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PLENARY SESSION

Anatomy and Pathology of the Lymph Nodes

K. Farkas: Presidential Address

Ladies and Gentlemen,

The program of our Congress reflects the sphere of interest of the Hungarian pathologists and their methods of approach to the current problems. It is worth while to consider the problem of methodology in detail. In our period of rapid developement, not only industrial technology but also the methodology of laboratory instruments has undergone radical changes. The trends of research changing in connection with methodology greatly determine the place of pathology in our knowledge of the diseases.

Pathology joined the research of disease only after the technique of necropsy had developed to such an extent as to make the detailed knowledge of organs and organ groups possible and mainly after the microscope and the cells had been discovered. The most farreaching inventions in the history of medicine — the microscope and the cell — have determined the place of pathology for a long time. The singular fruitfulness of this methodology had chained the researcher to the microscope for a long time and the finer the technique became the more was his activity confined to recognizing the changes in cells and tissues instead of establishing the real natura of the disease.

The pathologist had to realize at the price of repeated disappointments that, no matter how much the method has advanced, his view as to the origin of diseases could not get beyond the confines of his microscopic lens. At that time, though pathological departments were established in order to collaborate with the therapeutists, this could rarely be put into practice. In our days a fruitful connection has developed between clinical and theoretical medicine, promising to explain the origin of diseases. And all these at a time when the instrumental techniques have reached a height hardly conceivable some decades ago, a level when the question must again arise whether methodology with all its modern achievements will not be dromed to serve once more its own end?

The temptation doubtlessly exists. Nothing seems to be easier than the reappraisal of all the results achieved by the classical procedures. The danger of such simplification can only be averted by the right attitude of keeping the

priciple in mind, that the organism is a functional unit, and the individual and its environment are in the closest connection. Keeping is in mind the danger can be avoided to look for the essence of the disease only in a single cell or in some group of cells. To-day the pathologist must work not only with the microscope; his task is also to assist the clinician in his work.

What makes pathology, more strictly speaking, the pathologist fit to become a useful associate of the clinician in diagnosis the diseases?

First of all the circumstance that he has the opportunity to analyse the most interesting cases of the different indical fields. Perhaps no one has such a possibility for rich experience as the pathologist and if he makes the best of this possibility, he may give the most useful assistance to the clinician.

Nowadays we often hear the clinicians, — referring to the exaggerations of the instrumental methods — remembering the priciple. Back to the sick-bed ! On the analogy of this is may be said that the pathologist should turn to the therapy, to the patient. Pathology must be Janus-faced, with one face turned to research and the other to the patient fulfilling what DAVIDSOHN said, that of yesterdy, may become the routine of to-day.

A glance at the new methodological possibilities of pathology will show the perspective ahead of us. The histochemical method make possible the chemical or, which is even more important, the enzyme-chemical localization of pathological changes. Electron microscopy allows the analysis of morphological structures on a level where localization is bordering on function. Spectrophotometry has realized the analysis of chemical and morphological structures. Chromatography, electrophoresis, isotope methods all assist in the analysis of morphological and chemical structures. Each of these techniques is so fruitful that those making use of them are constantly exposed to the temptation of selfcentredness. We are, however, protected from the autotelic morphological view by the fact that electronmicroscopy the classical method of the highest order, is being used together with histochemistry and spectrophotometry, thus making research possible in a sphere where condition, in other words then morphological structure, meets function. On the practical plane this means pathology associated with therapy.

Considering the possibilities of methodology, enzyme histology and the analysis of ultrastructures seem to emerge more and more distinctly as the two trends of the greatest perspective in research. No doubt, both methods dominate our science nowadays and determine the direction of its development. These procedures require special equipment and such special skill as most of the leading pathologists do not possess for the time being.

What is the meaning of all these? In the first place the consultation mentioned above. The pathologist and the clinician should meet at the sick-bed as often as possible, and we should repeatedly seek the points of view of therapy in the course of cytological examinations and biopsy.

Biopsy is the very procedure which might establish sloser links in the collaboration of the clinician and the pathologis. This is only possible by analysing the biopsy material in addition to the classical methods also by means of up-to-date procedure. The enzyme histological and ultrastructural examinations make the diagnosis of the pathognomonic elements possible even within circumscribed changes. In this respect reference should be made only to the so-called collagenosis or the fibrinoid changes within them. The great importance attached to the fibrinoid change in diagnosis certain disease is well-known, though it is a relatively simple tissue phenomenon. The modern histochemical or rather microstructural examinations have disclosed the real nature of that peculiar homogeneous substance and it has been proved that, beneath the pattern which seems to be the same under the simple microscope, the most diverse structural changes are concealed, such changes as are really characteristic of certain diseases. The finer analysis of the changes in the connective tissue may also be mentioned as giving similarly a basis for the determination of the real nature of certain pathological processes. The practical application of the microstructural and spectrophotometric methods is similarly promising in diagnosis the benign or malignant nature of tumors.

The isotope method may also assist in diagnosis tumours and diseases of other nature, e. g. hyperthyreosis. Such examinations will allow to infer from localized changes to the disease of the whole organism. It also becomes possible to discriminate between local changes and the so-called general diseases affecting the whole of the organism. The analysis of such microstructures as the mitochondria and the chromosomes may explain the isolated appearance of some pathological changes, while the observation of some chemical alterations will know light on the conditions of generalization of certain diseases.

Light microscopy the most distinguished method in its time, became an autotelic means instrumental in ascribing the causes of the diseases *solely* to the cell and in explaining their origin of far beyond the given possibilities. Still, it has opened the way for reliably diagnosing tissue changes and thus determining the real nature of the diseases.

In our days the most important consultative role of the pathologist seems to be centered around the solution of the tumour problem. The recognition of this has prompted the Society of Pathologists to choose the granulation and the tumorous changes of lymphatic tissue as the main subject of this year's Conference. I think this is to-day one of the most interesting questions. The relation of granuloma and tumour of the lymphatic apparatus is important not only in connection with the origin of such diseases, but also the genesis of tumours in general.

I hope the Congress will bring us closer to the solution of this important question, with this in mind do I wish success to each lecturer and participant of the Congress.

RELATOR

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Histophysiological Problems Regarding the Lymphatic Tissue

Development, structure and function of the lymphatic tissue are still controversial problems. The facts that a special system of internal organs (lymph nodes, spleen, tonsils) is composed of lymphatic tissue; that it may appear in a diffuse as well as in a massive form; that it is sometimes to be found at certain definite points and sometimes all over the organism, e. g. in the intestinal wall, liver, periportal connective tissue, nasal mucosa; that its components assume incessantly varying forms, make it extremely difficult to find a common denominator for the different forms of lymphatic tissue but indicate, at the same time, the necessity of their adequate classification. Problems connected with the lymphatic tissue will appear especially interesting if we remember its high sensitivity to irradiation and, further, the report of DELIUS (Dtsche med. Wschr. **1**, 863 (1960) according to which the percentage of lymphocytes in normal blood was 25 thirty years ago against 35 in our days.

It is impossible to expatiate upon all existing problems of the lymphatic tissue within the frames of the present report; we shall, therefore, treat only those questions which are now in the foreground of interest and form, at the same time, the subject of our own investigations. We shall deal with some of our unpublished observations concerning the lymph nodes and their cellular elements, the lymphocytes in particular.

Phylogenesis and ontogenesis of the lymph node and its structural elements

Lymph nodes are present in all mammals, and, although their number varies from species to species, it is — within a certain limit — still more constant than what is generally assumed. In monkeys and humans, lymph nodes are small in size but large in number. It seems to be a general rule that, with advancing evolution, the size of lymph nodes decreases and their number increases. So-called lymphomyeloid tissue is encountered in lower animals, e. g. fishes, amphibians and reptiles, in which the lymphoid and the myeloid tissue form an undifferentiated single structure (DRZEWINA, 1905). Such tissue may appear in various organs, and is clearly distinguishable even in cyclostomes, although these animals have no spleen. The spleen appears in higher fishes, and bone marrow in the amphibians. The appearance of myeloid tissue precedes that of lymphoid tissue in the course of phylogenesis. The correctness of this

assumption seems to be confirmed by the observation that the white pulp undergoes gradual atrophy if the spleen is extirpated through a number of generations. Galliformes and Columbidae have no lymph nodes; these organs appear in some natatorial and grallatorial birds in the form of cervico-thoracic and lumbar nodes. Such nodes, of primitive structure, consist of lymphatic tissue which surrounds a duct; there is no reticulum in the duct so that one is really dealing with a mere accumulation of lymphocytes in the wall of the duct. It is only at a later stage of evolution that, with the ramification of the duct and the growing number of lymphocytes the primitive form of lymph node emerges. The development of a system of lymphatics and lymph nodes belongs to a later phase in vertebrate evolution. Thus, lymphatic tissue was first independent of the lymph stream. The separation of lymphoid from myeloid tissue is most pronounced in mammals, but even their bone marrow contains lymphoid, and their lymphatic tissue myeloid, elements.

The lymph nodes located in different parts of the organism show different degrees of maturity. The development of lymph vessels precedes that of lymph nodes; the latter appear with the so-called lymph sacs.

In embryonic life, the development of the reticulum precedes the growth of lymphocytes with which it is peopled. Follicles are important structures of the cortex. GYLLENSTEN distinguished three, and AWAYA four, stages in the differentiation of the lymphatic tissue (+, ++, +++, ++++). The stage marked with a single cross meant an early agglomeration of cells; two crosses indicated an enlarged and partially demarcated agglomeration; three crosses were used when one edge of the follicle showed a sharp line of demarcation, a circular arrangement of the lymphocytes could be seen and the number of reticular cells had multiplied; four crosses indicated the finished Flemming follicle provided with a lymphocytic sheath and bounded by several macrophages and connective-tissue fibres.

Lymph nodes are far from being structurally uniform. One does not invariably find a cortical substance around the medulla. Both the cortex and the follicles, especially the latter, are rich in radially arranged capillaries. The endothelium lining the capillaries and the postcapillary veins often consists of cuboidal cells. Some of the nodes contain erythrocytes phagocyted by macrophages. The term haemolymphatic node is used if the number of red corpuscles is large. Nodes of this kind can be seen in ruminants (sheep) and do not occur in humans. Certain authors regard the haemolymphatic nodes as accessory spleens; they have both capsule and hilus but contain neither vas efferens nor vas afferens; there is no direct communication between blood vessels and lymph sinuses. It is only in the swine where haemolymphatic nodes provided with lymph vessels have been observed.

Lymph follicles

Characteristic structures of the cortex, the so-called follicles, are actually conspicuous accumulations of cells with a bright centre. The latter is the germinal centre, so called on account of the numerous mitoses occurring in it. ASCHOFF distinguished between lymphatic and lymphoid tissue according to whether it does or does not contain follicles. The presence or absence of follicles cannot be accepted as a distinguishing feature, since follicles are not permanent structures. No germinal centre exists during intrauterine life and for a month after birth; the number and size of both the follicles and the germinal centre grow with advancing age, but disappear in old age or during certain diseases. No follicles were observed to have developed in the lymph nodes of guinea pigs raised by GLIMSTED (1936) under germ-free conditions. GREGOIRE (1945) succeeded in accelerating the growth of follicles by bacterial injections. GYLLENSTEN claims that the postnatal development of the lymphatic tissue does not depend on the contamination of the environment alone but is considerably influenced by nutritional and endocrine factors as well.

Follicles arise as densely filled formations, called compact follicles by EHRICH (1929) and primary follicles by GYLLENSTEN (1950). The development and ripening of the lymphatic tissue is a chronologically well defined process in which environmental contamination serves as a stimulus. One and the same stimulus does not elicit one and the same response from the lymphatic tissue of different species. GLIMSTED (1936) demonstrated the disappearance of lymphatic tissue from the intestinal wall which had been deprived of bacteria, i. e. of its physiological environment. While secondary follicles are present in the lymph nodes of animals kept on a sterile diet, they are lacking in animals raised in germ-free milieu.

The appearance and behaviour of the follicles seem to follow the cyclic process undergone by the lymphatic tissue in the course of life under the effect of external and internal stimuli (FLEMMING and MAXIMOW). The first trace of the follicle appears, for instance, as a centre of proliferation induced by environmental stimulus. Centres of this kind consist of rapidly dividing lymphocytes of medium size which accumulate and form primary follicles and are the precursors of future germinal centres. The follicle grows larger and larger on account of the newly-formed cells which migrate to the periphery so that the growing follicle pushes the surrounding tissues asunder and comes, thus, to form part of the basic structure. Accordingly, the primary follicle is surrounded by a multiple ring of steadily accumulating small lymphocytes. While the outermost ring becomes denser, the dense centre becomes looser; pluripotent young dividing cells remain in the latter, and we have the secondary follicle with its germinal centre. However, follicles may not only arise but disappear as well: the latter process begins, according to MAXIMOW, with the disappear-

ance of the bright germinal centre and leads to a state of follicular quiescence. The quiescent follicle may either fuse with the adjacent tissues or enter a new phase of activity. The theory of follicular function rests on this cyclic activity. The presence of the germinal centre indicates, therefore, the phase of activity which terminates with its disappearance. The phase of quiescence would, thus, be represented by the primary (compact) follicle. There is according to ALBERTINI (1936), an interval of 60 hours between the disappearance and reappearance of the secondary follicle. Opinions are especially contradictory in regard to the significance of Flemming's follicle. Part of the authors (FLEMMING — 1885, DOWNEY and WEIDENREICH — 1912, JORDAN — 1935) holds that the centre of the follicle is characterized by cell division and proliferation, and that, accordingly, the term germinal centre is correct. Others (e. g. HELLMANN — 1921, 1930) contend that a destruction of cells, induced by certain factors, is the most conspicuous feature in the central part of follicles: they, therefore, prefer the term "reaction centre". SELYE does not make the bacteria responsible for the development of the reaction centres, as centres may arise under the effect of any stress. The major part of the authors (WALJEM — 1925, MAXIMOW — 1927, 1928, TAKOFERRO and CANNON — 1936, TAKOFERRO and MULLIGAN — 1937) takes the middle course between the two extreme views. HELLMANN had mostly to deal with pathologic human material, and it is for this reason that he championed the theory of degeneration. It would nevertheless be wrong to share EHRICH's view (1929) who refuses FLEMMING's theory. Again, it would be likewise wrong to affirm that nothing but cytopoiesis occurs in the centre of the follicles: we know that various factors (infection, poisoning, etc.) may release a process of cellular breakdown there. It is not solely in the primary follicle but anywhere in the lymphatic tissue that an active phase of rapid lymphocyte production may ensue. Follicles arise as lymphocytic agglomerations of medium size. Whether they become subsequently marked off against their environment depends upon the nature of the adjacent tissues and the rate of lymphocyte production. No demarcation occurs if the surrounding tissues are loose. (The young cells form a circular pattern arround the primary follicle, a process due to the migration of the fresh lymphocytes of medium size.) Enlargement of the follicles goes hand in hand with a thickening of the cortex. The phase of activity is followed by the release of lymphocytes, and — after about 66 hours — a condition is reached in which the structure of the cortex becomes as loose as that of the medulla. The diffuse tissue of the cortex as good as disappears. However, this phenomenon does not occur invariably; there are follicles in which proliferation is the predominant feature.

The term "pseudo-secondary follicle" was applied by EHRICH (1931) to that intermediate stage between primary and secondary follicle at which a demarcation of the primary follicle has taken place. A study of the cycle reveals

that lymphocytic proliferation is the dominant and degeneration the secondary process in the centre of the follicle. (The onset of lymphocytic proliferation depends on the rate of the follicle's development.) RÖHLICH (1928) studied the follicles in cats, TAKAFERRO and CANNON (1936) in monkeys, and KINDRED (1938) in rats; the germinal centre consists, according to them, of two zones, an inner active one containing medium-sized lymphocytes, and an outer inactive zone containing small lymphocytes. RINGERTZ and ADAMSON (1950) studied the biphasic reaction of lymphoid tissue to the injection of bacterial antigens, and observed a diffuse hyperplasia of the cortical tissue one or two days after the injection. This process occurred in the first phase. The second phase followed between the 10th and 16th day; it remained active up to the end of the experiment. Numerous new germinal centres were formed during this phase. GREGOIRE (1932) suggested that the reaction was principally due to the presence of foreign protein, and that the destruction of the cells was accompanied by a great number of mitoses in the germinal centre, a theory confirmed by CONVAY. The cellular components of the lymph node are, according to BAILOFF (1951), in equilibrium, and changes therein occur under the influence of age, diet or hormones. GILLMAN (1949) observed, after the chronic administration of one per cent trypan-blue solution, a change in the cellular composition of the lymph nodes: the lymphocytes were replaced by polyblasts, plasmacytes, histiocytes and mobilized endothelial cells.

The normal development of follicles is analogous to the differentiation of the tissues of the lymph nodes as induced by the said stimuli. GYLLENSTEN, IMAMURA and HIDETOSHI observed the development of lymph nodes in guinea pigs between the last days of intrauterine life and the 35th day of postnatal life. The follicle appeared in two forms, either as a compact structure or as the pseudo-secondary follicle described by EHRICH (1929—1930). No true secondary nodule was observed before birth. The structure, termed tertiary nodule by FISCHER (1937) and DABELOW (1939), is really the pseudo-secondary follicle; as it belongs to an earlier stage, the term is not justified.

The cells in the lymph nodes are of different types and vary not only from species to species but even from individual to individual. TAKAFERRO and MULLIGAN regard the system of macrophages (inclusive of the so-called lymphomacrophages) as the principal component of lymphatic tissue. Lymphomacrophages are enlarged phagocyting lymphocytes, called also intermediary cells or polyblasts. The macrophages are detached and rounded reticular cells. Cortex and medulla are composed of the same cellular elements, while the medullary bundles include plasma cells in addition. According to MAXIMOW and BLOOM, fibrocytes, too, may arise from macrophages. This view is, however, refused by many authors.

Lymphocytes

Lymphocytes are undoubtedly the most characteristic cells of the lymphatic tissue. Although their origin, fate and functions have been investigated by many authors, opinions concerning them are still contradictory in many respects. Lymphocytes are important constituents of the blood but are nevertheless mostly to be found in the lymphatic tissues. (The total weight of the latter amounts to 600 to 1300 g.)

