survival studies. *Bentley, S. A., Glass, H. I., Lewis, S. M., Szur, L.* (Royal Postgraduate Medical School, London W12 0HS, England), p. 179

Urinary excretion of short-chain fatty acids in latent pernicious anaemia and related conditions. *Williams, D. L., Spray, G. H.* (Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford OX2 6HE, England), p. 185

Serum vitamin E levels with beta-thalassaemia major: Preliminary report. *Zannos-Mariolea, L., Tzortzatou, F., Dendaki-Svolaki, K., Katerellos, Ch., Kavallari, M., Matsaniotis, N.* (Pediatric Clinic of Athens University, St. Sophie's Children's Hospital, Goudi, Athens, Greece), p. 193

An electron microscopic study of the nuclear abnormalities in erythroblasts in beta-thalassaemia major. *Polliack, A., Yataganas, X., Thorell, B., Rachmilewitz, E. A.* (Department of Haematology, Hadassah University Hospital, P. O. Box 499, Jerusalem, Israel), p. 201

Corticosteroid therapy in Felty's syndrome and its effect on hypersplenic rats. *Robertson, J. H., Crozier, E. H., Hollinger, M.* (The Laboratories, Belfast City Hospital, Belfast BT9 7AD, Northern Ireland), p. 205

Rapid stem cell differentiation induced by 19-nortestosterone decanoate. *Gorshein, D., Hait, W. N., Besa, E. C., Jepson, J. H., Gardner, F. H.* (Presbyterian University of Pennsylvania Medical Center, Philadelphia, Pa. 19104), p. 215

Immunological responsiveness in idiopathic and drug-induced panmyelopathy: Discrepancy between sensitization with DNCB and haemocyanin. *Samson, J. P., De Gast, G. C., Nieweg, H. O.* (Division of Haematology, Department of Medicine, University of Groningen, Groningen, The Netherlands), p. 227

Regulation of human bone marrow leucopoiesis. *Golde, D. W., Cline, M. J.* (Division of Haematology and Oncology, UCLA Center for the Health Sciences, Los Angeles, Calif. 90024), p. 235

Changes in ^{32}P-content of phosphatidic acid and the phosphoinositides of rabbit platelets during aggregation induced by collagen or thrombin. *Lloyd, J. V., Mustard, J. F.* (Department of Pathology, Faculty of Medicine, McMaster University, Hamilton, Ontario, Canada), p. 243

Thrombin stimulated release of platelet microfibrils. *Webber, A. J., Budtz-Olsen, O. E.* (Department of Paramedical Studies, Queensland Institute of Technology, P. O. Box 246, North Quay, Qld. 4000, Australia), p. 255

The absorption of human factor VIII neutralizing antibody by factor VIII. *Biggs, R.* (Research Laboratory, Oxford Haemophilia Centre, Churchill Hospital, Headington, Oxford OX3 7LJ, England), p. 259

A new haemorrhagic disorder with defective fibrin stabilization and cryofibrinogenaemia. *Rosenberg, R. D., Colman, R. W., Lorand, L.* (Beth Israel Hospital, Boston, Mass. 02115), p. 269

Plasma fibrinogen and its fragments during streptokinase treatment. *Gaffney, P. J., Chesterman, C. N., Allington, M. J.* (National Institute for Biological Standards and Control, Holly Hill, London NW3 6RB, England), p. 285

Separation and partial characterization of a coagulant enzyme from *Bitis gabonica* venom. *Marsh, N. A., Whaler, B. C.* (Department of Physiology, Queen Elizabeth College, London W8 7AH, England), p. 295

British Journal of Haematology (Oxford) **26** (1974) No. 3

The megathrombocyte as an index of platelet production. *Karpatkin, S., Garg, S. K.* (Department of Medicine, New York University School of Medicine, New York, N. Y. 10016), p. 307

Jaundice and antibodies directed against factors VIII and IX in patients treated for haemophilia or Christmas disease in the United Kingdom. *Biggs, R.* (Oxford Haemophilia Centre, Churchill Hospital, Headington, Oxford OX3 7LJ, England), p. 313

Enzymatic basis for platelet aggregation and release: The significance of the "platelet atmosphere" and the relationship between platelet function and blood coagulation. *Ardlie, N. G., Han, P.* (Department of Clinical Science, John Curtin School of Medical Research, The Australian National University, P. O. Box 334, Canberra A. C. T. 2601, Australia), p. 331

Platelet aggregation and release by ADP and thrombin: Evidence for two separate effects of ADP on platelets, involvement of fibrinogen in release, and mechanism of inhibitory action of acetylsalicylic acid. *Han, P., Ardlie, N. G.* (Department of Clinical Science, John Curtin School of Medical Research, The Australian Na-

tional University P. O. Box 334, Canberra A. C. T. 2601, Australia), p. 357

The influence of pH, temperature, and calcium on platelet aggregation: Maintenance of environmental pH and platelet function for *in vitro* studies in plasma stored at 37°C. *Han, P., Ardlie, N.G.* (Department of Clinical Science, John Curtin School of Medical Research, The Australian National University, P. O. Box 334, Canberra A. C. T. 2601, Australia), p. 373

Trisomy-9 in the bone marrow of a patient with acute myelomonoblastic leukaemia. *Rutten, F. J., Hustinx, T. W. J., Scheres, J. M. J. C., Wagener, D. J. T.* (Department of Human Genetics, Faculteit der Geneeskunde, Katholieke Universiteit Nijmegen, Nijmegen, The Netherlands), p. 391

Identification of promonocytes and monocytoid precursors in acute leukaemia of adults: Ultrastructural and cytochemical observations. *Glick, A. D., Horn, R. G.* (Department of Pathology, Vanderbilt University School of Medicine, Nashville, Tenn. 37232), p. 395

Platelet antiheparin activity. Assay based on factor-Xa inactivation by heparin and antifactor Xa. *Walsh, P. N., Biggs, R., Gagnatelli, G.* (Specialized Center for Thrombosis Research, Temple University Health Sciences Center, Philadelphia, Penn. 19140), p. 405

Fibrinogen "Leuven", another genetic variant. *Verhaeghe, R., Verstraete, M., Vermylen, J., Vermylen, C.* (Laboratory of Blood Coagulation, AZ St. Rafael, 3000 Leuven, Belgium), p. 421

A variant of factor VIII related antigen. *Kernoff, P. B. A., Gruson, R., Rizza, C. R.* (University Department of Medicine, The Martin Wing, General Infirmary, Leeds LSI 3EX, England), p. 435

Erythroid cell proliferation in human bone marrow suspension cultures. *Wood, W. G.* (Division of Medical Genetics, Department of Medicine, University of Washington, Seattle, Wash. 98195), p. 441

Haemoglobin synthesis in suspension cultures of human bone marrow. *Wood, W. G.* (Division of Medical Genetics, Department of Medicine, University of Washington, Seattle, Wash. 98195), p. 451

Liver iron: Changes induced by cooking and acid-peptic digestion. *Naish, R., Kimber, C. L., Deller, D. J.* (Department of Medicine, University of Adelaide, Adelaide, South Australia 5000), p. 459

Investigation of the mechanism of false positive ^{125}I-labelled fibrinogen scans. *Kerrigan, G. N. W., Buchanan, M. R., Cade, J. F., Regoeczi, E., Hirsh, J.* (Department of Medical Oncology, St. Bartholomew's Hospital, London, E.C.1., England), p. 469

Haemoglobin Inkster (α_2 ^{85}aspartic acid → valine β_2) coexisting with β-thalassaemia in a Caucasian family. *Reed, R. E., Winter, W. P., Rucknagel, D. L.* (Departments of Internal Medicine, Veterans Administration Hospital and University of Michigan Medical School, Ann Arbor, Mich. 48105), p. 475

Leucocyte glycogen response in inflammatory exudates. *Scott, R. B., Cooper, V. W.* (Department of Medicine, Medical College of Virginia, Richmond, Va. 23298), p. 485

Coagulation activities in perfused organs: Regulation by addition of animal plasmas. *Dodds, W. J., Hoyer, L. W.* (Division of Laboratories and Research, New York State Department of Health, Albany, N. Y. 12201), p. 497

British Journal of Haematology (Oxford) **26** (1974) No. 4

Oxidative haemolysis and Heinz body haemolytic anaemia. *Gordon-Smith, E. C., White, J. M.* (Department of Haematology, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS, England), p. 513

A new variant of sickle-cell disease with high levels of foetal haemoglobin homogeneously distributed within red cells. *Makler, M. T., Berthrong, M., Locke, H. R., Dawson, D. L.* (Veterans Administration Hospital, Palo Alto, Calif. 94304), p. 519

Absence of haemoglobin A in an individual simultaneously heterozygous in the genes for hereditary persistence of foetal haemoglobin and β-thalassemia. *Fogarty, W. M., Jr., Vedvick, T. S., Itano, H. A.* (Labora-

tory of Molecular Biology, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Department of Pathology, University of California, San Diego, La Jolla, Calif. 92037), p. 527

The effect of various cytotoxic agents on the erythroid precursors in rat bone marrow. *Millar, J. L., Blackett, N. M.* (Biophysics Division, Institute of Cancer Research, Sutton, Surrey, Great Britain), p. 535

Vitamin E and oxidative damage by tryptophan metabolites in experimental enterogenous cyanosis and anaemia. *Westphal, R. G., O'Meara, T. M.* (College of Medicine, University of Vermont, Burlington, Vt. 05401), p. 543

Red-cell organic phosphates in patients with chronic renal failure on maintenance haemodialysis. *Chillar, R. K., Desforges, J. F.* (Tufts Hematology Laboratory Boston City Hospital, Boston, Mass. 02111), p. 549

A vitamin B_{12} binder with transcobalamin I characteristics synthesized and released by human granulocytes *in vitro*. *Rachmilewitz, B., Rachmilewitz, M., Gross, J.* (Department of Experimental Medicine and Cancer Research, Hebrew University Hadassah Medical School, P. O. B. 1172, Jerusalem, Israel), p. 557

Solubilized receptor for vitamin B_{12}—intrinsic factor complex from human intestine. *Katz, M., Cooper, B. A.* (Division of Hematology, Royal Victoria Hospital, Montreal 112, Quebec, Canada), p. 569

The separation of free and bound vitamin B_{12}. *Adams, J. F., McEwan, F. C.* (Medical Unit, Southern General Hospital, Glasgow G51 4IF, Scotland) p. 581

Studies of the anaemia in an acute rat leukaemia. *Harriss, E. B., Hoelzer, D.* (Abteilung für Klinische Physiologie der Universität Ulm, 79 Ulm, BRD), p. 593

Haematopoiesis measured by spleen colony and diffusion chamber techniques in mice treated with one or two injections of cyclophosphamide. *Bøyum, A., Carsten, A. L., Laerum, O. D.* (Norwegian Defence Research Establishment, Division for Toxicology, P. O. Box 25-N-2007, Kjeller, Norway), p. 605

Absence of B- and T-cell markers on acute lymphoblastic leukaemic cells and persistence of the T-cell marker on mitogen-transformed T-lymphocytes. *Collins, R. D., Smith, J. L., Clein, G. P., Barker, C. R.* (Department of Pathology, Vanderbilt Medical School, Nashville, Tenn.), p. 615

Delayed incorporation of (^{75}Se) selenomethionine into fibrinogen: Its effects upon kinetic studies of fibrinogen with (^{75}Se) selenomethionine in rabbits. *Seligsohn, U., Rapaport, S. I., Rostami, H. J.* (Department of Hematology, Chaim Sheba Medical Center, Tel Hashomer, Israel), p. 627

Platelet-aggregating activity in neuraminidase-treated human cryoprecipitates: Its correlation with factor-VIII-related antigen. *Vermylen, J., De Gaetano, G., Donati, M. B., Verstraete, M.* (Academisch Ziekenhuis St. Rafael, B-3000 Leuven, Belgium), p. 645

Microangiopathic haemolytic anaemia and experimental tumour-cell emboli. *Hilgard, P., Gordon-Smith, E. C.* (Universitätsklinik [Tumorforschung], Essen 1, BRD), p. 651

Studies on an inhibitor of plasminogen activators in human platelets. *Murray, J., Crawford, G. P. M., Ogston, D., Douglas, A. S.* (Department of Medicine, University of Aberdeen, Foresterhill, Aberdeen AB9 2ZD, Scotland), p. 661

Tissue localization and synthesis of factor-VIII-related antigen in the human foetus. *Tuddenham, E. G. D., Shearn, S. A. M., Peake, I. R., Giddings, J. C., Bloom, A. L.* (Department of Haematology, University Hospital of Wales, Wales, Cardiff), p. 669

British Journal of Haematology (Oxford) **27** (1974) No. 1

Hypersplenism: Mechanisms and management. *Jacob, H. S.* (Section of Haematology and Department of Medicine, University of Minnesota Medical School, Minneapolis, Minn. 55455), p. 1

Prolymphocytic leukaemia. *Galton, D. A. G., Goldman, J. M., Wiltshaw, E., Catovsky, D., Henry, K., Goldenberg, G. J.* (M. R. C. Leukaemia Unit, Royal Postgraduate Medical School, London W12 0HS, England), p. 7

Morphological criteria for prognostication of acute lymphoblastic leukaemia.

Pantazopoulos, N., Sinks, L. F. (Department of Pediatrics, Roswell Park Memorial Institute, Buffalo, N. Y. 14203), p. 25

Further evidence for the lymphocytic nature of leukaemic reticuloendotheliosis (Hairy-cell leukaemia). *Heak, H. L., De Man, J. C. H., Hijmans, W., Knapp, W., Speck, B.* (Department of Haematology, University of Leiden Medical Centre, Leiden, The Netherlands), p. 31

Mechanisms of resistance of human acute leukaemia cells to cytosine arabinoside. *Tattersall, M. H. N., Ganeshaguru, K., Hoffbrand, A. V.* (Department of Haematology, Royal Postgraduate Medical School, London W12 0HS, England), p. 39

Monocyte production of colony stimulating factor in familial cyclic neutropenia. *Moore, M. A. S., Spitzer, G., Metcalf, D., Penington, D. G.* (Walter and Eliza Hall Institute of Medical Research, Royal Melbourne Hospital P. O., Melbourne 3050, Australia), p. 47

Esterases in human neutrophil granulocytes: Evidence for their protease nature. *Rindler-Ludwig, R., Schmalzl, F., Braunsteiner, H.* (Department of Internal Medicine, University of Innsbruck, A-6020 Innsbruck, Austria), p. 57

Hyperviscosity syndrome in IgA multiple myeloma. *Tuddenham, E. G. D., Whittaker, J. A., Bradley, J., Lilleyman, J. S., James, D. R.* (Department of Haematology, Welsh National School of Medicine, Cardiff CF4 4XW, Wales), p. 65

Characterization of fibrin degradation products in patients on ancrod therapy: Comparison with fibrinogen derivatives produced by plasmin. *Prentice, C. R. M., Edgar, W., McNicol, G. P.* (University Department of Medicine, Royal Infirmary, Glasgow G4 0SF, Scotland), p. 77

Factor VIII of small molecular weight and its aggregation. *Austen, D. E. G.* (Oxford Haemophilia Centre, Churchill Hospital, Headington, Oxford, England), p. 89

Preparation, characterization, and activation of a highly purified factor XI: Evidence that a hitherto unrecognized plasma activity participates in the interaction of factors XI and XII. *Schiffman, S., Lee, P.* (USC Medical School, Los Angeles, Calif. 90033), p. 101

Kinetic evaluation of haemostasis during surgery and wound healing. *Slichter, S., Funk, D. D., Leandoer, L. E., Harker, L. A.* (King County Central Blood Bank, Terry and Madison, Seattle, Wash. 98104), p. 115

Platelet survival and platelet production in idiopathic thrombocytopenic purpura (ITP). *Branehög, I., Kutti, J., Weinfeld, A.* (Department of Medicine II, Sahlgren's Hospital, 413 45 Göteborg, Sweden), p. 127

Metabolic studies on the erythrocyte from patients with chronic renal disease on haemodialysis. II. ATP metabolism. *Wallas, Ch. H.* (Division of Hematology and Oncology, George Washington University Medical Center, Washington, D. C. 20037), p. 145

The synthesis of globin peptide chains in sickle-cell disease. *Sarup, B. M., White, J. M.* (Pathology Department, Postgraduate Institute of Medical Education and Research, Sector 12, Chandigarh, India), p. 153

The effect of some liver enzyme inhibitors on the hepatic inactivation of erythropoietin in mice. *Loeber, J. G., Bosch, E., Goudsmit, R., Kolk-Vegter, A. J.* (Department of Internal Medicine and Laboratory of Experimental Surgery, Bineengasthuis, University of Amsterdam, The Netherlands), p. 163

The anti-Rh_0(D) responses of immunized volunteers following spaced antigenic stimuli. *Gunson, H. H., Stratton, F., Phillips, P. K.* (Blood Transfusion Centre, Lancaster, England), p. 171

A serum haemolytic factor demonstrable at low ionic strength. *Riedler, G. F., Straub, P. W.* (Department of Medicine, Kantonsspital, University of Zurich, Zurich, Switzerland), p. 183

British Journal of Haematology (Oxford) **27** (1974) No. 2

Annotation. Anaemia in early infancy. *Oski, F. A., Stockman, J. A. III.* (Department of Pediatrics, State University of New York, Upstate Medical Center, Syracuse, N. Y. 13210), p. 195

Hereditary spherocytosis: The metabolism of erythrocytes in the peripheral blood and in the splenic pulp. *Mayman, D., Zipursky,*

A. (Department of Pediatrics, McMaster University, Hamilton, Ontario, Canada), p. 201

Transferrin iron, chelatable iron and ferritin in idiopathic haemochromatosis. *Beamish, M. R., Walker, R., Miller, F., Worwood, M., Jacobs, A., Williams, R., Corrigall, A.* (Department of Haematology, Welsh National School of Medicine, Cardiff CF4 4XW, Wales), p. 219

Characteristics of a novel serum vitamin-B_{12}-binding protein associated with hepatocellular carcinoma. *Waxman, S., Gilbert, H. S.* (Cancer Chemotherapy Laboratory, Division of Oncology, Department of Medicine, Mount Sinai School of Medicine, The City University of New York, New York, N. Y. 10029), p. 229

Functional immaturity of bone marrow bands and polymorphonuclear leucocytes. *Altman, A. J., Stossel, Th. P.* (Department of Pediatrics, University of Connecticut School of Medicine, Farmington, Conn. 06032), p. 241

Philadelphia-chromosome positive bone-marrow cells showing loss of the Y in males with chronic myeloid leukaemia. *Lawler, S. D., Lobb, D. S., Wiltshaw, E.* (Departments of Cytogenetics and Immunology, Division of Medicine, Royal Marsden Hospital, London SW3 6JJ, England), p. 247

Heparin, platelets and blood coagulation: Implications for low-dose heparin prophylactic regimens in venous thrombosis. *Han, P., Ardlie, N. G.* (Department of Clinical Science, The John Curtin School of Medical Research, The Australian National University, Canberra 2601, Australia), p. 253

Platelet-function studies in patients with glucose-6-phosphate dehydrogenase deficiency. *Schwartz, J. P., Cooperberg, A. A., Rosenberg, A.* (Hematology Service and Department of Medicine, Jewish General Hospital, Montreal, Canada), p. 273

The effect of calcium ions on the properties of factor IX and its activated form. *Chuang, T. F., Sargeant, R. B., Hougie, C.* (Department of Pathology, University of California, San Diego, La Jolla, Calif. 92037), p. 281

In vitro stimulation of chronic lymphocytic leukaemia lymphocytes. *Perera, D. J. B., Pegrum, G. D.* (Haematology Department, Charing Cross Hospital Medical School, London W6 8RF, England), p. 289

Cytotoxic ability of peripheral blood lymphocytes from patients with chronic lymphocytic leukaemia. *Perera, D. J. B., Pegrum, G. D.* (Haematology Department, Charing Cross Hospital Medical School, London W6 8RF, England), p. 297

Studies on the mechanism of cyanate inhibition of reticulocyte protein synthesis. *Freedman, M. L., Schiffman, F. J., Geraghty, M.* (Department of Medicine, New York University School of Medicine, New York, N. Y. 10016), p. 303

Haemoglobin F Port Royal ($\alpha_2^G\gamma_2^{125Glu \rightarrow Ala}$). *Brimhall, B., Vedvick, T. S., Jones, R. T.* (Department of Biochemistry, University of Oregon Medical School, Portland, Ore.), p. 313

Chemical heterogeneity of foetal haemoglobin in the Lepore haemoglobinopathy. *Efremov, G. D., Sadikario, A., Stojmirovic, E., Schroeder, W. A., Shelton, J. R., Shelton, J. B., Apell, G., Wilson, J. B., Brodie, A. R., Huisman, T. H. J.* (Division of Biochemistry, Faculty of Agriculture, University of Skopje, Skopje, Yugoslavia), p. 319

The effect of splenectomy on the haematological response to radiotherapy in Hodgkin's disease. *Begent, R. H. J., Wiltshaw, E.* (Department of Chemotherapy, Royal Marsden Hospital, London, S.W.3, England), p. 331

An association between aplastic anaemia and sideroblastic anaemia. *Geary, C. G., Dawson, D. W., Sitlani, P. K., Allison, H. A., Leyland, M. J.* (University Department of Clinical Haematology, Manchester Royal Infirmary, Manchester M13 9WL, England), p. 337

The syndrome of hepatitis and aplastic anaemia. *Ajlouni, K., Doeblin, Th. D.* (Medical Service/III, Veterans Administration Center, Wood, Wisc. 53193), p. 345

British Journal of Haematology (Oxford) **27** (1974) No. 3

Annotation. Infectious mononucleosis. *MacKinney, A. A., Cline, W. S.* (Veterans

Administration Hospital, Madison, Wisc.), p. 367

Treatment of acute myeloid leukaemia with daunorubicin, cytosine arabinoside, mercaptopurine, L-asparaginase, prednisone and thioguanine: Results of treatment, with five multiple-drug schedules. *Galton D. A. G.* (M.R.C. Working Party on Leukaemia in Adults, Medical Research Council, London W1N 4AL, England), p. 373

Factor VIII concentrates made in the United Kingdom and the treatment of haemophilia based on studies made during 1969—72. *Biggs, R.* (Oxford Haemophilia Centre, Churchill Hospital, Oxford OX3 7LJ, England), p. 391

Controlled trial of ancrod and streptokinase in the treatment of deep vein thrombosis of lower limb. *Tibbutt, D. A., Williams, E. W., Walker, M. W., Chesterman, C. N., Holt, J. M., Sharp, A. A.* (Nuffield Department of Clinical Medicine, The Radcliffe Infirmary, Oxford, England), p. 407

The effect of lead on total globin and α- and β-chain synthesis; *in vitro* and *in vivo*. *Piddington, S. K., White, J. M.* (Department of Haematology, Royal Postgraduate Medical School, London W12 0HS, England), p. 415

Cation content and membrane deformability of heterozygous β-thalassaemic red blood cells. *Vettore, L., Falezza, G. C., Cetto, G. L., de Matteis, M. C.* (Istituto di Patologia Medica, Ospedale Maggiore, 34129 Trieste, Italia), p. 429

Oxygen binding to haemoglobin in subjects with hypoproliferative anaemia, with and without chronic renal disease: Role of pH. *Lichtman, M. A., Murphy, M. S., Whitbeck, A. A., Kearney, E. A.* (Department of Medicine, University of Rochester Medical Center, Rochester, N. Y. 14642), p. 439

Association of type II congenital dyserythropoietic anaemia and von Willebrand's disease. *Hernández, P., Almagro, D., Corral, J. F., Opolski, A., Sánchez, J. A., Rodríguez, N.* (Instituto de Hematologia e Immunologia, Rpto. Altahabana, Habana 8, Cuba), p. 453

The mechanism of neutropenia in Felty's syndrome. *Vincent, P. C., Levi, J. A Macqueen, A.* (Medical Research Department, Kanematsu Memorial Institute, Sydney Hospital, Sydney, N.S.W. 2000, Australia), p. 463

Immunological rebound after cessation of long-term chemotherapy in acute lymphocytic leukaemia: Changes in distribution of T and B cell populations in bone marrow and peripheral blood. *Sen, L., Borella, L.* (Laboratories of Virology and Immunology, St. Jude Children's Research Hospital, Memphis, Tenn. 38101), p. 477

IgG anti-Le^a. *Holburn, A. M.* (M.R.C. Experimental Haematology Unit. St. Mary's Hospital Medical School, London W2 1PG, England), p. 489

Australia antigen (HB—Ag) subtyping by a sensitive tanned cell haemagglutination-inhibition technique. *Hopkins, R. M., Das, P. C.* (South-East Scotland Regional Blood Transfusion Service, Royal Infirmary, Edinburgh, Scotland), p. 501

The use of chicken serum for measurement of serum vitamin B_{12} concentration by radioisotope dilution: Description of method and comparison with microbiological assay results. *Green, R., Newmark, P. A., Musso, A. M., Mollin, D. L.* (Department of Haematology, South African Institute for Medical Research, Johannesburg, South Africa), p. 507

Observations on the ultrastructure of platelets in Glanzmann's disease. *Firkin, B. G., Howard, M. A., Farmer, S. J.* (Department of Medicine, Monash University Medical School, Alfred Hospital, Melbourne 3181 Victoria, Australia), p. 527

Effects of irradiation on red cells. *Goldstein, B. D., Paniker, N. V., Hartmann, R. C.* (Department of Medicine, New York University Medical Center, School of Medicine, New York, N. Y. 10016), p. 533

British Journal of Haematology (Oxford) **27** (1974) No. 4

Annotation. Use of platelet transfusions. *Gardner, F. H.* (Hematology Research Laboratory, Presbyterian University of Pennsylvania Medical Center, Philadelphia, Pa.), p. 537

Functional cellular maturation in cultures of human haematopoietic cells. *Barak, Y., Shore, N. A., Higgins, G. R., Vadakan, V. V.* (Division of Hematology-Oncology,

Children's Hospital of Los Angeles, Los Angeles, Calif.), p. 543

Measurement of red cell folate levels by ^{3}H-pteroylglutamic acid (^{3}H-PteGlu) radioassay. *Schreiber, C., Waxman, S.* (Cancer Chemotherapy Laboratory, Division of Oncology, Department of Medicine, Mount Sinai School of Medicine of the City University of New York, New York, N. Y. 10029), p. 551

Effect of various factors on iron absorption in mice with X-linked anaemia. *Sorbie, J., Hamilton, D. L., Valberg, L. S.* (Etherington Hall, Queen's University, Kingston, Ontario, Canada), p. 559

Studies in lipogenesis by red cells of mice. *Pushpendran, C. K., Eapen, J.* (Biology and Agriculture Division, Bhabha Atomic Research Centre, Bombay 400085, India), p. 571

Inhibition of uridine incorporation in proerythroblasts of patients with α-methyldopa induced haemolytic anaemia. *Djaldetti, M., Bessler, H., Lewinski, U., Mandel, E. M.* (Department of Internal Medicine "B" and Haematology Clinic, Hasharon Hospital, Petah-Tiqva, Israel), p. 579

Procarbazine induced oxidative haemolysis: Relationship to *in vivo* red cell survival. *Sponzo, R. W., Arseneau, J. C., Canellos, G. P.* (Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, Md.), p. 587

The role of the polyol pathway in methaemoglobin reduction in human red cells. *Travis, S. F., Morrison, A. D., Clements, R. S., Jr., Winegrad, A. I., Oski, F. A.* (Thomas Jefferson University, Cardeza Foundation, Philadelphia, Pa. 19107), p. 597

Anti-Bg antibodies in sera used for red cell typing. *Pavone, B. G., Issitt, P. D.* (Paul I. Hoxworth Blood Center of the University of Cincinnati, Cincinnati, Ohio 45229), p. 607

The high frequency of anti-Bg^{a}. *Eska, P. L., Grindon, A. J.* (Blood Bank, Johns Hopkins Hospital, Baltimore, Md. 21205), p. 613

Experimental hepatic porphyria induced by hexachlorobenzene as a model for human symptomatic porphyria. *Stonard, M. D.* (Biochemical Mechanisms Section, M.R.C. Toxicology Unit, Medical Research Council Laboratories, Carshalton, Surrey, England), p. 617

Delayed cutaneous hypersensitivity in leukaemic patients to autologous blast cells. *Baker, M. A., Taub, R. N., Brown, S. M., Ramachandar, K.* (Toronto Western Hospital, Toronto, Ontario, Canada M5T 2S8), p. 627