Small, medium and large lymphocytes are known. Their sizes are 9 μ, 9 to 14 μ and more than 14 μ, respectively (KAZUHIKO, AWAYA). While invariably present in the lymph nodes of animals, large lymphocytes do not occur in humans. They are mostly situated in the sinuses, and their number depends on functional factors. The cytoplasm contains a few vacuoles. The nucleus is indented and contains a diplosome surrounded by the Golgi apparatus. A few rod-shaped mitochondria can be seen beside the kidney-shaped nucleus. The chromatin of the nucleus is scattered, and one or two nucleoli of irregular shape are likewise included. Nuclei of this type divide by way of mitosis. A division of small lymphocytes has rarely been observed. Mitosis is most frequent in lymphocytes of medium size. MAXIMOW and BLOOM have claimed that small lymphocytes may grow and recover the faculty of division (e. g. in cell cultures isolated from patients suffering from chronic lymphoid leukaemia).

Lymphocytes are produced in the lymph nodes, in the lymphatic tissue of the digestive tract, in the spleen, in the thymus and in the bone marrow. Certain authors regard the lymphatic tissue of the mesentery as the main source of lymphocytes (JOFFEY — 1933, 1936, SANDERS, FLOREY and BARMES — 1940, MANN and CHRISTENSEN — 1949), an erroneous assumption. Experiments with a suspension of nuclei isolated from the lymphatic tissues of rats (KINDRED) showed that, in young animals, the thymus produced 4 to 6 times as many lymphocytes as did the lymphatic organs. This finding was confirmed by ANDREASEN and OTTESEN (1944) who studied the phosphorous contents of DNA with a view to ascertaining the number of lymphocytes dividing by way of mitosis in the different lymphatic tissues. By comparing the activity of the DNA-P with that of the blood, they obtained a clear picture of DNA synthesis. It was two and a half times more in the thymus than in other lymph organs. Autoradiography by means of P^{32} is well suited for following the processes of synthesis in the follicles.

Generally speaking, lymphocytes arise by mitosis from the so-called lymphoblasts. Another source is supplied by reticular cells whose division may result in the appearance of both reticular cells and lymphocytes. There are, according to MAXIMOW, two types of reticular cells, one is a phagocyte and belongs to the RES, the other is the primitive type which is not phagocytic

but lymphocytogenic. The generally recognized way of evolution is, reticular cell → large lymphocyte → medium lymphocyte → small lymphocyte (MAXIMOW and BLOOM — 1952, JOFFEY and COUSTICE — 1956). SÜNDBERG distinguishes two kinds of reticular cells, an undifferentiated reticular cell, and a haemopoietic one which develops into reticular lymphocyte and then to normal lymphocyte. Undifferentiated reticular cells are round or oval, with a large body and a nucleus which contains finely dispersed chromatin and an irregularly-shaped basophilic nucleolus. The haemopoietic type contains less cytoplasm and more vacuoles. Reticular lymphocytes resemble lymphoblasts, contain a small amount of cytoplasm, and their chromatin is more compact. Needle biopsy of human lymph nodes revealed a very small number of lymphoblasts. For all these theories, it is still possible that there exists but a single type of reticular cell. It is known that many aged lymphocytes are phagocytized by the reticular cells in the centre of follicles. Not less than about 35 per cent of the lymphocytes disappear from rats in this way according to KINDRED (1942). Cells, having ingested a small lymphocyte, turn into large lymphocytes. TROWELL (1955), employing his own technique of explantation, grew cells from rat lymph nodes in a synthetic medium and observed the differentiation of reticular cells into large lymphocytes after having phagocytized a lymphocyte. That this process is rarely seen *in vivo* may be due to a more rapid rate of differentiation and the scarcity of intermediate forms in the organism. It is quite possible that destroyed small lymphocytes are the natural food of reticulocytes and, at the same time, that agent which releases the process of their differentiation. This may be a sort of feed-back mechanism for the regulation of the number of lymphocytes.

Electron-microscopic investigations

Many interesting phenomena, occurring in lymph nodes, which remain invisible under the light microscope, can be observed with the aid of the electron microscope. Electron micrographs make the intricate labyrinthine structure of the sinuses very conspicuous. The sinuses appear to be profusely traversed by numerous bundles of fibres coated with endothelium, and the entire substance of the sinuses, including the cells, exhibits a spongy structure. One has the impression as if the sinuses were unstable formations of the lymph nodes which, depending on functional factors, may arise or disappear. The wall of the sinuses is lined by endothelium which, too, has a spongy structure; the endothelial cells become detached from the wall, turn into reticular cells, while the latter may become flat and turn into endothelial cells. The latter contain a few Palade granules, ribosomes and a variable amount of endoplasmic reticulum.

Reticular cells are most clearly observable in sinuses; they are similar to endothelial cells and have likewise numerous microvilli which are sometimes of considerable length. The villous apparatus of reticular cells is stronger than that of the endothelial cells, and also their spongy structure is more pronounced. They contain a centrosome, and also Palade granules, fairly large mitochondria and phagocyted granules are encountered in the cytoplasm. The nucleus is fairly large and of a loose structure. Intermediate forms between endothelial and reticular cells can also be seen.

Lymphocytes in the sinuses are more or less round and have microvilli on their surface. They contain some endoplasmic reticulum, a few small mitochondria, a centrosome and Golgi material.

Concentrically arranged endoplasmic reticulum which distends to flat sacs at some points, is a characteristic feature of plasma cells. These sacs contain granules which are scattered when the sacs become ruptured. They contain numerous Palade granules. Mitochondria in plasma cells are comparatively large; the surface is covered by microvilli. Lymphocytes and plasma cells are structurally so different that the lymphocytic origin of plasma cells appears to be improbable. They may have rather originated from reticular cells.

The capsule of lymph nodes consists of many laminae and flat interlaminal fibrocytes. Bundles of elementary collagenous fibrils are situated in the trabeculae which traverse the sinuses but may be encountered also in the cavities of endothelial or reticular cells, or beneath the endothelium. We saw no muscular elements in the capsule. The capillaries have narrow lumina with a protruding cushionlike villous endothelium. The adjacent cells are closely adhering to the thin basement membrane of the capillaries, and also collagenous fibres can be seen in close contact with the wall at certain points. This phenomenon argues in favour of a transport of materials occurring along the capillary walls. We failed to distinguish reticular fibres from collagenous fibres under the electron microscope.

Tissue culture experiments

Cinematography of tissue cultures reveals many features in the cells of the lymph node which cannot be distinguished in the usual histological pictures. The cells show an astounding variety. Apart from fibroblasts which are easily distinguishable on account of their size, there are numerous intermediary forms. It seems to be certain that there exist transitory types between the endothelial cells lining the sinuses, and the reticular cells. Not the lymphocytes but the histiocytes and fibroblasts are the first to appear in the cultures. The movement of emigrating lymphocytes is not the same as that of the thymocytes. The shape of the cells, that of the reticular cells in particular, is often elongated, sometimes starlike. One encounters forms which seem to be transitory

between histiocytes and lymphocytes. The movement of macrophages is ensured by means of a large undulating membrane which, too, contributes to the great variety of forms. Granular activity can be seen in the cytoplasm of these cells, and a transformation of reticular cells into macrophages has also been observed. It is by means of their long protoplasmic processes and not by loosening a coherent tissue that emigrating reticular cells form the reticulum. Straight cytoplasmic threads, growing longer and longer, emerge from the cells, a phenomenon observed otherwise in cultures of nerve tissue only. We observed a type of cell which moved in a characteristic way and has been regarded by us as a plasma cell. Its body looked like a plam leaf; it had an undulating membrane by means of which the cell seemed to be groping forward. There was an elongated thin process at the opposite pole which trailed after the cell. Before, we had not seen such cells on microfilms.

We are perfectly convinced that plasma cells do not originate from lymphocytes; they rather seem to be related to reticular cells. Details in this respect will be discussed in a separate paper. We saw remarkably large, strongly granular and round cells? We regarded them as endothelial cells loaded with phagocyted matter.

Up to quite recently, it was generally accepted that lymphocytes did not live longer than a few days. However, OSGOOD (1955), using DNA labelled with P^{32}, found that human lymphocytes had remained in the circulation for several months, an observation confirmed (1954—1956) by the labelling of lymphocytes with adenine 8—C^{14}. Even after the lapse of 300 days did HAMILTON find the activity of DNA in lymphocytes to be more than a third of the peak value. He concluded that there were two generations of lymphocytes; one with an average life span of 85, the other with one of 350 days. OTTESEN studied human blood lymphocytes labelled with P^{32} and described likewise two types — although with shorter lives? 20 per cent of the lymphocytes were said to have a live span of 2 to 3 days, and 80 per cent one of 100 to 200 days. Autoradiography with C^{14} proved that lymphocytes might remain in the lymph nodes for more than two months before passing into the circulation. This possibility is supported by the electron-microscopic structure of the lymph nodes, while the thymus has a structure which facilitates a more rapid passage of thymocytes into the blood stream. It is, therefore, possible that the lymphocytes with the longer life span belong to the category produced in the lymph nodes. Of course, there is another possibility; namely that parts of the decomposed labelled lymphocytes may be taken up by macrophages, and the activity may persist not only in these phagocytes but also in the lymphocytes arising from them. Experiments regarding the evacuation of lymphocytes are, therefore, worthy of note. MONDEN kept rats of 200 g body weight on a standard diet and examined their thymolymphatic organs as also their lymphocyte counts. He found that the lymphocyte count in the various organs was 32

times that of the peripheral count. GRÜNDMANN found in the blood stream only one per cent of the organism's lymphocytes. Lymphocytes are, thus, migratory tissue cells. It is in the thymus that the highest lymphocyte count per sq. mm of tissue is recorded (2.68×10^6 against 1.15×10^6 in the lymph nodes). The daily number of mitoses is likewise the highest in the thymus; it amounts to 50 per cent of the mitoses occurring in all lymphatic tissues, against a ratio of 1/7 for the lymph nodes. Provided all lymphocytes are produced by mitosis in the lymphatic tissues and enter the circulation, the average daily increase in the number of all lymphocytes is, according to KINDRED, 3.3 times more than the corresponding rate in respect of the circulating lymphocytes. It takes 7.2 hours for the circulating lymphocytes to be replaced; this is the so-called daily replacement factor (JOFFEY). Lymphocytes eliminated from the blood stream are replaced from the lymphatics 11 times per day. Replacement occurs via the thoracic duct and the right lymphatic duct. Lymphocytes gain constantly access to the blood through these channels. Lymphocytes are constantly eliminated from the blood, and their number would decrease were they not replaced by fresh lymphocytes from the tissues through the ducts; on the other hand, the tissues receive lymphocytes from the blood. CLARK and CLARK (1936—1937) demonstrated that lymphocytes were constantly passing from the blood to the connective tissue, so that they might return thence to the ducts and then to the blood. OSZOGOE (1943) injected rats' own lymphocytes into the tissues and observed that the injected cells were eliminated via the blood vessels and not through the lymphatics. JOFFEY and DUNTER (1939) found the peripheral lymphocyte count to be constant and from this they concluded to a constancy of the lymphocyte count in the connective tissue. This is, however, but a small fraction of the lymphocytes escaping through the thoracic duct. Not more than one cell out of 32 gains access to the lymph from the blood, the other 31 are newly formed. The respective lymphocyte counts in the blood and the lymph do not change in parallel. It is only natural to assume that if the number of lymphocytes passing through the duct is less, the lymphocyte count in the blood will decrease correspondingly. This would be in conformity with the principle of recirculation according to which lymphocytes escaping from the blood return to the blood vessels. Yet, the number of lymphocytes collected by the cannula from the lymphatic duct is always more than the number of lymphocytes escaping from the blood path, in fact 75 times more. It follows — an assumption supported by experimental findings — that the major part of lymphocytes entering the blood paths through the lymphatic duct consists of newly-formed cells. This has been confirmed by the study of mitoses, by experiments with P^{32}, DNA-analyses, further by experiments with various diets, starvation, the exstirpation and regeneration of lymphatic tissues. The lymphocyte count in the blood is fairly constant so that number of lymphocytes leaving the blood

stream must be approximately equal to that of lymphocytes passing into it. Lymphocytes may (1) pass into the connective tissue, hence to the lymph capillaries, and then back into the blood stream; (2) escape through the intestinal mucosa; (3) filter through the spleen and the bone marrow; (4) perish in the blood. It has been shown that in the dog the daily number of newly-formed lymphocytes is 8.5 to 10 times that escaping from the blood. It would follow that lymphocytes remain in the blood 12 hours; since, however, it is not solely through the duct that lymphocytes gain access to the blood stream, JOFFEY estimates their stay in the blood to not more than 2 1/2 hours. The intestinal mucosa is an important gate for the escape of lymphocytes. KINDRED (1942) found three times as many lymphocytes in the intestinal epithelium as in the blood. Their presumable function there is to bind toxins. FARR (1951) injected autologous lymphocyte suspension into rabbits by the intravenous route. The suspension was labelled with 3,6-diamino-10-methylacridine chloride, a fluorescent dye. He found that most lymphocytes escaped from the blood within 90 minutes, while some remained there for 3 hours, occasionally even as long as 72 hours. Most of the labelled lymphocytes were found in the bone marrow and the various lymphatic tissues. They changed into myeloid elements in the bone marrow, or started lymphocytopoiesis in the tissues. Lymphocytes were observed in the intestinal mucosa and the connective tissue 12 hours after the intravenous injection.

Let us now investigate the factors which regulate the above-outlined processes. It was demonstrated by SELYE that under the effect of stress, the thymolymphatic organs undergo a significant, though not specific, change which points to the great influence of the hormonal apparatus. A change in the lymphatic tissue is but a partial phenomenon in the general adaptation syndrome. The change in question is due to the alarm reaction and can be provoked by means of ACTH. Considerations of time and space prevent us from discussing the interconnections between lymphatic tissue and endocrine glands, a subject often treated in the literature. The effect on the lymphatic tissue of the adrenals and the pituitary and its interconnections with the thyroid gland has been demonstrated by numerous authors. It has been shown that the reactions of the thymus and the lymphatic tissue are not invariably analogous. Another conclusion following from the experimental results is that the balance of growth between thymus and lymphatic tissue stands under the regulation of the pituitary-thyroid system.

Endocrine factors explain the connections between lymphatic tissue and body weight. The involution of the lymphatic tissue begins at a time when the body weight decreases and the genitals have attained maximum size. With advancing age, changes occur in the distribution of the organism's total amount of lymphatic tissue (spleen, lymph nodes, thymus); the weight of lymph nodes is still increasing when, at a certain age, that of the thymus

is already diminishing. The behaviour of the thymus is in contrast with that of the spleen; the weight of the thymus is always higher in females than in males. As regards the interproportion between thymus, spleen and lymph nodes in connection with advancing age, the weight of the spleen increases, that of the lymph nodes is not affected, while the behaviour of the thymus depends on sex, a phenomenon indicative of gonadal influences upon the lymphatic tissues.

The existence of an interaction between thymus and endocrine glands contradicts the theory which regards the thymus as a lymph node. The close relationship between the two manifests itself rather through the control exercised by the thymus over the functions of the lymphatic tissue. Literature contains many reports dealing with the differences between thymus and lymph nodes. The development of the thymus precedes that of the lymph nodes. The thymus is, as a matter of fact, the first organ to appear in the course of ontogenesis. The structure of the thymus is formed in utero, that of the lymph nodes after birth. Endogenous factors suffice for the growth of the thymic structure and do not suffice for that of the lymph nodes. The very endothelial ground structure of the thymus distinguishes it from the lymph node fundamentally. It is, thus, natural that the reactions of the thymus are different from those of the lymph nodes. Response to stress, for example, is prompter in the thymus than in the lymphatic tissues. BAKER, INGLE and LI (1951) found that on prolonged administration, 1 mg of ACTH sufficed to affect the thymus of male rats, while doses of 3 to 6 mg were necessary to produce an effect on the spleen; the lymph nodes remained unchanged. The thymus undergoes atrophy more rapidly and more markedly than the lymph nodes in cases of inanition. MONEY, FAGER, LUCAS and RAWSON (1952) observed that testosterine diminishes the size of the thymus and enlarges the mesenteric lymph nodes. The weight of the thymus decreases and the lymph nodes are enlarged by treatment with thyroxine. SARAND and HOMBURGER (1949), after having inoculated mice with sarcoma, observed atrophy in the thymus and growth in the lymph nodes. STREWSBURY and REINHARDT (1956) found that, after castration the thymus grew in rats, while the lymph nodes remained unchanged.