Lymphocyte membrane markers in acute lymphoblastic leukaemia. *Aiuti, F., Papa, G., Lacava, V., Ciarla, M. V., D'Amelio, R., Garofalo, J.* (Istituto di Clinica Medica III, Cattedra di Ematologia, University of Rome, Rome, Italy), p. 635

Receptor sites for aggregated gammaglobulin (AGG) on lymphocytes in lymphoproliferative diseases. *Huber, Ch., Dworzak, E., Fink, U., Michlmayr, G., Braunsteiner, H., Huber, H.* (Medizinische-Universitätsklinik, A-6020 Innsbruck, Austria), p. 643

Endotoxin-induced intravascular coagulation and shock in dogs: The role of factor VII. *Garner, R., Evensen, S. A.* (Correspondence: S. A. Evensen, Medical Department A, Rikshospitalet, Oslo, Norway), p. 655

The identification of fibrinopeptide B as a chemotactic agent derived from human fibrinogen. *Kay, A. B., Pepper, D. S., McKenzie, R.* (Department of Respiratory Diseases, City Hospital, Edinburgh EH10 5SB, Scotland), p. 669

Experimental Hematology (Copenhagen) **1** (1973) No. 6

Regulators of cell division. A review. I. Endogenous mitotic inhibitors of hematopoietic cells. *Lozzio, B. B.* (University of Tennessee, Membrane Research Center and Hospital, Knoxville. Tenn. 37920), p. 309

Kinetic analysis of splenic erythropoiesis in mice under prolonged hypoxic stress. *Markoe, A. M., OKunewick, J. P., Schiffer, L. M.* (Allegheny General Hospital, Clinical Radiation Therapy Research Center, Pittsburgh, Pa. 15212), p. 340

Suppression of erythropoiesis by simultaneous proliferation of alloantigen-sensitive units. *Kitamura, Y., Kawata, T., Kanamaru, A., Seki, M.* (Osaka Univer-

sity, Medical School, Department of Pathology 2, Osaka City, Japan), p. 350

Investigations of a stochastic model of haemopoiesis. *Korn, A. P., Henkelman R. M., Ottensmeyer, F. P., Till, J. E.* (University of Toronto, Department of Medicine and Biophysics, Toronto Max 1K9, Ontario, Canada), p. 362

Influence of altered iron kinetics in the mouse on measurement of erythropoiesis, by radio-iron. *Schofield, R.* (Christie Hospital, Paterson Laboratories, Manchester M20 9BX, England) p. 376

Experimental Hematology (Copenhagen) **2** (1974) No. 1

Proliferation and differentiation of transplanted bone marrow from mice treated with nitrogen mustard. *Sharp, J. G., Thomas, D. B., Briscoe, C. V.* (University of Nebraska Medical Center, Department of Anatomy, Omaha, Nebr. 68105), p. 1

Colony forming unit suicide in normal and Rauscher leukemic mice given tritiated thymidine *in vivo*. *OKunewick, J. P., Phillips, E. L.* (Allegheny General Hospital, Division of Radiation Oncology, Pittsburgh, Pa. 15212), p. 9

Development of erythroleukemia in Rauscher virus infected mice treated with phytohemagglutinin. *Lozzio, B. B., Brown, A., Hewins, J. P.* (University of Tennessee, Memorial Research Center, Knoxville, Tenn. 37920), p. 16

Hemoglobin synthesis inhibiting factor (HSIF) chemical and biological characterization. *Molinari, P. F., Bulat, P., Chung, S. K., Menninger, F. F., Jr., Snyder, L. M.* (St. Vincent Hospital, Department of Medicine, Division of Hematology, Worcester, Ma. 01610), p. 28

Synergism between lymph node and bone marrow cells for production of granulocytes. I. Requirement for immunocompetent cells. *Kanamaru, A., Kitamura, Y., Kawata, T., Okano, K.* (Osaka University Medical School, Department of Pathology, Osaka 530, Japan), p. 35

Synergism between lymph node and bone marrow cells for production of granulocytes. II. Enhanced colony-stimulating activity of sera of mice with graft-versus-host-reaction. *Hara, H., Kitamura, Y., Kawata, T., Kanamaru, A., Nagai, K.* (Osaka University Medical School, Department of Pathology, Osaka 530, Japan), p. 43

Experimental Hematology (Copenhagen) **2** (1974) No. 2

Distribution and spread of ^{51}Cr-labeled leukemia cells in mice. *Boranić, M., Radačić, M., Gabrilovac, J.* (Rudjer Boskovic Institute, Laboratory of Experimental Therapy, 41001 Zagreb, Yugoslavia), p. 51

Serum inhibitors of *in vitro* colony formation: Relation to haemopoietic tissue *in vivo*. *Beran, M.* (Karolinska Institute, Medical School, Department of Medical Radiobiology, S-10401 Stockholm 60, Sweden), p. 58

The effect of prostaglandins on the *in vitro* blastogenic response of human peripheral blood lymphocytes (Review Article). *Stockman, G. D., Mumford, D. M.* (Baylor University, Texas Medical Center, College of Medicine, Department of Obstetrics and Gynecology, Houston, Texas 77025), p. 65

Mitogenic stimulation of human leukemic plasma cells. *Wetter, O., Van der Weert, M., Reis, H. E., Leiner, G.* (Gesamte Hochschule Essen, Universitäts Klinik, D-43 Essen, BRD), p. 73

Precursors for fibroblasts in different populations of hematopoietic cells as detected by the *in vitro* colony assay method. *Friedenstein, A. J., Deriglasova, U. F., Kulagina, N. N., Panasuk, A. F., Rudakowa, S. F., Lurià, E. A., Rudakow, I. A.* (NF Gamaleya Epidemiology and Microbiology Institute, Moscow, USSR), p. 83

The importance of the spleen on proliferation of erythropoietin-responsive cells induced by erythropoietin. *Bozzini, C. E., Martinez, M. A., Ugarte, C. A. A., Montángero, V., Soriano, G.* (University of Buenos Aires, Buenos Aires, Argentina), p. 93

Experimental Hematology (Copenhagen) **2** (1974) No. 3

The chemical and biological properties of busulphan ("Myleran"). *Dunn, C. D. R.*

(University Hospital of Wales, Department of Haematology, Cardiff CF4 4XW, Wales), p. 101

Light microscopy of scattered, unprocessed hemopoietic precursor cells in liver smears of a 6.35 mm crown-rump length human embryo. *Kelemen, E.* (Semmelweis University Medical School, 1st Department of Medicine, 1083 Budapest, Hungary), p. 118

The use of cell separation techniques and isoantibody to host antigens in the treatment of severe combined immunodeficiency disease with HL-A incompatible maternal marrow. *Gelfand, E. W., Phillips, R. A., Miller, R. G., McCulloch, E. A., Rosen, F. S.* (Hospital for Sick Children, Department of Immunology, Toronto, M5G 1X8, Ontario, Canada), p. 122

The relationship between granulocytic and erythroid repopulation ability. *Constable, T. B., Blackett, N. M.* (Institute for Cancer Research, Department of Biophysics, Belmont, Sutton, Surrey, England), p. 131

Treatment of blastic transformation of chronic granulocytic leukemia by high dose cyclophosphamide, total body irradiation and infusion of cryopreserved autologous marrow. *Buckner, C. D., Clift, R. A., Fefer, A., Neiman, P. E., Storb, R., Thomas, E. D.* (Providence Medical Center, Division of Oncology, Seattle, Wash. 98122), p. 138

CSF response to endotoxin in normal and leukopenic recipients. *Shadduck, R. K* (University of Pittsburgh, Montefiore Hospital, School of Medicine, Pittsburgh Pa. 15213), p. 147

Experimental Hematology (Copenhagen) **2** (1974) No. 4

Stimulation by human urine or plasma of granulopoiesis by human marrow cells in agar. *Metcalf, D.* (Royal Melbourne Hospital, Walter and Eliza Hall Institute, Cancer Research Unit, Melbourne, Victoria, Australia), p. 157

Liquid culture assays of mouse bone marrow granulopoiesis. *Morgan, D. A., McCredie, K. B., Durett, A. G.* (University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas 77025), p. 174

Inhibition of granulopoiesis in diffusion chambers by a granulocyte chalone. *MacVittie, T. J., McCarthy, K. F.* (Armed Forces Radiobiology Research Institute, Bethesda, Md. 20014), p. 182

Antilymphocytic antibodies and marrow transplantation. IV. Comparison of the effects of antibody fragments directed against immunoglobulin or lymphocyte antigens on acute secondary disease. *Rodt, H., Thierfelder, S., Eulitz, M.* (Gesell. Strahlen- und Umweltforschungs-Institut, D-8 München 2, BRD), p. 195

Comparison of hematopoiesis after treatment with antithymocyte serum and erythropoietin. *Kinnamon, K. E., Blackwell, L. H., Ledney, G. D.* (Walter Reed Army Medical Center, Institute of Research, Washington, D. C. 20012), p. 204

The role of anemia as a trigger of myeloid leukemia in irradiated rats. *Jarvis, J. H., Whittaker, J. A.* (Welsh National School of Medicine, Department of Haematology, Cardiff CF4 4XN, Wales), p. 212

Enhanced antibody production by grafted peripheral blood immunocytes in cyclophosphamide-treated allogenic chick embryo hosts. *Seto, F.* (University of Oklahoma, Zoology Department, Norman, Okl. 73069), p. 219

Quantitative changes with age in bone marrow cell populations of C3H mice. *Miller, S. C., Osmond, D. G.* (McGill University, Department of Anatomy, Montreal H3C 3G1, Quebec, Canada), p. 227

Experimental Hematology (Copenhagen) **2** (1974) No. 5

Human monocytopoiesis. *Meuret, G.* (Kantonsspital, Medical Clinic, Department of Oncology and Hematology, CH-9006 St. Gallen, Switzerland), p. 238

Separation of erythropoietin-responsive cells (ERC) from rat bone marrow. *Zucali, J. R., Van Zant, G., Rakowitz, F., Gordon, A. S.* (Roswell Park Memorial Institute, Department of Biological Researches, Buffalo, N. Y. 14203), p. 250

Human acute leukemia cells with membrane-bound immunoglobulin. *Falletta, J. M., Mukhopadhyay, N., Steuber, C. P., Starling, K. A., Fernbach, D. J.* (Texas

Children's Hospital, Hematology Laboratory, Houston, Texas 77025), p. 259

The influence of chloramphenicol on the bone marrow haemopoietic stem cell compartment. *Firkin, F. C., Sumner, M. A., Bradley, T. R.* (Melbourne University, St. Vincent's Hospital, Fitzroy 3065, Victoria, Australia), p. 264

Abstracts from the Third Annual Meeting of the International Society for Experimental Hematology, p. 271

Folia Haematologica (Leipzig) **101** (1974) No. 1

Gegenwärtiger Stand und Entwicklungstendenzen auf dem Gebiet der Thrombolytika. *Markwardt, F.* (Institut für Pharmakologie und Toxikologie der Medizinischen Akademie Erfurt, DDR-50 Erfurt), p. 5

Über die fibrinolytische Aktivität von Pilzen aus mikrobiologischer Sicht. *Koch, H. A.* (Mykologische Abteilung der Hautklinik der Medizinischen Akademie Erfurt, DDR-50 Erfurt), p. 9

Fibrinolytische und thrombolytische Wirkung von Proteasen einiger Pilzkulturen. *Andreenko, G. W., Silaev, A. B., Maksimova, R. A., Poch, L. I., Serebrjakova, T. N.* (Laboratorium für Physiologie und Biochemie der Blutgerinnung, Moskauer Staatliche Universität, Moskau W-234, UdSSR), p. 14

Review of the biochemistry and coagulation physiology of Brinolase. (Fibrinolytic enzyme from Aspergillus oryzae). *Roschlau, W. H. E., Ives, D. A. J.* (Department of Pharmacology, Faculty of Medicine, University of Toronto, Connaught Laboratories Limited, Willowdale-Toronto, Canada), p. 22

Experimentelle und klinische Untersuchungen mit einer Protease aus Aspergillus oryzae (Brinase): Fibrinogen-Turnover, Thrombozytenaggregation und Verschluß des Scribner-Shunts. *de Nicola, P., Cultrera, G., Gibelli, A., Manai, G.* (Institut für Gerontologie und Geriatrie der Universität Pavia, Pavia, Italy), p. 38

On the pharmacology of Brinase, a proteolytic enzyme from Aspergillus oryzae. *Svärd, P. O.* (Astra Läkemedel AB, Research and Development Laboratoy, Pharmacology, 151 85 Södertälje, Sweden), p. 45

Clinical review on Brinase, a protease from Aspergillus oryzae. *Frisch, E. P.* (Astra Läkemedel AB, Department of Clinical Investigations and Medical Statistics, 151 85 Södertälje, Sweden), p. 63

Mikrobiologische Gewinnung einer Protease mit fibrinolytischer Wirkung aus Aspergillus ochraceus. *Bärwald, G., Jahn, G., Volzke, K.-D.* (VEB Arzneimittelwerk Dresden, DDR-8122 Radebeul 1), p. 83

Charakterisierung einer alkalischen Protease aus Aspergillus ochraceus. *Töpfer, H., Piesche, K.* (VEB Arzneimittelwerk Dresden, Forschungsabteilung Biochemie, DDR-8122 Radebeul 2), p. 91

Studies on the proteolysis of fibrinogen and fibrin by Aspergillus ochraceus enzyme as compared to the action of plasmin. *Teisseyre, E., Latallo, Z. S., Kopeć, M.* (Department of Radiobiology and Health Protection, Institute of Nuclear Research, Warsaw, Poland), p. 99

Tierexperimentelle Untersuchungen mit einer Protease aus Aspergillus ochraceus. *Klöcking, H.-P., Hauptmann, J., Nowak, G.* (Institut für Pharmakologie und Toxikologie der Medizinischen Akademie Erfurt, DDR-50 Erfurt), p. 111

Thrombolyse experimentell erzeugter Shuntverschlüsse. *Bieselt, R., Sedlarik, K., Stanulla, H.* (Abteilung für Thorax- und Kardiochirurgie der Zentralklinik für Lungenkrankheiten und Tuberkulose, DDR-5303 Bad Berka), p. 118

Klinische und gerinnungsphysiologische Untersuchungen mit einer Protease aus Aspergillus ochraceus. (Vorläufige Mitteilung.) *Vogel, G., Großmann, K., Huyke, R., Zuber, W.* (Medizinische Klinik der Medizinischen Akademie Erfurt, DDR-50 Erfurt), p. 125

Zur Bestimmung der Fibrinolyseaktivatoren. *Astedt, B., Pandolfi, M.* (Koagulationslabor, Allmänna Sjukhuset, 214 01 Malmö, Sweden), p. 132

Klinische Untersuchungen über Aktivatoren und Inhibitoren der Fibrinolyse bei einigen inneren Krankheiten. *Smolenski, W. S., Bokarew, I. N., Jerschow, W. I. Mindlina, G. I.* (1. Moskauer Medizinisches Institut, Moscau, UdSSR), p. 138

Fibrinolytisches Potential des Blutes bei

Leberschädigungen. *Kotschy, M.* (Klinik für Angiologie des Institutes für Innere Krankheiten, Wrocław, Poland), p. 142

Folia Haematologica (Leipzig) **101** (1974) No. 2

Die Rezeptoren immunkompetenter Zellen. *Von Baehr, R., Schwenke, H.* (Institut für Impfstoffe, DDR-45 Dessau 2), p. 153

Praktische Aspekte der Lymphozyten- und Granulozytenisolierung aus dem Blut. *Frick, G.* (Medizinische Universitätsklinik, DDR-25 Rostock), p. 170

In-vivo-Verhalten der Lymphozyten bei Patienten mit chronischer Lymphadenose unter der Einwirkung von Anti-Lymphadenose-Gammaglobulin. *Preussner, S., Frick, G.* (Medizinische Klinik des Bereiches Medizin der Universität Rostock, DDR-25 Rostock), p. 183

Morphologische, zytochemische und autoradiographische Untersuchungen der Zellen in Lymphozytenkulturversuchen unter Zusatz von Phytohämagglutinin oder Tuberkulin. *Drescher, J., Rüßler, P.* (Universitäts-Kinderklinik, 23 Kiel, BRD), p. 196

Vergleichende Untersuchungen über die Brauchbarkeit des Lymphozyten-Transformations-Testes und des Monozyten-Testes in der Allergiediagnostik. *Brunner, H.-P.* (Bezirkskrankenhaus St. Georg, Leipzig, DDR-7021 Leipzig), p. 213

Amidinierungseffekte an Erythrozyten. *Halbhuber, K.-J., Benser, A., Brandt, H., Feuerstein, H., Geyer, G.* (Anatomisches Institut der Friedrich-Schiller-Universität Jena, DDR-69 Jena), p. 220

Wärmestabilität von Kaninchen-, Ratten- und Mäuseerythrozyten in vitro und ihre Überlebenszeit im Organismus. *Šebestík, V., Potměšilová, I., Jelínek, J.* (Institut für Hämatologie und Bluttransfusion, Prag, 2, Tschechoslovakia), p. 226

Zum Einfluß von Adenin und Guanosin auf die Überlebensrate von Erythrozyten nach Lagerung bei Temperaturen zwischen 4°C und 25°C. *Strauss, D., Raderecht, H. J.* (Bezirksinstitut für Blutspende- und Transfusionswesen, Berlin, DDR-113 Berlin), p. 232

Über den Einfluß von Lagerungstemperaturen zwischen 4°C und 25°C auf die Verwendbarkeit von Blutkonserven. *Strauss, D., Tänzer, S., Schmutzler, F., Gülke, L., Rettig, H. P., Roigas, H., Raderecht, H. J.* (Bezirksinstitut für Blutspende- und Transfusionswesen Berlin, DDR-113 Berlin), p. 243

Weitere Optimierung der ACD-AG-Konservierungslösung für Blut. I. *Stigge, V., Lun, A., Ziemer, S., Strauss, D., Raderecht, H. J.* (Institut für Laboratoriumsdiagnostik, Städtisches Klinikum Berlin-Buch, DDR-1115 Berlin), p. 256

Quantity of serum immunoglobulins IgG, IgA and IgM in Bulgarian blood-donors. *Toshkov, As., Abrashev, Ign., Prodanov, P.* (Institute of Microbiology, Department of Immunology, Bulgarian Academy of Sciences, Sofia 13, Bulgaria), p. 269

Die Antistreptokinaseaktivität bei Neugeborenen. *Weißbach, G., Domula, M., Keller, J., Künzel, R., Lenk, H.* (Kinderklinik des Bereiches Medizin der Karl-Marx-Universität, DDR-705 Leipzig), p. 272

Regelphysiologische Untersuchungen am Antithrombinsystem. *Zwiener, U.* (Pathophysiologische Abteilung der Nervenklinik, DDR-50 Erfurt), p. 281

Zur Kinetik der nichtaktivierten Euglobulin-Fibrinolyse in Humanplasma. *Hindersin, P., Zwiener, U., Fischer, W.* (Nervenklinik und Poliklinik der Medizinischen Akademie Erfurt, DDR-50 Erfurt), p. 293

Syndrome de coagulation intravasculaire disséminée dans la leucose blastique et certaines autres affections. *Génova, V., Georgief, Z.* (Institut de Recherche d'Hématologie et de Transfusion Sanguine, Sofia 56, Bulgarie), p. 300

Über die Anwendung von Fibrinogen und Thrombin zur lokalen Thrombosierung von Arterien. *Merkulov, M. F., Serbinenko, F. A., Oseledko, W. D., Padalko, P. I.* (Abteilung für Pharmakologie des Institutes für experimentelle und klinische Onkologie der Akademie der medizinischen Wissenschaften der UdSSR, Moscau, UdSSR), p. 313

Folia Haematologica (Leipzig) **101** (1974) No. 3

Die Bedeutung der Immunenzymtechnik in der immunologischen Diagnostik. *Storch,*

H. (Medizinische Universitätsklinik der Karl-Marx-Universität in Leipzig, DDR-701 Leipzig), p. 329

Quantifizierung der granulozytären Abwehr bei Hämoblastosen. *Senn, H. J., Jungi, W. F.* (Medizinische Klinik C, Kantonsspital St. Gallen, CH-9006 St. Gallen, Switzerland), p. 337

Die Erfassung der für die Infektabwehr "effektiven Leukozyten" bei Leukämien durch Auszählung der Speichelkörperchen. *Stobbe, H., Zimmermann, I., Strekker, B.* (I. Medizinische Klinik des Bereichs Medizin [Charité] der Humboldt-Universität zu Berlin, DDR-104 Berlin), p. 347

Autoimmunologische Reaktion im leukozytären Bereich mit besonderer Berücksichtigung arzneimittelinduzierter Formen. *Mey, U.* (Medizinische Klinik der Medizinischen Akademie Erfurt, DDR-50 Erfurt), p. 353

Über die serologische Verwendbarkeit tiefgefrorener Lymphozyten im Zellpanel. *Bube, F. W., Krebs, A., Siebel, E., Heumann, H.* (Blutspendezentrale der Universitätskliniken Köln, 5 Köln 41, BRD), p. 363

Arzneimittelallergische hämolytische Anämien. *Maas, D., Schubothe, H., Weber, S.* (Abteilung für klinische Immunopathologie, Medizinische Universitätsklinik Freiburg i. Br., BRD), p. 372

Qualitative and quantitative Kriterien der zytologischen Knochenmarkdiagnostik. *Boll, I.* (Städtisches Krankenhaus Neukölln, 1 Berlin-West 47), p. 384

Neue Untersuchungen im Bereich des HL-A-Systems: ein dritte Locus mit serologisch nachweisbaren Merkmalen. *Mayr, W. R.* (Institut für Blutgruppenserologie der Universität Wien, A-1090 Wien, Austria), p. 401

Zum Beweiswert von Vaterschaftsausschlüssen im HL-A-System. *Mayr, W. R., Hiller, Chr.* (Institut für Blutgruppenserologie der Universität Wien, A-1090, Wien, Austria), p. 412

Quantitative determination of aggregated IgG in gamma globulin preparations. *Noeva, K. K., Toshkov, As. S.* (Institute of Microbiology, Bulgarian Academy of Sciences, Sofia 13, Bulgaria), p. 419

Gerinnung und Fibrinolyse bei Unreif- und Reifgeborenen mit Atemnotsyndrom und intrakranieller Blutung. *Reddemann, H.* (Kinderklinik der Ernst-Moritz-Arndt-Universität Greifswald, DDR-22 Greifswald), p. 426

Vergleichende Untersuchungen zur Plättchenkinetik bei Verwendung unterschiedlicher Stabilisatoren. *Preußner, S., Frick, G., Konrad, H., Schulz, K.* (Medizinische Klinik des Bereiches Medizin der Universität Rostock, DDR-25 Rostock), p. 451

Ergebnisse verschiedener Sedimentationsverfahren zur Herstellung leukozytenarmer Human-Erythrozytenkonzentrate. *Brandstädter, W., Baborowski, H., Günzel, R.* (Bezirksinstitut für Blutspende- u. Transfusionswesen Magdeburg, DDR-309 Magdeburg), p. 461

Untersuchungen an Kryopräzipitaten. 3. Mitteilung: Konzentration einiger Plasmabestandteile in Kryopräzipitaten und deren Bedeutung für die klinische Praxis. *Sander, W., Uteg, K.-H.* (Bezirksinstitut für Blutspende- u. Transfusionswesen Schwerin DDR-27 Schwerin), p. 466

Standardisierungsvorschlag zur Serologie des Bed-side-Tests. *Hölke, D., Brandstädter, M.* (Bezirksinstitut für Blutspende- und Transfusionswesen Magdeburg, DDR-309 Magdeburg), p. 473

Ergebnisse der Anreicherung und elektronenoptischen Darstellung des Aus/SH-Antigens. *Fritzsche, L., Lambrecht, R., Kemnitz, P.* (Bezirksinstitut für Blutspende- u. Transfusionswesen, DDR-309 Magdeburg), p. 479

The effect of phenformin plus stanozolol on fibrinolysis, platelet adhesiveness and blood lipids in patients with recurrent venous thrombosis. *Bielawiec, M., Myśliwiec, M., Perzanowski, A.* (Haematology Clinic, Institute of Internal Medicine, Medical Academy, Białystok, Poland), p. 483

Haemostasis (Basel) **3** (1974) No. 2

Acquired inhibitors in nonhemophilic patients. *Lechner, K.* (Central Coagulation Laboratory, University of Vienna, Vienna, Austria), p. 65

Dilution of haemophilic plasma used as a reagent in the determination of anti-

haemophilic factor A (factor VIII). *Bouma, B. N., Starkenburg, A. E.* (Division of Haemostasis, Department of Internal Medicine, University Hospital, Utrecht, The Netherlands), p. 94

Platelet membrane function studies on platelets from patients with hereditary thrombopathic thrombocytopenia. *Baadenhuijsen, H., Haanen, C.* (Laboratory of Clinical Chemistry, Department of Internal Medicine, St. Radboudziekenhuis, University of Nijmegen, Nijmegen, The Netherlands), p. 98

Inhibition of fibrinolysis by the human vascular wall related to the presence of smooth muscle cells. *Hegt-Noordhoek, V., Brakman, P.* (Gaubius Institute, Health Research Organization TNO, Leiden, The Netherlands), p. 118

Nouvelle Revue Française d'Hématologie (Paris) **14** (1974) No. 1

The effect of incubated plasma and lysolecithin on the shape and membrane lipid composition of red cells studied "in vitro". *Lichtman, M. A., Marinetti, G. V., Gordesky, S. E.* (Departments of Medicine, Radiation Biology and Biophysics, University of Rochester School of Medicine, Rochester, N. Y.), p. 5

Transformation discocyte-échinocyte. Absence de transformation échinocytaire du plasma conservé de malades atteints d'abetalipoprotéinémie congénitale. *Féo, C.* (Institut de Pathologie Cellulaire, Unité 48. I.N.S.E.R.M., Hôpital de Bicêtre, F. 94270 Le Kremlin-Bicêtre, France), p. 25

L'activité folique du sérum sanguin chez les sujets agés. Observations personnelles et discussion des données de la littérature. *Lewi, S.* (Hôpital et Fondation de Rotschild, 75012 Paris, France), p. 29

L'anémie au cors du neuroblastome chez l'enfant. *Tchernia, G., Vieu, F., Parmentier, C., Schweisguth, O.* (Service de Pédiatrie, Laboratoire des Isotopes, Institut Gustave-Roussy, 94800 Villejuif, France), p. 45

Une nouvelle hémoglobine anormale (Hb Abruzzo, β 143 His $\rightarrow$ Arg) à haute affinité pour l'oxygène, chez deux frères avec syndrome hémolytique du type "méditerranéen" et érythrocytose marquée. *Chiaroni, T., Nardi, E., Papa, G., Sasso, G. F., Tentori, L.* (Istituto di Patologia Speciale Medica e Metodologia Clinica dell'Università, Policlinico "Umberto I", I-00161 Roma, Italy), p. 67

La mégacaryocytopoïèse hépatique et spénique post-natale chez la souris. *Tverdy, G.* (Institut d'Anatomie Pathologique de l'Université de Gand, Anvers, Belgium), p. 81

Les antigènes HL-A chez les porteurs sains de l'antigène Australia. *Seignalet, J., Robinet-Lévy, M., Lemaire, J. M.* (Institut d'Hématologie de Montpellier, 34010 Montpellier, France), p. 89

Anémie hémolytique auto-immune et cancer du rein. *Gorin, N.-C., Homberg, J.-C., Najman, A., Duhamel, G., André, R.* (Service d'Hématologie, Hôpital Saint-Antoine, 75012 Paris, France), p. 105

Transformation acanthocyte-discocyte. Étude *in vitro* de l'action hémolysante de l'azide de sodium vis-à-vis des érythrocytes de. sujets atteints d'abétalipoprotéinémie. *Féo, C., Maigné, J.* (Institut de Pathologie Cellularie, U-48. I.N.S.E.R.M., Hôpital de Bicêtre, F. 94270 Le Kremlin-Bicêtre, France), p. 119

On the precipitation of serum lipoproteins by heparin. *Burstein, M., Scholnick, H. R.* (Centre National de Transfusion Sanguine, F. 75739 Paris, Cedex 15, France), p. 131

Groupe d'études sur l'hémostase et la thrombose. VI[e] Réunion, 10 novembre 1973, Nancy, France), p. 137

Nouvelle Revue Française d'Hématologie (Paris) **14** (1974) No. 2

Ilot érythroblastique anormal dû au développement de jonctions intercellulaires. (Synartèse érythroblastique.) Un nouveau mécanisme d'anémie. Problèmes posés par le diagnostic. *Flandrin, G., Daniel, M. Th., Breton-Gorius, J., Brouet, J. C., Bernard, J.* (Institut de Recherche sur les Maladies du Sang, Hôpital Saint-Louis, Paris, France), p. 161

Syndrome leucémique singulier chez un nouveau-né trisomique 21: prolifération mégacaryocyto-plaquettaire; Syndrome de

coagulation intravasculaire diffuse. *Cosson, A., Despres, P., Gazengel, C., Breton-Gorius, J., Prieur, M., Josso, F.* (Département d'Hématologie et Service de Pédiatrie C.H.U. Necker-Enfants-Malades, F 75730 Paris, Cedex 15, France), p. 181

Société française d'Hématologie. Séance spéciale consacrée aux polynucléaires neutrophiles, Grenoble, 16 et 17 Juin 1973, p. 199

Nouvelle Revue Française d'Hématologie (Paris) **14** (1974) No. 3

Purification de l'antigène Australia par tamisage moléculaire et chromatographie d'affinité. *Cherchel, G. L., Valet, J.-P., Matte, J., Ackerman, H. W.* (Laboratoire de Recherche sur l'antigène Australia, Centre Hospitalier de l'Université Laval, Québec 10, Canada), p. 341

Protéines de la membrane érythrocytaire. I. Étude électrophorétique des protéines solubilisées des membranes d'érythrocytes humains normaux et pathologiques. *Bovin, P., Galand, C.* (Centre de Recherches sur les Enzymopathies de l'Association Claude-Bernard, Université Paris VII, Paris, France), p. 355

Ultrastructure des plaquettes sanguines chez deux nouveau-nés atteints de trisomie-21 avec hyperplaquettose et syndrome leucémique. *Boisseau, M., Le Menn, R.* (Département d'Hémostase, Hôpital du Tondu, 33000 Bordeaux, France), p. 371

Acanthocytose acquise chez une femme splénectomisée pour sphérocytose héréditaire. *Turpin, G., Leblond, P., Gouffier, E., Garnier, M., Lortholary, P.* (Hôpital de Bobigny, Laboratoire Central d'Hématologie, 93000 Bobigny, France), p. 383

Activités fonctionnelles et enzymatiques des granulocytes du sang de malades ayant une anémie réfractaire acquise. *Hakim, J. Boivin, P., Troube, H., Boucherot, J.* (Centre de Recherches sur les Enzymopathies de l'Association Claude-Bernard, Paris, France), p. 397

Réaction de microlymphocytotoxicité avec antiglobuline anti-IgG et réactivité croisée des antigènes HL-A. *Delmas-Marsalet, Y., Woodbury, M., Corley, R., Amos, D. B.* (Centre Régional de Transfusion Sanguine de Lille, 59000 Lille, France), p. 409

Symposium Franco-Britannique sur les dyshématopoièses, 17 et 18 mai 1973, Créteil, France.

Nouvelle Revue Française d'Hématologie (Paris) **14** (1974) No. 4

Anémie hémolytique congénitale avec sphérocytose et anomalies cationiques érythrocytaires. *Bernard, J.-F., Afifi, F., Hakim, J., Boivin, P.* (Centre de Recherches sur les Enzymopathies de l'Association Claude-Bernard, Hôpital Beaujon, 92110 Clichy, France), p. 439

Le déficit en glucose-6-phosphate-déshydrogénase érythrocytaire chez le nouveau-né à Alger. *Richard, F., Belhani, M., Colonna, P.* (Service d'Hématologie, Centre P. et M. Curie, Alger), p. 453

Chromosome Philadelphie et marqueur du groupe C dans un cas de leucose aiguë découverte sous traitement par noramidopyrine. *Moraine, C., Brémond, J. L., Despert, F., Leroy, J., Leroux, M. E., Maillet, M.* (Département de Cytogénétique du Laboratoire de Biologie Humaine. Tours 37033, France), p. 461

Insuffisance transitoire en mégacaryocytes et érythroblastes au cours d'infections bactériennes chez le nourrisson. *Bonnet-Gajdos, M., Navarro, J., Roy, C.* (No address), p. 471

Probabilité de paternité estimée à partir des groupes sanguins et des marqueurs génétiques. *Salmon, D.* (Groupe de Recherches en Méthodologie Informatique, U.E.R. Pitié-Salpêtrière, 75013 Paris, France), p. 477

Déficit en 3-phosphoglycérate kinase érythrocytaire et leucocytaire. Étude des propriétés de l'enzyme, de la fonction phagocytaire des polynucléaires et revue de la littérature. *Boivin, P., Hakim, J., Mandereau, J., Galand, C., Degos, F., Schaison, G.* (Centre de Recherches sur les Enzymopathies de l'Association Claude-Bernard, Hôpital Beaujon, 92110 Clichy, France), p. 495

Quelques problèmes d'actualité sur l'étude des vaisseaux lymphatiques. *Arvy, L.* (Laboratoire d'Histo-enzymologie, Faculté de Médecine, Paris VI^{e}, France), p. 509

Société Française d'Hématologie. Séance spéciale, p. 519

Nouvelle Revue Française d'Hématologie (Paris) **14** (1974) No. 5

Histoire naturelle des leucémies granulocytaires chroniques. *Baserga, A.* (Clinique Médicale de l'Université de Ferrara, Ferrara, Italy), p. 583

Anémie hémolytique congénitale non sphérocytaire par déficit en glucose-6-phosphate-déshydrogénase érythrocytaire. Description des deux nouvelles variantes: Gd (−) Saint Louis (Paris) et Gd (−) Hayem. *Kahn, A., Boulard, M., Hakim, J., Schaison, G., Boivin, P., Bernard, J.* (Centre de Recherche Claude-Bernard sur les Enzymopathies, Hôpital Beaujon, 92110 Clichy, France), p. 587

Un cas d'hémoglobine Korle Bu [β 73 (E17) Asp → Asn] en Côte-d'Ivoire. Arguments pour une diffusion de gene. Nouvel abord technique. *Labie, D., Belkhodja, O., Coquelet, M. L., Elion, J., Wajcman, H.* (Institut de Pathologie Moléculaire, Centre Hospitalo-Universitaire Cochin, 75014 Paris, France), p. 601

Histiocytes bleus et "cellules de Gaucher" avec surcharges splénique et ganglionnaire au cours d'une leucémie myéloïde chronique. Étude histochimique et ultrastructurale. *Hopfner, C., Potron, G. Adnet, J. J., Caulet, T., Boy, J.* (Reprint requests: Prof. T. Caulet, Service d'Anatomie Pathologique, Centre Hospitalier et Universitaire de Reims, 51100 Reims, France), p. 607

"In vitro" normal biosynthesis of an unstable ferri-hemoglobin: Hemoglobin Saint Louis B10 (β 28) leu → gln. *Cohen-Solal, M., Lebeau, M., Rosa, J.* (I.N.S.E.R.M., U. 91, Hôpital Henri-Mondor, 94010 Créteil, France), p. 621

Hémoglobine Sétif [α 94 (G1) Asp → Tyr]. Étude génétique, biochimique et hématologique. *Debray, J., Krulik, M., Méhaut, M., Benabadji, M., Trabuchet, G., Wajcman, H., Gacon, G., Labie, D.* (Clinique Médicale "A", Hôpital Saint-Antoine, 75571 Paris, France), p. 627

Les dépôts stellaires de fibrine dans la moëlle osseuse. *Nézelof, C., Soulier, J. P. Griscelli, C., Royer, P.* (Groupe de Pathologie Pédiatrique, I.N.S.E.R.M. U. 77, Hôpital Necker Enfants-Malades, 75730 Paris Cedex 15, France), p. 641

La polychimiothérapie des leucémies aiguës myéloblastiques. *Bauters, F., Mouton, J., Carrez, J., Goudemand, M.* (Service des Maladies du Sang, Hôpital Calmette, C.H.U. de Lille, 59000 Lille, France), p. 653

Sur un nouveau cas d'hémoglobine J Baltimore ($\alpha_2^A \beta_2$ 16 Gly → Asp). Étude clinique et biochimique. *Mauran, A., Manesse, B., Cohen-Solal, M., Garel, M. C., Thillet, J., Blouquit, Y., Caburi, J., Vergne, H., Rosa, J.* (I.N.S.E.R.M., U. 91, Hôpital Henri-Mondor, 94010 Créteil, France), p. 663

Fréquence et diffusion de l'hémoglobine Lepore. Intérêt d'une méthod simple d'analyse structurale. *Tayebi, B., Labie, D.* (Institut de Pathologie Moléculaire, 75014 Paris, France), p. 677

Nouvelle Revue Française d'Hématologie (Paris) **14** (1974) No. 6

Coexistence d'un myélome et d'une leucémie granuleuse en l'absence de tout traitement. Étude de quatre observations. *Tursz, T., Flandrin, G., Brouet, J. C., Seligmann, M.* (Institut de Recherches sur les Maladies du Sang, Hôpital Saint-Louis, 75475 Paris Cedex 10, France), p. 693

Étude du caryotype au cours des polyglobulies primitives. *Berger, R., Parmentier, C., Droz, J. P.* (Centre de Recherches Biologiques Néo-natales, Hôpital Port-Royal, 75014 Paris, France), p. 705

Sur un cas de leucémie aiguë chez une fillette atteinte d'anémie de Fanconi. Revue de la littérature. *Lévy, J. M., Korn, R., Stoll, C.* (Service de Pédiatrie IV, 67005 Strasbourg Cedex, France), p. 713

Étude statistique des pores nucléaires dans les cellules lymphoïdes. *Foa, C., Foa, R., Bazin, H., Lazar, P., Carcassonne, Y.* (INSERM-U-119, 13009 Marseille, France) p. 721

Précipitation des lipoprotéines par la protamine après lipolyse induite par l'héparine. *Burstein, M., Legmann, P.* (Centre National de Transfusion Sanguine, 75739 Paris Cedex 15, France), p. 727

La radiothérapie dans la leucémie lymphoide chronique. I. L'irradiation splénique. *Parmentier, C., Chauvel, P., Hayat,*

M., *Bok*, *B.*, *Tubiana*, *M.* (Département des Radiations, Institut Gustave-Roussy, Villejuif, France), p. 737

La lésion enzymatique dans la méthémoglobinémie congénitale récessive avec encéphalopathie. Description d'une nouvelle variante déficitaire de NADH-diaphorase (variante Beni-Messous). *Kaplan*, *J. C.*, *Leroux*, *A.*, *Bakouri*, *S.*, *Grangaud*, *J. P.*, *Benabadji*, *M.* (Cochin-Port Royal, Institut de Pathologie Moléculaire, Paris 75014, France), p. 755

Проблемы гематологии и переливания крови (Москва) 17 (1972) № 1

Влияние антилимфоцитарной сыворотки на регуляцию кроветворения. *Чертков И. Л.*, *Леменева Л. Н.*, *Менделевич О. А.* (Лаборатория экспериментальной гематологии Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва.) с. 3. — Effect of Antilymphocytic Serum on Regulation of Hemopoiesis. *Chertkov*, *I. L.*, *Lemeneva*, *L. N.*, *Mendelevich*, *O. A.*, p. 3

Исследование активности церулоплазмина и эритропоэтинов крови при гипо- и апластических анемиях. *Файнштейн Ф. Э.*, *Чижова А. И.*, *Винокурова Г. П.*, *Сущенко И. Б.*, *Липац А. А.* (Гематологическая клиника и лаборатория проблемы донорства Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва.) с. 15. — Activity of Ceruloplasmin and Erythropoietins in Hypo- and Aplastic Anemias. *Fainshtein*, *F. E.*, *Chizhova*, *A. I.*, *Vinokurova*, *G. P.*, *Suschenko*, *I. B.*, *Lipatz*, *A. A.*, p. 15

Вопросы клиники и дифференциальной диагностики гетерозиготных форм талассемии. *Идельсон Л. И.*, *Дидковский Н. А.* (Научная группа академика И. А. Кассирского АМН СССР на базе Центральной клинической больницы № 2 Министерства путей сообщения СССР, Москва). с. 20. — Clinical Picture and Differential Diagnosis of Heterozygous Forms of Thalassemia. *Idelson*, *L. I.*, *Didkovsky*, *N. A.*, p. 20

Изменения некоторых показателей периферической крови при тотальном облучении человека. *Бриллиант М. Д.*, *Воробьев А. И.* с. 27. — Changes in Certain Peripheral Blood Indices After Total Body Irradiation of Man. *Brilliant*, *M. D.*, *Vorobiev*, *A. I.*, p. 27

Цитохимическое изучение дигидрооротатдегидрогеназы лимфоцитов и бластных клеток детей. *Нарциссов Р. П.*, *Петерсон И. С.*, *Кошель И. В.* (Институт педиатрии АМН СССР.) с. 31. — Cytochemical Study of Dihydroorotic Dehydrogenase of Lymphocytes and Blast Cells in Children. *Nartsissov*, *R. P.*, *Peterson*, *I. S.*, *Koshel*, *I. N.*, p. 31

Применение 6-меркаптопурина при хроническом лимфолейкозе. *Бюр Л. С.*, *Козлова В. Я.*, *Чернцова Т. А.* (Научно-поликлиническое отделение и гематологическое отделение Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва.) с. 36. — The Use of 6-Mercaptopurine in Chronic Lymphoid Leukemia. *Byur*, *L. S.*, *Kozlova*, *V. Ya.*, *Cherntsova T. A.*, p. 36

Редкие гематологические варианты хронического миелолейкоза. *Лорие Ю. И.*, *Финогенова И. А.* (Институт экспериментальной и клинической онкологии АМН СССР, Москва). с. 39. — Rare Hematological Variants of Chronic Myeloid Leukemia. *Lorie*, *Yu. I.*, *Finogenova*, *I. A.*, p. 39

Ультрафиолетовая флюоресценция клеток крови. *Брумберг И. Е.*, *Брумберг Е. М.* (Государственный оптический институт им. С. И. Вавилова, Ленинград.) с. 42. — Ultra-Violet Fluorescence of Blood Cells. *Brumberg*, *I. E.*, *Brumberg*, *E. M.*, p. 42

Получение и химическая характеристика стромы эритроцитов и ее компонентов. *Найер М.*, *Абу Раваш*, *Дембо М. А.* (Лаборатория препаратов крови и кровезаменителей и биохимическая лаборатория Ленинградского института гематологии и переливания крови.) с. 47. — Chemical Characteristics of the Stroma of Erythrocytes and its Components. *Nayer*, *M. Abu Zawash*, *A*, *Dembo*, *M. A.*, p. 47

Остеомиелофиброз и хронический лимфо-

лейкоз у одного и того же больного. *Дыгин В. П., Шейпак Л. Н.* (клиника факультетской терапии Военно-медицинской академии им. С. М. Кирова, Ленинград.) с. 53. — Osteomyelofibrosis and Chronic Lymphoid Leukemia in the Same Patient. *Dygin, V. P., Sheipak, L. N.*, p. 53

Случай длительного (19 лет) лимфогранулематоза. *Селиванова И. П.* (Кафедра факультетской терапии Рязанского медицинского института им. акад. И. П. Павлова.) с. 55. — 19 Year Course of Lymphogranulomatosis. *Selivanova, I. P.*, p. 55

О варианте внепеченочной портальной гипертонии, сопровождающейся своеобразными изменениями гемопоэза. *Соболева С. С., Фриновская И. В., Новикова Э. З., Цукерман О. А., Неменова Н. М., Гласко Е. Н., Шельгас Л. Е., Отставнова Е. И.* (Гематологическое отделение, рентгенологическое отделение, патологоанатомическая лаборатория Центрально о института гематологии и переливания крови Министерства здравоохранения СССР, Москва.) с. 56. — A Variant of Extrahepatic Portal Hypertension with Peluciar Changes of Hemopoiesis. *Soboleva, S. S., Frinovskaya. I. V., Novikova, E. Z., Tsukerman, O. A., Nemenova, N. M., Glasko, E. N., Shelgas, L. E., Otstavnova, E. I.*, p. 56

Вопросы организации диспансеризации больных лейкозами. *Лебедев В. Н.* (Гематологическое отделение Сочинского онкологического диспанесра.) сн. 60. — Problems of Organization of Leukemia Dispensaries. *Lebedev, V. N.*, p. 60

Проблемы гематологии и переливания крови (Москва) 15 (1972) № 2

Метаболизм лейкоцитарных элементов костного мозга при хроническом миэлолейкозе. *Лапотников В. А., Лебедева Н. П., Москалик И. Г., Онущенко, И. А., Филев Л. В.* (Кафедра факультетской терапии 1 Ленинградского медицинского института им. акад. И. П. Павлова) с. 3. — Metabolism of Leukocytic Bone Marrow Elements in Chronic Myeloid Leukemia. *Lapotnikov, V. A., Lebedeva, N. P., Moskalik, I. G., Onuschenko, I. A., Filev, L. V.*, p. 3

Органные культуры костного мозга человека. *Лурия Е. А., Воробьев А. И., Кулагина Н. Н., Панасюк, А. Ф., Прусевич Т. О., Смирнов А. Н., Фриденштейн А. Я.* с. 6. — Cultures of Human Bone Marrow. *Luria, E. A., Vorobiev, A. I., Kulagina, N. N., Panasyuk, A. F., Prusevich, T. O., Smirnov, A. N., Fridenshtein, A. Ya.*, p. 6

К вопросу о роли сосудистых факторов в генезе кровоточивости при гипопластической анемии. *Лагутина Н. Я., Чижова А. И., Кочемасов В. В., Файнштейн Ф. Э.* (Гематологическое отделение центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва.) с. 12. — The Role of Vascular Factors in the Tendency to Hemorrhages in Hypoplastic Anemia. *Lagutina, N. Ya., Chizhova, A. I., Kochemasov, V. V., Fainshtein, F. E.*, p. 12

Состояние симпатико-адреналовой системы у детей с болезнью Верльгофа. *Данилина З. А., Колесов Д. В., Зиновьева Г. А., Новикова Л. С.* (Клиника детских болезней I. Московского медицинского института им. И. М. Сеченова) с. 16. — The Sympatho-Adrenal System in Children with Werlhof's Disease. *Danilina, Z. A., Kolesov, D. V., Zinovieva, G. A., Novikova, L. S.*, p. 16

К вопросу о генетической гетерогенности α-талассемии. *Дидковский Н. А., Идельсон Л. И., Цфасман А. З.* (Группа акад. АМН СССР проф. И. А. Кассирского на базе Центральной клинической больницы № 2 Мин. путей сообщения, Москва). с. 20. — Genetic Heterogeneity of α-Thalassemia. *Didkovsky, N. A., Idelson, L. I., Tsfasman, A. Z.*, p .20

Влияние плазмы и плацентина-3 на эритропоэз и эритропоэтическую активность крови больных железодефицитными аанемиями. *Морозова А. Д., Винокурова Г. П., Михайлова Л. И.* (Гемотерапевтическое отделение и лаборатория проблемы донорства Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва.) с. 26. — Effect of Plasma and of Placentin-3 on Erythropoiesis and

Erythropoietic Activity in Iron Deficiency Anemia. *Morozova, A. D., Vinokurova, G. P., Mikhailova, L. I.*, p. 26

Поражение легких при остром лейкозе. *Касымходжаев Э. С.* (Узбекский институт гематологии и переливания крови, Ташкент.) с. 28. — Affection of the Lungs in Acute Leukemia. *Kasymkhodzhaev, E. S.*, p. 28

Данные о заболеваемости лейкозами в Сочи и Туапсе (1960—1969 гг.). *Лебедев В. Н., Беликова С. Г. Бецкий Б. А., Корнеева Л. А., Лебедева Ю. Л., Моисенко М. И., Юничева Р. Х.* (Гематологическое отделение Сочинского онкологического диспансера). с. 30. — Incidence of Leukemia in Sochi and Tuapse in 1960—1969. *Lebedev, V. N., Belikova, S. G., Betsky, B. A., Korneeva, L. A., Lebedeva, Yu. L., Moiseenko, M. I., Yunicheva, R. Kh.*, p. 30

Заболеваемость лейкозами в Самарканде и Самаркандской области в 1966—1969 гг. *Богданов, И. С., Хакимов Х. А.* (Узбекский институт гематологии и переливания крови, Ташкент и Самаркандская областная станция переливания крови) с. 33. — Incidence of Leukemia in Samarkand Town and Region. *Bogdanov, I. S., Khakimov, Kh. A.*, p. 33

Исследование эритрокинетики и гликолитической активности эритроцитов здоровых детей. *Матвеева Л. А., Балашева И. И., Сурикова Н. И., Ольховатенко Л. И., Рыбка В. И.* (Кафедра факультетской педиатрии и биохимическая лаборатория Томского медицинского института) с. 35. — Electrokinetics and Glycolytic Activity of Erythrocytes in Healthy Children. *Matveeva, L. A., Balasheva, I. I., Surova, N. A., Olkhovatenko, L. I., Rybka, V. I.*, p. 35

Определение колониеобразующих клеток в селезенке. *Черткова И. Л., Леменева Л. Н., Менделевич О. А.* (Лаборатория экспериментальной гематологии и переливания крови Министерства здравоохранения СССР, Москва) с. 37. — Colony-Forming Cells in the Spleen. *Chertkov, I., L., Lemeneva, L. N., Mendelevich, O. A.*, p. 37

Возможность продления выживания аллотрансплантатов с помощью воздействия антилимфоцитарной и антитромбоцитарной сыворотками. *Худанов Л. Л., Вербицкий М. Ш., Арцимович Н. Г., Кипервассер Е. М., Лагутина Н. Я., Намятышева А. М., Кирзон С. С., Ефимов Е. А., Кривский И. Л.* (Центральный институт гематологии и переливания крови Министерства здравоохранения СССР, Институт хирургии им. А. В. Вишневского АМН СССР, Институт медицинской генетики АМН СССР, Москва) с. 42 – Prolongation of Survival of Allotransplants by Antilymphocytic and Antithrombocytic Sera. *Khudanov, L. L., Verbitsky, M. Sh. Artsimovich, N. G., Kiperwasser, E. M., Lagutina, N. Ya., Namyatysheva, A. M., Kirzon, S. S., Evimov, E. A., Krivsky*, p. 42

Ингибирующее метафазу действие параоксифенилмолочной кислоты в первичной культуре человеческой эмбриональной ткани. *Кузнецова Л. Е., проф. Раушенбах М. О.* (Лаборатория системных заболеваний крови Института экспериментальной и клинической онкологии АМН СССР, Москва) с. 50. — Inhibition by Paraoxyphenyl-Lactic Acid of Metaphase in a Primary Culture of Human Embryonic Tissue. *Kuznetsova, L. E., Saushenbakh, M. O.*, p. 50

Применение радиоактивного хрома для одновременного определения продолжительности жизни и костномозговой продукции эритроцитов. *Илюхин А. В., Семашко Л. Л., Бураковская Т. Е., Шафиркин А. В.* с. 53. — Use of Radioactive Chromium for Simultaneous Determination of Life Span and Marrow Production of Erythrocytes. *Ilyukhin, A. V., Semashko, L. L., Burkovskaya, T. E., Shafirkin, A. V.*, p. 53

Проблемы гематологии и переливания крови (Москва) 17 (1972) № 2

О гипопластической анемии, протекающей с синдромом пароксизмальной ночной гемоглобинурии, и некоторые вопросы дифференциальной диагностики этого заболевания с болезнью Маркиафава-Микели. *Файнштейн Ф. Э., Турбина Н. С., Родина Р. И., Соболева Ю. Г., Розанова Н. С., Воронина А. Н., Шитикова М. Г., Фетисов В. В., Любимова Л. С.*

(Гематологическое отделение, клиническая лаборатория и цитологическая лаборатория Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва). с. 3. — Hypoplastic Anemia with Paroxysmal Nocturnal Hemoglobinuria: the Differentiation from Marchiafava-Micheli's Disease. *Fainshtein, F. E., Turbina, N. S., Rodina, R. I., Soboleva, Yu. G., Rozanova, N. S., Voronina, A. N., Shitikova, M. G., Fetisov, V. V., Lyubimova, L. S.*, p. 3

Протеин и его применение при состояниях белковой недостаточности и протеинопривных анемиях. *Альперин П. М., Фром А. А., Жеребцов Л. А., Мелехова О. П., Русанов В. М., Баронина М. А., Воронина Л. Н., Дубровина Н. А., Замчий А. А., Кочина Е. Н., Шарова Ю. А.* (Гемотерапевтическая клиника, экспериментально-производственная лаборатория Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва) с. 8. — Protein, and Its Use in Protein Deficiency Anemias. *Alperin, P. M., From, A. A., Zherebtsov, L. A., Melekhova, O. P., Rusanov, V. M., Baronina, M. A., Voronina, L. N., Dubrovina, N. A., Zamchy, A. A., Kochina, E. N., Sharova, Yu. A.*, p. 8

Свертывающая система крови у больных серповидноклеточной болезнью. *Орлова Л. Д., Хуцишвили Г. Э.* (Гематологическое отделение Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва и грузинский институт гематологии и переливания крови, Тбилиси) с. 12. — Blood Coagulation in Patients with Sickle-Cell Disease. *Orlova, L. D., Khutsishvili, G. E.*, p. 12

Влияние витаминов А и Е на кислотную резистентность эритроцитов. *Мельник В. П.* (Кафедра биохимии Алтайского медицинского института) с. 15. — Effect of Vitamins A and E on the Acid Resistance of Erythrocytes. *Melnik, V. P.*, p. 15

Изменения показателей периферической крови и миелограммы в первом периоде ожоговой болезни. *Муразян Р. И., Илюхин А. В., Турбина Н. С., Сидорова Л. Г., Максимова П. И., Стрижевская Л. Н., Герасимова Л. И.* (Хирургическое отделение Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва) с. 17. — Change in the Peripheral Blood Indices and Myelogram During the First Period of Burns. *Murazyan, R. I., Ilyukhin, A. V., Turbina, N. S., Sidorova, L. G., Maximov, P. I., Strizhevskaya, L. N., Gerasimova, L. I.*, p. 17

Состояние гемопоэза и показания к переливанию крови у обожженных детей. *Воронина Г. В., Егоров П. И., Евхаритская З. Е.*, (Военно-медицинская академия им. С. М. Кирова, Ленинград) с. 22. — Hemopoiesis and Indications of Blood Transfusion in Burned Children. *Voronina, G. V., Egorov, F. I., Evkharitskaya, Z. E.*, p. 22

Применение алломиелотрансплантации в терапии гипоплазий гемопоэза, вызванных цитостатическими препаратами. *Михайлов В. Г., Алиева Т. М., Олендер С. К., Глиндеман В. П.* (Лаборатория консервации тканей Узбекского института гематологии и переливания крови и Ташкентский городской онкологический диспансер, Ташкент) с. 25. — Allomyelotransplantation in Hemopoietic Disturbances due to Cytostatics. *Mikhailov, V. G., Alieva, T. M., Oleander, S. K., Glindeman, V. P.*, p. 25

Содержание в крови здоровых людей некоторых микроэлементов и возможные потери их в процессе взятия крови. *Тимакин Н. П., Гольдберг Е. Н., Петраковская Е. А.* (Центральная научно-исследовательская лаборатория Томского медицинского института и Томская областная станция переливания крови) с. 27. — Microelements in the Blood of Healthy Persons and Their Losses after Blood Sampling. *Timakin, N. P., Goldberg, E. D., Petrakovskaya, E. A.*, p. 27

Ограждающее действие полиэтиленоксидов на клетки при глубоком замораживании. *Пушкарь Н. С., Шенберг М. Г., Наконечный А. А., Симонова Л. И. Цуцаева А. А., Обозная Э. И., Дроздова О. А., Останкова Л. В., Бодня В. М., Карева Л. В., Михайличенко З. П., Гайсенюк Л. А.* (Проблемная лаборато-

рия низкотемпературной консервации костного мозга и крови Украинского института усовершенствания врачей Министерства здравоохранения СССР, Харьков) с. 30. — Protective Action of Polyethyleneoxide on Cells during Deep Freezing. *Pushkar, N. S., Shenberg, M. G., Nakonechny, A. A., Simonova, L. I., Tsutsaeva, A. A., Oboznaya, E. I., Drozdova, L. A., Ostankova, L. V., Bodnya, V. M., Kareva, L. V., Mikhailichenko, Z. P., Gaisenyuk, L. A.*, p. 30

Применение сополимеров винилпирролидона с кротоновой кислотой в качестве криопротектора клеток костного мозга трупов. *Медведева П. М., Фисанович Т. И., Кропачев В. А., Трухманова Л. Б., Алферова Л. В.* (Ленинградский институт гематологии и переливания крови и Институт высокомолекулярных соединений АН СССР) с. 34. — Use of Crotonic Acid Copolymers of vinylpyrrolidone as Cryoprotectors of Cadaver Bone Marrow Cells. *Medvedeva, P. M., Fisanovich, T. I., Kropachev, V. A., Trukhmanova, L. B., Alferova, L. V.*, p. 34