The cardinal problem in connection with these observations is whether the thymocytes are or are not identical with lymphocytes. Recent investigations point — as has already been noted — to the existence of two types of lymphocytes in the blood: one with a longer, the other with a shorter lifetime. Experiments with colchicine enabled TANAKA to demonstrate that two different kinds of cells were produced in the thymus by way of mitosis. According to OTTESEN, the DNA of the thymus regenerates rapidly, that of lymphocytes of the lymph nodes slowly. Our observations support this statement: the thymus incorporated P^{32} into DNA intensively, and the rate of

incorporation continued to increase during the experiment. Injection of protein induces hypertrophy in the lymph nodes but leaves the thymus unaffected. Even P^{32} produces certain effects. BLOOM and JAKOBSON (1948) WARREN, MCMILLAN and DICHSON (1950) found that the administration of P^{32} induced first hypoplasia and then hyperplasia in the lymphatic tissues. Thymus, spleen and bone marrow increased in size, while the lymph nodes remained unaltered (WISEMON). There is, according to the evidence of our investigations, a difference between thymus and lymph node as well as a difference between thymocytes and lymphocytes. Thymocytes are of epithelial origin: they originate from reticular cells. This seems to be confirmed by the observations of ACKERMANN and KNOUFF who found that thymocytes originated from epithelial cells in the bursa Fabricci of birds, an organ that may be regarded as a rectal thymus. BALL and AUERBACH cultured thymic epithelium and showed that thymocytes arose from the epithelial cells in vitro. The differences between cultures of thymocytes and lymphocytes are considerable. In thymus cultures a mass of rapidly moving small cells is seen to emigrate after the first second hour. One may, moreover, observe the growths of the epithelium and the emigration of epithelial macrophages. Proliferation starts after 12 hours and is abundant. On the other hand growth in lymph-node cultures starts after a few days period of latency, the rate of emigration of cells is low and growth of the mesenchymal reticulum feeble. Lymphocytes contain considerably more total N and protein than thymocytes. There is no proteolytic enzyme in the small lymphocytes under normal contitions; they contain, however, protease in cases of chronic lymphoid leucaemia. Lymph-node extracts contain cathepsin (optimum pH between 4 and 5) and some trypsin. BARNES (1940) found cathepsin, nuclease, lipase and lysozyme in the lymphocytes of cats, while also amylase and adenosinase were present in those of rabbits. The cell membranes of thymocytes — and so also the thymus itself — give a positive alkaline phosphatase reaction, while neither acid nor alkaline phosphatase reaction can be obtained from lymph-node cells. Except the reticular cells the cells of the lymph node do not give esterase or succinodehydrogenase reactions either, while all these reactions are positive in the thymus. The tetrazonium reaction is positive in the cytoplasm, nucleus and the fibres alike. Lymph nodes give a weak but positive sulphhydryl reaction and they contain lipids. FAERBER (1939) failed to detect cytochrome in lymphocytes and assumed, therefore, that their reserve energy was negligible. Lymphocytosis is looked upon by EHRLICH and ZEIFLER (1953) as something more than a simple means of proliferation; they regard it as a source of energy required for processes of syntheses. Lymphocytes in the blood are, according to RABIMONTSCH and ANDRENCU, sudanophobe but become sudanophile in cases of hypertrophy. Lymphocytes outside the blood paths are Nadi-positive, contain PAS and sudanophile granules (GRAF). A great number of additional arguments could

be adduced to prove that, while similar in some respects, thymocytes and lymphocytes are of different origin and significance. Another noteworthy difference between the two structures should nevertheless be mentioned: lymph nodes contain many, and the thymus contains no, plasma cells. These cells are important factors in the production of anti-bodies. FAGRAEUS affirms that the production of antibodies is accompanied by an increase in the basophilia and the RNA-content of the plasma cells. According to DOUGHERT and WHITE (1946), cortical hormones have the effect of increasing the number of plasma cells in lymph nodes within a few hours. EHRLICH, DROBBIN and FORMAN (1949) injected typhoid vaccine into the paw of animals, and found the lymph node beneath the knee to have grown after six days, with a simultaneus increase in the amount of DNA and especially RNA, i.e. a proliferation of plasma cells and not that of lymphocytes.

Although, according to the traditional view, plasma cells originate from lymphocytes, recent investigations point rather to their reticular origin. There are no plasmacytes in the embryo, and but a very few in infants (GOOD — 1954, JANEWAY and GITTLIN — 1957). Birth means a turning point for lymphatic tissues. Postnatal adaptation occurs under new alimentary and hormonal conditions. These involve essential quantitative and qualitative changes for the lymphatic tissues, connected with the beginning production of antibodies. The appearance of mature plasma cells coincides with that of the secondary follicle. Employing antigen labelled with fluorescent stain as a specific histochemical dye, COONS, LEDUC and CONOLLY (1953) observed the formation of antibodies in plasma cells. After penetrating into, and being transformed in, the macrophage, the antigen enters the slightly differentiated neighbouring cell, releases there a process of protein synthesis, and the cell assumes the characteristics of plasma cells.

Small lymphocytes circulating in the blood are, in our opinion, of thymic provenience. Only a limited number of lymphocytes finds access to the circulation from the nodes under normal conditions. That this is so is supported by the structure of the lymph nodes as revealed by the electron microscope; it follows from their spongy consistency that, unless forced to do so by some mechanical force, lymph nodes do not discharge a large number of lymphocytes. Lymphocytes produced in the nodes may gain direct access to the blood stream through the wall of the capillary veins whose cuboid endothelium is suggestive of splenic sinuses. The production of macrophages — transformed reticular and endothelial cells — is an important task of the lymph nodes. The task of the follicles consists in lymphocytopoiesis, the neutralization of toxins, and the production of antibodies. The digestion of foreign matter is performed by macrophages, endothelial cells and reticular cells alike. While doing so, they turn into plasma cells in which antibodies are produced. What is then the function of lymphocytes? Why are so many lymphocytes discharged into the

blood stream? These cells play a significant part in the adaptation of the tissues as is indicated by the escape of so many lymphocytes into the digestive tract, and further by the fact that the presence of foreign matter induces lymphocytic accumulations not only in the lymphatic tissues but also in other parts of the organism. There are authors who think that lymphocytes produced in the lymph nodes may change into plasma cells and even histiocytes. On the other hand, mature thymocytes are incapable of transformation, and only their young forms may turn into mast cells. Mature thymocytes convey nucleoproteins or heparin to different parts of the organism and are doomed to disintegration. They do not produce antibodies but stimulate this process in the lymph nodes. Small and medium-sized lymphocytes, apart from being involved in immunogenesis, have the faculty of changing into forms which are especially suitable for certain functions. Thymocytes are short-lived, while lymphocytes live longer and pass most of their life in the tissues, outside the blood paths. There are according to GRÜNDMANN, two types of lymphocytes: one with many nucleoli and the other with a single nucleolus. The first originates from the sinuses of the spleen and the lymph nodes, the other is presumably formed in the follicles. Studying the differentiation of lymphocytes by means of cytophotometry and interferometry, DEUTSCH demonstrated that reticular cells — in contrast to the lymphocytes and lymphoblasts originating from them — contained diploid DNA. Lymphocytes in the lymph nodes have the basic protein-methyl-green bond, a property not shared by those circulating in the blood paths. The concept that thymocytes are not identical with lymphocytes throws light on many hitherto incomprehensible phenomena and raises, at the same time, a number of new problems.

Lymphatic organs stand under endocrine regulation. The thymus — a meeting point of endocrine interactions — plays an important part in this process. The assumption that the thymus is the principal regulator of the lymphatic organs does not exclude the possibility that certain hormones may produce a direct effect on the lymphatic tissues. This would explain the observation that reactions on the part of the thymus always precede those of the lymph nodes.

A characteristic property of the lymphatic tissue is its sensitivity to irradiation, a subject the discussion of which would require a separate treatise.

It should be clear that the above considerations do not present a full picture of all the problems which exist in connection with the lymphatic tissue. All we can hope to have succeeded in presenting is a review of the most important questions in this field. We hope that we have succeeded in proving that investigations into the structure of the lymphatic tissue and the lymphocytes are inseparable from histological and physiological considerations. The search after truth requires complex investigations.

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Granulomatous Diseases of the Lymph Nodes

The proliferative diseases of the lymph nodes obviously cannot be discussed in $^3/_4$ of an hour, because if we extend the concept of proliferation to every increase in tissue, specific or non-specific, we should include in this group many toxic, infectious, allergic, tuberculous, syphilitic, mycotic and other conditions as well. And a paper cannot have the aim of summing-up text-book evidence, but it should identify controversial problems in the focus of interests in this field and should tell the audience what the relator thinks about them. It is also obvious that the relator of a subject must be one who has studied the problems in question in extensive detail and who has formulated individual opinions in the course of his investigations. I think that the principal aim is that a research worker well-versed in the problems to be discussed should submit his personal views to debate, and he should point out the problems concerning which opinion is not uniform. I shall therefore omit speaking about fundamental data, and deal instead with problems which I think merit discussion.

In the lymph nodes 5 areas can be distinguished from the point of view of tissue reactivity. The germinative centres, which according to the investigations of HELLMANN and myself, are reactive areas, showing characteristic changes in response to infection, toxic effects, X-ray irradiation and other factors. The second area is the sinusoid system, the inner surface of which is covered by cells belonging to the reticuloendothelial system; besides, however, there are reticulum cells anchored by their processes in the cavity of the sinus; thes cells are in contact with the circulating lymph through their entire surface. The third area is the fixed reticular supporting structure of the lymph node, the cells of which, however, can become activated at any time. This means that they may become free, mobile elements after detaching themselves from the reticular bonds. The fourth area is the lymphatic tissue proper, the lymphatic bundles; and the fifth the peculiar tissue area of the vascular system and the pericytes.

The lymph nodes are known to participate actively in the local and systemic reaction to inury. This is only natural, because the lymph node is exposed to every kind of stimulation and disturbance by way of the lymph and the blood. It is not astonishing therefore that the lymph nodes near to a disintegrating tumour should develop changes, just like the lymph nodes throughout the organisen do so, in response to some systemic infection. The changes will be obviously complex, since according to my investigations some poisons, for example ricin, act first of all on the reticular elements in the germinative centres, while others, for example typhoid endotoxin activate

the sinus endothelium in the first place. The reticuloendothelial system is a group of cells present in every tissue throughout the body and built up of essentially equivalent elements. It should be remembered that it was just the discovery of the reticuloendothelial system that showed us how absolutely false had been the localisation doctrine, according to which the organs would function as isolated units, almost entirely independently of one another. Nevertheless, the above statement does not mean that certain areas of the reticuloendothelial system should have no special functions other than that common to all of them. My investigations concerning the spleen in typhoid fever have shown long ago that the activation of the germinative centres and sinuses in the spleen differed in degree from case to case, and that for example hypertoxic typhoid fever caused first of all an activation of the sinus cells. It is therefore understandable that the reactive processes of the lymph nodes present a most variable pattern, manifesting themselves once with proliferative, disintegrative processes of the germinative centres, then with a proliferation of the sinus cells, or with other phenomena. These changes must not be considered to have some specific significance in the individual diseases. Even the activation of the splenic sinuses in hypertoxic typhoid fever is not an exclusive phenomenon, since it occurs in many other diseases, in pradically every severe toxic condition, and I have observed if for example in a lethal case of bronchial asthma. I shall not go into the details of these reactive phenomena, but deal exclusively with the processes producing so-called granulomatous changes in the lymph nodes. However, no matter how easy it seems to restrict this paper to the granulomatous diseases, it is in deed most difficult to realize this aim. Let us take an example. In cat-scratch disease the regional lymph nodes are enlarged and the swelling may persist for weeks or even months. In the lymph nodes we often find yellow necroses and abscesses and sometimes fistulae. In some cases, at least, in the early phase, an acute lymphadenitis is the only change. Later, however, intense proliferation of the reticulohistiocytary cells ensues and ultimately a proliferation similar to that seen in Nicolas—Favre's disease occurs, so that FRANCESCO and SIMONATO are fully justified in suggesting, that cat-scratch disease is accompanied by granulomatous lymphadenitis. Or let us take a more common example. In generalised septic processes we find local or systemic lymph node changes ranging from moderate reticuloendothelial activation to lymphadenitis and septicaemic reticulosis, depending on what toxic symptoms are produced by the disease, wheter there is bacteriaemia, how severe the local inflammations are, what course the disease takes, etc.

The changes of the lymph nodes can therefore be explained exclusively on the basis of the clinicopathological conception and the pathological changes observed in the lymph nodes must be analysed in the light of the clinical evidence. It is also natural that the changes found in a single lymph node often

fail to reveal the nature of the disease, and in such cases it is necessary to compare the changes displayed by the lymph nodes located in different part of the body. If this is not done, it may occur that in a systemic disease no change will be found in the lymph node examined, or the changes found in the lymph nodes of a region will be overestimated.

The question now is that apart from the general changes mentioned, what is our opinion concerning the alterations called specific granulation. An inflammation is called specific, when the morphological changes by themselves can be relied upon in drawing conclusions as to the pathogenic microorganism, even without isolating it. Such a change is for example the tuberculous granulation, with the tubercle as its characteristic structure, the histological examination of which will be itself reveal that the process is tuberculous. There is, however, no essential difference between specific and non-specific inflammation. The fundamental inflammatory changes (hyperaemia, immigration of cells) are the same in either case. The form of appearance may differ in many respects with the inflammations caused by different pathogens. For example, the anthrax bacillus causes first of all an extravasation of blood, while for example streptococci produce purulent processes in the first place. But the character of inflammation may also vary according to the systemic resistance of the affected person. The interaction between the pathogen and the organism attacked by it depends equally on the quality of the two factors and on the condition of the subject. This statement applies in full to specific inflammation. Let us think for example of tuberculosis, one of the most specific kinds of inflammation, in which we may find every type of change, ranging from a total absence of changes and non-specific exudative inflammation to the tubercle. The characteristic picture of specific inflammation arises solely as a result of the fact that owing to their peculiar biological properties many microorganisms activate certain cells in the first place, so that inflammatory granulations of special structure may be produced. For example, if systemic reactivity is adequate, the tuberculosis bacillus mobilizes the reticuloendothelial elements and initiates the formation of special giant cells, whereas bacterial toxins inhibit the formation of vascular elements. Many other pathogenic agents have similar properties. For example, Eberthella typhosa stimulates first of all the reticuloendothelial cells, and in response to Treponema pallidum giant cells closely similar to those found in tuberculosis may be formed. Thus, the changes outlined above cannot be considered specific for tuberculosis, the less so, because they will not develop if the systemic resistance is poor.

Many authors claim that the focal form of appearance of specific inflammation is sharply distinct from the non-specific inflammation of diffuse character and suggest it to be a characteristic change. As a matter of fact, specific inflammation often appears in circumscribed form, sharply delineated

from adjacent tissues in the lymph nodes, too. The focal character of inflammation is correlated with two factors. One of them is the direct action of the pathogenic agent, the leukocytes lined up around the pyogenic bacteria create in the lymph nodes focal structures, abscesses, just like the giant cells active around a thread of silk left in the tissues do. The other factor is the hyperergic nature of the process. The tissues responding stormily to the hypersensitivity factor develop inflammation in every area in which the sensitising stimulus makes itself felt. And since the hyperergic effects are spread by the blood stream or the nervous network, inflammatory changes will develop in or around the vascular bed or nerve receptors at a time when the other tissues are still in a resting state. The focus thus created is spherical in shape, because according to the laws of physics stimulative effects spread spherically, just like waves extending from one point do. Accordingly, the genesis of the spherical granulation caused by tuberculosis bacilli and composed mainly of reticuloendothelial elements is explained by the reticuloendothelial effects of the metabolites of the tuberculosis bacillus, and is made understandable, by the fact that in the hypersensitized organism even a minimum quantity of the pathogen suffices to produce a spherical, hyperergic structure of tissue excitation, i.e. a tubercle. That a tubercle is actually produced in this way, is proved among others by the fact that in different diseases reticuloendothelial foci similar to the tubercle may develop in the lymph nodes. Foci of granulation resembling a tubercle may occur in the lymph nodes in syphilis, Besnier—Boeck—Schaumann's disease, tularaemia, lymphogranuloma inguinale, various mycoses, in the lymph nodes near to the area of regionalis ileitis, different allergic conditions, and even in the lymph nodes near to malignant tumours. The latter has been described by BARBOLINI, as a special condition called epithelial granulomatosis, although the process is in fact nothing else but a state of mesenchymal excitation in the tumorous organism, arising in the way outlined above. Thus, ultimately, the formation of structures similar to the tubercle is explained by the fundamental inflammatory phenomena and by the hyperergic processes. They are differentiated from one another only for certain purposes, and not because such a distinction is justified by essential differences. I certainly cannot deal here with all these processes of granulation, all I can do is just to mention in a few words some illustrative examples. We all know what the caseous lymph node of the primary complex looks like. The changes developing later in the lymph nodes are classified differently by different authors. I have distinguished proliferative tuberculous lymphadenitis from caseous and fibrous tuberculous lymphadenitis, as well as from the macrocellular hyperplasia of ZIEGLER, the macrocellular tuberculous lymphadenitis. The latter is pointed out emphatically, because it may be a source of serious error when studied by inexperienced observers. When still a beginner, the pathologist may be too much impressed by the picture

he has in his mind as regards the tuberculous lymph node, with the giant-cell tubercle as the most outstanding feature, and may fail to realize that if the systemic reaction is altered, tubercles may not be formed at all, or the pattern of the changes may be profoundly different. One of such characteristic tuberculous patterns is the above mentioned macrocellular hyperplasia of ZIEGLER, where under the tuberculotoxic effect, the reticulum cells proliferate excessively, without caseation or the formation of giant cells of the Langhans type. On the other hand, many pathological processes may produce changes similar to those occurring in tuberculosis. I refer here for example to the well known granulation in inguinal lymphogranuloma, as well as to the lymph node changes in histoplasmosis, one of the granulations accompanied by the formation of giant cells. This shows that similar changes may equally be produced by specific and non-specific inflammations, and it must be stressed that a histological diagnosis is reliable exclusively when analysed together with the clinical, bacteriologic, mycologic or virologic evidence. In text-books we often point out certain fine differences. We write for example that in the tubercle there are just a few leukocytes, or none at all, while in the granuloma of inguinal lymphogranuloma there are leukocytes and in the necrosed area intact and disintegrated leukocytes. In most cases this is in fact so. But every experienced pathologist knows that the picture of the granulation may often be modified, and for example in the early phase the granuloma of inguinal lymphogranuloma may contain just a few leukocytes. Moreover, it should be borne in mind that there are granulations resembling a tubercle, which have no specific disease in the background, but arise merely as a result of local tissue excitation. I just refer to one example. As it is known, the Merlkerson—Rosenthal syndrome is associated with swelling of the mucosa of the lips (usually of the upper lip), of the tongue and with unilateral facial paralysis. In the mucosa, and even in the submaxillary lymph nodes granulomas closely similar to tubercles may be found, although in most cases there is no evidence of tuberculosis. Thus, the so-called specific granulations in the lymph nodes, arise as a result of an excitation of the reticuloendothelial components of the lymph node and, depending on the quality of interaction between the pathogen and the affected organism. Thus focal or non-focal granulation is produced, which is often, but not always, characteristic of the pathogenic agent involved. I mention just in passing, that there is quite a variety of special processes that must be remembered when making our diagnosis on the basis of the histological pattern of the lymph nodes sent in for examination. For example, there is the cerviconuchal lymphadenitis of PIRINGER—KUCHINKA, composed of foci of epitheloid cells and due according to some authors to toxoplasmosis, as well as the reticular abscedeng lymphadenitis of WILENSKY—STRUTTHERS, and, which is the same, of WILLY—MASCHOFF, caused by Pasteurella pseudotuberculosis infection.