Выявление австралийского антигена и антител к нему в крови у доноров и гематологических больных — рання диагностика заражения вирусом гепатита и профилактика трансмиссионной передачи его. *Голосова Т. В. Фром А. А., Марголина А. Н., Бурлев В. А., Никитенко А. А.* (Центральный институт гематологии и переливания крови Министерства здравоохранения СССР, Москва) с. 30. — Detection of Australia Antigen and its Antibodies in Blood Donors and Hematological Patients, for Early Diagnosis of Hepatitis Virus Infection and Prophylaxis of Its Transmission. *Golosova, T. V., From, A. A., Margolina, A. N., Burlev, V. A., Vikitenko, A. A.*, p. 30

Морфологические изменения в почках при введении синтетического плазмозамещающего раствора поливинола. *Касымходжаев Э. С., Аверьянова С. Г.* (Узбекский институт гематологии и переливания крови Ташкент) с. 45. — Morphological Changes in the Kidneys Induced by Polyvinyl Plasma Substitutes. *Kasymkhodzhaeva, Z. S., Averyanova, S. G.*, p. 45

Сравнительная оценка электролитного состава отмытых эритроцитов, взвешенных в различных плазмозамещающих средах. *Бородай Э. И., Вовк Г. П., Сеник Я. К.* (Отдел консервирования крови Львовского института гематологии и переливания крови, кафедра факультетской терапии Львовского медицинского института и Львовская городская клиническая больница № 5). с. 46. — Comparative Evaluation of an Electrolyte Composition of Washed Erythrocytes Suspended in Various Plasma Substitutes. *Borodai, E. I., Vovk, G. P., Senik, Ya. K.*, p. 46

Современные представления о патогенезе анемии при хроническом миелоидном и лимфатическом лейкозах (Обзор литературы и собственные данные). *Канаев С. В., Тушинская М. М., Розанова Л. М., Егоршин Э. В., Абдулкадыров К. М., Федоров В. В., Лапченков В. И., Осипов И. С., Доценко М. С.* (Кафедра факультетской терапии I Ленинградского медицинского института им. акад. И. П. Павлова, гематологическая клиника Ленинградского научно-исследовательского института гематологии и переливания крови, лаборатория изотопных методов исследования Центрального научно-исследовательского рентгено-радиологического института Министерства здравоохранения СССР) с. 48. — Pathogenesis of Anemia in Chronic Myeloid and Lymphatic Leukemias (Survey of the Literature and Own Data). *Kanaev, S. V., Tushinskaya, M. M., Rozanova, L. M., Egorshin, E. V., Abdulkadyrov, K. M., Fedorov, V. V., Laptsenkov, B. I., Osipov, I. S., Dotsenko, M. S.*, p. 48

Проблемы гематологии и переливания крови (Москва) 17 (1972) № 4

Новые данные о природе и функции противосвертывающей системы. *Кудряшев Б. А.* (Кафедра физиологии и биохимии свертывания крови Московского государственного университета им. М. В. Ломоносова) с. 3. — New Data on the Nature and Function of the Anticoagulation System. *Kudryasov, B. a.*, p. 3

О так называемой противосвертывающей системе. *Ойвин И. А.* (Отдел патологической физиологии Института медицинской радиологии АМН СССР, Обнинск) с. 13. — The So-called Anticoagulation System. *Oyvin, I. A.*, p. 13

Аспекты гемостаза и гемокоагуляции. *Маркосян А. А.*, (Институт физиологии детей и подростков АПН СССР, Москва) с. 16. — Aspects of Hemostasis and Hemocoagulation. *Markosyan, A. A.*, p. 1

Гемокоагулирующие и фибринолитические свойства кожи и подкожной жировой клетчатки. *Скипетров В. П., Горбитская В. Т.* (Кафедра нормальной физиологии Медицинского факультета Мордовского университета, Саранск) с. 19. — Hemocoagulating and Fibrinolytic Properties of the Skin and of Subcutaneous Adipose Tissue. *Skipetrov, V. P., Gorbitskaya, V. T.*, p. 19

О механизме возникновения несвертываемости крови при поступлении в кровоток веществ с тромбопластиновой активностью. *Ойвин И. А., Балуда В. П.* (Институт медицинской радиологии АМН СССР, Обнинск) с. 23. — Noncoagulability of Blood Following Entrance into the Circulation of Substances with Thromboplastin Activity. *Oivin, I. A. Baluda, V. P.*, p. 23

Комплексные соединения плазминогена с гепарином (ПГГ) и плазмина с гепарином (ПГ) и их значение в регуляции жидкого состояния крови. *Кудряшев Б. А., Ляпина Л. А.* (Лаборатория физиологии и биохимии свертывания крови Московского университета им М. В. Ломоносова) с. 28. — Complex Compounds of Plasminogen with Heparin (PGH) and of Plasmin with Heparin (PH) and Their Significance in Regulation of the Fluid Condition of the Blood. *Kudryasov, B. A., Lyapina, L. A.*, p. 28

К вопросу о нервной и эндокринной регуляции свертывания крови на органотканевом уровне. *Гланц Р. М.* (Экспериментальный отдел Львовского института гематологии и переливания крови) с. 30. — Nervous and Endocrine Regulation of Blood Coagulation at the Organic-Tissue Level. *Glantz, R. M.*, p. 30

Особенности диагностики, клиники и лечения гемофилий с циркулирующими специфическими антикоагулянтами. *Баркаган З. С., Суховеева Е. Я., Еремин Г. Ф., Толочко Н. И., Шевченко В. И., Тарасова Н. И.* (Клиника пропедевтики внутренних болезней Алтайского медицинского института, Барнаул) с. 35. — Diagnosis, Clinical Picture and Treatment by Specific Anticoagulants of Hemophilia. *Barkagan, Z. S., Sukhoveyeva, E. Ya., Eremin, G. F., Tolochko, O. I., Shevchenko, V. I., Tarasova, N. I.*, 35

Зависимость фибринолитической активности от содержания лейкоцитов в крови у больных лейкозами. *Красик Я. Д., Кузник Б. И.* (Кафедра нормальной физиологии и кафедра факультетской терапии Читинского медицинского института) с. 41. — Dependence of Fibrinolytic Activity on Leukocyte Count in Leukemia. *Krasik, Ya. D., Kuznik, B. I.*, p. 41

Сравнительная оценка методов определения фибринолитической активности крови у больных хроническим миелолейкозом. *Наумова Г. А., Орлова Л. Д., Андреенко Г. В.* (Гематологическая клиника Центрального института гематологии и переливания крови Министерства здравоохранения СССР и лаборатория физиологии и биохимии свертывания крови Московского университета им. М. В. Ломоносова) с. 44. — Comparative Assessment of Blood Fibrinolytic Activity in Chronic Myeloid Leukemia. *Naumova, G. A., Orlova, L. D., Andreyenko, G. V.*, p. 44

Результаты спеленэктоми про болезни Верльгофа. *Гроздов Д. М., Цепа Л. С.* (Хирургическая клиника Центрального института гематологии и переливания крови Министерства здравоохранения, Москва) с. 49. — Results of Splenectomy in Werlhof's Disease. *Grozdov, D. M., Tsepa, L. S.*, p. 49

Беременность и болезнь Верльгофа. *Павлова Л. С., Цепа Л. С., Дидина Н. М.,-Киселева К. С.* (Московский областной научно-исследовательский институт акушерства и гинекологии и Центральный институт гематологии и переливания крови Министерства здравоохранения СССР, Москва) с. 55. — Pregnancy and Werlhof's disease. *Pavlova,*

L. S., Tsepa, L. S., Didina, N. M., Kiselyeva K. S., p. 55

Случай врожденной афибриногенемии с гипопротромбинемией. *Салиев К. К.* (Кафедра биологии с общей генетикой Андижанского медицинского института) с. 57. — A Case of Congenital Afibrinogenemia with Hypoprothrombinemia. *Saliev, K. K.*, p. 57

О патогенезе тромботических осложнений антикоагулянтной терапии. *Рзаев Н. М., Закирджаев Д. Д.* (Научно-исследовательский институт клинической и экспериментальной медицины Министерства здравоохранения Азербайджанской ССР, Баку) с. 58. — Thrombotic Complications of Anticoagulant Therapy. *Rzaev, N. M., Zakirdshaev, D. D.*, p. 58

Проблемы гематологии и переливания крови (Москва) 17 (1972) № 5

Австралийский антиген (А) и связь его с сывороточным гепатитом. *Киселев А. Е., Голосова Т. В., Марголина А. Н. Бурлев В. А.* (Центральный институт гематологии и переливания крови Министерства здравоохранения СССР, Москва) с. 3. — Australia Antigen and its Association with Serum Hepatitis. *Kiselev, A. E., Golosova, T. A., Margolina, A. N.*, p. 3

Спленэктомия у беременных и родильниц с болезнью Верльгофа. *Гроздов Д. М., Романова Е. П., Кукель А. С., Саутина В. О., Иванова Е. С.* (Центральный институт гематологии и переливания крови, Всесоюзный институт акушерства и гинекологии Министерства здравоохранения СССР, Москва) с. 8. — Splenectomy in Pregnant and Puerperal Women with Werlhof's Disease. *Grozdov, D. M., Romanova, E. P., Kukel, A. S., Sautina, V. O., Ivanova, E. S.*, p. 8

Клинико-морфологические особенности болезни Верльгофа при кортикостероидной терапии. *Покровский П. И., Цепа Л. С., АнохинаЮ. В.* (Хирургическая клиника, патологоанатомическая лаборатория и лаборатория эпидемиологии и гистопатологии лейкозов Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва) с. 13. — Werlhof's Disease Treated with Corticosteroid Hormones. *Pokrovsky, P. I., Tsepa, L. S., Anokhina, Yu. V.*, p. 13

Морфологические особенности селезенки при болезни Верльгофа. *АнохинаЮ. В., Хохлова М. П.* (Патологоанатомическая лаборатория, лаборатория эпидемиологии и гистопатологии лейкозов Центрального института гематологии и переливания крпви Министерства здравоохранения СССР, Москва) с. 15. — Morphology of Spleen in Werlhof's Disease. *Anokhina, Yu. V., Khokhlova, M. P.*, p. 15

Некоторые особенности изменений стенки сосудов у больных гипо- и апластической анемиями. *Кочемасов В. В., Розанова Н. С.* (Гематологическая клиника и патологианатомическая лаборатория Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва) с. 21. — Changes of the Vascular Wall in Hypo- and Aplastic Anemias. *Kochemasov, V. V., Rozanova, N. S.*, p. 21

К вопросу о метаболизме серотонина у больных гипопластической анемией. *Лагутина Н. Я., Чижова А. И.* (Гематологическое отделение Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва). с. 26. — Serotonin Metabolism in Hypoplastic Anemia. *Lagutina, N. Ya., Chizhova, A. I.*, p. 26

К вопросу об обмене железа у больных хронической железодефицитной анемией. *Харятьян А. М.,Юлдашев У. И., Цветков В. В., Калугина В. И., Закирова М. А.* (Радиологическая группа Ташкентского медицинского института и Узбекский институт гематологии и переливания крови) с. 28. — Some Indices of Ferrokinetics in Chronic Iron Deficiency Anemia. *Kharatyan, A. M., Yuldashev, U. I., Tsvetkov, V. V., Kalugina, V. I., Zakirova, M. A.*, p. 28

Значение уровня фактора VIII в крови при оперативных вмешательствах у больных гемофилией А. *Рутберг Р. А., АндреевЮ. Н.*, (Отдел кровезаменителей и головной центр по гемофилии Центрального института гематологии и

переливания крови Министерства здравоохранения СССР, Москва) с. 30. — Significance of Factor VIII Level in Surgical Interventions on Patients with Hemophilia A. *Ruthberg, R. A., Andreev, Yu. N.*, p. 30

К вопросу о механизме нарушения вязкого метаморфоза тромбоцитов при гемофилиях. *Громнацкий Н. И.* (Львоский институт гематологии и переливания крови) с. 34. — Disturbance of Platelet Viscosity in Hemophilia. *Gromnatsky, N. I.*, p. 34

Влияние графит-бензалконий-гепаринового комплекса и его отдельных компонентов на гемокоагуляцию. *Чепуров А. К.,Юдин А. А.* (Отделение трансплантации и искусственных органов Института клинической и экспериментальной хирургии Министерства здравоохранения СССР, Москва) с. 37. — Effect on Hemocoagulation of Graphite-Benzalconium-Heparin Complex and of its Individual Components. *Chepurov, A. K., Yudin, A. A.*, p. 37

К вопросу о нормализации белкового состава крови у ожоговых больных. *Стальков Е. А.* (Кафедра анатомии и физиологии человека и животных Калининградского университета) с. 41. — Normalization of Blood Protein Composition in Burns. *Stalkov, E. A.*, p. 41

Влияние переливания крови на функциональное состояние тканевого звена системы гемостаза. *Гланц Р. М., Ткач Е. А.* (Экспериментальный отдел Львовского института гематологии и переливания крови) с. 45. — Effect of Blood Transfusion on the Functional Condition of the Tissue Link of the Coagulation System. *Glantz, R. M., Tkach, E. A.*, p. 45

Методы диагностического применения витамина B_{12}—Co^{58} в клинической медицине. *Харятьян А. М., Воловой В. Л.* (Биофизическая лаборатория Ташкентского медицинского института) с. 54. — Diagnostic Application of ^{58}Co Vitamin B_{12} in Clinical Medicine. *Kharatyan, A. M., Ъolovoy, V. L.*, p. 54

Новые методы разделения крови на компоненты и отмывания от ограждающих растворов эритроцитов, хранившихся в замороженном состоянии, при автоматизации этих процессов с помощью макета отечественного фракционатора. *Виноград-Финкель Ф. Р., Рутберг Р. А., Воробьева Г. С., Федорова Л. И., Семенова Н. В.* (Лаборатория консервирования крови Центрального института гематологии и переливания крови Министерства здравоохранения СССР, Москва) с. 59. — New Method of Blood Separation into Components and Washing from Preservatives of Erythrocytes Stored in Frozen Condition. Automation of these Processes by means of a Soviet Fractionator. *Vinograd-Finkel, F. R., Rutberg, R. A., Vorobieva, G. S., Fedorova, L. I., Semenova N. V.*, p. 59

Revue Française de Transfusion (Paris) **17** (1974) No. 2

Nécrologie. p. 119

Ordinateur et phénotypage des donneurs de sang. *Chateau, G., Delmas-Marsalet, Y., Goudemand, M.* (Centre Régional de Transfusion Sanguine, 59012 Lille Cedex, France), p. 121

Les nucléotides adényliques comme indicateurs de la qualité des sangs ACD et CPD conservés. *Saint-Blancard, J., Allary, M., Bouchet, J., Fabre, G.* (Centre de Transfusion Sanguine des Armées "Jean Julliard", 92140 Clamart, France), p. 137

Un cas de dysérythropoièse congénitale de type II. Mise en évidence de l'antigène par les extraits de Helix pomatia. Étude comparée avec les antigènes de la série Cad. *Bizot, M., Monis, M.* (Centre de Transfusion Sanguine de Montpellier, 3400 Montpellier, France), p. 147

Ictère hémolytique néonatal par anti-D réagissant préférentiellement en milieu enzymatique. *Bizot, M., Monis, M., Rieu, D.* (Centre de Transfusion Sanguine de Montpellier, 34010 Montpellier Cedex, France), p. 151

Phénotype Rh nul. *Habibi, B.* (Service d'Immunologie, C.D.T.S., 75012 Paris, France), p. 159

Revue Française de Transfusion (Paris) **17** (1974) No. 3

L'antigène D^u. *Salmon, Ch., Gerbal, A.* (Centre Départemental de Transfusion Sanguine, 75012 Paris, France), p. 195

Étude comparée de diverses méthodes de mise en évidence de l'antigène D^u. *Yvart, J., Gerbal, A., Cartron, J., Salmon, Ch.* (Centre Départemental de Transfusion Sanguine, 75571 Paris Cedex 12, France), p. 201

Détermination du facteur D^u sur Groupamatic. Étude comparée avec les techniques manuelles. Bilan sur 203,240 examens. *Garretta, M., Muller, A., Gener, J.* (Centre National de Transfusion Sanguine, 75739 Paris Cedex 15, France), p. 211

Facteur D^u et groupage sanguine de routine. *Jouvenceaux, A., Chataing, B.* (Centre Régional de Transfusion Sanguine Hôpital Edouard-Harriot, 69374 Lyon Cedex 2, France), p. 229

Comportement électrophorétique sur différents supports du plasminogène humain. *Steinbuch, M., Audran, R., Lambin, P., Fine, J.-M.* (Centre National de Transfusion Sanguine, 75015 Paris, France), p. 235

Préparation de suspensions leucocytaires injectables par leucophérèse en flux continu. *Malinvaud, G., Gaillard, S.* (Centre de Transfusion Sanguine, 87000 Limoges, France), p. 251

Fréquence de l'antigène Australie chez 13.658 donneurs espagnols bénévoles. *Galvé, C.* (Service d'Hématologie et de Transfusion des Armées, Instituto de Medicina Preventiva, Madrid 15, Spain), p. 267

Scandinavian Journal of Haematology (Copenhagen) **12** (1974) No. 1

Diagnostic laparotomy in Hodgkin's disease. *Andersen, E., Videbaek, Aa.* (Medical Department C, Gentofte Hospital, DK-2900 Copenhagen, Hellerup, Denmark), p. 5

Cyclic thrombocytopenia. Case report and review of literature. *Cohen, T., Cooney, D. P.* (Reprint requests: D. P. Cooney, Division of Hematology, Stanford University School of Medicine, Stanford, Calif. 94305), p. 9

Composition and mitotic activity of the erythropoietic part of the bone marrow in chronic myeloid leukaemia. *Sjögren, U., Brandt, L.* (Department of Internal Medicine, University Hospital, S-22185 Lund, Sweden), p. 18

β-Glucuronidase activity in Sezary cells. *Flandrin, G., Daniel, M. T.* (Institut de Recherche sur les Maladies du Sang, Hôpital Saint-Louis, 75475 Paris Cédex 10, France), p. 23

Myelomatosis and acute monocytic leukaemia. *Marcović, N., Hansson, B.-G., Hällén, J.* (Reprint requests: J. Hällén, Medical Department, Centrallasarettet, S-721 89 Västeras, Sweden), p. 32

Sinus repair in the bone marrow of hypoxic mice. Possible relationship to cellular migration. *Ben-Ishay, Z.* (Department of Anatomy, Hebrew University Hadassah Medical School, Jerusalem, Israel), p. 37

The influence of technical factors on the NBT test. *Björkstén, B.* (Department of Virology, University of Umeå, S-901 85 Umeå Sweden), p. 46

Platelet factor 4 (PF-4). A study on methodology and physiology. *Gjesdal, K.* (Institute of Clinical Medicine, University of Tromsø, Tromsø, Norway), p. 51

IgG subclasses: Relationship to clinical aspects of multiple myeloma and frequency distribution among M-components. *Schur, P. H., Kyle, R. A., Bloch, K. J., Hammack, W. J., Rivers, Sh. L., Sargent, A., Ritchie, R. F., McIntyre, O. R., Moloney, W. C., Wolfson, L.* (Robert B. Brighton Hospital, Boston, Mass. 02120), p. 60

Platelet survival and platelet production in idiopathic thrombocytopenic purpura (ITP) before and during treatment with corticosteroids. *Branehög, I., Weinfeld, A.* (Department of Medicine II, Sahlgren's Hospital, S-413 45 Göteborg, Sweden), p. 69

Scandinavian Journal of Haematology (Copenhagen) **12** (1974) No. 2

Erythrocyte δ-aminolaevulinic acid dehydratase in homozygous β-thalassaemia. *Lyberatos, C., Mitsiou, Ch., Philippidou, A., Papayannis, A. G., Chalevelakis, G., Gardikas, C.* (Medical Unit, Evangelismos Hospital, Athens 140, Greece), p. 81

Platelet factor 3 activity and platelet aggregation in patients submitted to coronarography. *Renaud, S., Gautheron, P., Arbogast, R., Dumont, E.* (INSERM, Unité 63, 69500 Bron, France), p. 85

Human platelet aggregation by thrombofax. An electron-microscopic study of the sequence of events. *de Clerck, F., Borgers, M., Vermylen, J., de Gaetano, G.* (Cardiovascular Department, Janssen Research Laboratories, B-2340 Beerse, Belgium), p. 93

Ultrastructural features of the granulocytes in Down's syndrome. *Djaldetti, M., Bessler, H., Fishman, P., van der Lÿn, E., Joshua, H.* (Department of Internal Medicine "B", Hasharon Hospital, Petah-Tiqva, Israel), p. 104

Serum immunoglobulin levels in chronic lymphatic leukaemia. *Slungaard, A., Smith, M. J.* (Department of Internal Medicine, Gundersen Clinic, La Crosse, Wis. 54601), p. 112

Trisomy G-21 in adult myelomonocytic leukaemia. An abnormality common to granulocytic and monocytic cells. *Brandt, L., Levan, G., Mitelman, F., Olsson, I., Sjögren, U.* (Reprint requests: F. Mitelman. Department of Internal Medicine A, University Hospital, S-22185 Lund, Sweden), p. 117

Autonomy of the PHA-responsive cells in the mouse thymus. *Jacobsson, H., Blomgren, H.* (Department of Tumor Biology, Karolinska Institutet, S-10401 Stockholm 60, Sweden), p. 123

The effect of fractionated administration of erythropoietin in splenectomized or sham-operated erythraemic mice. *Fogh, J.* (Department of Nuclear Medicine, Rigshospitalet, DK-2100 Copenhagen Ø ,Denmark), p. 133

Unusual cases of myelomatosis. *Ghosh, M. L., Sayeed, A.* (Department of Haematology, District General Hospital, Barnsley, Yorkshire, England), p. 147

Myeloperoxidase-mediated extracellular iodination during phagocytosis in granulocytes. *Odeberg, H., Olofsson, T., Olsson, I.* (Research Department II, E-blocket, Hospital of Lund, S-220 05 Lund, Sweden), p. 155

Scandinavian Journal of Haematology (Copenhagen) **12** (1974) No. 3

Pseudotumour of bone in a haemophiliac with circulating antibodies to factor VIII. Recovery after rupture of cyst wall without necrosis or perforation of the skin. *Stavem, P., Egeberg, O., Kolmannskog, F., Nökleby, K.* (Section of Haematology, Medical Department A, Rikshospitalet, Oslo 1, Norway), p. 161

The effect of products D and E on the thrombin induced conversion of fibrinogen to fibrin. *Arnesen, H.* (Haematological Laboratory, Department IX, Ullevål Hospital, Oslo, Norway), p. 165

Red-cell carbonic anhydrase isoenzymes in megaloblastic anaemia. *Dunbar, A. P., Tudhope, G. R.* (Department of Pharmacology and Therapeutics, University of Dundee, Dundee, DD1 4HN, Scotland), p. 173

Possible mechanism of vinblastine-induced thrombocytosis. *Klener, P., Donner, L., Hynčica, V., Šafránková, D.* (Second Department of Medicine, Division of Haematology, Charles University Hospital, 12808 Prague 2, Czechoslovakia), p. 179

Particulate emboli retained by bypass blood filters. *Schneider, M. D.* (Medical Engineering Research Division, IIT Research Institute, Chicago, Ill. 60616), p. 185

The role of fibrin monomer and an in vivo thrombin-induced anticoagulant in experimental venous thrombosis. *Wetmore, R., Gurewich, V.* (Vascular Laboratory, Lemuel Shattuck Hospital, Jamaica Plain, Mass. 02130), p. 204

Studies on coagulation and fibrinolysis in experimental pulmonary embolism in dogs. *Rø, J. S., Bergan, A., Amundsen, E.* (Institute for Thrombosis Research, Rikshospitalet, Oslo 1, Norway), p. 213

AHF related protein in clinical praxis. *Holmberg, L., Nilsson, I. M.* (Coagulation Laboratory, Allmänna Sjukhuset, S-21401 Malmö, Sweden), p. 221

Studies on plasma coagulation and fibrinolysis during oral contraception of various types, with special reference to cold activation of factor VII. *Gjønnaess, H., Fagerhol, M. K.* (Institute for Thrombosis Research, University of Oslo, Norway), p. 232

Scandinavian Journal of Haematology (Copenhagen) **12** (1974) No. 4

The effect of RA 233 on platelet function in vitro and after administration to man.