I do not think the various authors would seriously disagree with what I have said until nowthere is, however, a group of granulomatous diseases of the lymph nodes, in which not only the pathogen is unknown, but where it is questionable whether the condition is granulomatous or tumorous in nature. We should mention first of all the reticuloses of the lymph nodes, Hand—Schüller—Christian's disease, lipioid granulomatosis, lymphogranulomatosis and mycosis fungoides, leaving a few other, rare granulomatous conditions unconsidered.

The behaviour of the reticuloendothelial system in allergic processes has been studied extensively. As early as 22 years ago I dealt with these pathological processes in a paper read at a meeting of the Hungarian Pathological Society. Since then we have learnt much about these processes, but the essence of the problem is still the same, notably that the reticuloendothelial system reacts sensitively to allergic processes and shows intense excitatory phenomen as a result of hyperergic processes. The lymph nodes are stations of the reticuloendothelial system dispersed throughout the body, which become almost invariably involved in the allergic, hyperergic processes, though their participation may be different in degree. The excitation of the single reactive centres of the lymph nodes may vary according to the degree of systemic reaction, and may be so intense in certain conditions that it may dominate the picture, for example in allergic granulomatous angiitis, so heatedly discussed in the literature. In this group belong the granulomatosis of WEGENER, the allergic granulomatosis and angiitis described by CHURG and STRAUSS, etc. In these conditions granulomatous changes may develop in the lymph nodes, too. The centre of the granuloma may be necrosed and contains fibrinoid material at sites. The necrotic centre is surrounded by a zone of epitheloid cells and fibroblasts, containing variable numbers of leukocytes, plasma cells, macrophages and occasionally multinuclear giant cells. From our Institute MÁRK and FEHÉR reported on such a case in which excessive changes of this nature developed in the lymph nodes. The cause of these diseases is unknown, or the factor directly responsible for the allergic process cannot be identified. Since the changes may vary from case to case, it is most difficult to make a diagnosis on the basis of the histological pattern of the lymph node specimen.

As I have already emphasized, the reticuloendothelial system responds to the greatest variety of extrinsic effects and almost any kind of change may develop, ranging from mild activation and proliferative phenomena to systemic reticuloendothelial proliferation. The reticuloendothelial system is a dynamic, in other words a continuously proliferating, tissue, which responds most sensitively to every kind of effect and whether its response will be normergic, anergic or hyperergic, it will be determined by the metabolism, neurohormonal and immunological conditions of the organism. In connexion with a mild metabolic disorder we shall find at the most fine changes in the

lymph nodes, whereas in the various disturbances of lipid metabolism, for example in Gaucher's disease, we see marked changes in the lymph nodes throughout the body. There are some further conditions in which we can detect the systemic metabolic disorder in the background only by analysing the changes in the reticuloendothelial system or in the lymph nodes. For example, in the lipomelanotic reticulosis or Pautriez—Woringer's syndrome a mixture of melanin cholesterol and lipid was demonstrated in the hyperplastic reticuloendothelial cells in the lymph nodes. The disease occurred in conjunction with other diseases, for example in the case of LINDER and KÄRCHTER together with erythroderma and other cutaneous changes, while SUSLOV found the same process in association with a tumour.

The situation is similar in the case of septic infectious processes. In animals inoculated with bacteria the reticuloendothelial system shows intense proliferation. Depending on the experimental methods employed and on the immunebiological conditions this phenomenon may be considered to be an immunemorphological or hypersensitivity reaction. I described these phenomena in 1932, pointing out that in hyperergic states proliferation of the reticuloendothelial system may dominate the picture. Proliferationof the reticuloendothelial system is a symptom commonly occurring in numerous human infections diseases. There are also processes (whose aetiology is mostly unclear), in which the progressive changes of the reticuloendothelial system are in the foreground. GOLDSCHMIDT and ISAAC were the first to describe a disease involving excessive proliferation of the sinus and endothelial cells, respectively, of the reticuloendothelial system. Then EWALD reported on a septic condition associated with reticuloendothelial proliferation, in which the cells released by the reticular bond appeared in the blood stream. Shortly thereafter LETTERER described an excessive, at many sites focal, proliferation following otitis media in an infant. Since then, many entities called reticuloendotheliosis or reticulosis have benen made known. The diseases described under those names are far from uniform; they differ from one another in many features of the course and pathological changes. In some cases the changes are definitely systemic in character, in others they are restricted to the bone marrow, liver, spleen and lymph nodes, and sometimes tumour-lika proliferations are seen. The different authors have made different classifications in this big group of diseases. I have classified the reticuloses in my text-book in the following way: *a)* reticuloendothelioses based on disturbances of storage or metabolism; *b)* reticuloendothelioses of infectious, toxic origin; *c)* the so-called essential reticuloendothelioses of unclear aetiology, based presumably on infectious, septic, hyperergic mechanism; *d)* tumorous reticuloendothelioses.

I now intend to say a few words about the so-called essential i.e. nontumorous, reticuloendothelioses of septic, infectious, or mostly hyperergic nature. The principal forms of this are the acute infantile reticulosis or Letterer-

Siwe's disease, the reticulosis of older children and adults, as well as the so-called eosinophilic granuloma. In acute infantile reticulosis the lymph nodes are enlarged throughout the body and contain granulation tissue composed of polymophous reticulum cells. The septic nature of the disease is often quite cospicuous. Most authors, including for example GLANZMANN, WALTHART, WENDT and others, consider the disease to be a reactive process due to infection and call attention to the fact that in a considerable percentage of the cases streptococci or other pathogenic bacteria could be isolated, on the one hand, and on the other hand, that in some cases antibiotic treatment cured the patient. For example, in Aranson's case streptomycin, in Biermann's aureomycin proved to be effective. The reticulosis of older children and adults takes an acute or a chronic course and the changes in the lymph nodes are similar to those in acute infantile reticulosis. The final picture of the disease is characterized by septic symptoms. The so-called eosinophilic granuloma mostly develops in a single bone. The bones become swollen and in them a granulation composed of proliferating reticulum cells appears. The reticulum cells are partly in contact with the reticular structure and are partly in an epitheloid-like arrangement. The lymph nodes are mostly free from eosinophilic granulation, but there are observations, including my own case, where intense reticular proliferation has been found in the regional lymph nodes. The reticuloses and bone destroying proliferations may occur also in the reticuloses accompanied by systemic lymph node enlargement. Such cases have been described for example by GRIEDER, FITTING and MUNDT, and others. Some of these cases undoubtedly correspond to a reticular proliferation of neoplastic nature. In many a case it is, however, most difficult to decide whether the reticulosis is due to or to neoplastic proliferation. More often than not the histological picture is uncharacteristic. For example, in one of our cases occurring in association with septicaemia of rapid course reticular proliferation was excessive, while in another case, which we present at this meeting, reticular foci destroying the bones had arisen and at the same time the reticular proliferation in the enlarged lymph nodes scattered throughout the organism was rather monomorphous. In fact, all that we can say to-day about the reticuloses is that in all likelihood septicaemic, infectious, hyperergic and neoplastic processes equally occur among them and more often than not we cannot decide whether the reticular proliferation observed in the lymph nodes is hyperergic or tumorous in nature, even if we know the entire course of the disease. No matter how valuable the histochemical studies are (for example the cytotechnical studies for the demonstration of sulphhydryl groups made by TURA, PIERAGNOLI and GALUPPI), they have not produced results allowing definitely to differentiate tumorous reticuloses from non-tumorous ones.

Conditions related in many respects to the reticuloses are Hand—Schüller—Christian's disease, or more properly lipoid granulomatosis, then lympho-

granulomatosis and mycosis fungoides. It has been emphasized by several authors that these are related conditions, and for example BODIAN, SUTCLIFFE, MACNAB, I. G. WILLIAMS, H. WILLIAMS, HAJDU and others went as far as to suggest that all of them, including Letterer—Siwe's disease, were variants of the same pathologic process. It is beyond doubt that in all of these pathological conditions there is a proliferations of the reticuloendothelial system, or, more correctly, of the active mesenchyma, which appear once in the lymph nodes, then in the viscera, or in the bones. Essentially they correspond to an unlimited proliferation of the reticuloendothelial system in the wider sense of the word, or of the active mesenchyma.

Hand—Schüller—Christian's disease is well—known to produce the most marked changes in the bones. It cannot be doubted that it is a primarily granulomatous process and the deposition of lipid is only secondary and, according to LETTERER, is due to an enzyme deficiency associated with the granulomatosis. I was the first in 1942 to describe in a monograph that form of the disease in which osseous changes are absent and also described the changes of the lymph nodes, pointing out that the granulomatous process preceded the deposition of lipid and in some lymph nodes only the granulomatous process was detectable. The disease is less rare than generally believed and on the basis of the evidence obtained by lymph node biopsy studies the cases without osseous changes are listed among the proliferative reticuloses, because the character of the condition is characterised merely by the subsequent deposition of lipid, and that may still be absent in the early biopsy specimens. This is the explanation for the belief that the two diseases may develop into each other.

Among the granulomatous conditions mentioned, the most significant is undoubtedly lymphogranulomatosis I wrote my first work on the subject nearly 30 years ago and summed up the results of my investigations in a monograph published in 1944. More recently, I have again analysed 76 biopsy and post-mortem cases and found my earlier views fully confirmed. Nothing has emerged in the latest literature, either, that would have made any alterations necessary. More recently, JACKSON and PARKER have differentiated among the lymphogranulomatous proliferations one of slower course rich in lymphocytes from the one with a rapid course and rich in neutrophil leukocytes and necroses. The former has been called paragranuloma. It is to be noted that it is fully unjustified to call lymphogranulomatosis Hodgkin's disease. My view agrees with that of HAMPERL, who says that "It is doubtful how many of the cases published by Hodgkin were really lymphogranulomatosis (apparently only 2 cases of the total of 7). Under such conditions it is senseless to use in the German literature in a subservient manner, the term Hodgkin's disease, as a result of which the most fitting name; lymphogranulomatosis, is pushed to the background." Among our cases 23 corresponded to paragranulomatous

proliferation, 43 were cases of typical proliferation with many Sternberg cells and eosinophils, and 10 showed a tumorous character.

As to the aetiology of lymphogranulomatosis, there are three prevalent theories. Some authors consider the disease to be a chronic inflammation of unclear aetiology, others think it to be due to viral infection and still others believe it to be a neoplastic disease. From among the views ascribing the disease to infection and granulation I mention only three. BUDAY stated: "The similarity of the lymphogranulomatous cells to tumour cells is indeed no justification to claim that lymphogranulomatosis is a tumour." More recently, Letterer has pointed out: "Alles spricht aber dafür, dass das Lymphogranulom wie der gleichen Gruppe angehörige Mykosis fungoides eine Infektionskrankheit darstellt." In the recent book of Kaufmann and Staemmler ROTTER and BÜNGELER put forward the following critical opinion after surveying the literature on lymphogranulomatosis: "Abschliessend stellen wir fest, dass es sich bei dem Lymphogranulom um eine Granulomatose unbekannter Ätiologie handelt, dass jedoch bei einer kritischen Sichtung des Bekannten alles dafür spricht, dass das Lymphogranulom eine spezifische Infektionskrankheit darstellt, die vermutlich durch ein lymphotropes Virus erzeugt wird". I have expressed my views on the subject in a paper presented at the 1943 Congress of the Hungarian Pathological Society (and which appeared in print later), as well as in a monograph published in 1944. In those works I have summed up my views concerning lymphogranulomatosis in the following.

Lymphogranulomatosis is an inflammatory process (accompanied by phenomena of pathological mobilisation) of the haemolymphatic tissue possessing special tendency to growth and rich in indifferent cells, in the course of which the intense tendency of the cells to grow in connexion with the inflammatory, activatory tissue excitation may reach the limit separating tumorous from non-tumorous growth. In some cases the inflammatory increase in the number of cells merely approaches the border of neoplastic proliferation and the disease it not a tumour, but it is justified to assume that sometimes the proliferation of cells goes beyond this boundary and the growth will become tumorous. However, until we cannot compare experimentally the biological properties of tumorous tissue with those of lymphogranulomatous tissue, we have no definite proof of the two processes being identical, and for the time being the correct thing to do is not to use the term sarcoma for the single forms of lymphogranulomatous inflammation. We should instead emphasize that the pathological process in question is one of the chronic tissue excitation phenomena, which is certain forms may show tumorous signs. The latter statement does not alter the fact that lymphogranulomatosis, at least in its early phase, is essentially an inflammatory process, and does not make it necessary to subdivide lymphogranulomatosis into various tumorous and non-tumorous forms on the basis of the severity of tissue excitation. For the time being

we should emphasize that in some cases the tumorous features of the pathological process are very much in the foreground.

According to those outlined above we may sum up our views on lymphogranulomatosis in that its aetiology is unknown and that there are observations to indicate that the inflammatory pattern is due to a peculiar responsiveness of the tissues, a special condition of the mesenchyma, and in its development excessive growth bordering tumorous proliferation plays the leading role. Some authors still expect that bacteriological or virological investigations will clarify the true nature of the pathological process and devote little attention to the reaction of the organism. Thus, far this trend has yielded no reliable results and after surveying all the information available in this field we are justified in pointing out that lymphogranulomatosis, too, is a disease the true nature of which will be known only after we shall detect much more about the details of systemic reactivity. On the other hand, the cellular changes in the direction of neoplastic growth, as they occur in lymphogranulomatosis, will not be understood until after the fundamental phenomena of tumorous growth will have become known and thus a full explanation of the disease will presumably be offered by pathological, biochemical and tissue culture studies associated with morphological investigations and relying upon experimental research. It would be beyond the scope of the present paper to go into the details of this problem, and therefore I wish to point out only the following.

The proliferation in lymphogranulomatosis in the early phase and in the cases with a protracted course often remains granulomatous in character, without any sign indicative of tumorous growth. I have observed many cases in which proliferation remained inflammatory in character till the end. The early changes are endothelial proliferations, then granulations rich in eosinophile cells and relatively poor in Sternberg-cells develop, in some cases there are more giant cells, sometimes there are also necroses, finally loose and then rough fibrous scar tissue is formed. This may be the pattern of changes for years. It is to be emphatically stressed that vascular changes are common and they sometimes correspond to hyperergic vascular phenomena. In about 20 to 25 per cent of the cases tuberculous infection, or tubercles may be found. It is difficult to claim that these cases, in which the disease may last as long as 15 to 20 years, are tumorous ones. In any mentioned monograph I described the development of the Sternberg type giant cells from the hypochromic mononuclear cells to the multinucleated ones, from the reticuloendothelial elements and from the active mesenchymal elements, respectively, in great detail. I ponted out the features which according to the view of BUDAY and my own, make these cells similar to tumour cells, without identifying them with tumour cells. Among the Sternberg type cells, as it was shown by BUDAY, JOHANN and myself, even atypical nuclear mitoses may occur. On the other hand, these cells, when they occur together with tuberculosis, may exception-

ally phagocyte tubercle bacilli, and penetrate into the lymphatics and tissue interspaces, but they form no true metastases. We must emphasize that the marked polymorphism and the cytological properties of the cells correspond to the active reticuloendothelial elements. However, in the lymph nodes from septicaemic cases accompanied by a leucaemoid reaction the activated reticuloendothelial elements sometimes also show a conspicuous polymorphism, and the cells occurring in malleus may also show an excessive polymorphism, though they are not tumorous cells. In my paper and monograph as well as in a paper by BUDAY published in the 'thirties we find descriptions of cases which showed a tumorous character. In some instances the lymphogranulomatous proliferation does not differ in appearance from the usual pattern rich in Sternberg-cells, but it grows most destructively, destroying the lymph nodes and invading adjacent tissues. On the other hand, I observed a case, which showed every undoubtable sign of tumorous growth, marked polymorphism, destructive growth, etc.; such cases are called Sternberg's or Hodgkin's sarcoma. At Kolozsvár we saw a woman, 59 years of age, in whom a tumour developed almost before our eyes. The tumour grew most destructively, contained areas resembling macrocellular reticular sarcoma and others closely similar to cancer. Thus, according to my final view lymphogranulomatosis, in its early phase and in many cases throughout its course, cannot be considered to be a tumour, because if joining some fashionable hypothesis we declare that it is a tumorous process without analysing the details, we shall be just as wrong, as we are when we say right away that every precancerosis is a tumour, although they develop into tumour in a certain percentage of the cases only.

The correlation between mycosis fungoides and lymphogranulomatosis has been emphasized by many authors and I, too, stated in my monograph that the two conditions were similar. As it has been pointed out by GIARELLI and MIANI, as well as by KÜHL and HARMANN and others, the proliferation in the lymph nodes may so closely resemble that seen in lymphogranulomatosis that it is difficult to differentiate the two conditions on the basis of biopsy studies. In my experience mycosis fungoides may sometimes, but not always, contain such giant cells in the lymph nodes which in their cytological properties are similar to the cells of the basic tissue and differ from them only in their gigantic size; in other cases, mycosis fungoides may present a bizarre tumorous picture.

Recapitulating the above we may arrive at the conclusion that in the lymph nodes processes of granulation may arise, which in response to metabolic disorders, infectious, and toxic disturbances may lead to an intense excitation of the reticuloendothelial system and the development of granulation tissue. These conditions, the reticuloses, lipid granulomatosis, lymphogranulomatosis, mycosis fungoides, beside having individual features, are the manifestations of essentially the same process, of an mesenchymal excitation, which

may reach such intensity that it turns into autonomic, i.e. tumorous proliferation. It is often difficult to interpret the changes and this applies to the lymph node biopsy specimens, too. There are few fields in pathology in which so many diagnostic errors are made as in this one. As I have devoted much attention to the study of lymphogranulomatosis, I have had occasion to re-examine many biopsy diagnoses. Experience has shown me that quite often the pathologist or physician diagnoses lymphogranulomatosis, a lethal disease at present, much too hastily, although pathological phenomena of similar character certainly occur in a wide variety of reactive conditions, against which we are by far not so helpless as we are in the case lymphogranulomatosis. To recognize and properly interpret the reactive processes of the lymph nodes is one of the most important tasks of the practising pathologist, because it is only in the possession of such knowledge that he will be able to establish such important diagnoses as that of lymphogranulomatosis.

RELATOR

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Tumours of the Lymph Nodes

In typical cases it is not difficult to diagnose tumours of the lymph nodes. However, every pathologist often encounters cases, in which the diagnosis is dubious; these cases represent one of the most difficult and responsible tasks in morbid anatomical practice. In the present paper I intend to expose the causes of the difficulties in diagnosis and shall attempt to show how diagnosis could be placed on more solid foundations.

The difficulties of pathohistological diagnosis can be often traced back to the fact that in connexion with inflammatory reactive processes, endocrinological changes etc. we find such morphological changes in the lymphatic apparatus, as may resemble very closely one or another kind of haemoblastosis. This problem will not be delt with here. Frequently, an inadequacy of clinical or pathological analysis or a lack of clinico-pathological cooperation may be held responsible for the diagnostic difficulties.

In most cases reliable clinical data are essential for making a correct pathological diagnosis. We must know when the first lymph node was noticed, what was the blood count, had the patient been treated with irradiations or chemotherapeutics, had he fever, in short: we must know the course and symptoms of the disease. In the overwhelming majority of the cases the clinical diagnosis is based on the histological diagnosis. It is a frequent error that owing to technical difficulties or to examinations which were not thorough

enough it is not the most characteristic lymph node which is sent in for histological study. Diagnosis is made easier if two or three adjacent lymph nodes are taken out. Lymphatic tissue is most sensitive to mechanical trauma and therefore diagnosis may be impossible if the lymph node is injured at excision. This is the chief source of error in the aspiration diagnosis of lymph nodes.

Usually, we cannot do without a detailed analysis of the cell structure: this, however, has the prerequisites that fixation should be executed with care, one or two adequate fixatives should be used, embedding should be extremely gentle and both thin and thick sections should be cut. Many authors have stressed that the sections should be thin, but such sections are not always the best. A Sternberg cell of 60 to 80 microns in size, or a reticulum cell, can be identified better in thicker sections. As to the special staining methods, it is still the silver and fibre-staining ones that are most relevant and mostly we cannot do without them. Much is revealed by the PAS reaction. With adequate practice, the Giemsa pictures will tell us much. The Feulgen reaction is not of great diagnostic value, and seldom can methylgreen-pyronine preparations of adequate quality be made, because with large routine material the fixation required for such staining is seldom employed. I think that for staining fat with Sudan thin sections are most valuable. The use of a cover glass is necessary, lacquel covered preparations cannot be used. For the time being, histochemical and submicroscopic studies have no practical use.

It is important to have a collection of pathohistological material together with the pertaining clinical data.

More important than the technical problems just discussed is, however, that many a fundamental problem must be solved to overcome some or another of the diagnostic difficulties. I should like to deal with a few such questions.

Because of the fact that some of its basic problems are unclarified, there is no uniform standpoint as regards the classification of haemoblastosis. According to Table I., which bears resemblence in many respects to those found in most papers and books, tumours of the lymph nodes may originate from lymphoid or reticular elements. This is true also for lymphogranulomatosis. We have taken into account the changes of the myeloid apparatus and the changes originating from the plasma cells, because these, too, may be associated with enlargement of the lymph nodes. We have left out, on the other hand, the diseases based on changes in erythropoiesis, because these are usually not accompanied by enlargement of the lymph nodes. There is a more precise classification, which has been made on the basis of the progression of the tumours, but this is leading to many a controversial issue.

Little is known about the preblastomatosis of the lymph node tumours. As a result of the advance in diagnostic and operative techniques we get more and more lymph nodes suspected of showing the earliest phase of neoplastic growth. Long clinical follow-up studies offer a possibility to compare the

morphological findings with the clinical course after the lapse of 5 to 10 years. Most valuable such observations have been described by KREYBERG and IVERSEN, for instance. Much may be expected also from the studies on the histogenesis of experimental haemoblastosis.

Among the fundamental problems still awaiting elucidation those concerned with aetiology have been studied most intensely and it is also in this field that we have obtained the most important informations. Since, however, the evidence thus obtained is for the time being of little if any diagnostic value, I do not wish to deal with such data here. Clarification of the problems of pathogenesis, and of morphogenesis, in the first place, may bring us nearer to an overcoming of pathohistological difficulties. For an early histological diagnosis we ought to know on the basis of what diseases does haemoblastosis develop and what morphological changes are indicative of a neoplastic transformation in its initial phase.

At present, we know hardly anything about the preblastomatosis of lymphosarcoma and reticular sarcoma. In case reports we often find claims that repeated inflammation and inflammatory hyperplasia would precede the growth of these tumours. The commonest condition mentioned in this connection is pharyngeal catarrh, which leads to enlargement of the cervical lymph nodes and after long years to sarcoma. The number of such reports is too small to enable one to accept them as proofs. Somewhat more is known about the malignant lymphoma starting out from certain internal organs. Most characteristic of them is Hashimoto's thyroiditis, which, presumably rather infrequently, may turn malignant. One or another of the reticuloses may also develop into reticular sarcoma. There are, for example, reports on the sarcomatous transformation of genuine reticulosis, eosinophilic granuloma, Hand—Schüller—Christian's disease, etc. Malignisations of the focal lymphoid hyperplasia and reticuloses of the skin, and of the lymphomatosis of the orbita are more common. As to the so-called pregranulomatous changes of lymphogranulomatosis, we cannot say whether it is a preblastomatosis or a change marking the onset of neoplastic growth. In lymphogranuloma there are often lymph nodes exhibiting no characteristic changes, in which histiocytosis, foci of epitheloid cells, hyperplasia of the follicles and lymphoid elements, sinus catarrh, and increase in the number of plasma cells and eosinophils can be detected. These changes may be present in some enlarged lymph nodes in patients who later develop lymphogranulomatosis. However, diagnosis should not be based on these pregranulomatous changes. When we see such changes, we may find at the same time characteristic infiltrations in another area of the same lymph node, or in another lymph node. We must therefore study a number of sections in every case and every lymph node should be examined. The clinician should be warned that the patients with this diagnosis must be kept under thorough observation and later every enlarged lymph

node must be examined histologically until the diagnosis can be established with certainty.

There are certain entities which invariably lead to malignant haemoblastosis. These may therefore be compared to the so-called "obligatory precancerosis". Here belong follicular lymphoma or Brill—Symmers' disease. Such case have been known for long. BRILL, BEAR and ROSENTHAL, then SYMMERS described them as pathological entities. The lymph nodes are enlarged, the cortex and medulla contain enormous follicles. These are composed of cells similar to the reticular elements of reactive centres, surrounded by a halo of closely packed small lymphocytes. After 5 to 10 years the changes turn as a rule into lymphosarcoma or reticular sarcoma. Correspondingly, we may consider the condition either borderline case between benign changes and malignancy, or a malignant tumour. The condition is difficult to differentiate from reactive follicular hyperplasia, it is especially in children that the lymph nodes may show such changes near the sites of inflammation. Diagnosis is easier if the follicles merge and the proliferating reticular elements invade the environment, the cells are polymorphous, atypical. These are namely the morphological signs of malignisation. Very often the changes are not characteristic enough and therefore the diagnosis has to be confirmed by repeated excisions and by following up the course of the disease.

More or less the same applies to paragranuloma, a term used for the first time by JACKSON and PARKER. Also some of the so-called atypical cases of lymphogranulomatosis belong here. The classical term "early Hodgkin" seems a better characterization of condition's essence. In the lymph node as a whole, or in part of it, the original structure disappears, but mostly one or two follicles may still be recognized. Among the masses of lymphocytes we may sometimes find eosinophil and plasma cells as well. The most characteristic feature is the large number of proliferating reticular cells, of which one or another has turned into a multinuclear Sternberg cell. The number of the latter is always small and therefore we must search for them thoroughly. If we find no Sternberg cell, the diagnosis of lymphogranulomatosis or paragranuloma must not be made. The big mononuclear, so-called Hodgkin cell, cannot be considered so characteristic that its presence should ensure the diagnosis; it only means that the patient might suffer from the disease in question. A condition similar to those outlined beforehand is mycosis fungoides, identified by many with lymphogranulomatosis. We think it to be comparable in the first place with paragranuloma, because it begins with inflammatory infiltration and goes over as a rule into reticular sarcoma.

The localized tumours. Haemoblastoses are thought by many workers to be systemic diseases. On the other hand, clinical reports often point out that tumourous growth starts in single groups of lymph nodes and it is thence the process becomes generalized. In favour of this evidence is the fact that

the patient may remain free of symptoms for many years after the surgical removal of one or two enlarged lymph nodes.

The most illustrative examples of localized lympho- or reticular sarcoma occur in the internal organs; most often in the tonsils and pharynx, the stomach, the iliocoecal region and appendix, the thyroid gland. It is remarkable that such tumours may start togrow also in tissues not containing lymphoreticular elements, for example in the meninges. According to certain data, the visceral lymphoreticular sarcoma grows somewhat slower and forms secondary deposits later than do the other malignant tumours.

All those stated for the localized forms of lympho- or reticular sarcoma apply to the localized forms of lymphogranulomatosis as well. The clinicians claim that Hodgkin's disease, too, tends to begin in one lymph node or in one region. It may remain circumscribed and the patient may be free of symptoms for years following the removal of the enlarged lymph nodes. Although rarely, lymphogranulomatosis may be restricted to one or another of the internal organs. (I have found typical lymphogranulomatosis in a removed spleen; the patient died shortly after splenectomy. Gross and microscopic post-mortem study showed lymphogranulomatosis nowhere else in the body.)

The view that malignant lymphoma begins locally is supported by the evidence of animal experiments. Many strains could be bred (C58, AK, etc.) in which the adult animals are often affected by leukaemia, lymphosarcoma or reticular sarcoma. According to FURTH, KAPLAN and many other authors, thymectomy may prevent the development of haemoblastosis. At our institute we are now investigating a mouse strain, in which the disease begins with the enlargement of one or two cervical lymph nodes and the subsequent course takes up the form of either a lymphosarcoma, or reticular sarcoma, or occasionally of lymphoid leukaemia. On the basis of these data it may be assumed that like the other tumours the haemoblastoses arise, in a few lymph nodes or in one single organ and spread by forming secondary deposits throughout the body. It is likely that spreading takes place easily and fast.

Lymphosarcoma was widely discussed early in this century, because owing to its generalized appearance many authors had doubted that it would be truly sarcomatous in nature. There still are advocates of the view that it is a systemic disease.

Usually, the morphological diagnosis of lymphosarcoma is not difficult. In the area of tumourous infiltration theoriginal structure disappears, the tumour tissue infiltrates the capsule and the environment, resulting in a conglomeration of lymph nodes. We usually distinguish two morphological forms, one composed of small mature lymphocytes and the other of large cells reminiscent of lymphoblasts. The two types do not differ either in course, or in prognosis. There is no evidence to indicate that the more differentiated small-cell lymphosarcoma would turn into the large cell form in the course of its progression. In general,

the lymphosarcoma has a scanty reticular structure, but it may occur that the two kinds of tissue proliferate together. These lymphoreticular sarcomas turn into the purely reticular form in the course of their progression. In advanced cases we find the KUNDRAT—PALTAUF type of generalized lymphosarcomatosis, with diffuse infiltrations in all the lymph nodes, the bone marrow and spleen, and secondary deposits in the internal organs. A certain tumour has been termed retothelsarcoma by ROULET, most authors call this neoplasm reticulo-sarcoma. As to its essence, the view has been adopted since the early 'thirties that tumours with a characteristic structure and different from lymphosarcoma may originate from the reticular tissue of lymph nodes and from the other elements of the reticulo-endothelial apparatus (Kupffer's cells, spleen, thymus). The reticular tissue may exhibit widely variable degrees of differentiation, correspondingly the reticular tumours may present highly variable histological patterns. Not infrequently nuclei of equal size occur dispersed in the synplasma and the cell complex as a whole is surrounded by reticular fibres. In other instances the tumour is composed of a network of cells producing ample numbers of reticular fibres, which are often closely related with the cytoplasm as well. This is what ROBB—SMITH called the diktyocytary form. Sometimes the tumour cells resemble the littoral cells of the lymph node, the endothelial, littoral cells of the sinus, become elongated and form longitudinal or starshaped bundles. The forms producing fibre may resemble spindle cell sarcoma. The commonest form is the histiocytary reticular sarcoma, the cells of which are rounded and separated. This form is difficult to differentiate from the lymphoblastic lymphosarcoma. However, these forms may occur alternatingly within the same tumour, and the young or more mature secondary deposits in the different organs may present an even more complex picture.

The typical cases of lymphogranulomatosis are easy to diagnose. Most authors see the essence of the disease in a malignant proliferation of reticular elements. Because of the increased number of additional cell types (lymphocytes, leucocytes, eosinophils, plasma cells), many authors have suggested that this peculiar disease would develop on grounds of an inflammatory process.

This is the only one of the haemoblastoses which we do not find in animals and which could not be induced experimentally. Although changes similar to it have been described in many animal species, they are different from the human disease. The course taken by the disease is variable. Sometimes the patient is killed by it in a few weeks, while sometimes he may live for years or even decades without symptoms or complaints. Therefore not infrequently the histologist's diagnosis is given the benefit of doubt. The many attempts made thus far at finding a correlation between the histological pattern and the course of the disease have all failed. In general, an increase of round-cell elements and fibrosis are believed to be favourable morphological signs. The poly-

morphism of the proliferating reticular cells is considered to be a sign of malignancy.

Dedifferentiated tumours. If the patients live long enough, ultimately an anaplastic tumour develops, which we diagnose as polymorphocellular, or reticular sarcoma. In such cases we are mostly unable to say what the original tumour could have been like. Sometimes we find in a few distant lymph nodes or in the secondary visceral deposits areas in which the structure of the original tumour persists.

In the course of leukaemia the lymph nodes sooner or later become enlarged. In this connexion we are interested in the first place in the lymphocytic and monocytic leukaemias, because they start from the lymphatics. There seems to be some agreement in that leukaemias are malignant tumours, differing from the tumour-forming forms only in that the cells produced again and again continue to flow into the blood stream, like the corpuscular elements of blood. The lymph node may increase in size in leukaemia, because the corpuscular elements of blood infiltrate the lymph nodes just as well as they infiltrate the liver or spleen.

Most authors consider lymphosarcoma and the leukaemias to be different forms in which the same disease becomes manifest. The two conditions can be distinguished from one another exclusively on the basis of the blood count. Under experimental conditions once leukaemia, then lymphosarcoma appear alternatingly. Terminally, every leukaemia produces tumour-like infiltrations in the lymph nodes; when these merge, enormous tumour-like conglomerates of lymph nodes arise. This is most marked in the cases of lymphoid and the acute "paramyeloblastic" leukaemia.

One of the most characteristic properties of malignant lymphomata, that I have repeatedly mentioned when discussing the various kinds of tumour and that often leads to diagnostic error, is that one form turns into another, and that one disease combines with another. It is not frequently seen with other tumours that one kind of neoplastic growth goes over into another. This problem is interesting also because it may have a significance in the understanding of pathogenesis. First of all, we should survey the information concerning the progression of tumourous growth.

The tumours are changing continuously in the course of their development and growth. The fundamental changes in biological behaviour are reflected by the increase in their autonomy. One sign of this is that the milieu, for example the hormones, gradually lose their influence on the activity of the cells. The functions of the cells and tissues, for example their secretory activity or hormone production, decrease. The tumours become more easily transmissible. We are interested, however, in the morphological changes, in the progressive anaplasia, in the first place. As a sign of this, the cells do not differentiate, the number of mitotic forms increases, distorted mitoses and amitoses become

prevalent. The tumour infiltrates the environment and forms secondary deposits in the lymph nodes and the organs.

When trying to formulate a view concerning the pathogenesis of haemoblastosis we should take into account certain data concerning the production of the blood's corpuscular elements.

The corpuscular elements of blood live for a short time and are produced continuously. Tumour cells perish and are reproduced even faster. An acceleration of physiological regeneration is of particular significance in the cases of haemoblastosis.

According to the universal view, tumour cells arise from a primitive, ancient cell, and become lymphocytes, myelocytes, leukocytes, etc. only in the course of differentiation. Thus, in this case anaplasia means that the cells become similar to the primitive mesenchymal cell type.

Necrobiotic processes take place as a rule in tumours. In tumours of the haematopoietic organs necrosis is a rarity. In contrast, an occasional disintegration of single cells is a common occurrence, especially in lymphosarcoma. I have suggested that we should try to differentiate lymphoid leukaemia from investigations the destruction of tumour cells is invariably accompanied by a loosening-up of the tumour. The tumour cells thus set free enter the circulation.

Taking into account this phenomenon, I shall try to explain the progressive transformation, the turning of one type of tumour into another in the course of malignant growth.

Lymphoid leukaemia and lymphosarcoma are two forms of the same disease. The leukaemic cells flow into the blood stream similarly to the lymphocytes, the sarcomatous cells accumulate locally and produce a tumour. Leukaemia is such a tumour, in which the proliferating cells have not yet lost the tendency to swarming-out, a characteristic property of the corpuscular elements of blood. However, in the course of progression they become more and more tumourous in character. In the course of lymphosarcoma, especially terminally and following therapeutic intervention, we see a leukaemic increase of cells in the blood. This is explained by assuming that in such cases the tumour cells are set free as a result of degenerative changes and the cells thus detached from those around them swarm out into the blood. This leukaemic increase in the number of cells is equivalent to a tumourous cytaemia. Cytological examination can distinguish the tumour cells from the leukaemic ones. On the other hand, in the course of their progression the leukaemias often become tumourous in character, because the proliferating cells lose the property of flowing into the blood stream, like the corpuscular elements of blood do.

We may interpret in the same way the genesis of chloroleukaemia, leukosarcoma. stem-cell leukaemia associated with reticular sarcoma, etc.