Warlow, C., Forman, K., Ogston, D., Douglas, A. S. (Department of Medicine, Medical School, Aberdeen, AP9 2ZD, Scotland), p. 241

Failed Schilling tests. *Chanarin, I., Waters, D. A. W.* (Department of Haematology, Northwick Park Hospital, Harrow, Middlesex, HA1 3UJ, England), p. 245

Platelet responses to ristocetin in von Willebrand's disease. *Sanderson, J. H., Burn, A. M., Cooke, S.* (Industrial Hygiene Research Laboratories, Cheshire, SK10 4TJ, England), p. 249

Acute leukaemia associated with an abnormal genotype. *Garson, O. M., Milligan, W. J.* (University of Melbourne, Department of Medicine, St. Vincent's Hospital, Fitzroy, Victoria, Australia 3065), p. 256

Depletion of thymus dependent lymphocytes in Hodgkin's disease. *Andersen, E.* (Medical Department C, Gentofte Hospital, Copenhagen/Hellerup, Denmark), p. 263

The Radner needle, a bone-marrow biopsy device. *Dombernowsky, P., Worm, A.-M., Hainau, B., Hansen, H. H., Nissen, N. I.* (Finsen Institute, Department of Internal Medicine, DK-2100 Copenhagen, Denmark), p. 270

Myeloma producing nonsecretory IgM and secretory IgG. *Stein, H., Kaiserling, E.* (Pathologisches Institut der Universität, D-2300 Kiel, BRD), p. 274

Ribonuclease. Ribonuclease inhibitor patterns in lymphocytes of chronic lymphocytic leukaemia. *Månsson, P. E., Deutsch, A., Nordén, Å.* (Reprint requests: A. Deutsch, Department of Biochemistry, Kemicentrum, 220 07 Lund 7, Sweden), p. 284

The effect of splenectomy on the megakaryocyte and platelet count in the blood of rats. *Pedersen, N. T.* (University of Copenhagen, Anatomy Department C, DK-2200 Copenhagen N, Denmark), p. 291

Growth stimulation of normal human bone marrow cells in agar culture by human serum. *Knudtzon, S.* (Department of Medicine, Finsen Institute, DK-2100 Copenhagen, Denmark), p. 298

Familial IgA defects. *Beermann, B., Holm, G.* (Medicinska Kliniken, Serafimerlasarettet, S-112 83 Stockholm, Sweden), p. 307

The effect of continuous cell removal on blast cell kinetics in acute leukaemia. *Hoelzer, D., Kurrle, E., Dietrich, M., Meyer-Hamme, K.-D., Fliedner, T. M.* (Department of Clinical Physiology, Ulm University, 79 Ulm/Donau, FRG), p. 311

Scandinavian Journal of Haematology (Copenhagen) **12** (1974) No. 5

Study on the fibrillar formation surrounding the nuclear bridge in some types of leukaemic cells. *Ito, S., Hattori, A.* (Department of Internal Medicine, Niigata University School of Medicine, Niigata City, Japan 951), p. 321

The effect of alimentary hyperlipaemia and primary hypertriglyceridaemia on platelets in man. *Nordøy, A., Strøm, E., Gjesdal, K.* (Department of Medicine, Sentralsykehuset, 9012 Tromsø, Norway), p. 329

Combination chemotherapy of acute leukaemia in adults. Comparison of two schedules. *Ikkala, E.* (Second Department of Medicine, University Central Hospital, 00290 Helsinki 29, Finland), p. 341

Factor VII during warfarin treatment. *Howarth, D. J., Brozović, M., Stirling, Y., Reed, M.* (Coagulation Laboratory, MRC-DHSS Epidemiology and Medical Care Unit, Northwick Park Hospital, Harrow, Middlesex, England), p. 346

Study on the in vitro Rieder cell. *Ito, S.* (Department of Internal Medicine, Niigata University School of Medicine, Niigata City, Japan 951), p. 355

Simple, semiquantitative test for partial factor XIII (FSF) deficiency. *Jakobsen, E., Godal, H. C.* (Medical Department IX, Haematological Research Laboratory, Ullevål Hospital, Oslo, Norway), p. 366

Relation between life expectancy and composition of the bone marrow at diagnosis of chronic myeloid leukaemia. *Sjögren, U., Brandt, L., Mitelman, F.* (Department of Internal Medicine A, Lasarettet, S-221 85 Lund, Sweden), p. 369

The erythrocyte sedimentation rate in Rh-positive and Rh-negative donors. *Hilden, J., Rønnike, F.* (Institute of Human Genetics, University of Copenhagen, DK-2200 Copenhagen N, Denmark), p. 374

Granulopoiesis in chronic myeloid leukaemia. I. In vitro cloning of blood and bone marrow cells in agar culture. *Moberg,*

C., Olofsson, T., Olsson, I. (Reprint requests: I. Olsson, Research Department 2, E-blocket, Lasarettet, S-221 85 Lund, Sweden), p. 381

DNA-synthesizing myeloid and lymphoid cells in the blood of haemodialysis patients and kidney graft recipients. *Virolainen, M., Lalla, M., Pasternack, A., Wasastjerna, C., Häyry, P.* (Third Department of Pathology, SF-00290 Helsinki 29, Finland), p. 391

Scandinavian Journal of Haematology (Copenhagen) **13** (1974) No. 1

Corticosteroids and experimental intravascular coagulation. *Gerrits, W. B. J., Prakke, E. M., van der Meer, J., Feltkamp-Vroom, Th. M., Vreeken, J.* (Department of Blood Coagulation Research, Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, 91910 Amsterdam, The Netherlands), p. 5

The effects of β-adrenergic blockade on the responses of leucocyte counts to intravenous epinephrine in man. *Gader, A. M. A.* (University Department of Physiology, Khartoum, Sudan), p. 11

Adenosine diphosphate-induced platelet aggregation of hospitalized men. *Davis, J. W., Yue, K. T. N., Phillips, Ph. E., McField, J. R.* (Veterans Administration Hospital, Kansas City, Mo. 64128), p. 17

Complement components on the surface of normal human lymphocytes. *Osther, K., Dybkjaer, E.* (The Blood Bank, Bispebjerg Hospital, DK-2400 Copenhagen NV, Denmark), p. 24

Factor VII antigen in the vessel walls in von Willebrand's disease and haemophilia A. *Holmberg, L., Mannucci, P. M., Turesson, I., Ruggeri, Z. M., Nilsson, I. M.* (Coagulation Laboratory, Malmö General Hospital, S-21401 Malmö, Sweden), p. 33

Kinetics of rat bone marrow cells cultured in diffusion chambers: Effect of heterologous implantation and irradiation of the host. *Petersen, B. H., Meyer, T., Tjernshaugen, H.* (Norwegian Defence Research Establishment, Division for Toxicology, N-2007 Kjeller, Norway), p. 39

Haemoglobin M Saskatoon and haemoglobin M Hyde Park in two Yugoslavian families. *Efremov, G. D., Huisman, T. H. J., Stanulovic, M., Zurovec, M., Duma, H., Wilson, J. B., Jeremic, V.* (Department of Pediatrics, Faculty of Medicine, Skopje, Yugoslavia), p. 48

Progression of polycythaemia vera to malignant myelofibrosis and reticulum cell sarcoma. *McVie, J. G., MacMichael, A. C., Ramsay, D. M.* (Department of Therapeutics, The Royal Infirmary, Edinburgh, EH3 9YW, Scotland), p. 61

Free fatty acids (FFA), blood clotting, fibrinolysis and platelet function. *Korsan-Bengtsen, K., Holm, T.* (Coagulation Laboratory, Department of Medicine II, Sahlgren's Hospital, S-41345 Göteborg, Sweden), p. 64

The effect of heparin on plasma and platelet lipids during alimentary hyperlipaemia in man. *Nordøy, A., Strøm, E., Berntsen, H.* (Institute for Clinical Medicine, University of Tromsø, N-9000 Tromsø, Norway), p. 72

Scandinavian Journal of Haematology (Copenhagen) **13** (1974) No. 2

The pathogenesis of the anaemia of chronic disorders and the role of fever in erythrokinetics. *Karle, H.* (Division of Haematology, Department of Medicine A, Rigshospitalet, DK-2100 Copenhagen Ø, Denmark), p. 81

Cytogenetic evidence for splenic origin of blastic transformation in chronic myeloid leukaemia. *Mitelman, F., Brandt, L., Nilsson, P. G.* (Department of Internal Medicine A, University Hospital, S-22185 Lund, Sweden), p. 87

Studies of human peripheral lymph. II. Low lymphocyte count and few B-lymphocytes in peripheral lymph of patients with chronic lymphocytic leukaemia. *Engeset, A., Frøland, S. S., Bremer, K.* (Haematological Laboratory, The Norwegian Radium Hospital, Montebello, Oslo 3, Norway), p. 93

A biochemical study of erythrocytes in Swedish families with β-thalassaemia minor. *Hjelm, M., Samuelson, G.* (Reprint requests: G. Samuelson, Department of Pediatrics, University Hospital, S-901 85 Umeå, Sweden), p. 101

Platelet production and survival in cyanotic

congenital heart disease. *Goldschmidt, B., Sarkadi, B., Gárdos, G., Matlary, A.* (Second Department of Paediatrics, Semmelweis University Medical School, 1094 Budapest, Hungary), p. 110

Differences in morphology and mitotic activity between intra- and extra-medullary erythropoietic tissue in chronic myeloid leukaemia. *Sjögren, U., Brandt, L.* (Department of Internal Medicine A, University Hospital, S-22185 Lund, Sweden), p. 116

Isolation and characterization of an *in vivo* thrombin-induced anticoagulant activity. *Hyde, E., Wetmore, R., Gurewich, V.* (Vascular Laboratory, Lemuel Shattuck Hospital, Jamaica Plain, Mass. 02130), p. 121

Characterization of R-type vitamin B_{12}-binding proteins by isoelectric focusing. I. The relationship between transcobalamin I, transcobalamin III and the granulocyte R protein. *Stenman, U.-H.* (The Minerva Institute, P. O. Box 819, SF-00101 Helsinki 10, Finland), p. 129

Study of granulocytopoiesis in drug-induced agranulocytosis using ^{3}HTdR autoradiography. *Ruvidić, R.* (Interna Klinika B, Medicinski Fakulter, Beograd, Yugoslavia), p. 135

Prevention of thromboplastin-induced intravascular coagulation in rabbits by warfarin as monitored by thrombotest. *Slaastad, R. A.* (Department IX, Ullevål Hospital, Oslo 3, Norway), p. 140

Quantitation of erythropoiesis by a new method. IV. Studies using ^{59}Fe and DF^{32}P simultaneously in haematological diseases. *Lockner, D.* (Department of Medicine, Huddinge University Hospital, S-141 86 Huddinge, Sweden), p. 146

Soluble fibrin and fibrinogen-derived material in the kidneys during low-graded disseminated intravascular coagulation (DIC) in rabbits. *Slaastad, R. A., Husby, G., Skjörten, F.* (Haematological Research Laboratory, Medical Department IX, Ullevål Hospital, Oslo 3, Norway), p. 152

Scandinavian Journal of Haematology (Copenhagen) **13** (1974) No. 3

The effect of factor IX and factor X on blood platelets. *Osterud, B., Holm, T., Prydz, H.* (Institute of Medical Biology, University of Tromsø, 9001 Tromsø, Norway), p. 161

Hypertonic saline induced abortion as pathophysiologic model of low grade intravascular coagulation. *van Royen, E. A., Treffers, P. E., ten Cate, J. W.* (Coagulation Laboratory, Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, P. O. Box 9190 Amsterdam, The Netherlands), p. 166

Cold induced retraction of reptilase clots. *Kubisz, P.* (Haemostasis Laboratory, Department Hospital, 02201 Cadca, Czechoslovakia), p. 175

Preleukaemic abnormal myelopoiesis induced by chlorambucil: A case study. *Tulliez, M., Ricard, M. F., Jan, D., Sultan, C.* (Reprint requests: Service Central d'Hématologie, Hôpital Henri Mondor, 94010 Créteil, France), p. 179

Blood platelet production and red cell leakage to lymph during thrombocytopenia. *Aursnes, I.* (Institute of Physiology, University of Oslo, Oslo 1, Norway), p. 184

Platelet stain preventing factor in serum or plasma. An early sign of leiomyosarcoma? *Stavem, P., Berg, K., Flatmark, A., Refsum, S.* (Section of Haematology, Medical Department A, Rikshospitalet, Oslo 1, Norway), p. 196

Blood lymphocytes in Hodgkin's disease. Lymphocytopenia related to stages and histological groups. *Heier, H. E., Normann, T.* (Haematological Laboratory, The Norwegian Radium Hospital, Montebello, Oslo 3, Norway), p. 199

Familial bleeding disorder with a moderate thrombocytopenia and giant blood platelets. *Evensen, S. A., Solum, N. O., Grøttum, K. A., Hovig, T.* (Medical Department A, Rikshospitalet, Oslo 1, Norway), p. 203

Platelet function abnormalities in the myeloproliferative disorders. *Adams, T., Schutz, L., Goldberg, L.* (Bay Area Hematology-Oncology Group, Santa Monica, Calif. 90404), p. 215

The pulmonary vessels as a filter for circulating megakaryocytes in rats. *Pedersen, N. T.* (Anatomy Department C, DK-2200 Copenhagen N, Denmark), p. 225

Platelet factor 4 (PF-4). An electroimmune assay for PF-4 in human plasma. *Gjesdal,*

K. (Institute of Clinical Medicine, University of Tromsø, N-9012 Tromsø, Norway), p. 232

Scandinavian Journal of Haematology (Copenhagen) **13** (1974) No. 4

Effect of acetylsalicylic acid and dipyridamole on platelet survival and aggregation in patients with atherosclerosis obliterans. *Abrahamsen, A. F., Eika, C., Godal, H. C., Lorentsen, E.* (Radiumhospitalet, Montebello, Oslo, Norway), p. 241

Evaluation of celloscope 421 for the simultaneous measurement of red blood cells, haematocrit and mean cell volume. *Borud, P., Strømme, J. H.* (Department of Clinical Chemistry, Institute of Medical Biology, University of Tromsø, N-9000 Tromsø, Norway), p. 246

The effect of the ^{51}Cr-labelling procedure on platelet aggregability. *Björnson, J.* (Haematological Research Laboratory, Medical Department IX, Ullevål Hospital, Oslo, Norway), p. 252

Erythrophagocytosis by pathological erythroblasts in the di Guglielmo syndrome. *Søndergaard-Petersen, H.* (Medicinsk afdeling II, Amtssygehust, DK-8000 Århus C, Denmark), p. 260

Immunoglobulin-containing intranuclear inclusions in plasma cells in a case of IgG myeloma. *Stavem, P., Hovig, T., Frøland, S., Skrede, S.* (Section of Haematology, Medical Department A, Rikshospitalet. Oslo 1, Norway), p. 266

Congenital erythroid hypoplastic anaemia: Autosomal dominant transmission. *Lawton, J. W. M., Aldrich, J. E., Turner, T. L.* (Blood Transfusion Service, The Royal Infirmary of Edinburgh, Edinburgh EH3 9YW, Scotland), p. 276

Binding of fluorescein labelled concanavalin A to human bone marrow cells in leukaemias and lymphomas. *Juhlin, R., Sällström, J. F., Stenkvist, B.* (Department of Clinical Cytology, Academic Hospital, S-750 14 Uppsala, Sweden), p. 281

Vitamin B_{12} absorption evaluated by a dual isotope test (Dicopac). Results of radioactivity measurements in plasma and in urine. *Knudsen, L., Hippe, E.* (Medical Department C, Bispebjerg Hospital, DK-2400 Copenhagen NV, Denmark), p. 287

Amoeboid movement configuration. A cell configuration observed in tumour cells from 3 cases of bone marrow neoplasia. *Norberg, B., Rydgren, L., Stenstam, M.* (Department of Internal Medicine, University Hospital of Lund, S-221 85 Lund, Sweden), p. 294

Polymorphonuclear leucocyte chemotaxis in Boyden chambers. Effect of low concentrations of vinblastine. *Bandmann, U., Norberg, B., Rydgren, L.* (Reprint requests: Dr. B. Norberg, Department of Internal Medicine A, University Hospital of Lund, S-221 85 Lund, Sweden), p. 305

Hb D Punjab. Alpha thalassaemia combination in a Turkish family. *Cavdar, A. O., Arcasoy, A.* (Division of Haematology, Department of Pediatrics, Ankara University Medical School, Ankara, Turkey), p. 305

Scandinavian Journal of Haematology (Copenhagen) **13** (1974) No. 5

Chromosome banding pattern in acute myeloid leukaemia. *Mitelman, F., Brandt, L.* (Department of Internal Medicine, University Hospital, S-221 85 Lund, Sweden), p. 321

Platelet aggregation and haemolysis induced in rats by intravenous infusion of ADP. Effect of potentially antithrombotic drugs. *Innocenti, I. R.-D., Poggi, A., De Gaetano, G.* (Reprint requests: Dr. G. de Gaetano, Laboratory for Haemostasis and Thrombosis Research, Istituto di Ricerche Farmacologiche "Mario Negri", 20157 Milano, Italy), p. 331

The action of erythropoietin on erythroid cells in vitro. *Silver, R. K., Erslev, A. J.* (Cardeza Foundation, Thomas Jefferson University, Philadelphia, Pa. 19107), p. 338

Enrichment of PHA-responsive lymphocytes in chronic lymphocytic leukaemia after removal of Ig-bearing cells. *Blomgren, H., Andersson, B., Johansson, B.* (Radiumhemmet, Karolinska Hospital, S-104 01 Stockholm 60, Sweden), p. 352

Technical aspects of the rosette technique for detecting human circulating B and T lymphocytes. Normal values and some remarks on null lymphocytes. *Jønsson, V.*

(Medical Department C, Gentofte University Hospital, DK-2900 Hellerup, Denmark), p. 361

Phenotypic variation in sickle cell trait. *Esan, G. F. J., Adesina, T. A. O.* (Department of Haematology, University College Hospital, Ibadan, Nigeria), p. 370

Influence of two different beta-adrenergic blocking agents on the increase in fibrinolytic activity and factor VIII activity during submaximum and maximum exercise. *Korsan-Bengtsen, K., Conradson, T.-B.* (Department of Medicine I, Sahlgren's Hospital, 41345 Göteborg, Sweden), p. 377

Seminars in Hematology (New York) **11** (1974) No. 2

Current concepts in chronic myelogenous leukemia. *Stryckmans, P. A.* (Service de Médecine Interne et d'Investigation Clinique de l'Institut Jules Bordet, Centre des Tumeurs de l'Université Libre de Bruxelles, Bruxelles, Belgique), p. 101

Chronic myelomonocytic leukemia in adults. *Miescher, P. A., Farquet, J. J.* (Division of Hematology, Hôpital Cantonal, Geneva, Switzerland), p. 129

Hematologic malignancies and other marrow failure states: Progress in the management of complicating infections. *Levine, A. S., Schimpff, S. C., Graw, R. G., Jr., Young, R. C.* (National Institutes of Health, Bethesda, Md. 20014), p. 141

Chemotherapy after synchronization of tumor cells. *Klein, H. O., Lennartz, K. J.* (Medical Clinic and Institute of Pathology, University of Cologne, Cologne, FRG), p. 203

Seminars in Hematology (New York) **11** (1974) No. 3

Introduction. *van Rood, J. J.* (Department of Immunohaematology, Academisch Ziekenhuis, Leiden, The Netherlands), p. 229

The HL-A system. I. Genetics and molecular biology. *Ceppelini, R., van Rood, J. J.* (Basel Institute for Immunology, Basel, Switzerland), p. 233

The HL-A system. II. Clinical relevance. *van Rood, J. J.* (Department of Immunohaematology, University Hospital, Leiden, The Netherlands), p. 253

Serologic recognition of the histocompatibility antigens using agglutination and cytotoxicity techniques. *Bruning, J. W.* (Department of Immunohaematology, University Hospital, Leiden, The Netherlands), p. 263

Serologic recognition of histocompatibility antigens using complement fixation. *Colombani, J., Colombani, M.* (Unité de Recherche sur l'Immunogénétique de l'Histocompatibilité Humaine, U93 I.N.S.E.R.M. Hôpital Saint-Louis, 75475 Paris Cédex 10, France), p. 273

Neutrophil-specific antigens: Immunology and clinical significance. *Lalezari, P., Radel, E.* (Division of Immunohematology, Department of Medicine, Montefiore Hospital and Medical Center, New York, N. Y.), p. 281

Immunogenetic disparity and graft-versus-host reactions. *Bach, M. L., Bach, F. H.* (Departments of Pediatrics, Pharmacology, Medical Genetics and Surgery, University of Wisconsin, Madison, Wis. 54706), p. 291

The cellular recognition in vitro of antigens related to human histocompatibility. *Eijsvoogel, V. P.* (Laboratory for Experimental and Clinical Immunology, University of Amsterdam, Amsterdam, The Netherlands), p. 305

The double barrier in bone marrow transplantation. *van Bekkum, D. W.* (Radiobiological Institute of the Organization for Health Research TNO, Rijswijk [ZH], The Netherlands), p. 325

Immunosuppression for clinical marrow transplantation. *Santos, G. W.* (Division of Oncology, Department of Medicine, The Johns Hopkins University, Baltimore City Hospitals, Baltimore, Md. 21224), p. 341

Marrow transplants in aplastic anemia and leukemia. *Fefer, A., Thomas, E. D., Buckner, C. D., Storb, R., Neiman, P., Glucksberg, H., Clift, R. A., Lerner, K. G.* (Division of Oncology, Department of Medicine, University of Washington School of Medicine, Seattle, Wash. 98195), p. 353

Bone marrow transplantation in children. *Dooren, L. J., Kamphuis, R. P., de Koning,*

J., *Vossen*, *J. M.* (Department of Pediatrics, University Hospital, Leiden, The Netherlands), p. 369

Seminars in Hematology (New York) **11** (1974) No. 4

Introduction. *Ranney*, *H. M.* (University of California San Diego, University Hospital, San Diego, Calif. 92103), p. 382

Human hemoglobin mutants with abnormal oxygen binding. *Nagel*, *R. I.*, *Bookchin*, *R. M.* (Albert Einstein College of Medicine, Bronx, N. W. 10461), p. 385

The oxyhemoglobin dissociation curve and pulmonary gas exchange. *Wagner*, *P. D.* (Department of Medicine, University of California, San Diego, La Jolla, Calif. 92037), p. 405

Human hemoglobin stability and instability: Molecular mechanisms and some clinical correlations. *Rieder*, *R. F.* (Department of Medicine, State University of New York, Downstate Medical Center, Brooklyn, N. Y. 11203), p. 423

Denaturation of the normal and abnormal hemoglobin molecule. *Rachmilewitz*, *E. A.* (Department of Hematology, Hadassah University Hospital, Hebrew University-Hadassah Medical School, Jerusalem, Israel), p. 441

The biosynthesis of hemoglobin. *Benz*, *E. J., Jr.*, *Forget*, *B. G.* (Reprint requests: Dr. B. G. Forget, Division of Hematology, Children's Hospital Medical Center, Boston, Mass. 02115), p. 463

Regulation of fetal hemoglobin production. *Kazazian*, *H. H., Jr.* (Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Md. 21205), p. 525

Abnormal globin synthesis in thalassaemic red cells. *Schwartz*, *E.* (Division of Hematology, Children's Hospital, Philadelphia, Pa. 19104), p. 549

Therapy of sickle cell disease: An approach with sodium cyanate. *Peterson*, *C. M.*, *Cerami*, *A.* (The Rockefeller University, New York, N. Y. 10021), p. 569

Interactions between human hemoglobins: Sickling and related phenomena. *Bookchin*, *R. M.*, *Nagel*, *R. L.* (Department of Medicine, Division of Hematology, Albert Einstein College of Medicine, Bronx, N. Y. 10461), p. 577

Thrombosis et Diathesis Haemorrhagica (Stuttgart) **30** (1973) No. 1

Reports from the International Committee of Haemostasis and Thrombosis. I. A genetic nomenclature for human blood coagulation. *Graham*, *J. B.*, *Barrett II*, *D. A.*, *Blombäck*, *B.*, *Cann*, *H. M.*, *Hardisty*, *R. M.*, *Larrieu*, *M. J.*, *Renwick*, *J. H.* (University of North Carolina, Department of Pathology, Chapel Hill, N. C. 27514), p. 2

A controlled trial of aspirin in childhood glomerular disorders. *Trygstad*, *C. W.*, *Bang*, *N. U.*, *Heidenreich*, *R. O.*, *Csiscko*, *B. M.*, *Rodda*, *B.* (Department of Pediatrics, Harbor General Hospital, UCLA School of Medicine, Torrance, Calif. 90509), p. 12

Trial of aspirin and RA 233 in prevention of post-operative deep vein thrombosis. *Wood*, *E. H.*, *Prentice*, *C. R. M.*, *McGrouther*, *D. A.*, *McNicol*, *G. P.* (University Department of Medicine, Division of Surgery, Royal Infirmary, Glasgow, Scotland), p. 18

Induction of disseminated intravascular coagulation in the factor XII-deficient fowl. Morphological effects of liquoid, bacterial endotoxin and tissue thromboplastin in the normal and anticoagulated fowl. *Skjørten*, *F.*, *Evensen*, *A.* (Ullevål Hospital, Department of Pathology, Oslo, Norway), p. 25

Leucocytes and thrombosis. I. A simple test of leucocyte behaviour. *Banks*, *D. C.*, *Mitchell*, *J. R. A.* (Department of Medicine, University of Nottingham, Nottingham, England), p. 36

Leucocytes and thrombosis. II. Relationship between leucocyte behaviour and divalent cations, sulphydryl groups, red cells and adenosine diphosphate. *Banks*, *D. C.*, *Mitchell*, *J. R. A.* (Department of Medicine, University of Nottingham, Nottingham, England), p. 47

Leucocytes and thrombosis. III. Effect on white cell behaviour of substances which induce or inhibit platelet aggregation. *Banks*, *D. C.*, *Mitchell*, *J. R. A.* (Depart-

ment of Medicine, University of Nottingham, Nottingham, England), p. 62

Chicken fibrinogen and human fibrinogen. Comparative immunological studies. *Ménaché, D., Cesbron, N., Guillin, M.-C., Schlegel, N.* (Service Central d'Immunologie et Hématologie, Hôpital Beaujon, 92-Clichy, France), p. 72

Quantitative determination of total antithrombin III in plasma. *Yue, R. H., Starr, T., Gertler, M. M.* (Cardiovascular Research, Institute of Rehabilitation Medicine, New York University Medical Center, New York, N. Y. 10016), p. 84

Antiheparin activity of human serum and platelet factor 4. *Sear, C. H. J., Poller, L., Path, F. R. C.* (Haematology Department, Withington Hospital, University Hospital of South Manchester, Manchester, England), p. 93

Blood coagulation inhibitor in a snake plasma (*Bothrops jararaca*). *Nahas, L., Betti, F., Kamiguti, S., Sato, H.* (Department of Physiopathology, Instituto Butantan, S. Paulo, Brazil), p. 106

Evaluation of a new preparation of urokinase. *Prentice, C. R. M., Rogers, K. M., McNicol, G. P.* (University Department of Medicine, Royal Infirmary, Glasgow G4 OSF, Scotland), p. 114

Fibrinocoagulopathy in maturity onset diabetes mellitus and atherosclerosis. *Banerjee, R. N., Sahni, A. L., Kumar, V.* (Department of Haematology and Nuclear Medicine, Safdarjang Hospital, New Delhi-16, India), p. 123

Fibrinolytic activity of human carcinomas. A comparative methodological study. *Peterson, H.-I., Petrusson, B., Korsan-Bengtsen, K.* (Departments of Surgery I, Oto-Rhino-Laryngology and Medicine II, Sahlgrenska Sjukhuset, University of Göteborg, Göteborg, Sweden), p. 133

The filter loop technique as a method of measuring platelet aggregation in the flowing blood of the rat; the inhibitory activity of 5-oxo-1-cyclopentene-1-heptanoic acid (AY-16,804) on platelet aggregation. *Muirhead, Ch. R.* (Department of Pharmacology, Ayerst Research Laboratories, P. O. Box 6115, Montreal 101, Quebec, Canada), p. 138

A preliminary study on the acetylcholinesterase and butyrylcholinesterase of human platelets. *Chuang, H. Y. K., Mason, R. G.* (Department of Pathology, School of Medicine, University of North Carolina, Chapel Hill, N. C.), p. 148

Platelet factor 3 activity made available from human platelets by ADP. Inhibition by colchicine. *Gold, M., Evensen, S. A., Belamarich, F. A., Shepro, D.* (Biological Science Center, Boston University, Boston, Mass. 02215), p. 155

Evaluation of a semi-micro method for measuring platelet aggregation in whole blood samples. *Gordon, J. L.* (Department of Pathology, Cambridge University, Cambridge, England), p. 160

The migration of human platelets in vitro. *Nathan, P.* (Shriners Burns Institute, Cincinnati Unit, University of Cincinnati College of Medicine, Cincinnati, Ohio), p. 173

Systemic effects of ADP-induced platelet aggregation and their modification by aspirin and by pyridinolcarbamate. *Kobayashi, I., Didisheim, P.* (Section of Laboratory Hematology, Department of Laboratory Medicine, Mayo Clinic, Rochester, Minn. 55901), p. 178

Impairment of human platelet aggregation and serotonin release caused in vitro by *Echis colorata* venom. *Biran, H., Dvilansky, A., Nathan, I., Livne, A.* (Blood Research Laboratory, Soroka Medical Center and Biology Department, University of the Negev, Beer Sheva, Israel), p. 191

Metabolic properties of human platelet membranes. I. Characterization of platelet membranes prepared by sucrose and ficoll density gradients. *Kaulen, H. D., Gross, R.* (Medical Clinic, University of Cologne, Cologne, FRG), p. 199

The effect of apyrase on platelet retention in normal subjects and in patients with abnormal cardiac valves or with von Willebrand's disease. *Rifkin, P. L., Friedberg, N. M., Zucker, M. B.* Departments of Medicine and Pathology, New York University Medical Center, New York, N. Y. 10016), p. 215

Thrombosis et Diathesis Haemorrhagica (Stuttgart) **30** (1973) No. 2

Preparation of modified bovine factor VIII with enhanced biological activity using

insoluble-trypsin columns. *Vogel, Ch. N., Parfitt, H. E., Jr., Kingdon, H. S., Lundblad R. L.* (Dental Research Center, University of North Carolina, Chapel Hill, N. C. 27514), p. 229

Potentiation of the anti-factor VIII effect of thrombin in plasma by the plasminolytic derivatives of fibrinogen and fibrin. *Chandra, S., Triantaphyllopoulos, D. C.* (Department of Hematology, St. Vincent Hospital, Worcester, Mass. 01610), p. 235

Observations on the hydrolysis of *p*-nitrophenyl acylates by purified bovine thrombin. *Lundblad, R. L.* (Dental Research Center, University of North Carolina, Chapel Hill, N. C. 27514), p. 248

Detection of carriers of haemophilia. *Ekert, H., Helliger, H., Muntz, R. H.* (Royal Children's Hospital Research Foundation, Parkville, Victoria 3052, Australia), p. 255

Incidence and course of inhibitors among patients with classic hemophilia. *Kasper, C. K.* (University of Southern California School of Medicine, Los Angeles, Calif.), p. 263

Tranexamic acid in the control of spontaneous bleeding in severe haemophilia. *Rainsford, S. G., Jouhar, A. J., Hall, A.* (Lord Mayor Treloar Hospital, Alton Hampshire, England), p. 272

On the complex formation of antithrombin III with thrombin. *Binder, B.* (Department of Physiology, School of Medicine, University of Vienna, Vienna, Austria), p. 280

Behaviour of the portal clotting time in cats following the intraduodenal administration of heparin. *Kokot, B.* (Third Surgical Clinic, Medical Academy in Gdansk, Gdansk, Poland), p. 284

Characterization of clotting factors associated with blood platelets after gel filtration. *Tangen, O., Lestrup, E. B., Berman, H. J.* (Department of Experimental Medicine, Pharmacia AB, Uppsala, Sweden), p. 289

Role of platelet factor 3 in the hypercoagulability induced by pregnancy and oral contraceptives. *Renaud, S., Gautheron, P.* (Laboratory of Experimental Pathology, Montreal Heart Institute, Montreal, Canada), p. 299

The presence of glycogen synthetase in preparations of platelet plasma membranes. *Greenberg, J. H., Fletcher, A. P., Jamieson, G. A.* (American National Red Cross Blood Research Laboratory, Bethesda, Md. 20014), p. 307