	Lymphoid	Reticular	Lymphogranulomatosis	Plasmocytic	Myeloid
Basic disease? Praeblastomatosis?	Reactive lymphadenitis Lymph-hyperplasia	Reticular hyperplasia Reticuloses	Paragranulomatous changes?	?	Myeloid reaction?
Obligatory praeblast. Beginning tumour? Benign tumour, multiple or silitary?	Follicular lymphoma Localized lymphoma of lymph nodes or viscera	Certain reticuloses	Paragranuloma	Plasmocytoma Myeloma multiplex	
Localized or multiple sarcoma	Lympho-	Reticular sarcoma (from localized to one region or organ)	Lymphogranulomatosis		Chloroma
Sarcoma of the generalised mature type	Lymphosarcomatosis	Reticular sarcoma	Typical lymphogranulomatosis	Generalised plasmocytoma	Myeloid lymph node infiltration Leukosarcoma Myelosarcoma
Sarcoma of the generalised immature type	Lymphoblastic lymphosarcomatosis	Rich in cells, transient form toward polymorphocellular immature sarcoma			
Dedifferentiated	Anaplastic (reticular) lymphosarcomatosis	Polymorphocellular sarcoma	Hodgkin's sarcoma	—	—
Leukaemia	Lymphoid leukaemia	Stem-cell leukaemia Monocytic leukaemia Acute paramyeloblastic leukaemia Megakaryocytic leukaemia?	—	Plasmacell leukaemia	Acute and chronic myeloid leukaemia Eosinophilic leukaemia Basophilic leukaemic

Thus, the haemoblastoses cannot be considered to be systemic diseases, but they are solitary or multiplex tumours forming secondary deposits early and extensively. We may also point out that the cells carried away by the lymph and blood show a great preference to become lodged in the haematopoietic apparatus.

The haemoblastoses are progressing in the direction of immature reticular elements. The more advanced the progression, i. e. the more marked the anaplasia, the more will be lost of the special properties of the tumour, and the more one tumour will become similar to the other. The anaplastic reticular elements may undergo secondary differentiation, and then fibre production will come to the fore. It is in this way that we interpret the conversion of Brill-Symmers' disease and lymphosarcoma to reticular sarcoma, the development of Hodgkin's sarcoma.

Follicular lymphoma turns into lymphosarcoma in one case, because lymphoid elements are formed from the reticular cells corresponding to the germinative centre, while in another case the cells jump over this phase in the course of progression and reticular sarcoma is formed right away. This leukaemia-like swarming-out of reticular cells occurs rarely in lymphogranulomatosis, the anaplasia is accompanied by a conversion to the polymorph-cell „Hodgkin's sarcoma".

DISCUSSION

Anna Vécsei

(Department of Pathology, Postgraduale Medical School, Budapest)

The Histology of Lymph Nodes in Granulomatous Intestinal Disease

The lymph nodes, owing to their location and anatomical structures, are usually involved in the diseases of the neighbouring organs. The causative agent of a disease frequently releases a characteristic reaction in the lymph node from which it may be possible to infer to the responsible condition. This is what sometimes happens in connection with granulomatous intestinal inflammation. It is known that intestinal tuberculosis involves a tuberculous granulation in the environmental lymph nodes. Landouzy's acute tuberculosis, however, gives rise in the lymph nodes to a reactionless necrosis of the same type as the one occuring in the intestines in other similar cases. Characteristic changes may occur furthermore in Boeck's sarcoid if this involves the intestines, in ulcerative colitis and necrotic enteritis. In Crohn's disease the mesenteric and mesocolic lymph nodes always present a typically granulated structure. In typhoid fever the salmonella endotoxin activates the reticuloendothelial system and the lymph nodes show large round cells, the so-called typhoid cells, which originate from mobilized reticular cells. It is remarkable that in actinomycosis, one of the most specific granulomatous intestinal diseases, the lymph nodes do not undergo any morbid change.

These changes raise a few problems for discussion. Attention is drawn to the fact that only the local lymph nodes are involved in the intestinal lesion. Furthermore it seems important to ascertain which was the primary lesion in each disease, that of the intestines or of the lymph nodes.

A thorough knowledge of the characteristic changes is all the more desirable as lymph node biopsy allows for some inference as to the nature of the inflammatory intestinal process.

L. Barla-Szabó

(Department of Histopathology, Municipal Hospital, Uzsoki u. Budapest)

Eosinophilic Granuloma in Lymph Nodes

The development of eosinophilic granuloma in the region of the cervical lymph nodes has been studied in two out patients. The diesease manifested itself with conspicuous hypertrophy of the cervical lymph nodes. Histology revealed granulation accompanied by strong eosinophilic infiltration, a process leading to the accumulation of scar tissue. There appeared many Charcot-Leyden crystals among the eosinophils. A tuberculoid structure consisting of central fibrinoid necrosis surrounded by epitheloid and giant cells was observed in one of the two cases. This structure was similar to that which Bergstrand, further Churg and Strauss, had found at the autopsy of patients who had been suffering from severe asthma accompanied by high temperatures, eosinophilia and vascular lesions of allergic origin. Similar lesions were encountered by Zuelzer and Apt in the biopsy material obtained from the liver of eosinophilic children. Such lesions are, essentially, allergic reactions of the connective tissue. Since eosinophilia persisted after removal of the granuloma, it is safe to conclude that the disease was not local but represented a general allergic response of the entire organism.

Localization of the condition in the cervical lymph nodes must have been due to that the allergen had acted through the naso-pharyngeal tract.

The cases in question were interesting because, so far, typical allergic tuberculoid reactions have been observed at autopsy only (the said biopsies of Zuelzer and Apt excepted). Literature contains no reports on lymph nodes (wherever they be in the body) affected by allergic granuloma.

I. Besznyák

(Ist Department of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest)

A Case of the Letterer-Siwe Disease

A female child 11 years of age had been admitted to hospital with Letterer-Siwe's disease. The first diagnosis had been Hodgkin's disease. The mediastinal lymph nodes, liver and spleen had been considerably enlarged, there had been fever up to 40° C of a septic character, and signs of marked anaemia and moderate leukopenia. Polymorphous cutaneous eruptions had appeared all over the body, there had been no response to treatment and the child died after 2 months in the hospital. Pronounced leukocytosis and cellular structures reminiscent of monocytes in the peripheral blood smear, had been observed a few days before death.

The gross and microscopic lesions, and the clinical course, of Letterer-Siwe disease's have been together with the aetiological factors and the relations of the condition to other reticuloendothelioses (Hand-Schüller-Christian's disease, eosinophilic granuloma). This was the third case of Letterer-Siwe's disease recorded in Hungarian literature.

H. Jellinek, I. Márk

(2nd Institute of Pathology, Medical University, Budapest)

Granulomatous Changes in the Lymph Nodes in a Case of Histoplasmosis

A case of histoplasmosis in Hungary was described by Csillag, and Wermer, Juba, as well as Simkovics. The infant aged 9 months had developed bronchopneumonia 8 to 10 weeks earlier. Clinical data: the liver was enlarged by two fingers' width, the spleen by one finger's width. The right lung was missing. A Mantoux test was negative.

At autopsy agenesis of the right lung, ductus Cuvieri persistens and diverticulum Meckeli were found. The lymph nodes, mainly the thoracic and deep cervical ones, were slightly increased in size; the cut surface was granular. The left lung was denser. In an area similar to a small apple in size the gyri of the left frontal lobe were atrophied and dense to touch.

Microscopic examination showed in the cerebral perivascular spaces in the cells with foamy cytoplasm spheroidal bodies 0.5 to 3 microns in size. They stained blue with haematoxylin, pale blue with Giemsa, lively red with PAS, Griedly, red with Ziehl-Neelsen, black with Sudan black, and were surrounded by a light capsule. These were pathogens corresponding to histoplasma capsulatum. Similar pathogens were found in the liver, spleen and lung. In the lymph nodes granulomata containing histiocytes, epitheloid cells and giant cells were visible. The pathogens could be detected here, too, but besides them substances similar to ceroid and apparently originating from disintegrated pathogens were also found. The pathogenic agent accumulates in the cells of the reticuloendothelial system and produces granulomatous changes in the RES, that may bear resemblance to the changes seen in tuberculosis, lymphogranulomatosis and in mycotic diseases.

I. Rózsa, Á. Csontai

(2nd Institute of Pathology, Medical University, Budapest)

Granulomatosis Manifesting itself with Chronic Otitis

Diseases classified under the term of reticuloendothelyosis include unnervous conditions with different aetiology, clinical course and morphological pattern. A certain category of these diseases is characterized by a diffuse proliferation of the RES, while the formation of foci is characteristic of another. HARANGHY's statemenet, that a precise classification is impossible has not lost its validity.

It was TARATYNOW who described eosinophilic granuloma; than JAFFE and LICHTENSTEIN and — almost simultaneosuly — OTANI and EHRLICH studied the condition. One or more foci of destruction or a swelling of bones (principally in childhood) and an abundance of reticuloendothelial tissue in the osteolytic foci are the principal features of the disease. Eosinophils in focal or diffuse distribution are most characteristic of it. The aetiology is obscure, the course usually benign, and the bone lesions respond readily to X-ray irradiation as also to surgery.

The case, of a child 3 years of age is reported. History and local symptoms pointed to chronic otitis. Histology and serial X-rays showed the condition to belong to the reticuloendothelioses. Local treatment and X-ray irradiation put an end to the complaints and the bone foci to disappear. Follow-up examinations proved the benignity of the condition.

I. Loránt, D. Schuler

(2nd Institute of Paediatrics, Medical University, Budapest)

Comparison fo the Clinical and the Histological Findings in Children Suffering from Hodgkin's Disease

JACKSON and PARKER divided Hodgkin's disease into paragranuloma, granuloma and Hodgkin's sarcoma. This division has been claimed to correspond to the clinical course of the disease. In spite of this and some recent classifications it is still unclear whether a parallelism exists between the clinical course and the histological picture of the disease. Most reports contain data only in regard to adults. According to some authors, the prognosis of the disease is worse in children than in adults, while — according to others — both clinical course and duration of the condition are identical in all age groups. —

The material of the Department contained 15 cases of Hodgkin's disease in the last 10 years. 11 were in the 3 to 6 years age group, 14 were boys. These proportions are in keeping with those described in literature. Biopsy was performed in every case: on two or three occasions in 8 cases and not less than 6 times in one case. The first clinical symptom was in 13 out of 15 cases an enlargement of the cervical lymph nodes, and only in 2 cases that of the inguinal ones, without any other general manifestation.

According to the nomenclature of JACKSON and PARKER, 3 cases proved to be paragranulomas, 12 cases typical Hodgkin-granulomas and 2 cases had developed into sarcomas.

The cases under review justify the conclusion that, while diagnosis can be established from the histological picture, it does not allow inferences as to the clinical course of the disease.

S. Keresztury, Ágnes Kőrakó, J. Gál

(Institute of Pathology, Medical University, Debrecen)

Re-Examination of Lymph Nodes Biopsy Material of Children

The biopsy material obtained during the last 5 years from the lymph nodes of those paediatric cases in which it was not possible to establish a definite diagnosis has been re-examined. Out of a total of 146, in 25 cases (17.4%) the lymph nodes afforded no reliable basis to ensure diagnosis. Twenty of these patients (average age, 7 years) were alive and summoned to report for follow-up examination. Fresh lymph nodes were excised and the patients were observed during the following 33 months, a period which was not always sufficient for the establishment of definite conclusions. Repeated lymph-node biopsies were performed at various intervals in 18 children. The cases so observed belonged to four categories.

Group 1. After an uncertain initial histological picture, subsequent observation justified the diagnosis of a malignant lymph-node tumour (5 cases).

Group 2. Although previous examinations had pointed to the probability of malignancy, the fresh biopsy material did not justify a definite diagnosis (6 cases). Members of this group had no complaints at subsequent follow-up examinations, while the general histological picture was still unchanged.

Group 3. Most members of this group displayed histological changes pointing to infectious granuloma (6 cases). With a single exception, these children had no symptoms, and complaints and may be regarded as recovered.

Group 4. This comprised 8 cases in which the clinical picture was very variable, while the lymph nodes showed various and uncertain changes, characterized by diffuse reticulocyte proliferation. Histological picture and clinical course of the disease were rarely in accordance in these cases. To form a definite opinion of the histologically unidentifiable lymph-node lesions would require a long period of clinical and histological observation. The further fate of the patients is being followed up.

J. T. Kelemen

(Institute of Pathology, Medical University, Debrecen)

Clinical Pathology and Histopathologic Diagnosis in Sarcoidosis

36 cases of thoracic sarcoidosis are reported. All of them exhibited the clinical picture characteristic of Boeck's sarcoid. The age of the patients varied between 10 and 50, with an average of 21, years. According to Heilmayer and Wurm's classification, 27 patients were in the first, 9 in the second phase at admission. The Mantoux test was negative in 22 cases, positive in 9 cases at a dilution 1 : 100, and likewise positive in 5 cases at a dilution of 1 : 10.000. Old scarred foci were observed in the lungs in the latter cases. Author's opinion was, that a positive Mantoux reaction did not exclude the possibility of sarcoidosis. Thoracic lesions were combined with erythema nodosum in 10 cases, with uveoparotitis in one case. Tubercle bacilli could not be isolated. The diagnosis was histologically verified in 20 cases and in 4 cases by means of the Nickerson-Kveim test. Pathological changes were always demonstrable in the tu biopsy material obtained from the paratracheal or broncho-pulmonary lymph nodes and the lungs, even if several peripherial lymph nodes had proved negative. Diagnosis was based on the characteristic clinical picture, the negativ bacteriology, and — histologically — on the absence of caseation, the lack of tubercle bacilli, the lack of a lymphocytic margin ttu tendency to form fibres of the tuberculoid granuloma and ttu positive result of the Nickerson-Kveim test. Inoculation of guinea pigs with the triturated lymph nodes and simultaneous cortisone treatment was performed in 5 cases without any observable effect.

K. Lapis

(Research Institute of Oncopathology, Budapest)

Histological and Histochemical Investigation of Lymph Nodes in the Vicinity of Tumours

Approximately 3000 lymph nodes (regional, tributary and remote) have been examined in about 200 cases (partly operated and partly autopsied). The material did not include lymph nodes containing metastases.

The observed changes, affecting all tissue elements of the lymph nodes, can be divided into three main groups according to the nature and trend of the changes, further into nine types according to the affected tissue element and the kind of damage suffered by them.

I. Hyperplastic reactions

1. Follicular hyperplasia
2. Reticular hyperplasia
   a) sinus histiocytosis
   b) pulpar-reticular hyperplasia

II. Desquamative catarrhal processes

1. Acute (Schüppel's sinus catarrh)	56.2%	Changes characteristic of regional tributary lymph nodes
2. "Chronic" sinus catarrh		
a) with phenomena of atrophy in the lymphoid substance	30.7%	
b) with a change in the cellular composition of the lymphoid substance, and with plasmacyte proliferation		

III. Atrophic-sclerotic lesions

1. Lympho-reticular atrophy
2. Fibrous atrophy
3. Hyalinosis
4. Fibrosis-sclerosis
5. Lipomatous atrophy

It is evident from the Table that the nature of the lesions is different according to whether they occur in regional, tributary or those lymph nodes which are distant from, and have no direct lymph communication with, the tumour.

The cellular elements in the lymph nodes undergo notable histochemical changes in connection with the above-mentioned reactions. Increased alkaline and acid phosphatase activity was found to accompany the hyperplastic changes in the activated reticuloendothelial elements. Plasmacytic reaction was observed to be associated with the appearance of a considerable amount of PAS-positive substance. The accumulation of PAS-positive and sudanophile granules was seen in the course of desquamation: it occurred in the cytoplasm of the detached cells without a coincident increase in phosphatase activity.

Fluorescence microscopy of preparations stained according to Haitinger revealed an increased permeability of the capillary walls.

The morphological changes observed in the lymph nodes were not specific. Their study is nevertheless useful in order to gain insight into the behaviour of the tumour-infested organism and its reactive capacity.

Zofia Czechovska

(Warszawa)

Histopathology of the Spleen in Patients with Hypersplenism

Of 58 surgically removed and pathohistologically examined spleens, 17 showed thrombocytopenia, 13 haemolytic anaemia, 19 pancytopenia, 7 hepatolienal syndrome and 2 malignant lymphoma.

In cases of hypersplenism the histological findings subsequent to splenectomy are not specific, but when considered in their totality, they still reveal certain characteristic features.

In thrombocytopenia there were large and active lymphfollicles, large reticulum cells of the red pulp without multiplication of their cell elements, and not very numerous megakariocytes.

Characteristic of haemolytic anaemia is the oversaturation of the red pulp with erythrocytes, further the swelling and hyperchromatism of the sinal endothelium.

In pancytopenia two basic pathohistological forms are conspicuous viz. (1) a cell-abundant type with hyperplasia mainly in the reticulum cells, and (2) a cell-poor type with hyperplasia mainly of the connective tissue. There are intermediate forms and the hypothesis is set forth that type (1) may represent the primary form and type (2) a subsequent secondary form of the splenic change.

The fourth group of hypersplenic changes which is associated clinically with the hepatolineal syndrome, exhibits significant hyperthrophy of the connective tissue and may be regarded as an advanced stage of lienal fibrosis.

The repeatedly established presence of eosinophilia in the spleen together with the active, doublecontoured follicles apparently suggests the immunological character of the underlying morbid process.

Ilse Kühl

(Jena)

Reactions of the Reticuloendothelial, Lymphatic and Haemopoietic Systems to Experimentally Induced Tumours

With a view to studying the condition of and changes in certain tissues, histological, haematological and serological examinations have been performed in mice with tumour induced by means of different cancerogenic hydrocarbons and mice with spontaneous malignant and benign tumours of the mammary gland.

The most essential reactions in mice with malignant tumours are the activation of the reticuloendothelial system and a degeneration of the lymphatic tissues. These changes are much more pronounced in cases of malignancy than in those of benign tumours, and they manifest themselves especially in the spleen and the lymph nodes. Disorders of haemopoiesis, have been discussed in detail. The question to be decided is whether the processes in question are specific for and characteristic of tumours or whether the described reactions should be regarded as belonging to a defence mechanism of immune-biological nature.