The effect of barbituric acid derivatives on platelet function in vitro and in vivo. *Joist, J. H., Cazenave, J.-P., Mustard, J. F.* (Department of Pathology, McMaster University, Hamilton, Ontario, Canada), p. 315

The platelet of the newborn infant. 5-hydroxytryptamine uptake and release. *Whaun, J. M.* (Division of Paediatrics, University of Calgary, Faculty of Medicine, Calgary, Alberta, Canada), p. 327

Inhibition by phenol and phenolic acids of platelet release reaction. *Molinas, F. C.* (Instituto de Investigaciones Medicas, Facultad de Medicina, Universidad de Buenos Aires, Buenos Aires, Argentina), p. 334

Generalized Shwartzman reaction induced by liquoid in the rat. Increased DNA-synthesis in aortic endothelium. *Evensen, S. A., Shepro, D.* (Medical Department A, Rikshospitalet, Oslo 1, Norway), p. 347

Formation and embolization of thrombi after electrical stimulation. On the method and evaluation of drugs. *Spilker, B. A., van Balken, H.* (Department of Pharmacology, Sterling-Winthrop Research Institute, Rensselaer, N. Y. 12144), p. 352

A 3.5-second phenomenon in haemostasis. A scanning electron microscopic study. *Thilo, D., Böhm, E.* (Gerinnungslabor, Kantonsspital, CH-4004 Basel, Switzerland), p. 363

Volume distribution and ultrastructure of platelets in acute hog cholera. *Weiss, E., Teredesai, A., Hoffmann, R., Hoffmann-Fezer, G.* (Veterinär-Pathologisches Institut, D-63 Gießen, BRD), p. 371

Studies on activator formation in human plasma with streptokinase. I. Experimental studies. *Martin, M.* (Aggertalklinik Engelskirchen bei Köln, D-525 Engelskirchen, BRD), p. 381

Studies on activator formation in human plasma with streptokinase. II. Quantitative activator and plasminogen measurements during continuous and intermittent streptokinase infusion. *Martin, M.* (Aggertalklinik Engelskirchen bei Köln, D-525 Engelskirchen, BRD), p. 393

Preferential degradation of soluble fibrin monomers in streptokinase-activated plas-

ma. *Konttinen, Y. P., Lalla, M. L. T., Turunen, O.* (Medical and Laboratory Departments of Maria Hospital, 00180 Helsinki, Finland), p. 403

Studies on an inhibitor of plasminogen activation in human serum. *Hedner, U.* (Coagulation Laboratory, Allmänna Sjukhuset, Malmö, Sweden), p. 414

Thrombosis et Diathesis Haemorrhagica (Stuttgart) **30** (1974) No. 3

Human prothrombin: A new method of preparation from a single individual. *Benarous, R., Labie, D., Josso, F.* (Institut de Pathologie Moléculaire, 75014 Paris, France), p. 425

Human coumarin prothrombin. Chromatographic, coagulation and immunologic studies. *Cesbron, N., Boyer, C., Guillin, M.-C., Ménaché, D.* (Service Central d'Immunologie et Hématologie, Hôpital Beaujon, 92 Clichy, France), p. 437

Congenital hypoprothrombinemia in a Portuguese family. *Pina-Cabral, J. M., Justiça, B.* (Department of Physiology, Oporto School of Medicine, Oporto, Portugal), p. 451

Further evidence for a humoral control of factor VIII plasma levels. *Landaburu, R. H., Castellanos, D. E.* (Laboratoro de Hemoderivados, Universidad Nacional de Córdoba. Córdoba, Argentina), p. 460

The measurement of heparin. A method based on the potentiation of anti-factor Xa. *Denson, K. W. E., Bonnar, J.* (John Radcliffe Hospital, Oxford, England), p. 471

Clinical studies concerning factor XIII; with special reference to hyperlipemia. *Cucuianu, M. P., Vasile, V. V., Popescu, T. A., Opincaru, A., Crisnic, I., Tapalaga, D.* (Institute of Public Health and Medical Research, Medical Clinic I, Cluj, Romania), p. 480

Effect of Aspirin on the thrombelastogram of human blood. *de Gaetano, G., Vermylen, J.* (Laboratory of Blood Coagulation, Medical Research Department, Academisch Ziekenhuis St. Rafäel, University of Leuven, Leuven, Belgium), p. 494

Effects of puff adder venom on the coagulation mechanism. II. In vitro. *Phillips, L. L., Weiss, H. J., Christy, N. P.* (Department of Medicine, The Roosevelt Hospital and College of Physicians and Surgeons, Columbia University, New York, N. Y.), p. 499

Treatment of tissue thromboplastin membranes with phospholipase C. *Bjørklid, E., Otnaess, A.-B., Storm, E., Prydz, H., Johansen, B. V., Frøholm, L. O.* (Institute of Medical Biology, University of Tromsø, Tromsø, Norway), p. 509

Controlled-flow instruments for stimulating *in vivo* thrombosis. *Clark, H. G., Shinoda, B. A., Mason, R. G.* (Department of Biomedical Engineering, Duke University, Durham, N. C. 27706), p. 519

Effect of corticosteroids upon fibrinogen metabolism in rabbits. *Seligsohn, U., Rapaport, S. I., Shen, S. M.-C., Kuefler, P. R.* (Department of Medicine, University of Southern California School of Medicine, Los Angeles, Calif. 90033), p. 531

Leucocytes and thrombosis. IV. The effect of various diseases on leucocyte adhesiveness. *Banks, D. C., Mitchell, J. R. A.* (Department of Medicine, University of Nottingham, Nottingham, England), p. 541

A comparison of the effects of antihistamines on platelet function. *Thomson, C., Forbes, Ch. D., Prentice, C. R. M.* (University Department of Medicine, Royal Infirmary, Glasgow, G4 OSF, Scotland), p. 547

Platelet factor 3 activity in washed platelets. *Renaud, S., Gautheron, P., Rosenstein, H.* (Laboratory of Experimental Pathology, Montreal Heart Institute, University of Montreal, Montreal, Canada), p. 557

Platelets and clot retraction. Effect of divalent cations and several drugs. *Bottecchia, D., Fantin, G.* (Institute of Human Physiology, Faculty of Medicine, University of Padua, 35100 Padova, Italy), p. 567

Effect of aspirin and benadryl on human platelet oxidative phosphorylation and aggregation. *Yue, K. T., Davis, J. W., Aldridge, E. G.* (Hematology Research Laboratory, Veterans Administration Hospital, Kansas City, Mo. 64128), p. 577

Influence of platelet count on haemostatic plug formation and plug stability. An experimental study in rabbits with graded thrombocytopenia. *Bergqvist, D., Arfors,*

K.-E. (Department of Experimental Medicine, Pharmacia AB, Uppsala, Sweden), p. 586

The *in vivo* and *in vitro* effect of antihistamine on platelet aggregation. *Ungaro, P. C., Beck, Th. M., McCaa, W. M., Hershgold, E. J.* (Division of Hematology, University of Utah Medical Center, Salt Lake City, Utah), p. 597

Thrombosis Research (New York) **4** (1974 No. 1

Editorial. Bleeding time, other in vivo hemostasis tests and the arrest of hemorrhage. *Copley, A. L.* (Department of Medicine, New York Medical College, New York, N. Y. 10029), p. 1

The effect of propranolol, alprenolol and practolol on the fibrinolytic and factor VIII response to adrenaline and salbutamol in man. *Gader, A. M. A., da Costa, J., Cash, J. D.* (S-E Scotland Regional Blood Transfusion Centre, Royal Infirmary, Edinburgh, Scotland), p. 25

On the metabolism of the thrombin-like enzyme from the venom of *Bothrops atrox. Egberg, N.* (Department of Blood Coagulation, Karolinska Institutet, Stockholm, Sweden), p. 35

Enzymatic reduction of disulfide bonds in fibrinogen by the thioredoxin system. I. Identification of reduced bonds and studies on reoxidation process. *Blombäck, B., Blombäck, M., Finkbeiner, W., Holmgren, A., Kowalska-Loth, B., Olovson, G.* (Chemistry Department, Karolinska Institutet, Stockholm, Sweden), p. 55

Growth rate and volume of haemostatic plugs in the mesentery of normal and thrombocytopenic rabbits. *Bergqvist, D., Arfors, K.-E.* (Department of Experimental Medicine, Pharmacia AB, Uppsala, Sweden), p. 77

Degradation products and heterogeneity of bovine fibrinogen. *Paturel, L., Hudry-Clergeon, G., Suscillon, M.* (Laboratoire d'Hématologie, D.R.F., Centre d'Études Nucléaires de Grenoble, 38041 Grenoble Cedex, France), p. 89

Isolation and characterization of a prealbumin activator of prekallikrein from acetone-activated human plasma. *Venneröd, A. M., Laake, K.* (Department of Pharmacology, Institute of Pharmacy, University of Oslo, Oslo, Norway), p. 103

Further variant of the thrombocytopathy with abnormalities in platelet release reaction. *Kubisz, P., Suranova, J.* (Hemostasis Laboratory, Department Hospital, Cadca, Czechoslovakia), p. 119

A search for fibrinopeptides in urine during experimental intravascular coagulation in dogs. *Teger-Nilsson, A.-C., Gröndahl, N. J.* (Department of Clinical Chemistry and Thoracic Surgery Research Laboratory, Karolinska Sjukhuset, Stockholm, Sweden), p. 131

The influence of insulin on plasma fibrinolytic system. *Kleniewski, J., Gladecki, K., Cybulska, J.* (Department of Biochemistry, Postgraduate Medical School, Warsaw, Poland), p. 137

Major operations, hemostatic parameters and venous thrombosis. *Korvald, E., Abildgaard, U., Fagerhol, M. K.* (Surgical Department and Medical Department A, Aker Hospital, Oslo, Norway), p. 147

Factor VIII, a series of homologous oligomers and a complex of two proteins. *van Mourik, J. A., Bouma, B. N., LaBruyère, W. T., de Graaf, S., Mochtar, I. A.* (Laboratory of Biochemistry of the Pediatric Clinic, Binnengasthuis, University of Amsterdam, Amsterdam, The Netherlands), p. 155

Experimental venous thrombosis in agranulocytic rabbits. *Lerner, R. G., Wiener, J., Goldstein, R.* (Department of Medicine and Department of Pathology, New York Medical College, New York, N. Y. 10029), p. 165

Circulating platelet levels in the rat during rejection of xenogeneic skin. *Ballantyne, D. L., Jr., Harper, A. D., Hawthorne, G. A., Nathan, P., Coburn, R. J.* (Institute of Reconstructive Plastic Surgery, New York University Medical Center, New York, N. Y. 10016), p. 177

Studies on soluble fibrin in plasma. V. Isolation and characterization of the clottable proteins obtained from patient plasma upon gelation with ethanol. *Kierulf, P.* (Hematological Research Laboratory, Department IX, University Clinic, Ullevål Hospital, Oslo, Norway), p. 183

Mechanical recording of reptilase-clot retraction. Effect of adenosine-5'-diphosphate and prostaglandin E_1. *de Gaetano, G. Franco, R., Donati, M. B., Bonaccorsi, A., Garattini, S.* (Istituto di Recerche Farmacologiche "Mario Negri", 20157 Milano, Italy), p. 189

The reducing action of highly purified globulin and lipoprotein on the viscous resistance of surface layers of fibrinogen. *Copley, A. L., King, R. G.* (Hemorrhage and Thrombosis Research Laboratories, Departments of Medicine and Pharmacology, New York Medical College, New York, N. Y. 10029), p. 193

Thrombosis Research (New York) **4** (1974) No. 2

Thrombelastographic patterns of Ancrod and thrombin fibrin formation and dissolution. *Caprini, J. A., Kwaan, H. C., Zuckerman, L., Verduin, R.* (Department of Surgery, Evanston Hospital, Chicago, Ill.), p. 199

Activation of factor X: Kinetic properties of the reaction. *Kosow, D. P., Furie, B., Forastieri, H.* (American National Red Cross, Blood Research Laboratory, Bethesda, Md. 20014), p. 219

The effect of moderate doses of chlorpromazine on the haemostasis in dogs defibrinogenated with defibrase. *Johnsson, H., Niklasson, P. M.* (Department of Blood Coagulation Research, The Thoracic Surgery Research Laboratory, Karolinska Sjukhuset, Stockholm, Sweden), p. 229

Preparation of heparin-linked agarose and its interaction with plasma. *Danishefsky, I., Tzeng, F.* (Department of Biochemistry, New York Medical College, Valhalla, N. Y. 10595), p. 237

Platelet consumption in chronically induced plasma platelet factor 4-like activity reflecting rate of intravascular coagulation in dogs. *Fuster, V., Bowie, E. J. W., Kazmier, F. J., Owen, Jr., C. A.* (Mayo Clinic and Mayo Foundation, Rochester, Minn. 55901), p. 247

Interaction between red cell membranes and fibrinogen. *Murray, M., Rearick, D. E.* (Department of Pathology, University of Louisville School of Medicine, Louisville, Ky.), p. 261

Thrombus formation in stainless steel tubes used as vascular implants in the dog. *Olson, P. S., Ljungqvist, U., Bergentz, S.-E.* (Department of Surgery I, University of Gothenburg, Gothenburg, Sweden), p. 271

Factor XII-induced fibrinolysis: Studies on the separation of prekallikrein, plasminogen proactivator, and factor XI in human plasma. *Laake, K., Venneröd, A. M.* (Department of Pharmacology, Institute of Pharmacy, University of Oslo, Norway), p. 285

The behaviour of isotope labelled blood proteins in thrombosis. *Strachan, C. J. L., Scully, M. F., Kakkar, V. V.* (Department of Surgery, King's College Hospital Medical School, London SE5 8RX, England), p. 303

ADP-induced aggregation studied with a screen filtration pressure test. Correlation with the photometric test. *Stoltz, J. F., Alexandre, P., Nicolas, A., Streiff, F., Larcan, A.* (Regional Blood Transfusion Center and Resuscitation Department, C.H.U., 54000 Nancy, France), p. 319

Influence of human ceruloplasmin on the aggregation of human platelets by adenosine diphosphate. *Soria, J., Soria, C., Samama, M., Mester, L.* (Laboratory of Haematology, Hôtel Dieu, Paris IV, France), p. 327

Plasma factor X_a-inhibitory activity in alcoholic liver disease and the effect of heparin. *Gavrilis, P., Lerner, R. G., Goldstein, R.* (Hematology Section, Department of Medicine, New York Medical College, New York, N. Y. 10029), p. 335

Influence of fibrinolysis and coagulation on haemostatic plug formation. An experimental study in rabbits. *Bergqvist, D., Arfors, K.-E.* (Department of Experimental Medicine, Pharmacia AB, Uppsala, Sweden), p. 345

Effects of intravenous administration in rabbits of dipyridamole and five related agents on platelet aggregation, blood pressure and heart rate. *Philp, R. B.* (Department of Pharmacology, The University of Western Ontario, London, Canada), p. 361

Thrombolytic agents: Are suitable methods

used for their assessment? Are our investigative efforts directed toward the right goal? *von Kaulla, K. N.* (Coagulation Laboratories, Department of Medicine, University of Colorado Medical Center, Denver, Col. 80220), p. 367

Thrombosis Research (New York) **4** (1974) No. 3

Safety of intraaortic balloon pumping. I. Biochemic and hematologic values influenced by use of balloon. *Schneider, M. D., Kaye, M. P., Blatt, S. J., Tobin, H. G., Eckner, F. A. O.* (Medical Engineering Research Division, IIT Research Institute, Chicago, Ill. 60616), p. 387

Safety of intraaortic balloon pumping. II. Physical injury to aortic endothelium due to mechanical pump action. *Schneider, M. D., Kaye, M. P., Blatt, S. J., Tobin, H. G., Eckner, F. A. O.* (Medical Engineering Research Division, IIT Research Institute, Chicago, Ill. 60616), p. 399

The tanned red cell hemagglutination-inhibition immunoassay of fibrinogen-fibrin degradation products. Methodological and statistical aspects. *Hahn, L.* (Department of Obstetrics, Sahlgren's Hospital, Göteborg, Sweden), p. 417

Phospholipid requirements in thrombin formation. *Zolton, R. P., Seegers, W. H.* (Department of Physiology, Wayne State University, School of Medicine, Detroit, Mich.), p. 437

Influence of blood flow velocity on experimental haemostatic plug formation. *Arfors, K.-E., Bergqvist, D.* (Department of Experimental Medicine, Pharmacia AB, Uppsala, Sweden), p. 447

Identification of two distinct heparin cofactors in human plasma: II. Inhibition of thrombin and activated factor X. *Bringinshaw, G. F., Shanberge, J. N.* (Hemostasis and Thrombosis Research Laboratories, Department of Pathology, Mount Sinai Medical Center, Milwaukee, Wis. 53233), p. 463

Inhibition of platelet aggregation by medium-chain fatty acids. *Tangen, O., Wallenbeck, I. A. M., Bergqvist, D.* (Department of Experimental Medicine, Pharmacia AB, Uppsala, Sweden), p. 479

Competitive adsorption of plasma proteins onto polymer surfaces. *Lee, R. G., Adamson, C., Wan Kim, S.* (Division of Materials Science and Engineering, University of Utah, Salt Lake City, Utah 84112), p. 485

The fibrinogenolytic pathway of fibrinogen catabolism: A reply. *Collen, D., Semeraro, N., Verstraete, M.* (Laboratory of Blood Coagulation, Medical Research Department, University of Leuven, 3000 Leuven, Belgium), p. 491

Thrombosis Research (New York) **4** (1974) No. 4

Incorporation of fibrinogen into soluble fibrin complexes. *Jakobsen, E., Ly, B., Kierulf, P.* (Hematological Research Laboratory, Department IX, University Clinic, Ullevål Hospital, Oslo, Norway), p. 499

Stabilization of soluble fibrin/fibrinogen complexes by fibrin stabilizing factor (FSF). *Ly, B., Kierulf, P., Jakobsen, E.* (Hematological Research Laboratory, Department IX, University Clinic, Ullevål Hospital, Oslo, Norway), p. 509

Effets "in vitro" du gliclazide, nouvel agent hypoglycémiant, sur les plaquettes humaines normales. *Vainer, H., Verry, M.* (Institut de Recherches sur les Maladies du Sang, Hôpital Saint-Louis, 75010 Paris, France), p. 523

Enhancement of plasminogen activator by vasopressin and adrenaline: A role of cyclic AMP? *Mannucci, P. M.* (Institute of Medical Pathology, Hemophilia and Thrombosis Centre, 15 Milano, Italy), p. 539

Effect of steroids, including progestin and estrogen components of oral contraceptive drugs, on the esterase activity of thrombin. *Cole, E. R.* (Coagulation Laboratories, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Ill. 60612), p. 551

New nonimmunological method of measuring fibrinogen-fibrin degradation products. *Finkelstein, A. E., Alexander, B., Roisman, F.* (Department of Rheumatology, Fundacion CIMAE, Buenos Aires, Argentina), p. 567

Fibrinolytic activity in rabbit kidney after the endotoxin injections. *Szczepański, M.*

(Department of Biochemistry and Department of Pathomorphological Diagnostics, Medical Centre of Postgraduate Education, Warsaw, Poland), p. 587

A continuous registration method in experimental arterial thrombosis in the rat. *Bourgain, R. H., Six, F.* (Laboratorium voor Fysiologie en Fysiopathologie Eenheid voor Hart- en Bloedvatenonderzoek, Vrije Universiteit Brussel, Brussels, Belgium), p. 599

A plasminogen proactivator-activator system in human blood effective in absence of Hageman factor. *Astrup, T., Rosa, A. T.* (The James F. Mitchell Foundation, Institute for Medical Research, Washington, D. C.), p. 609

Thrombosis Research (New York) **4** (1974) No. 5

Factor-VIII-related antigen in platelets. *Howard, M. A., Montgomery, D. C., Hardisty, R. M.* (Department of Haematology, Institute of Child Health, Hospital for Sick Children, Great Ormond Street, London WC1N 3JH, England), p. 617

Platelet aggregation by platelet-clumping substance. *Yamazaki, H., Sano, T., Shimamoto, T., Shimamoto, T.* (Institute for Cardiovascular Diseases, Tokyo Medical and Dental University, School of Medicine, Tokyo, Japan), p. 625

Isolation and chemical analyses of platelet-clumping substance in blood. *Yamazaki, H., Ijiri, H., Sano, T., Anan, K., Shimamoto, T.* (Institute of Cardiovascular Diseases, Tokyo Medical and Dental University, School of Medicine, Tokyo, Japan), p. 639

Isolation and characterization of multiple forms of human thrombin. *Gorman, J. J., Castaldi, P. A.* (Department of Haematology, Austin Hospital, Heidelberg, Victoria 3084, Australia), p. 653

Ion exchange and affinity chromatography during the purification of human plasminogen on Sepharose-L-lysine. *Silverstein, R. M.* (Armour Pharmaceutical Co., Kankakee, Ill. 60901), p. 675

Polyphloretinphosphate, an antithrombogenic substance which inhibits platelet adhesion. *Swedenborg, J., Olsson, P., Lagergren, H.* (Surgical Research Laboratory, Thoracic Clinics, Karolinska Sjukhuset, Stockholm, Sweden), p. 687

Vascular injury and thrombosis: A scanning electron microscopic study. *Stoner, G. E., Chisolm, G. M., Lucas, T. R., Srinivasan, S., Sawyer, P. N.* (University of Virginia, Charlottesville, Va. 22901), p. 699

Progressive inactivation of factor VII in the cold by heparin. *Godal, H. C., Gravem, K., Laake, K.* (Hematological Research Laboratory, Department IX, University Clinic, Ullevål Hospital, Oslo, Norway), p. 707

Proteolytic specificity of thrombin. *Walz, D. A., Seegers, W. H., Reuterby, J., McCoy, L. E.* (Department of Physiology, Wayne State University, School of Medicine, Detroit, Mich.), p. 713

Thrombosis Research (New York) **4** (1974) No. 6

Determination of plasma prothrombin with a reaction rate analyzer using a synthetic substrate. *Bergström, K., Blombäck, M.* (Department of Clinical Chemistry, Karolinska Sjukhuset, Stockholm, Sweden), p. 719

Some properties of the tissue plasminogen activator from the pig heart. *Hijikata, A., Fujimoto, K., Kitaguchi, H., Okamoto, S.* (Department of Physiology, Kobe University School of Medicine, Kobe, Japan), p. 731

The inhibition of thrombocyte adhesion by bencyclane. Experimental and clinical results. *Martin, M., Schäfer, G., Martin, U., Juraschek, H., Knüll, W.* (Aggertalklinik Engelskirchen, Clinic for Vascular Diseases, Bonn, FRG), p. 741

Dependence of staphylococcal clumping activity of fibrinogen on conformation. *Stemberger, A., Hörmann, H.* (Max Planck-Institut für Biochemie, München-Martinsried, BRD), p. 753

The semiquantitative classification of thrombus size by the ^{125}I-labeled fibrinogen technique. *Wolf, E., Hume, M.* (Vascular Laboratory, Lemuel Shattuck Hospital, Tufts University School of Medicine, Boston, Mass. 02111), p. 757

Cold-promoted activation of factor VII in human plasma: Studies on the associated

acyl-arginine esterase activity. *Laake, K., Venneröd, A. M., Haugen, G., Gjönnaess, H.* (Department of Pharmacology, Institute of Pharmacy, University of Oslo, Oslo, Norway), p. 769

Effect of *in vivo* produced fibrinogen. Fibrin intermediates on viscosity of human blood. *Blättler, W., Straub, P. W., Peyer, A.* (Hematology Division, Department of Medicine, Kantonsspital, University of Zurich, Zurich, Switzerland), p. 787

Reduction of insolubilized fibrinogen. *Matthias, F. R., Heene, D. L., Wegrzynowicz, Z.* (Department of Medicine, Justus Liebig University, Giessen, FRG), p. 803

Platelet aggregation and clot retraction by two preparations of staphylocoagulase. *Semeraro, N., Fumarola, D., Pasquetto, N., Vermylen, J.* (Laboratory of Blood Coagulation, Medical Research Department, Academisch Ziekenhuis St. Rafaël, University of Leuven, Leuven, Belgium), p. 819

Isolation and some properties of thrombin-E and other prothrombin derivatives. *Seegers, W. H., Walz, D. A., Reuterby, J., McCoy, L. E.* (Department of Physiology, Thrombosis Specialized Center of Research, Wayne State University School of Medicine, Detroit, Mich.), p. 829

Characterization of fibrinogen and fibrin degradation products by isoelectric focusing in polyacrylamide gel. *Arnesen, H.* (Hematological Research Laboratory, Department IX, University Clinic, Ullevål Hospital, Oslo, Norway), p. 861

Formation of prothrombin-E, thrombin, and thrombin-E and their inhibition with antithrombin and enzyme inhibitors. *Seegers, W. H., Andary, T. J.* (Department of Physiology, Thrombosis Specialized Center of Research, Wayne State University School of Medicine, Detroit, Mich.), p. 869

Human and bovine prothrombin similarities. *Walz, D. A., Seegers, W. H., Hassouna, H. I., Reuterby, J.* (Department of Physiology, Wayne State University, School of Medicine, Detroit, Mich.), p. 875

Uptake and utilization of free fatty acids (FFA) by human endothelial cells. *Hoak, J. C., Czervionke, R. L., Lewis, L. J.* (Specialized Center of Research in Atherosclerosis, Department of Medicine, University of Iowa College of Medicine, Iowa City, Iowa), p. 879

Amino acid sequence of O fragment of bovine prothrombin. *Reuterby, J., Walz, D. A., McCoy, L. E., Seegers, W. H.* (Department of Physiology, Wayne State University School of Medicine, Detroit, Mich.), p. 885

The fibrinogenolytic pathway of fibrinogen catabolism: Additional comments. *Lipinski, B., Lipinska, I., Gurewich, V.* (Vascular Laboratory, Lemuel Shattuck Hospital, Tufts University School of Medicine Boston, Mass. 02130), p. 891

The fibrinogenolytic pathway of fibrinogen catabolism: A rebuttal. *Mosesson, M. W., Finlayson, J. S.* (State University of New York, Downstate Medical Center, Brooklyn, N. Y. 11203), p. 895

Reply to the fibrinogenolytic pathway of fibrinogen catabolism. A comment. *Sherman, L. A.* (Division of Laboratory Medicine, St. Louis, Mo. 63110), p. 901

Thrombosis Research (New York) **4** (1974) Suppl. No. 1

Mechanisms and frequency of thrombosis in the coronary circulation. *Chandler, A. B.* (Department of Pathology, Medical College of Georgia, Eugene Talmadge Memorial Hospital, Augusta, Ga.), p. 3

Dietary fats and arterial thrombosis. *Renaud, S.* (Unité de Recherche de Physio-Pathologie Vasculaire, 69500 Lyon-Bron, France) p. 25

Biological membranes. *Chapman, D.* (Department of Chemistry, University of Sheffield, Sheffield, England), p. 37

Hyperlipoproteinemia. Relation to platelet lipids, platelet function and tendency to thrombosis. *Miettinen, T. A.* (Second Department of Medicine, University of Helsinki, 00280 Helsinki 29, Finland), p. 41

Prostaglandins in platelet function. *Smith, J. B., Ingerman, C., Kocsis, J. J., Silver, M. J.* (Cardeza Foundation and Department of Pharmacology, Thomas Jefferson University, Philadelphia, Pa. 19107), p. 49

The platelet synthesis of prostaglandins in pathological conditions. *Clausen, J., Srivastava, K. C.* (Department of Hygiene,

Social and Preventive Medicine and Environment Science, University of Odense, Odense, Denmark), p. 57

Ultrastructure of the vessel wall in fat embolism and electron microscopy of fat phagocytosis and transport by blood platelets. *Schulz, H.* (Pathologisches Institut der Städtischen Kliniken, 45 Osnabrück, BRD), p. 59

Abstracts. Proceedings of the IIIrd Tromsø Seminar in Medicine, University of Tromsø, Tromsø, Norway, p. 61

Transfusion (Philadelphia) **14** (1974) No. 1

Factors influencing the 24-hour posttransfusion survival and the oxygen transport function of previously frozen red cells preserved with 40 per cent W/V glycerol and frozen at −80 C. *Valeri, C. R.* (Naval Blood Research Laboratory, Chelsea, Mass. 02150), p. 1

Frozen blood: A method for low-glycerol, liquid nitrogen freezing allowing different postthaw deglycerolization procedures. *Åkerblom, O., Högman, C. F.* (Blood Center, University Hospital, S-75014 Uppsala, Sweden), p. 16

The high incidence of anti-HL-A antibodies in anti-D typing reagents. Illustrated by a case of Matuhasi-Ogata phenomenon mimicking a "D with anti-D" situation. *Wilkinson, S. L., Vaithianathan, T., Issitt, P. D.* (The Paul I. Hoxworth Blood Center, University of Cincinnati, Cincinnati, Ohio 45229), p. 27

Accumulation of DI-2-ethylhexyl phthalate (DEHP) in whole blood, platelet concentrates, and platelet-poor plasma. *Contreras, T. J., Sheibley, R. H., Valeri, C. R.* (Naval Blood Research Laboratory, Chelsea, Mass.), p. 34

The influence of dialysis in 2-mercaptoethanol reduction of erythrocyte antibodies. *Rosner, E. R., Pirofsky, B., Smith, K.* (Department of Clinical Pathology, University of Oregon Medical School, Portland, Ore. 97201), p. 47

Pseudomonas septicemia in neutropenic dogs. I. Treatment with granulocyte transfusions. *Epstein, R. B., Waxman, F. J., Bennett, B. T., Andersen, B. R.* (V. A. West Side Hospital, Chicago, Ill. 60612), p. 51

Complement-fixing antibodies to the AD-169 strain of cytomegalovirus in banked blood. *Monif, G. R. G., Adams, W. R., Flory, L. F.* (Department of Obstetrics and Gynecology, University of Florida College of Medicine, Gainesville, Fla. 32610), p. 58

Unnecessary albumin therapy in a jaundiced patient. *Peters, R. W., Myhre, B. A., Ellis, R. R., Fu, P. C.* (Harbor General Hospital, Torrance, Calif. 90509), p. 61

Hepatitis carriers among soldiers who have returned from Vietnam. Australia antigen studies. *Blumberg, B. S., London, W. T., Sutnick, A. I., Camp, F. R., Jr., Luzzio, A. J., Conte, N. F.* (Department of Medicine, University of Pennsylvania, Institute for Cancer Research, Philadelphia, Pa.), p. 63

Evaluation of the use of albumin controls in Rh phenotyping. *White, W. D., Issitt, C. H., McGuire, D.* (The Paul I. Hoxworth Blood Center, University of Cincinnati, Cincinnati, Ohio 45229), p. 67

Auto anti-N: An additional example. *Hysell, J. K., Gray, J. M., Beck, M. L.* (Blood Bank, St. Joseph Mercy Hospital, Ann Arbor, Mich. 48104), p. 72

A rapid and simple method for freezing small volumes of erythrocytes in liquid nitrogen. *Reid, M. E., Ellisor, S. S.* (Educational Service, Spectra Biologicals, Oxnard, Calif.), p. 75

Blood component calculator. *Tenczar, F. J., Best, W. R.* (Abraham Lincoln School of Medicine, University of Illinois, College of Medicine, Chicago, Ill.), p. 77

Transfusion (Philadelphia) **14** (1974) No. 2

Evaluation of commercial antiglobulin sera over a two-year period. Part I. Anti-beta 1A, anti-alpha 2D, and anti-beta 1E levels. *Issitt, P. D., Issitt, C. H., Wilkinson, S. L.* (The Paul I. Hoxworth Blood Center of the University of Cincinnati, Cincinnati, Ohio 45229), p. 93

Evaluation of commercial antiglobulin sera over a two-year period. Part II. Anti-IgG and anti-IgM levels and underirable contaminating antibodies. *Issitt, P. D., Issitt, C. H., Wilkinson, S. L.* (The Paul I. Hoxworth Blood Center of the University of Cincinnati, Cincinnati, Ohio 45229), p. 103

Coagulation studies after transfusion of hydroxyethyl starch protected frozen blood in primates. *Weatherbee, L., Spencer H. H., Knorpp, C. T., Lindenauer, S. M., Gikas, P. W., Thompson, N. W.* (Veterans Administration Hospital, Ann Arbor, Mich. 58105), p. 109

Bacteriocidal properties of platelet concentrates. *Myhre, B. A., Walker, L. J., White, M. L.* (U.C.L.A. School of Medicine, Department of Pathology, Torrance, Calif. 90509), p. 116

Automated blood typing of patients. *Taswell, H. F., Nicholson, L. L., Cochran, M. L.* (Mayo Clinic Blood Bank and Transfusion Service, Mayo Clinic and Mayo Foundation, Rochester, Minn. 55901), p. 124

The platelet response to hypotonic shock. Its value as an indicator of platelet viability after storage. *Kim, B. K., Baldini, M. G.* (Division of Hematologic Research, The Memorial Hospital, Pawtucket, R. I.), p. 130

Platelet preservation by freezing. Use of dimethylsulfoxide as cryoprotective agent. *Murphy, S., Sayar, S. N., Abdou, N. L., Gardner, F. H.* (Hematology Research Laboratory, Presbyterian-University of Pennsylvania Medical Center, Philadelphia, Pa. 19104), p. 139

Cooling mattress induced acute hemolytic anemia. *Niejadlik, D. C., Lozner, E. L.* (Wilford Hall, USAF Medical Center, Lackland AFB, Tex. 78236), p. 145

American National Red Cross experience with hepatitis B antibody (HBAb or anti-HBAg) testing. *Ni, L. Y., Lama, S., Krakaur, R. B., Greenwalt, T. J., Levin, J. J.* (Special Projects Laboratory, American National Red Cross, Washington, D. C. 20006), p. 148

Microaggregates in frozen and saline washed red blood cells. *Goldfinger, D., Solis, R. T., Meryman, H. T.* (Blood Bank Department, Clinical Center, National Institutes of Health, Bethesda, Md. 20014), p. 151

Clotting factors in supernatant plasma following cryoprecipitation. *Roth, G. J., Tobias, K. I.* (U. S. Army Medical Research Laboratory, Blood Research Division, Fort Knox, Ky. 40121), p. 155

A study of weak subgroups of blood group A with an antiglobulin-latex test. *Poskitt, T. R., Fortwengler, H. P., Jr.* (Blood Research Division, U. S. Army Medical Research Laboratory, Fort Knox, Ky. 40121), p. 158

Procurement and identification of HL-A lymphocytotoxic antibodies in sera of nonpregnant, multiparous blood donors. *Rodey, G. E., Kunicki, J., Anderson, J., Aster, R. H.* (Immunology Section, The Milwaukee Blood Center, Inc., Milwaukee, Wis. 53233), p. 167

Platelet concentrates: Sterility of 400 single units stored at room temperature. *Wrenn, H. E., Speicher, C. E.* (Clinical Pathology Service, Wilford Hall USAF Medical Center, Lackland AFB, Tex. 78236), p. 171

Transfusion (Philadelphia) **14** (1974) No. 3

Transfusion of the neonatal patient. *Oberman, H. A.* (No address) p. 183

Chemical specifications for adenine for medical use. Committee of the Division of Medical Sciences, National Academy of Sciences, National Research Council. (Reprint requests: E. L. May, National Institute of Arthritis, Metabolism and Digestive Diseases, National Institutes of Health, Bethesda, Md.), p. 185

The purification of red cells for transfusion by freeze preservation and washing. I. The mechanism of leukocyte removal from washed, freeze preserved red cells. *Crowley, J. P., Valeri, C. R.* (Naval Blood Research Laboratory, Chelsea, Mass.), p. 188

The purification of red cells for transfusion by freeze preservation and washing. II. The residual leukocytes, platelets and plasma in washed, freeze-preserved red cells. *Crowley, J. P., Valeri, C. R.* (Naval Blood Laboratory, Chelsea, Mass.), p. 196

Jaundice and hepatitis B antigen/antibody in hemophilia. *Lewis, J. H., Maxwell, N. G., Brandon, J. M.* (Department of Medicine, University of Pittsburgh, Pittsburgh, Pa.), p. 203

Combined maternal erythrocyte autosensitization and materno-fetal Jk^a incompatibility. *Doerner, I., Moore, J. A., Chaplin, H., Jr.* (Barnes Hospital Blood Bank, Washington University School of Medicine, St. Louis, Mo.), p. 212

The risk of immunization to IgG following Rh immune globulin therapy. *Sebring*

E. S., Polesky, H. F., Schanfield, M. S. (Minneapolis War Memorial Blood Bank, Minneapolis, Minn. 55404), p. 220

Autoimmune hemolytic anaemia in Hodgkin's disease associated with anti-I^T. *Garratty, G., Petz, L. D., Wallerstein, R. O., Fudenberg, H. H.* (Harkness Community Hospital and Medical Center, San Francisco, Calif.), p. 226

The incubation of long term in vitro incubation on the intermediates of red cell metabolism. *Henderson, R. J., Jr., Mills, G. C.* (Department of Biochemistry and Molecular Biology, Louisiana State University School of Medicine, Shreveport, La. 71130), p. 232

A bradykinin-like substance in heat-treated human plasma protein solution. *Izaka, K., Tsutsui, E., Mima, Y., Hasegawa, E.* (Green Cross Corporation, Miyakojuma-Nakadori, Miyakojima-ku, Osaka 534, Japan), p. 242

Storage, rejuvenation and restorage of human red cells for periods up to 56 days. *Moore, G. I., Failla, M. L., Blake, B. H., Gray, J. L., Manalo, F. W.* (Army Medical Research Laboratory, Fort Knox, Ky., 40121) p. 249

Increased efficiency of leukocyte collection from patients with chronic myelocytic leukemia. *Wheeler, T. G., McCredie, K. B., Freireich, E. J., Daniels, T. V.* (Department of Neural Sciences, University of Texas at Houston, Houston, Texas), p. 253

Evidence for two anomalous I blood group determinants. *McGinniss, M. H., Grindon, A. J., Schmidt, P. J.* (Blood Bank Department, Clinical Center, National Institutes of Health, Bethesda, Md. 20014), p. 257

Contamination of cord blood with maternal blood during delivery. *Milam, J. D., Reeves, A. E., Bush, R. W., Gardner, H. L.* (St. Luke's Episcopal Hospital, Houston, Texas), p. 261

Tetrycycline-induced immune hemolytic anemia. *Wenz, B., Klein, R. L., Lalezari, P.* (Division of Immunohematology, Department of Medicine, Montefiore Hospital and Medical Center, New York, N. Y.), p. 265

The composition of several commercial rapid tube and saline anti-D reagents. *Howard, P. L., Dopp, S. L.* (Pathology Department, University of Vermont, Burlington, Vt.), p. 270

The effect of ascorbate and dihydroxyacetone on the 2,3-diphosphoglycerate and ATP levels of stored human red cells. *Wood, L., Beutler, E.* (Division of Medicine, City of Hope Medical Center, Duarte, Calif. 91010), p. 272

Effects of centrifugation on erythrocytes. *Miller, W. V., Wilson, M. J.* (Missouri-Illinois Regional Red Cross Blood Program, St. Louis, Mo.), p. 278

The preparation of cryoprecipitate in a mobile laboratory: A five-year experience. *Keating, L. J.* (Northern Ohio Red Cross Blood Program, Cleveland, Ohio 44115), p. 283

Further evaluation of a latex agglutinination test for detection of hepatitis B antigen. *Perkins, H. A., Perkins, S. L., Vyas, G. N.* (Irwin Memorial Blood Bank, San Francisco Medical Society, University of California, San Francisco, Calif.), p. 287

Hematologic parameters and transfusion: Weekly summary by computer. *Buchholz, D. H., Hopper, J. K., Yamamoto, L. A.* (Saint Barnabas Medical Center, Livingston, N. J. 07039), p. 291

Transfusion (Philadelphia) **14** (1974) No. 4

A perspective of Soviet blood banking. *Cohen, E.* (Clinical Immunology, Hematology and Blood Bank, Roswell Park Memorial Institute, New York State Department of Health, Buffalo, N. Y.), p. 315

Platelet preservation. What temperature? A rationale for strategy. *Kattlove, H. E.* (Division of Hematology, Harbor General Hospital, Torrance, Calif. 90509), p. 328

The relation between response to hypotonic stress and the ^{51}Cr recovery in vivo of preserved platelets. *Valeri, C. R., Feingold, H., Marchionni, L. D.* (Naval Blood Research Laboratory, Chelsea, Mass.), p. 331

Rejuvenation of human red blood cells during liquid storage. *DeVenuto, F., Brenneman, G., Wilson, S. M.* (Blood Research Division, U. S. Army Medical Research Laboratory, Fort Knox, Ky. 40121), p. 338

Washing of red blood cells previously frozen in liquid nitrogen. Experience with the elutramatic ultra-flo system. *Åkerblom, O., Kreuger, A.* (Blood Center, University Hospital, S-750 14 Uppsala, Sweden), p. 345

Hydroxyethyl starch and dexamethasone as an adjunct to leukocyte separation with the IBM blood cell separator. *Mishler, J. M., Higby, D. J., Rhomberg, W., Cohen, E., Nicora, R. W., Holland, J. F.* (McGaw Laboratories, Glendale, Calif. 91201), p. 352

Increased granulocyte collection with the blood cell separator and the addition of etiocholanolone and hydroxyethyl starch. *McCredie, K. B., Freireich, E. J., Hester, J. P., Vallejos, C.* (Department of Developmental Therapeutics, M. D. Anderson Hospital and Tumor Center, Houston, Texas 77025), p. 357

Effects of in vitro storage on red blood cell agglutinogens. *Greendyke, R. M., Banzhaf, J. C.* (Department of Pathology, University of Rochester School of Medicine and Dentistry, Rochester, N. Y. 14642), p. 365

Hepatitis B virus subtypes ad and ay among blood donors in the greater Los Angeles, area. *Mosley, J. W., Edwards, V. M. Wapplehorst, B., Hajduk, P.* (Hepatic Epidemiology Laboratory, John Wesley County Hospital, Los Angeles, Calif. 90007), p. 372

Kidd blood group antigensof leu kocytes and platelets. *Marsh, W. L., Øyen, R., Nichols, M. E.* (Serology and Genetics Laboratory, New Yoork Blood Center, New York, N. Y. 10021), p. 378

Hemoglobin catabolism following a hemolytic transfusion reaction in a patient with sickle cell anemia. *Duvall, C. P., Alter, H. J., Rath, C. E.* (Division of Hematology, Department of Medicine, Georgetown University Hospital, Washington, D. C.), p. 382

Intensive multiunit plateletpheresis of normal donors. *Schiffer, C. A., Buchholz, D. H., Wiernik, P. H.* (Baltimore Cancer Research Center, Baltimore, Md.), p. 388

Transfusion (Philadelphia) **14** (1974) No. 5

Anti-C3d antiglobulin reagents. I. Characteristics of the anti-C3c and anti-C3d response during hyperimmunization in rabbits. *Moore, J. A., Chaplin, H., Jr.* (Department of Preventive Medicine, Washington University School of Medicine, St. Louis, Mo.), p. 407

Anti-C3d antiglobulin reagents. II. Preparation of an antiglobulin serum monospecific for C3d. *Moore, J. A., Chaplin, H., Jr.* (Department of Preventive Medicine, Washington University School of Medicine, St. Louis, Mo.), p. 416

Microcapillary agglutination for the detection of leukocyte antibodies: Evaluation of the method and clinical significance in transfusion reactions. *McCullough, J., Burke, M. E., Wood, N., Carter, S. J., Weiblen, B. J., Yunis, E. J.* (Laboratory of Medicine and Pathology, University of Minnesota Medical School, Minneapolis, Minn.), p. 425

Red cell D antigen sites and titration scores in a family with weak and normal D^u phenotypes inherited from a homozygous D^u mother. *Bush, M., Sabo, B., Stroup, M., Masouredis, S. P.* (Philip Levine Laboratories of Immunohematology, Ortho Diagnostics, Inc., Raritan, N. J.), p. 433

The prophylactic treatment of thrombocytopenic leukemic patients with platelets: a double blind study. *Higby, D. J., Cohen, E., Holland, J. F., Sinks, L.* (Department of Medicine A, Roswell Park Memorial Institute, Buffalo, N. Y.), p. 440

Altered filterability of CPD-stored sickle trait donor blood. *Hipp, M. J., Scott, R. B.* (Department of Medical Technology, St. Joseph's Hospital, Towson, Md.), p. 447

Effect of chilling on membrane related functions of platelets. *Ando, Y., Steiner, M., Baldini, M.* (Division of Hematology Research, The Memorial Hospital, Pawtucket, R. I.), p. 453

Studies of MNSsU antigen activity on leukocytes and platelets. *Marsh, W. L., Øyen, R., Nichols, M. E., Charles, H.* (Serology and Genetics Laboratory, New York Blood Center, New York, N. Y. 10021), p. 462

Blood group U antigen on Rh_{null} leukocytes. *Marsh, W. L., Øyen, R., Moulds, J., Polesky, H. F.* (Serology and Genetics Laboratory, New York Blood Center, New York, N. Y. 10021), p. 467

Evidence for heterogeneity of LW antigen revealed in a family study. *Swanson, J. L., Azar, M., Miller, J., McCullough, J. J.* (Department of Laboratory Medicine and Pathology, University of Minnesota Hospitals, Minneapolis, Minn. 55455), p. 470

Another example of human chimerism. *Carr, E. O., McDonald, L. A.* (Central Florida Blood Bank, Inc., Orlando, Fla.), p. 475

Development of a nonelectrical refrigerant. *McPeak, D. W., Camp, F. R., Jr.* (U. S. Army Medical Research Laboratory, Fort Knox, Ky.), p. 477

Accomplishments of a salaried blood donor recruiter in a municipal hospital. *McBarnette, L., Rosner, F., Bisserup, R.* (Queens Hospital Center, Affiliation of the Long Island Jewish-Hillside Medical Center, New York, N. Y.), p. 478

Experience with frozen erythrocytes in a private hospital. *Bryant, L. R., Wallace, M. E.* (Department of Hemotherapy, Charity Hospital, New Orleans, La.), p. 481

Vox Sanguinis (Basel) **26** (1974) No. 4

Instrumented PVP-augmented antiglobulin tests. I. Detection of allogeneic antibodies coating otherwise normal erythrocytes. *Burkart, P., Rosenfield, R. E., Hsu, T. C. S., Wong, K. Y., Nusbacher, J., Shaikh, Sh. H., Kochwa, Sh.* (Department of Pathology, Mount Sinai School of Medicine, City University of New York, New York, N. Y.), p. 289

Instrumented PVP-augmented antiglobulin tests. II. Evaluation of acquired hemolytic anemia. *Hsu, T. C. S., Rosenfield, R. E., Burkart, P., Wong, K. Y., Kochwa, Sh.* (Department of Pathology, Mount Sinai School of Medicine, City University of New York, New York, N. Y.), p. 305

Instrumented PVP-augmented antiglobulin tests. III. IgG-coated cells in ABO incompatible babies; depressed hemoglobin levels in type A babies of type O mothers. *Hsu, T. C. S., Rosenfield, R. E., Rubinstein, P.* (Department of Pathology, Mount Sinai School of Medicine, City University of New York, New York, N. Y.), p. 326

Observations on the reproducibility of the bromelised test cell anti-D assay using the auto-analyser. *Gunson, H. H., Phillips, P. K., Stratton, F.* (Blood Transfusion Centre, Lancaster, England), p. 334

Antigenic alteration of red cell surfaces exposed to enzymatic actions of autologous polymorphonuclear leukocytes. Leukocyte-induced alteration. *Arend, P., Malchow, H.* (Research Laboratories, Chemie Grünenthal GmbH, 519 Stolberg [Rhld], FRG), p. 344

Efficiency of anti-D IgG prevention after induced abortion. *Simonovits, I.* (National Institute of Haematology and Blood Transfusion, 1113 Budapest, Hungary), p. 361

Recipient's hepatitis, an inevitable side-effect of blood transfusion. *Fiedler, H.* (DRK-Blutspendedienst, D-44 Münster/Westf., FRG), p. 368

Serology and genetics of the A_1 high H subgroup. *Sathe, M., Bhatia, H. M.* (Blood Group Reference Centre [ICMR], Seth G.S. Medical College, Parel, Bombay 4000 12, India), p. 374

Blood-group-like substances in some marine invertebrates. I. Blood-group A reactive substances in the ascadian *Phallusia mammilata* (Cuvier) and in the lancelet *Amphioxus (Branchiostoma) lanceolatus* (Pallas). *Renwrantz, L., Uhlenbruck, G.* (Zoologisches Institut und Zoologisches Museum, Universität Hamburg, Hamburg, BRD), p. 385

Screening of blood donors with twelve biochemical tests. *Heistö, H., Knuds, F., Rosenlund, B., Godal, H. C., Skaga, E.* (Blood Bank and Department of Immunohaematology, Ullevål Hospital, Oslo, Norway), p. 392

The successful culture of sheep blood lymphocytes despatched over long distances. *Dain, A. R., Curtain, C. C.* (ARC Institute of Animal Physiology, Babraham, Cambridge, England), p. 396

Further observations on the In^a (Indian) antigen in Indian populations. *Badakere, S. S., Parab, B. B., Bhatia, H. M.* (Blood Group Reference Centre [ICMR], Seth G. S. Medical College, Parel, Bombay 4000 12, India), p. 400

Vox Sanguinis (Basel) **26** (1974) No. 5

Separation of H-activity from isolated glycoproteins of human O erythrocyte membranes. *Brennessel, B. A., Goldstein, J.* (New York Blood Center, Department of Biochemistry, New York, N. Y. 10021), p. 405

Effects of repeated heating on human albumin. *Roelands, J. F., Moody, M. F., Cohen, P.* (Bureau of Biologics, Food and Drug Administration, Bethesda, Md. 20014), p. 415

Le^x, the spurned antigen of the Lewis blood group system. *Arcilla, M. B., Sturgeon, P.* (The Gwynne Hazen Cherry Memorial Laboratories, Department of Pediatrics, Hematology Division, UCLA School of Medicine, Los Angeles, Calif. 90024), p. 425

Mercaptoethanol-stable antibody test predicting hemolytic disease of the newborn due to ABO incompatibility. *Hasekura, H.* (Department of Legal Medicine, The Saitama Medical School, Moroyama, Saitama 350-04, Japan), p. 439

Distribution of the HL-A antigens of the Japanese population in Japan. *Tsuji, K., Aizawa, M., Itakura, K., Nakayama, E., Hasekura, H., Yoshida, T., Akaza, T., Orita, K., Kodama, T., Nomoto, K., Goya, T., Miyamoto, H., Ito, M.* (Renal Transplantation Center, Hyogo Prefectural Nishinomiya Hospital, Nishinomiya City, Hyogo-Ken, Japan 662), p. 449

Dissociation of human albumin dimer by heating. *Finlayson, J. S., Reamer, B. L., Young, A. M.* (Bureau of Biologics, Food and Drug Administration, Bethesda, Md. 20014), p. 457

Cad receptor in Thai blood donors. *Springarm, S., Chiewsilp, P., Tubrod, J.* (National Blood Centre, The Thai Red Cross Society, Bangkok, Thailand), p. 462

Demonstration of M antigen on human lymphocytes by liquid phase electrophoresis. *Stoltz, J. F., Streiff, F., Genetet, B.* (Groupe de Recherches Hémorrhéologiques, Centre Régional de Transfusion Sanguine et d'Hématologie, Vandoeuvre-lès-Nancy, F54500, France), p. 467

Relations of HL-A and Rh systems to immune reactivity. *Petrányi, G. Gy., Iványi, P., Hollán, S. R.* (National Institute of Haematology and Blood Transfusion, 1113 Budapest, Hungary), p. 470

Vox Sanguinis (Basel) **26** (1974) No. 6

Contribution to the inheritance of the Ag groups. A population genetic study. *Bütler, R., Brunner, E., Morganti, G.* (Central Laboratory of the Blood Transfusion Service, Swiss Red Cross, CH-3000 Berne, Switzerland), p. 485

Red cell hydrolases. III. Neuraminidase activity in isolated human erythrocyte plasma membranes. *Bosmann, H. B.* (Department of Pharmacology and Toxicology, University of Rochester, School of Medicine and Dentistry, Rochester N. Y. 14642), p. 497

Immunocompetent lymphocytes in previously frozen washed red cells. *Crowley, J. P., Skrabut, E. M., Valeri, C. R.* (Naval Blood Research Laboratory, Chelsea, Mass. 02150), p. 513

Studies on the biosynthetic pathway of human P erythrocyte antigens using somatic cells in culture. *Fellous, M., Gerbal, A., Tessier, C., Frezal, J., Dausset, J., Salmon, C.* (Institut de Recherche sur les Maladies du Sang, Hôpital Saint-Louis, 75010 Paris, France), p. 518

Blood group A_{bantu} population and family studies. *Jenkins, T.* (South African Institute for Medical Research, Johannesburg, S. A.), p. 537

Prevalence of irregular red cell antibodies and their significance in blood transfusion and antenatal care. *Spielmann, W., Seidl, S.* (Blood Donor Service Hessen, D-6 Frankfurt/M. 73, FRG), p. 551

Stability of normal human IgG in saline and glycine solutions. *Patterson, M. R., Smith, J. K.* (Scottish National Blood Transfusion Association, Protein Fractionation Centre, Royal Infirmary, Edinburgh EH3 9HB, Scotland), p. 560

P phenotype in two successive generations of a Japanese family. *Miwa, S., Matuhasi, T., Yasuda, J.* (Third Department of Internal Medicine, Yamaguchi University School of Medicine, Kogushi, Yamaguchi-ken 755, Japan), p. 565

Vox Sanguinis (Basel) **27** (1974) No. 1

Relationship of blood transfusions to appearance of mixed leukocyte culture blocking factor activity in plasma of uraemic patients and renal allograft recipients. *Sengar, D. P. S., Rashid, A., Harris, J. E.* (Laboratory of Immunology, Department of Medicine, University of Ottawa, Ottawa General Hospital, Ottawa, Canada), p. 1

Serology for automated cytotoxicity assays. Contrast fluorescence test. *Martel, J. L., Jaramillo, S., Allen, F. H., Jr., Rubinstein, P.* (Request reprints: F. H. Allen, The New York Blood Center, New York, N. Y. 10021), p. 13

Leukocyte-poor CPD blood. *Frey-Wettstein, M., Bachmann, M.* (Blutspendezentrum Limmattal SRK, CH-8952 Schlieren/Zürich, Schweiz), p. 21

Cryptic A-like receptor sites in human erythrocyte glycoprotein: Proposed nature of Tn-antigen. *Dahr, W., Uhlenbruck, G., Bird, G. W. G.* (Medizinische Universitätsklinik Köln, Abteilung für Immunobiologie, D-5 Köln 41, BRD), p. 29

An antibody in the serum of an MN patient which reacts with the M_1 antigen. *Giles, C. M., Howell, P.* (MRC Blood Group Reference Laboratory, London SW1W 8QJ, England), p. 43

Anti-Lu 11: Another antibody defining a high-frequency antigen related to the Lutheran blood group system. *Gralnick, M. A., Goldfinger, D., Hatfield, P. A., Reid, M. E., Marsh, W. L.* (Blood Bank Department, Clinical Center, National Institutes of Health, Bethesda, Md.), p. 52

An unusual expression of Ii antigens in erythrocytes of a healthy adult person. *Dzierżkowa-Borodej, W., Lisowska, E., Leśkiewicz, A., Leszczak, L.* (District Blood Transfusion Centre, 50345 Wroclaw, Poland), p. 57

Studies on the agglutinin specificities and blood group O(H)-like activities in extracts from the molluscs *Pomacea paludosa* and *Pomacea urceus*. *Baldo, B. A., Uhlenbruck, G.* (Clinical Immunology Unit Children's Medical Research Foundation, Princess Margaret Hospital, Perth, W. A. 6001, Australia), p. 67

Wk^a (Weeks), a new antigen in the Kell blood group system. *Strangle, J. J., Kenworthy, R. J., Webb, A. J., Giles, C. M.* (Regional Transfusion Centre, Churchill Hospital, Headington, Oxford OX3 7LJ, England), p. 81

Selective IgA deficiency in Rh-negative women. *Pal, M. K. R., Davison, M., Bedritis, I., Zipursky, A.* (Department of Pediatrics, Medical Centre, McMaster University, Hamilton, Ont. L8S 4J9, Canada), p. 87

Haemolytic disease of new-born due to anti-D antibodies in a D^u-positive mother. *Hill, Z., Vacl, J., Kalasová, E., Calábková, M., Pintera, J.* (Institute of Blood Transfusion and Haematology KUNZ, 65720 Brno, Czechoslovakia), p. 92

Vox Sanguinis (Basel) **27** (1974) No. 2

Reversed haemagglutination test for the detection of hepatitis B antigen. *Schuurs, A. H. W. M., Kacaki, J.* (Organon Scientific Development Group, Oss, The Netherlands), p. 97