J. Juhász, Magda Horváth

(1st Institute of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest)

Tuberculoid Reaction in the Regional Lymph Nodes of Malignant Tumours

Five cases are described in which a malignant tumour had induced epitheloid aud giant cell proliferation in the regional lymph nodes. The histological picture resembled that of sarcoidosis; the tumour lipids may have caused the process. Administration of the lipid extract of human cancer tissue has provoked hyperplasia of the endothelial cells in the lymph-node sinus of guinea pigs, but it has failed to give rise to a tuberculoid reaction. Immune-biological processes probably play a part in the development of the tuberculoid reaction. The distinction of tuberculoid reaction, caused by malignant tumour, from the epitheloid proliferation cansed by other factors, is important in differential diagnosis.

B. Szendi, V. Heim, I. Gy. Lakatos

(Department of Gynaecology, County Hospital, Gyula)

Pelvic Lymph Nodes at 104 Cases of Wertheim's Operation

The results of treatment for cancer of the cervix are not satisfactory and did not improve much during the past 15 to 20 yerars. Absolute cure is achieved in not more than 40 to 50 per cent of the cases and it is only in a few institutes that the 5-year survival rates of stages I and II are higher (50 to 75 per cent). This was a gained by irradiation by some authors, and by a combination of radical surgery with irradiation by others. Many authors claim that the radical surgery and an extensive removal of the pelvic lymph nodes and of the tissues of the pelvic base may be expected to improve the results. Many surgeons explore extra- or intraperitoneally the lymph nodes even at the vaginal radical operation too. It is observed, that irradiation therapy alone does not destroyed the lymph node metastases. After irradiation morphologically intact cellnest of cancer in lymph nodes have been demonstrated in from 20 to 71 per cent at operation. In order to improve the results and particularyl of preventing the metastases and recidivs, the lymph nodes of the vascular triangle, those of the internal, external and obturator blood vessels, the uterine, rectal, aortic, etc. lymph nodes should be taken into consideration. In 104 cases of Wertheim's operations the stage of the cervix cancer the morphological, histological and metastatic distribution of the lymph nodes was as follows

Stage of cervix ca. (clinical)	Case	Enlargement of lymph node	Metastases in lymph nodes
I.	36(3)	20 = 55%	6 = 14%
II.	63(7)	54 = 86%	24 = 38%
III.	5	5 = 100%	5 = 100%
Total	104	79 = 76%	35 = 33%

Beside the 33 per cent lymph nodes with metastasis 43 per cent of the enlarged lymph nodes showed inflammation or congestion. In many cases there were caseation or colliquation and free cancer cells in the lymph nodes, as signs of an increase or decline (respectively) of the defensive capacity. Other authors found lymph node metastases in even higher percentages at carcinoma of the cervix.

It has been suggested that in the classification according to stages the metastatic cases of the cervix cancer must be separated from the nonmetastatic ones. Discussing the problem of the obligatory or facultative removal of lymph nodes in the light of the extension of the genital lymphatic apparatus, its involved nature and its protective role as well as of the bad results of irradiation for metastases, the authors are of the opinion that the lymph nodes should be better removed.

J. Kövi, J. Hidas

(1st Institute of Pathology and Experimental Cancer Research, Medical University, Budapest)

Inclusion Bodies and Phagocytized Structures in Lymph Nodes

The diameter of several hundreds of Flemming's "stainable corpuscles" has been determined in the germinal centre of lymph nodes; it was found to vary between 0.8 and 5.0 μ. The examination was easiest in toluidine blue and Feulgen preparations. Most of the corpuscles were crescent shaped. In a further form the DNA was condensed circularly on the inner side of the nuclear membrane. The condensed nuclear substance adhering to the nuclear membrane was frequently fragmented. Most of the "stainable corpuscles" presented, therefore, a picture of cellular necrosis, a hyperchromasia of the nuclear membrane.

While only few lymph nodes contained such corpuscles, they were present in the germinal centre of about 90 to 95 per cent of the examined 300 vermiform appendages. It has been concluded, that the appearance in the germinal centre of "stainable corpuscles" is due to the destruction of certain cells by bacteria, toxins and other substances which are not potent enough to induce diffuse necrosis of the lymphatic tissue.

A. Haraszti, G. Papp, Magda Stipula

(Institute of Pathological Anatomy, Medical University, Debrecen)

The Lymph-Nodes in Measles

It has long been known that there occur characteristic changes in the lymph nodes during the prodromal phase of measles. A typical phenomenon of this kind is the appearance of the Warthin-Finkeldey-type giant cells which disappear after the prodromal stage. Out of six children who had died of measles we found the said giant cells in a single case only. Still, histological picture was characteristic. Apart from giant cells resembling the Sternberg type observable in Hodgkin's disease,the picture was dominated by pronounced reticulosis and macrophage reaction.

Severe damage of the RES is suggested to play a significant role in the development of different complications associated with measles.

I. Márk, F. Király

(2nd Institute of Pathology, Medical University, Budapest)

Reticulosis Associated with Extensive Nephrocalcinosis

Malignant reticulosis taking an acute course has been observed in an adult subject. The reticular cells destroyed the bony substance, formed calcium metastases and grave nephrocalcinosis. The change in mineral metabolism caused by the calcium mobilized from the bones and the calcium metastases and nephrocalcinosis gave rise to a group of symptoms characteristic of hypercalcaemia.

N. Ratkóczy

(Institute of Radiology, Medical University, Budapest)

Differential Diagnosis of Mediastinal Tumours by Means of Radiography

Radiography makes it possible to recognize mediastinal tumours early and easily. A differentiation of the numerous, anatomically different kinds of tumours is not so easy.

Special X-ray examinations require special apparatuses. Those necessitating surgical intervention involve certain risks. Therefore, "simple" procedures (radioscopy and simple roentgenograms) are preferred; the situation of the tumour shadows, their contours and demarcation, as also their possible segmentation offer a possibility of differentiation in many a case. The present study has the purpose to widen this possibility.

It was demonstrated by the author more than 10 years ago that — especially in overexposed roentgenograms the tuberculous lymph-nodes display a certain complexity or segmentation, while the shadow in Hodgkin's disease is always massive and uniformly homogeneous. This distinction between the two kinds of shadow is known in literature under the term "Ratkóczy's sign".

As to the differentiation of reticulosarcomas, it is a characteristic feature of these tumours that they grow to a large size in a short time without causing symptoms. The first X-ray already shows them to be of the size of a fist or even of a child's head.The shadow is characteristic, being a sharply circumscribed, rounded and homogeneous, *emerging symmetrically* and bilaterally from the hilum *suggestive of the image of a butterfly with outspread wings*. The author claims that the tumour, extending to the anterior mediastinum and leaving free the posterior one, originates from the remaine of the tyhmus.

The said characteristics are still more conspicuous in tomograms. A recognition of such features in lymph-node tumours may ensure the differential diagnosis and save the patient from examinations requiring a major intervention.

G. Kendrey, J. Juhász

(1st Institute of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest)

Hodgkin Paragranuloma

The division of Hodgkin's disease into paragranuloma, granuloma and sarcoma (JACKSON and PARKER) gave rise to numerous arguments. Opinions especially differ as to the proper place and nature of paragranuloma. JACKSON and PARKER regard it as a phase of Hodgkin's disease, with a similar histology but its course is benign.

The separation of the histological pattern of paragranuloma from the other changes of the lymph nodes seems to be justified and it has been convincingly illustrated by several authors (HARRISON, LUMB, SYMMERS, WRIGHT).

In the routine material of our Institute during the ten years between 1951 and 1960, among 79 cases of Hodgkin's disease there were 5 cases of paragranuloma.

According to our examinations the paragranuloma is a histologically well defined disease with a most varying outcome. It can be present for years without causing complaints (1 case). According to some data in the literature it may even disappear.

In 3 cases the condition was transformed into Hodgkin's disease; in 1 case the ultimate result was reticular sarcoma.

The authors do not regard paragranuloma as a phase or variant of Hodgkin's disease; it is considered a disease of lymph nodes corresponding to facultative preblastomatosis.

M. Sellyei, J. Juhász

(1st Institute of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest)

Lymphogranulomatosis and Amyloidosis

In 21 patients who had died in lymphogranulomatosis the post-mortem examination revealed concomitant generalized amyloidosis in 5 cases (3 males, 2 females). The average age was 43 years, and — on an average — 5 years and 9 months had elapsed from the clinical diagnosis of lymphogranulomatosis to the death. All patients suffering from lymphogranulomatosis combined with amyloidosis had received X-ray and cytostatic treatment. Other 16 patients who had received a similar treatment did not develop amyloidosis. Analysis of the serum proteins showed a slight increase of alpha globulins in patients suffering from lymphogranulomatosis alone, and a simultaneous considerable increase of gamma globulins in cases combined with amyloidosis.

It is emphasized that the simultaneous appearance of lymphogranulomatosis and amyloidosis is more frequent than what could be expected on the evidence of literary data. Therapeutic interventions are not regarded as factors contributing to the development of amyloidosis in association with lymphogranulomatosis.

L. Németh, B. Kellner

(Oncopathological Research Institute, Budapest)

Mouse Lymphoid Leukaemia Transferred in the Form of Ascites

In the sandy inbred mouse strain of the Oncopathological Research Institute of Budapest, 10 per cent of the animals younger than one year have been observed to present enlarged lymph nodes. In some animals enlargement of the spleen haematologic alterations and symptoms charasteristic of lymphoid leukaemia presented themselves.

The splenic suspensions of these mice inoculated first into juvenile and later in adult animals induced ascites tumour, which now runs in the 37th passage and permits of a ready transfer into every kind of mouse strain. Passaging produces a generalized tumour without a leukaemic character. Histology of the donor organs and the transferred suggests the condition to be a lymphosarcomatous variation of lymphoid leukaemia.

The high susceptibility of the transferred tumour to chemotherapeutics makes it greatly suitable for screening purposes. Some other features such as malignity, uniformity of devel-

opment, the certainity to take in every kind of mouse strain, provide excellent opportunities for a variety of experimental oncobiological virological and biochemical studies.

Attempts at non-cellular transfer have been unsuccessful.

This ascites tumour we have labelled: NK/Ly

G. Kelényi, J. Pongrácz

(Institute of Pathology, Medical University, Pécs)

Quantitative Studies on the Porphyrin and Myeloperoxidase (Verdoperoxidase)

In earlier investigations (Acta haemat. 1959) it has been observed that in animals inoculated with cells of the transplantable rat chloroleukaemia pathological processes different in character developed, depending on the route of inoculation (subcutaneous, intraperitoneal and intravenous), that differed also in biological behaviour (regressing and progressing solitary chloroma, disseminated chloroma, leukaemic type). In these types the greenish colour and the purple fluorescence of the infiltrates, otherwise marked in chloroleukaemia were most variable. In the present studies the concentration of the porphyrins responsible for the purple fluorescence and the activity of the enzyme myeloperoxidase (verdoperoxidase) giving the green colour were determined quantitatively. In tissues high in porphyrin the myeloperoxidase activity was low, while with low porphyrin concentrations enzyme activity was high. Thus for example the slowly growing solitary chloroma contains much porphyrin and little myeloperoxidase; just the opposite was the case with leukaemic forms. Further studies will may elucidate the causes of the inverse ratio of the two components and clarify the functional correlation between the porphyrins and myeloperoxidase.

J. Pongrácz, G. Kelényi

(Institute of Pathology, Medical University, Pécs)

Enzyme Activity in Regressive Chloromas

Earlier studies concerned with transplantable chloroleukaemia of the rat have shown that on subcutaneous inoculation the tumour rarely takes in adult animals and, if it does take, it develops into a subcutaneous solitary chloroma of slow growth, with subsequent graduai but complete regression. In newborn and infant rats the tumour so induced shows a progressive and frequently disseminating course until it kills the animal. Subcutaneous chloromas can therefore be classified into a regressive and a progressive variant.

Regression of the chloroma following subcutaneous transfer in the adult animal may be due to some immunological effect, the mechanism of which has not yet been explored.

It is assumed that in the regression of subcutaneous chloromas some intracellular hydrolytic enzymes with acid pH optimum may be involved, and which are active during the catabolic phase of the metabolism and bound, according to De Duve, to a submicroscopic cell structure, called lysosome.

In the present experiments acid and alkaline phosphatase and β-glucoronidase activity has been studied quantitatively and qualitatively in both progressive and regressive subcutaneous chloromas. Acid phosphatase and β-glucoronidase activity was found to be significantly higher in regressive tumours than in progressive ones. This support the view that the lysosome-bound enzymes with and acid pH optimum may play role in the regression of chloromas.

I. Kiss

(Department of Pathology, Municipal Hospital, Tétényi út Budapest)

Malignant Thymoma

Two cases of thymic tumour are described. The structure was of an epithelial character in one case and lymphoid in nature in the other. The different cell types of the thymus are supposed to be able to give rise to tumours of one or several cell types simultaneously. Both tumours were malignant and had brought about extensive metastases. In neither of the two cases did myasthenia gravis or insufficiency of the haemopoietic apparatus develop.

L. Józsa, G. Lusztig

(Department of Pathology, County Hospital, Kecskemét)

Primary Reticulosarcoma of the Liver

Primary malignant tumours of the liver are comparatively rare. FRIDERICI collected 215 hepatic sarcomas in the literature up to 1952; of these, reticulosarcoma occurred with the least frequency. We found only 9 such cases in the available literature up to 1955.

Our case was that of a male patient of 58 years, admitted with a diagnosis of apoplexy. Hypertension of a few years standing was mentioned in the history. An ESR of 107 mm was noteworthy among the results of physical examinations and laboratory tests. The patient died after two days of hospitalization.

Autopsy revealed a hypertrophic heart, grave pulmonary oedema and hazelnut-sized tumour nodes in the lungs. The digestive tract, kidneys, genitals, brain and the endocrine organs appeared to be essentially unimpaired. Several fasciculate, sporadically hemorrhagic, soft nodes, some having the size of hazelnuts, others that of a child's fist, were encountered in the liver. Their cut surface was greyish pink, and they were not sharply demarcated from hepatic tissue. Gömöri's impregnation revealed the presence of a delicate fibrous network.

The diagnosis was reticulosarcoma.

Kupffer cells and endothelial cells constitute the reticular elements of the liver. TÖRŐ, WOLF-HEIDEGGER and other authors regard them as being to different developmental phases of one and the same cell. Accordingly, HARANGHY and KABISCH refuse to distinguish between hepatic reticulosarcoma and haemangioendothelial sarcoma. RICHTERICH and WOLF observed high alkaline-phosphatase activity in the Kupffer cells and failed to find it in the endothelial cells.

We regard the Kupffer cells and the endothelial cells as distinct types, and trace reticulosarcomas to the former, haemangioendothelial sarcomas to the latter. Our view seems to be supported apart from other data by the alkaline phosphatase activity in the examined reticulosarcoma.

Erzsébet Füredi, I. Márk, Éva Groholy

(2nd Institute of Pathology, Medical University, Budapest)

Polypous Reticulosarcoma of the Stomach

A case of metastasizing gastric polyposis is described which had assumed a clinically malignant form. Autopsy revealed macrofollicular reticulosarcoma (Brill-Symmers' disease) involving the gastrointestinal tract, lymph nodes and spleen. The process led to characteristic polypoid growth in the stomach.

L. Szijártó, A. Kálló, G. Liszka

(Department of Pathology, János Hospital, Budapest)

Intestinal Lymphomatous Polyposis

Female patient of 24 years. Appendicitis. Appendectomy. Typical ulcerophlegmonous appendicitis, lymphoreticular hyperplasia in appendix. Complaints persist after operation. 14 months later second operation. Crohn's disease in suspected. An intestinal segment 40 cm long is resected, with the larger part of it corresponding to the lower portion of the ileum, the smaller to coecum. At to border of the two an egg sized diverticle. The resecate is filled with smaller pedunculated polyps orally and with bigger flat eminences caudally. The former represented simple lymphatic follicular hyperplasia, the latter an infiltrative proliferation of the lymphoreticular tissue. Examination of a rectal growth a few months later showed the same picture as the small intestinal polyps.

Adenomatous polyposis of the intestine is a well-known condition. Much less in known about lymphomatous polyposis, classified by SCHMIEDEN and WESTHOUSE among the pseudopolyposes. One case was described from the museum of the Frankfurt am Main Institute of Pathology, and LEHMAN described lymphomatous polyps in the rectum. These are all the cases thus far, reported, though similar or related changes have been described recently in the literature.

Similar changes have been observed by radiologists in the terminal ileum. GOLDEN called the radiological pattern of the terminal ileum in various diseases (inflammations, neoplastic reticulopathies) "cobblestone ileum". Among the latter he mentions also lymphatic pseudopolyposis. Still more recently similar changes have been reported by french authors. They think their cases to be alimentary tract manifestations or polypous forms of KUNDRAT's lymphosarcomatosis.

It is undecided whether these observations correspond to several kinds of similar or related diseases, or to different forms, or stages of the same disease. Our case, in which benign and malignant changes occurred side by side, indicates that the different findings may represent different phases of the same disease.

Thus, tumour-like systemic changes similar to adenomatous polyposis may start from the lymphatic follicles of the intestine (lymphomatous polyposis). They are usually develop diffuse, regionally or in many foci at a time and affect exclusively the lymphoreticular tissue of the digestive canal. Similarly to adenomatous polyposis, the changes are beningn at first, but later may become partially or in toto malignant. Even then, however, no true metastases are formed. All these properties tend to indicate that they may be listed with the pseudoleucaemias rather than among tumours. In support of this view is also the relatively benign clinical course.

J. Baló, B. Szende

(1st Institute of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest)

The Pathology of Mycosis Fungoides

Observations were made in five middle-aged males who had died of mycosis fungoides.

The disease has three phases, (i) the premycotic, (ii) the infiltrative, and (iii) the tumorous phase. Cutaneous manifestations of the disease are accompanied by extensive lesions of the internal organs.

Histopathologically, the disease consists in a proliferation of the reticulocytes, accompanied by polymorphous inflammatory infiltration. With the development of the process, the inflammatory reaction becomes weaker and reticular proliferation more and more marked. There exist certain data to indicate that mycosis fungoides may develop into reticulosarcoma or leukemia.