The reactions of IgG and IgM anti-A and anti-B group antibodies with ^{125}I-labelled blood group glycoproteins. *Holburn, A. M., Masters, C. A.* (MRC Experimental Haematology Unit, St. Mary's Hospital Medical School, London W2 1PG, England), p. 115

Association between HL-A and red cell antigens. II. Absorption and titration analyses. *Nordhagen, R.* (National Institute of Public Health, Postuttak, Oslo 1, Norway), p. 124

Sa 1, a possible new HL-A specificity found in the Japanese population. *Nakayama, E., Itakura, K., Yakura, H., Aizawa, M., Kuroda, M., Hanada, K.* (Department of Pathology, Hokkaido University School of Medicine, Sapporo, Japan), p. 134

Reliability in automatic determination of the ABO group by the groupamatic system. *Garretta, M., Muller, A., Gener, J., Matte, C., Moullec, J.* (Centre National de Transfusion Sanguine, 75015 Paris, France), p. 141

The role of enzymes and albumen in haemagglutination reactions. A serological and ultrastructural study with ferritin-labelled anti-D. *Voak, D., Cawley, J. C., Emmines, J. P., Barker, C. R.* (Regional Transfusion

and Immuno-Haematology Centre, Cambridge CB2, 2PT, England), p. 156

A second example of anti-Yt^a with rapid *in vivo* destruction of Yt(a+) red cells. *Göbel, U., Drescher, K. H., Pöttgen, W., Lehr, H. J.* (Universitäts-Kinderklinik, D-4 Düsseldorf, BRD), p. 171

Plasma fibrinogen levels in 1016 regular blood donors. I. The influence of age and sex on mean values and percentiles. *Weisert, O., Jeremic, M.* (State Laboratory of Microbiology, N-2600 Lillehammer, Norway), p. 176

Increased elevation of peripheral leukocyte count by infusion of histocompatible granulocytes. *Higby, D. J., Mishler, J. M., Cohen, E., Rhomberg, W., Nicora, R. W., Holland, J. F.* (Department of Medicine A and Department of Clinical Laboratories, Roswell Park Memorial Institute, Buffalo, N. Y.), p. 186

Cytogenetic investigation of the Rh_{null} phenotype. *Marsh, W. L., Chaganti, R. S. K., German, J., Seidl, S., Spielmann, W.* (Serology and Genetics Laboratory, New York, N. Y. 10021), p. 190

Vox Sanguinis (Basel) **27** (1974) No. 3

Contributions to the optimal use of human blood. IV. Quantitative analysis of the immunoglobulin isolation. *Vogelaar, E. F., d. Boer v. d. Berg, M. A. G., Brummelhuis, H. G. J., Beentjes, S. P., Krijnen, H. W.* (Reprint requests: H. G. J. Brummelhuis, Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam-W, The Netherlands), p. 193

Contributions to the optimal use of human blood. V. A method to increase the yield of anti-D immunoglobulin by processing Cohn's fraction III. *Vogelaar, E. F., d. Boer-v. d. Berg, M. A. G., Reijnierse, E., Brummelhuis, H. G. J., Krijnen, H. W.* (Reprint requests: H. G. J. Brummelhuis, Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam-W, The Netherlands), p. 207

The purification of human factor II (prothrombin) and the preparation of a specific antiserum. *Heystek, J., Maier-v. d. Zande, G. M., Brummelhuis, H. G. J., Krijnen, H. W.* (Reprint requests: H. G. J. Brummelhuis, Central Laboratory of the Netherlands Red Cross Blood Transfusion Service Amsterdam-W, The Netherlands), p. 216

Separation of hepatitis-associated antigen (HAA) from human plasma for the production of rabbit anti-HAA. *Booth, J. R., Wiseman, I. C., Lee, D.* (National Blood Transfusion Service, Sheffield S5 7JN, England), p. 227

Two new cases of Rh mosaicism. Selective study of red cell population. *Habibi, B., Lopez, M., Salmon, C.* (Centre Départemental de Transfusion Sanguine, F-75012 Paris, France), p. 232

Quantitative, kinetic and thermodynamic analysis of weak B_{60} erythrocyte phenotypes. Heterogeneity among families. Identity within a family. *Lopez, M., Bouguerra, A., Lemeud, J. Badet, J., Salmon, C.* (Service d'Immunologie, Centre Départemental de Transfusion Sanguine, F-75012 Paris, France), p. 243

Some notes on the concept of cross-reactivity. *Hirschfeld, J.* (Statens rättskemiska laboratorium, Stockholm 60, Sweden), p. 254

Scianna blood group system. *Lewis, M., Kaita, H., Chown, B.* (Rh Laboratory and Department of Paediatrics, University of Manitoba, Winnipeg, Man., Canada), p. 261

Another HL-A27 recombinant. *Berry, P. R., Mills, K. R.* (Blood Transfusion Centre, P. O. Box 5546, Auckland, New Zealand), p. 265

Influence of orally administered antibiotics on anti-T agglutinin of normal subjects and of cirrhotic patients. *Boccardi, V., Attina, D., Girelli, G.* (Istituto di Patologia Medica I, Università di Roma, I-00100 Roma, Italia), p. 268

Vox Sanguinis (Basel) **27** (1974) No. 4

Release of a low molecular weight Fc-like fragment on reduction of water-insoluble IgG myeloma proteins. *Morris, G. G., Osterland, C. K., Chaplin, H. jr.* (Department of Preventive Medicine, Washington University School of Medicine, St. Louis, Mo. 63110), p. 273

Automated determination of the IgG and IgM fractions of rhesus antibodies.

Coulter, C. D. (Department of Haematology, Royal Victoria Hospital, Belfast, Ireland), p. 287

Anti-immunoglobulin antibodies in immunodeficiencies: Their influence on intolerance reactions to γ-globulin administration. *Ropars, C., Caldera, L. H., Griscelli, C., Homberg, J. C., Salmon, C.* (Groupe de Recherche U 76, INSERM, Centre Départemental de Transfusion Sanguine, 75012 Paris 12e, France), p. 294

Recovery of hepatitis B antibody from human plasma products separated by a modified Cohn fraction. *Berg, J. V. R., Berntsen, K. O., Björling, H., Holmström, B., Vyas, G. N.* (Reprint requests: J. V. R. Berg, Virus Department, Central Microbiological Laboratory of the Stockholm County Council, S-101 22 Stockholm, Sweden), p. 302

Elution of HL-A-specific antibodies from platelets. *Heinrich, D., Mueller-Eckhardt, C., Czitrom, A.* (Zentrum für Innere Medizin der Justus-Liebig-Universität, D-63 Giessen, BRD), p. 310

Complement-fixing and lymphocytotoxic antibodies in serum of pregnant women at delivery. *Nymand, G.* (Regional Blood Transfusion Center, P. O. Box 561, DK-9100 Aalborg, Denmark), p. 322

ABH receptors and red cell survival in a "Bombay" blood. Immunofluorescence studies by phytohemagglutinins and Helix agglutinins. *Poschmann, A., Fischer, K., Seidl. S., Spielmann, W.* (Department of Immunotherapy, University of Hamburg, Hamburg, FRG), p. 338

Purification and characterization of anti-A agglutinin from *Euhadra callizoma amaliae*. *Mukaida, M., Takatsu, A., Ishiyama, I.* (Department of Legal Medicine, University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113, Japan), p. 347

Severe ABO haemolytic disease due to high titre IgG anti-B in an A_2 mother. *Graham, H., Morrison, M., Casey, E.* (Clinical Laboratory, Bellshill Maternity Hospital, Bellshill, Scotland), p. 363

The Lu(a-b-) syndrome and an apparent upset of P_1 inheritance. *Contreras, M., Tippett, P.* (Reprint requests: P. Tippett, MRC Blood Group Unit, The Lister Institute, London SW 1W 8RH, England), p. 369

Antibodies against human immunoglobulin A allotypes, the genetic marker A_2m (1) of IgA. *Scherz, R., Pflugshaupt, R., Bütler, R.* (Central Laboratory, Blood Transfusion Service, SRC, CH-3000 Bern, Switzerland), p. 372

Polymorphism of phosphoglucomutase (PGM_3) in leucocytes: gene frequencies and family studies. *Goedde, H. W., Stender, D., Stahn, M., Benkmann, H.-G.* (Institut für Humangenetik der Universität Hamburg, D-2 Hamburg, BRD), p. 376

Exclusion of paternity in the HL-A system without testing the deceased accused man. *Speiser, P., Mayr, W. R., Pacher, M., Pausch, V., Bleier, I., Melzer, G., Weirather, M., Groer, K.* (Institute for Blood Group Serology, University of Vienna, Vienna, Austria), p. 379

Linkage of HL-A and GBG. *Allen, F. H. jr.* (The New York Blood Center, New York, N. Y. 10021), p. 382

Vox Sanguinis (Basel) **27** (1974) No. 5

Positive antiglobulin reactions with thawed deglycerolized red blood cells. *Moore, J. A. Dorner, I., Chaplin, H. Jr.* (Department of Preventive Medicine, Washington University School of Medicine, St. Louis, Mo. 63110), p. 385

"True" genotype of chimeric twins revealed by blood-group gene products in plasma. *Wrobel, D. M., McDonald, I., Race, C., Watkins, W. M.* (Toronto Centre, Canadian Red Cross Blood Transfusion Service, Toronto M5T, IV4 Ont., Canada), p. 395

Biochemical changes on storage of blood. Decrease in rate of methemoglobin reduction and increase in oxygen affinity on storage of ACD blood. *Ioppolo, C., Amiconi, G., Currell, D. L., Maffei, G., Zolla, L., Antonini, E.* (Institute of Chemistry, Faculty of Medicine, University of Rome, Rome, Italy), p. 403

Comparative effects of dextrans, gelatin and stable plasma protein solution (SPPS) on the experimental disseminated intravascular coagulation (DIC). *Moraiu, M., Rodhain, J., Noel, H., Masure, R.* (Laboratory for Haemostasis and Thrombosis Research, University of Louvain, Louvain, Belgium), p. 411

Demonstration of low-titer anti-Pr agglutinins. *Roelcke, D., Ebert, W., Anstee, D. J.* (Institute of Immunology and Serology, University of Heidelberg, D-6900 Heidelberg, FRG), p. 429

Anti-IP: An antibody defining another product of interaction between the genes of the I and P blood group system. *Allen, F. H. Jr., Marsh, W. L., Jensen, L., Fink, J.* (The New York Blood Center, New York, N. Y. 10021), p. 442

Characterization of a human saliva antigen precipitated by a lectin from *Lotus tetragonolobus*. *Napier, P. W., Everhart, D. L., Grundbacher, F. J.* (Reprint requests: Dr. D. L. Everhart, Peoria School of Medicine, Peoria, Ill. 61606), p. 447

Antibody to vaccinia. I. Detection by immunoelectroendosmophoresis. *Entwistle, C. C.* (National Tissue Typing Reference Laboratory, Southmead, Bristol, England), p. 459

Report 1973/1974 of the Reference Laboratory for the polymorphism of the third component (C3) of the human complement system. *Rittner, C., Rittner, B.* (Institut für Gerichtliche Medizin der Universität, D-53 Bonn, BRD), p. 464

Anti-ce (anti-f) in a CDe/cD-mother, as a cause of haemolytic disease of the newborn. *Spielmann, W., Seidl, S., von Pawel, J.* (Blutspendedienst Hessen, D-6 Frankfurt/M, BRD), p. 473

Erythroblastosis fetalis caused by anti-Wr^a (Wright). *Jørgensen, J., Jacobsen, L.* (Blood Bank and Blood Grouping Laboratory, Kommunehospitalet, Århus, Denmark), p. 478

DDT test: A new method to differentiate IgM and IgG erythrocyte antibodies. *Pirofsky, B., Rosner, E. R.* (Division of Immunology and Allergy, University of Oregon Medical School, Portland, Ore. 97201), p. 480

Vox Sanguinis (Basel) **27** (1974) No. 6

Cell electrophoresis for the detection of platelet antibodies. *Van Boxtel, C. J., Van der Weerdt, C. M., Engelfriet, C. P.* (Department of Immunohematology, Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, The Netherlands), p. 489

Partial purification of ABO blood group antigens: Sodium deoxycholate fractionation of human erythrocyte membranes. *Zuckermann, S. H., Uretsky, S. C., Douglas, S. D.* (Reprint requests: Dr. S. D. Douglas, Laboratory of Immunology, University of Minnesota School of Medicine, Minneapolis, Minn. 55455), p. 504

Anti-I (A + B): An autoantibody detecting an antigenic determinant of I and a common part to A and B. *Doinel, C., Ropars, C., Salmon, C.* (Centre Départemental de Transfusion Sanguine, F-75571 Paris 12, France), p. 515

Incidence of "Bombay" (Oh) phenotype and weaker variants of A and B antigen in Bombay (India). *Bhatia, H. M., Sathe, M. S.* (Blood Group Reference Centre, Seth GS Medical College, Bombay, India), p. 524

Further data on HBs antigen subtypes. Geographical distribution. *Couroucé-Pauty, A.-M., Soulier, J. P.* (Reprint requests: Dr. J. P. Soulier, Centre National de Transfusion Sanguine, F-75015 Paris, France), p. 533

Ag(i): Detection of an antithetical factor to Ag(h). *Bütler, R., Brunner, E.* (Central Laboratory of the Blood Transfusion Service, Swiss Red Cross, CH-3000 Basel, Switzerland), p. 550

Agarose gel electrophoresis of the human red cell acid phosphatase. *Sorensen, S.. A.* (University Institute of Medical Genetics, DK-Copenhagen N, Denmark), p. 556

Contents

Volume 9

Author Index

Subject Index

Card Indexes

A. D. Hoyes, D. J. Riches, B. G. H. Martin

The fine structure of haemopoiesis in the human fetal liver. Haematologia *9*, 179 (1975).

The differentiation of the megakaryocyte was studied at the ultrastructural level in the liver of human fetuses of between 49 and 134 mm crown-rump length. The development of the cells was traced from lymphoid elements with the features of haemopoietic stem cells and was divided on the basis of nuclear morphology into three stages. Granula formation commenced during the first stage and demarcation membranes could be demonstrated in the perinuclear cytoplasm early in the second stage. Late stage 2 cells often contained more than one nucleus, and the possibility that this was due to cellular fusion is discussed. The third stage was characterized by the appearance of cytoplasmic zoning and by the gradual extension of the demarcation system throughout the cytoplasm. There was evidence that the demarcation membranes were initially formed directly from the Golgi apparatus, but that their further development was due to the incorporation of elements of the agranular endoplasmic reticulum. The surface projections associated with platelet release were observed only in fully developed cells, and the formation of a zone of clear cytoplasm at the periphery was related to events occurring during the later stages of platelet release.

Ch. Coutelle, H. H. Reineke, E. Steindamm, W. Meurer, M. Grieger, S. Rosenthal

Synchronization of rabbit bone-marrow cells in vivo. Haematologia *9*, 195 (1975).

The recovery of the rabbit bone-marrow from anaemia was investigated during an eight-day period of daily puncture of the tibiae after six days of phenylhydrazine treatment. A maximum of erythroid (range, 37.1 to 44.0%) and a minimum of leukoid cells (range, 8.4 to 13.4%) was observed on the fifth day of recovery. The rest, about 50% cells were reticulum cells. Signs of recovery were observed in peripheral blood as soon as on the first day after phenylhydrazine treatment. This led to the assumption that the tibiae became repopulated with active erythropoietic cells during anaemia, and that the reticulum cells might play a role as erythroid precursors in this process.

G. Csaba, T. Richter

Histamine fluorescence in group forming peritoneal cells of the rat embryo. Haematologia *9*, 205 (1975).

In the peritoneal fluid of 18—21-day-old rat embryos the lymphocytes form groups and give an intensive yellow—histamine—fluorescence. The groups contain myeloid elements, too. After birth the fluorescence disappears.

R. A. Muraviev, V. V. Rogovin, V. M. Frolova, N. G. Geranina, L. A. Piruzyan

Ultrastructural cytochemistry of peroxidase and acid phosphatese in mouse eosinophils. Haematologia *9*, 209 (1975).

The distribution of peroxidase and acid phosphatase activity in the bone marrow of mouse eosinophils was investigated by electron microscopy. Peroxidase activity was found in the perinuclear space, the endoplasmic reticulum, the Golgi complex, non-mature and mature specific crystal-containing granules. In the course of development peroxidase activity disappears from the cisternal system. In mature eosinophils the enzyme is stored in specific granules, but some of these failed to reveal peroxidase activity. A hypothesis is offered concerning the complete condensation into crystal of the enzyme. In cells incubated in peroxide-free media some granular components stained weakly. Their activity probably depended on the presence of endogenous non-organic peroxidase. In developing eosinophils acid phosphatase was found in the Golgi complex and in non-mature specific granules. In the course of development, acid phosphatase disappears from the granules.

R. A. Muraviev, V. V. Rogovin, V. M. Frolova, N. G. Geranina, L. A. Piruzyan

Ultrastructural cytochemistry of peroxidase in mouse neutrophils. Haematologia *9*, 219 *(1975)*.

The distribution of peroxidase activity of developing neutrophils in mice was investigated by electron microscopy. The enzyme was found in the rough endoplasmic reticulum, the Golgi complex and azurophilic granules. The heterogeneity of azurophilic granules and their endogenous non-organic peroxide content are discussed.

N. M. Emanuel, L. M. Dronova, V. N. Erokhin, E. I. Belich

A kinetic model of experimental leukosis. Regularities in the development of reticulosarcomatosis in mice. Haematologia *9*, 227 (1975).

The kinetics of development of a new transplantable reticulosarcomatosis was studied in $CC_{57}Br$ mice. Tumour development was estimated from changes in the weight of metaplastic organs by means of kinetic curves constructed on the basis of changes of all parameters characterized by exponential and power functions. The kinetic model of reticulosarcomatosis is recommended for use in quantitative research in experimental oncology.

A. S. Wiener, G. J. Moon

A "new" blood factor, Cl, demonstrated with extracts of seeds of the Korean Clerodendron trichotomum Thunberg. Haematologia *9*, 235 (1975).

By absorbing extracts of seeds of the Korean *Clerodendron trichotomum* Thunberg with selected human group O red cells, a lectin has been prepared, which defines a hitherto undescribed specificity, designated Cl, defining individual differences in human red cells. The specificity Cl appears to characterize a structure associated with the A–B–H–Le macromolecule, both of red cells and of saliva, which is distinct from the combining groups for A, B, H and Le. Moreover, the reactivity of red cells with anti-Cl lectin is destroyed by treatment of the red cells with proteolytic enzymes, unlike the reactions for A, B, H and Le.

T. R. Tovell

Rh_0 or D, -D- and the blocking patterns. A genetic (template) explanation. Haematologia *9*, 243 (1975).

By the use of the gene template it will be shown that D appears at two different sites on the Rh locus, and that the locus cannot simply be DCE — or a similar one. Further, -D- does not appear to be a super Rh_0 as described by Wiener. Finally, a simple explanation is offered for the action of incomplete (blocking) and agglutinating antibodies.

D. Valló, G. Halmosdi, J. Perkedi

Lack of immune tolerance to hepatitis B antigen in offsprings of guinea pigs infected with HB Ag during pregnancy. Haematologia *9*, 253 (1975).

Immune tolerance to hepatitis B antigen has been examined in the guinea pig. The offsprings of guinea pigs injected with purified HB Ag during pregnancy were found capable of producing HB antibodies. Purified HB Ag is suitable for producing immune serum for the systemic screening of blood donors for HB Ag.

U. Mintz, S. Bar-Meir, M. Shaklai, J. Pinkhas, A. de Vries

Blastic crisis in previously clinically silent chronic myelogenous leukemia. Haematologia *9*, 257 (1975).

A patient is described in whom CML first presented as blastic crisis. The diagnosis of CML was based upon the findings of Ph^1 chromosome in the bone marrow, basophilia in the peripheral blood, absence of NAP activity in the leukocytes, elevated serum vitamin B_{12} and an enlarged firm spleen. CML with blastic crisis as its first expression is relatively rare, as compared to CML in which blastic crisis appears as a phase of prolonged clinically manifest disease.

J. Jákó, Sz. Virágh, M. Boga, G. Brooser, Gy. Dóbiás, J. Domán, Sz. Ottó, Z. Riskó, P. Szemere

A case of IgD-lambda myeloma. Haematologia *9*, 261 (1975).

A case of IgD myeloma is presented. The severe damage of both kidneys resulted in uraemia, and death. Fluorescein angiography failed to reveal a typical paraproteinaemic fundus. The elevated serum IgD level decreased from 1000 mg to 400 mg per 100 ml during cytostatic therapy. The effect of the antineoplastic drugs on the plasmocytes was demonstrated by microphotograms. The caryograms revealed multiple changes.

G. Nagy, Valéria Stenszky, Irma Timár, Katalin Murvay

Tissue antigens and cytotoxic antibodies in polycythaemia rubra vera. Haematologia *9*, 279 (1975).

The distribution of tissue antigens for 22 antigens was studied in 46 patients suffering from polycythaemia rubra vera (PRV), using antibody containing sera from 80 multigravidae. The incidence of HL-A 5 was highly significant and that of HL-A 7 significant, while the frequency of HL-A 13 was remarkably lower than in the normal population. No difference was found in ABO and Rh (D) antigen distribution for erythrocytes. No antibodies against erythrocytes, thrombocytes or lymphocytotoxic ones could be demonstrated.

G. Nagy, Mária Léhi, Gy. Petrányi

Cytostatic treatment of polycythaemia rubra vera. Comparison of the effects of some cytostatics in 100 patients in a period of five years. Haematologia *9*, 283 (1975).

Experience with cytostatic treatment performed in patients with polycythaemia rubra vera is reviewed. The effectivity and side effects of the drugs applied are evaluated. Nannosulfan and mitobromitol. were the drugs most suitable for treatment. In certain special cases, 5-hydroxyurea was also satisfactory, while mitolactol was the least suitable.

NOTICE TO CONTRIBUTORS

HAEMATOLOGIA is designed for the publication of original papers, preliminary reports and reviews which contribute to the advancement in all fields related to haematology and blood transfusion. Papers in English, French, German and Russian are accepted on the condition that they have not been previously published or accepted for publication.

Manuscripts with a clear carbon copy should be sent to the Editor-in-Chief

Susan R. Hollán, M. D.
Central Research Institute of the
National Blood Service
Daróczi út 24
1113 Budapest, Hungary.

If in addition to the original typewritten copy, a duplicate copy, complete with figures, tables and references, is submitted, this will speed publication. Although every effort will be made to guard against loss, it is advised that authors retain copies of all material which they submit. The editorial board reserves the right to make literary corrections.

Manuscripts should be typed double-spaced on one side of good quality paper with proper margins and bear the title of the paper, name, address and degrees of the author together with the name of the hospital, laboratory or institute where the work has been carried out. The name and full postal address of the author who will be responsible for reading proofs should also be given. An abstract of 50 to 100 words should precede the text of the paper. The paper should not exceed 15 pages including tables and references. The approximate location of tables and figures should be indicated in the margin.

References. Only papers closely related to the author's work should be referred to. The citations should include the name of the author and/or the reference number in parenthesis. A list of numbered references should follow the end of the manuscript.

References to periodicals should mention: (1) name(s) and initials of the author(s); (2) title of paper; (3) international abbreviation of the periodical; (4) volume; (5) number of the first page; (6) year of publication in parenthesis. Thus: 14. Bean, W., Mills, A.: Coronary occlusion, heart failure and environmental temperature. *Amer. Heart J. 16*, 701 (1938).

References to books should include: (1) author(s)' name; (2) title; (3) publisher; (4) place and year of publication. Thus: 8. Alsted, G.: The incidence of peptic ulcer in Denmark. Danish Science Press Ltd., Copenhagen 1953.

Illustrations should be selected carefully and only up to a quantity required. Black-and-white photographs should be in the form of glossy prints. The author's name and the title of the paper together with the serial number of the figure should be written on the back of each print. Coloured illustrations should be given only if indispensable. Legends should be brief and attached on a separate sheet. Tables, each bearing a title, should be self-explanatory and numbered consecutively.

Authors will receive page proofs which must be sent back by return mail.

Authors are entitled to 50 reprints free of charge.

Reviews of the Hungarian Academy of Sciences are obtainable at the following addresses:

AUSTRALIA

C.B.D. Library and Subscription Service
Box 4886, G.P.O.
Sydney, N.S.W. 2001

Cosmos Book and Record Shop
145 Acland Street,
St. Kilda, 3182

Read and Co.
694—696 George Street,
Sydney, N.S.W.

AUSTRIA

Globus,
Vertrieb Ausländischer Zeitschr.
Höchstädtplatz 3,
A—1200 Wien XX.

BELGIUM

Du Monde Entier S.A.
Rue du Midi 162
1000 Bruxelles

Office International de Librairie S.A.,
Avenue Marnix 30,
1050 Bruxelles

BULGARIA

Direkzia R.E.P.
11 pl. Slaveikov,
Sofia

CANADA

Pannonia Books,
P.O. Box 1017, Postal Station „B",
Toronto, Ont. M5T 2T8

CHINA

Beijing Waiwen Shudian,
Periodical Division,
P.O. Box 50.
Peking

Peking Post Office,
Branch No. 106,
Peking

CZECHOSLOVAKIA

Mad'arská Kultura,
Václavské nám 2.
110 00 Praha 1.

Poštova Novinova Služba — dovoz tisku
Vinohradská 46.
Praha 2.

Poštova Novinova Služba — dovoz tlace
Leningrádská 14.
Bratislava

DENMARK

Munksgaard's Boghandel,
Norregade 6.
DK—1165 København K.

FINLAND

Akateeminen Kirjakauppa,
Keskuskatu 2.
SF—00100 Helsinki 10.

FRANCE

Agence Litteraire et Artistique Parisienne
25 rue Royale,
Paris 8.

Office International de Documentation et Librairie
48, rue Gay-Lussac
Paris 5.

GERMAN DEMOCRATIC REPUBLIC

Zeitungsvertriebsamt
Strasse der Pariser Kommune 3—4.
1004 Berlin

GERMAN FEDERAL REPUBLIC

Kunst und Wissen,
7000 Stuttgart 1
Postfach 46,
Wilhelmstrasse 4.

GREAT BRITAIN

Blackwell's Periodicals
P.O. Box 40
Hythe Bridge Street,
Oxford OX1 2EU

Collet's Holdings Limited
Denington Estate,
Wellingborough, Northants NN8 2QT

Wm. Dawson and Sons Ltd.,
Cannon House, 10/14 Macklin Street,
London WC2B 5NG

Robert Maxwell and Co. Ltd.
4—5 Fitzroy Square,
London, W.1.

HOLLAND

Martinus Nijhoff,
P.O. Box 269,
Den Haag

Pegasus Import,
Leidsestraat 25,
Amsterdam

Swets and Zeitlinger,
Keizersgracht 487,
Amsterdam C.

ITALY

Libreria Commissionaria Sansoni
Via Lamarmora 45,
Casella Postale 552.
50121 Firenze

So. co. Lib. Ri.
Export-Import
Piazza Margana 33,
00186 Roma

JAPAN

Maruzen Co. Ltd.
P.O. Box 5050
5050 Tokyo International, 100—1 Japan

Nauka Ltd.
2—30—19 Minami-Ikebukuro,
Toshima-ku,
Tokyo 171 Japan

NORWAY

A/S Narvesens Litteraturtjeneste
Bertrand Narvesensvei 2.
Box 6140,
Oslo 6.

POLAND

B.K.W.Z. Ruch,
ul. Wronia 23.
00—840 Warszawa

ROUMANIA

D.E.P.
Bucureşti
D.E.P.
Arad

SOVIET UNION

Pochtamt-Import
Moscow
Pochtamt-Import
Leningrad

SWEDEN

Nordiska Bokhandeln,
Fack,
10110 Stockholm 1.

SWITZERLAND

Karger Libri,
Arnold-Böcklin-Strasse 25.
4000 Basel 11.

USA

Fam Book Service,
69 Fifth Avenue,
New York, N.Y. 10003

Hungarian Books and Records
11802 Buckeye Road,
Cleveland, Ohio 44120

Intercontinental Medical Book Corporation
381 Park Avenue South
New York, N.Y. 10016

Medical Market Research
East Washington Square,
Philadelphia, Penn. 19105

Stechert-Hafner, Inc.
31 East 10th Street,
New York, N.Y. 10003

YUGOSLAVIA

Jugoslovenska Knjiga,
Terazije 27
Beograd

Prosveta Export-Import
P.O.B. 555,
Terazije 16/1.
11001 Beograd

Index: 826861