Examination of the skin invariably revealed lesions characteristic of the infiltrative and the tumorous phases. In one of the subjects, a 46 year-old male, a tumour in the right infraclavicular fossa presented the picture of reticulosarcoma. Infiltrations in the internal organs were found in four of the five subjects, in three in the lung, in two in the kidney, heart and stomach, and in one each in the spleen, lymph node, liver, prostate and the epididymis. The infiltrates were often situated around vessels and nerves. Vascular lesions, regarded as specific, were observed in the small and middle-sized arteries, and in one case in the abdominal aorta. These lesions consisted in intimal proliferation with leukocytic infiltration of the media and adventitia.

Cellular inclusions in the epidermis were observed in one instance, a phenomenon which seems to support the theory of APLAS who, on the evidence of animal experiments, has claimed the viral origin of mycosis fungoides.

L. Bakos

(State Institute of Onkology, Budapest)

Interrelations between Mycosis Fungoides and Reticulosarcoma

The clinical picture of mycosis fungoides raises a number of problems. It is still unsettled whether the disease by itself is a syndrome, whether it is caused by some infection and whether it is of inflammatory, granulomatous or neoplastic nature. Out of 10 observed cases, three were "d'emblée" and seven showed the standard features. In each case histology revealed the typical skin symptoms and it was always after their appearance that changes in the lymph nodes had become manifeste. The thermodifference values were negative during the second stage in the standard cases but positive in the areas of mycotic tumours. The low positive values appear to prove the preblastomic character.

In four of the classic cases lymphoreticular blastomas have been observed to arise during treatment.

S. Eckhardt

(State Institute of Oncology, Budapest)

Haematological Data Regarding the Interconnection between Mycosis Fungoides and other Forms of Lymphomatoid Diseases

Haematological analyses have been made in 6 cases of mycosis fungoides. Three of the subjects had had this disease, while the condition had been associated with lymphosarcoma in one, with Hodgkin's disease in another, and with reticulosarcoma in a third case.

Blood and bone marrow counts were normal in the 3 subjects with mycosis fungoides alone.

A transitory leukhaemic pattern appeare din the patient suffering from mycosis associated with lymphosarcoma. The leukocyte count reached 47600; 90 per cent of the lymphocytes were not typical. The sternal bone marrow at the time of the greatest changes in the peripheral count appeared normal, except for a moderate accumulation of lymphoid elements. The leukhaemoid reaction lasted three weeks, and the patient died after the lapse of further four weeks at which time no irregularity except a shift of myelopoiesis to the left was observed. This was explained by the temporary appearance in the circulation of sarcoma cells.

The patient in whom mycosis fungoides was associated with Hodgkin's disease developed pancytopenia.

Leukocytosis and a shift of myelopoiesis to the left were observed in the patient with reticulosarcoma, a phenomenon presumably due to concurrent infection.

The observations justify the following conclusions. (1) Mycosis fungoides is frequently associated with other forms of haemoblastosis. (2) Mycosis fungoides alone produces no characteristic change in the blood counts. (3) If the condition is combined with other forms of lymphomatoid disease, the clinical course, treatment and the complications may give rise to various haematological changes. (4) These changes may call the attention to the possibility of another disease, concurrently existing with mycosis fungoides, whithout the necessity of performing further biopsies.

K. Lapis

(Oncopathological Research Institute, Budapest)

Interconnections between Mycosis Fungoides and Malignant Lymphomas

In 6 (4 men and 2 women) out of 10 cases of mycosis fungoides, it was possible to follow the further course of the disease by way of repeated subsequent biopsies.

Biopsy was made 6 months after the cutaneous manifestations in 4 cases, after 4 months in one, and after several years in another case. The clinical picture showed the process to be in the infiltrative or plaque phase in 4 cases, while the diagnosis was mycosis fungoides d'emblée in 2 cases.

Histology revealed infiltration of the deeper layers in 3 cases, and only circumscribed infiltration of the upper layers in the rest. As a rule, infiltration was perivascular.

The skin usually showed changes suggestive of acanthosis or parakeratosis, sometimes of psoriasis. Pautier's micro-abscesses, of almost pathognomonic value according to Lever, were encountered in 3 cases.

The infiltrates contained several cell types: histiocytes, mature and immature reticulocytes, mycosis cells, lymphocytes, neutrophils, eosinophils, plasmacytes and fibrolasts in varying amounts and proportions. Histiocytes were the predominant elements.They showed a high degree of polymorphism. Silver impregnation revealed a fibrous network in most cases.

Infiltrates in cases of mycosis fungoides d'emblée and, generally, in the tumorous phase were more widespread and displayed fewer cell types, an increased polymorphism of the predominating reticulohistocytic elements and a greater number of mycosis cells and mitotic figures.

Marked or less marked vascular changes were observed in all cases. Sections stained according to Haitinger revealed significant disorders of permeability.

Clinically observable lymph-node lesions were subsequent encountered in 4 of the 6 cases, with sarcoma in one case, atypical lymphogranulomatosis in another case, and Hodgkin's sarcoma in two cases.

The fact that, in three of these four cases, the lymph-node lesions supervened many months and even years after the cutaneous manifestations seems to prove that such lesions indicate a progress of the pathological process. Both these observations and literary data lead to the conclusion that Paltauf-Zumbusch's original conception of the disease has to be revised and that we should regard mycosis fungoides as a peculiar disease of granulation or as a special form of polymorphocytic reticulosis which has a preblastomatous character and may give rise to the prompt or subsequent development of various lympho-reticular blastomas.

T. Venkei

(State Institute of Onkology, Budapest)

Presumable Relations between Mycosis Fungoides and Reticulosarcoma

Although the authors are at variance about the nosology of mycosis fungoides, most of them agree in two essential points, namely, that the disease is not confined to the skin but is of a more general nature, and that the primary symptoms frequently manifest themselves only with a dermal affection and always assume a secondary character in the lymph nodes and inner organs.

On the basis of ten own cases mycosis fungoides is considered granulomatous disease or a peculiar form of polymorphocellular reticulosis. After a certain time, the disease it may as already emphasized by Gottron, give rise to lymphoreticular blastomas.

The relationship of mycosis fungoides and lymphogranulomatosis is not clear. One of the ten cases presented the histological picture of both conditions.

Mycosis fungoides should not be classified with the group of blastomas, it being a distinct condition with certain preblastomatous traits.

S. Braun, Márta Erdélyi, Z. Harmath, A. Udvardy

(Department of Pathology, Municipal Hospital, Péterffy u., Budapest)

Biological and Cytomorphological Effect of Oxygenation on Amytal-Ascites Sarcoma Treated with Janus Green B

The damaging action of ionizing rays is well-known to be more marked if irradiation occurs in the presence of oxygen, and less if exposure to the rays occurs in a completely anaerobic gas phase. No tests seem to have been made concerning the effect of chemical agents in the oxygen phase, and the present experiments, performed with Janus green B, are the first of this kind. A new apparatus has been devised to ensure maximum oxygenation. A total of 1110 test animals were in the experiments used. The ascites tumour of 275 mice was treated in vitro in a constant 15-minute oxygen phase by 2.5×10^{-4} to 0.625×10^{-4} M Janus green B, or at varying times of oxygenation and a constant 2.5×10^{-4} M concentration of the dye. Irrespective of whether the time or the concentration was constant, the increase in survival time became significant when treatment had lasted 15 minutes and the O_2 concentration amounted to 2.5×10^{-4} M. With longer oxygenation or higher concentrations of the dye, the time of survival increased from 30.2 to 185.6 days. A mixture of tumour and dye, treated with oxygen, which leads subsequently to a decomposition of the dye in the N_2-phase, provoked tumorous growth in white mice.

On inoculation with oxygenated amytal ascites sarcoma cells treated with Janus green B the survival of animals was prolonged if the dye concentration had reached 2.5×10^{-4} M and increased with increasing concentrations. The tumor, becoming manifest after a longer or shorter latency, was characterized by a frequency of solid growths and haematogenic and lymphogenic metastases in the parenchymatous organs and, beyond a certain concentration, by the disappearance of ascites. The megakaryocytes of the non-tumorous spleen and the cells of the liver revealed a typical nuclear effect; the latter even developed into hepatoma-like structures. Chromosomal bridges, dicentric chromosomes left out of the mitotic process, as also amitotic symplast-like structures, all of their characteristic of poisons affectively the interphase, were observable in the tumour cells.

I. Kádas

(Department of Pathology, County Hospital, Pécs)

Cancer and Arteriosclerosis

A total of 450 tumorous and non-tumorous cases of subjects over 50 years of age have been studied post-mortem. Our data agrees with those given in the literature, in the group of malignant tumours arteriosclerosis and its complications either did not occur at all, or less frequently than in the non-tumorous cases. We mainly did the microscopic examination of the aorta in 30 cases (aged between 60—70) from either group, in order to demonstrate eventual finer structural differences in the vascular wall; polarisation optical methods seemed eminently suitable for that purpose. Elastic fibres were examined by staining with resorcin fuchsin and by applying Romhányi's aniline reaction combined with digestion by elastase. The fibrillar structure of the ground substance of the vascular wall was studied by Romhányi's precipitating toluidine blue process combined with hyaluronidase treatment. Ebner's phenol reaction and PAS reaction were also applied. All the results indicate that in the tumorous group the negative birefringence of elastic fibres was definitely stronger than in the control group, and the resistance to elastase digestion was more accentuated. All these indicate that the elastic elements are biologically younger and more resistant in the tumorous group. Between the two groups there was no difference in the fibrillar structure of the ground substance in the media, but in the case of the intima a moderate increase of the negative birefringence occurred in the non-tumorous group. This decreased by 43,8 per cent following digestion with hyaluronidase, as compared to the decrease of 20.9 per cent in the tumorous group. Therefore these facts suggest that in addition to the macroscopic vascular differences the two groups differ conspicuously in the stability of vascular wall structures as well.

A. Bajtai

(Department of Pathology, Municipal Hospital, Tétényi út, Budapest)

On the Pathology of Primary Malignant Duodenal Tumours

Five cases of malignant duodenal tumour are discussed. Four were found among about 4000 autopsy findings accumulated during 10 years in a municipal hospital, while the fifth case formed part of the material of the Institute of Pathology and Experimental Cancer Research.

Of the five tumours, four were cancers and one was a sarcoma. The neoplasm was in the superior portion of the duodenum in 2 cases, in the inferior portion in 3 cases. Three of the patients were men, two women. The sarcomatous patient was 57 years old, all the carcinomatous ones were past 60. Symptoms had appeared 3 years before death in 2 cases, 4 months before death in one case, and a month prior to the fatal outcome in one other case. The clinical course was suggestive of ulcer, with typical remissions, in two cases, but only one of them proved to be a carcinomatous ulcer. The history and clinical course of another case of cancerous ulcer were not typical. The of the suprapapillary tumours induced typical pyloric stenosis with cyclic vomitings. No symptom pointing to a disease of the gastrointestinal tract had been noted in the patient with sarcoma.

The joint evidence of the gross and microscopic findings bore out the ulcerous origin of the tumour in two cases of carcinoma. The malignant degeneration of Brunner's glands was clearly visible at the margin of the ulcer in one case, while in two other cases a malignant degeneration of originally beningn tumours seemed to have occurred. Microscopic adenomas issuing from Brunner's glands, found in the submucosa, revealed the tendency to malignant degeneration beyond doubt in one of the latter two cases. The sarcoma proved to be a lymphoreticular tumour, originating in the lymph nodes of the intestinal wall. It was noteworthy in this case that fulminant pulmonary embolism was induced by a fragment detached from a mural thrombus in the vena cava inferior, a phenomenon which appeared to be in association with the tumorous growth.

The correct diagnosis had been get in a single case at operation. Radical operation had been performed on one patient only but even this case had terminated fatally on the 5th postoperative day. The patient had died with symptoms of hepatic coma due to acute yellow atrophy.

Á. Csontai, H. Jellinek, Zsuzsa Halmai

(2nd Institute of Pathology, Medical University, Budapest)

Changes in the Statistics of Pathologico-Anatomical Diagnoses due to the Progress of Therapeutics in the Last Ten Years

It was DOERR, who, first at the congress of the Association of German Pathologists in 1955 and then in a publication of 1957, called attention to a fact that had long been known but had never been scientifically studied, viz. that the nature of diseases was subject to changes with the passage of time. While certain diseases are no longer or hardly ever encountered in our days, new forms are seen to arise. Again, it frequently happens that well-known diseases present new features. Phenomena of this kind are ascribed by DOERR to two factors: (i) to changes in our notions concerning pathology; (ii) to changes in the clinical course of the diseases, be they spontaneous or induced by therapeutic elements.

A survey of the material examined in the IInd Department of Path. Anatomy of the Budapest Medical University (of which 5800 specimens were derived from dissections and 23900 specimens received from other institutes) proved that the number of certain diseases had considerably diminished and that of others increased during the examined period. There were, moreover, diseases which had changed in respect of their clinical manifestations but remained practically unaltered in respect of their fundamental pathological properties. A survey of statistics concerning cancerous diseases showed that their total number had increased, and that — within the overall increase — it was especially the incidence of pulmonary, mammary and rectal carcinomas that showed a conspicous rise. The surveyed material being far from complete, the possibility of errors must be taken into account, but certain changes seem to be very conspicuous nevertheless.

P. Endes, I. Dévényi, Sz. Gomba

(Institute of Pathological Anatomy, Medical University, Debrecen)

Behaviour of Juxtaglomerular Granular Cells Following Heminephrectomy

Reports on the behaviour of the granular cells of the juxtaglomerular apparatus after heminephrectomy are few and contradictory. This behaviour has been studied in white rats at different intervals (from 6 hours to 180 days) after unilateral nephrectomy. A total of 97 animals were used: 54 test animals, 36 controls and 7 animals upon which a sham operation had been performed. Sham operations had the purpose to exclude the possibility of anaesthesia and surgical intervention affecting the behaviour of the examined cells. On the average, 900 glomeruli per animal were examined from the two kidneys in order to determine the juxtaglomerular index. The respective indexes of the removed left kidney and the remaining right kidney were compared, and the difference between the two values was expressed in per cents.

In experiments of short duration (6, 24, 48 hours), granulation seemed to have significantly diminished in the remaining organ, evidently because of the enhanced activity following removal of the contralateral kidney. The granulation index of the remaining kidney rose after one or two weeks, an obviously compensatory process. This index decreased once more very considerably between the 30th and 180th days. This decrease was not a physiological reaction since in such cases hypertensive changes occurred in the remaining kidney, such as a thickening of the glomerular basement membrane, coalescence of the glomerular tufts, hyaline degeneration of the arterioles and the tubular epithelium. Heminephrectomy in rats is well-known to be followed by hypertension and hypertension to be accompanied by a reduced granulation of the juxtaglomerular cells.

J. Balogh

(Department of Pathology, Municipal Hospital, Hódmezővásárhely)

Effect of Conditioning Factors on the Early Vascular Changes due to Neurogenic Hypertension

A rise in the blood pressure of white rats has been observed after regularly repeated unpleasant stimuli, a phenomenon in harmony with the observations of other authors. Morphological changes in the endothelium, the muscular and the elastic layers of the vessels occurred at the very onset of hypertension.

The lesions were gravest in the muscular layer, with degeneration in the form of hyperhydration droplets. Small doses of mineralocorticoids did not provoke either hypertension or tissue lesions; if, however, they were administrered in addition to electric shocks which served as unpleasant stimuli in the experiments, the lesions became much more serious. The observed moderate rise in blood pressure could not have caused the considerable aggravation of the lesions; this must have been due to the disturbed neuro-humoral equilibrium provoked by nervous factors.

Magda Frank

(Department of Pathology, János Hospital, Budapest)

Perirenal Apoplexy of Periarteritic Origin

A 49 year-old male patient had been suffering from multiple sclerosis for 10 years, and developed symptoms of laryngeal tuberculosis 3 years before death. He had had bilateral apical fibrocavernous tuberculosis in the last 2 years of his life. Slitting and increasingly sharp pains in the legs had appeared 10 weeks before death, associated with paresis and atrophy of the calf muscles. Peroneal biopsy had revealed endangiitis obliterans; Blood counts: 10.000 to 20.000 WBC, no eosinophils but many young and monocytic elements. Following a collapse during defecation the patient died within 3 hours with symptoms of acute abdomen, shock, and anoxia.

At autopsy, after removal of the intestines, a large retroperitoneal haematoma was found; it protruded into the left half of the abdominal cavity and extended from the diaphragm to the pelvis; it consisted of both fresh and clotted blood. No rupture was found on the aorta neither on the renal vein and artery nor in the left kidney. There was a narrow strip-haemorrhage under the capsule of the left kidney, with the major part in the fatty capsule of the kidney. The surface of the kidney was uneven, its cut-surface pale. The cortex contained two small necrotic spots with a vessel filled with a pea-sized coagulum in their vicinity. The right kidney revealed a similar picture. The white substance of the brain and spinal cord contained numerous greyish transparent foci of verious sizes. Histologic examination revealed the typical subacute and acute lesions of polyarteritis nodosa in nearly all organs; they were most extensive in the kidneys. The gravest lesions were seen in the renal arteries, with fibrinoid necrosis of the coats, beside some obstructed and recanalizing vessels. Demyelinized foci were present in the grey matter of the brain, but without vascular changes, giving so the pattern of multiple sclerosis. The post-mortem diagnosis was: multiple sclerosis, pulmonary tuberculosis and polyarteritis nodosa. The latter was as usually most pronounced in the kidneys. It was from these diseased renal vessels that the perirenal haematoma had originated, which, due to its large mass, led to the fatal outcome. This haemorrhage was presumably promoted by the increased intraabdominal pressure during defecation too. The nervous system showed no polyangitic lesions. According to the clinical data and the histologic picture the three diseases found in our case seem independent from one another.

Perirenal haematoma (called "apoplexy of the renal bed" by WUNDERLICH in 1856, "massive haemorrhage into the renal bed" by LENK, and its present name got by COENEN) may arise either spontaneously or from an injury. Since the first case of perirenal haematoma, recorded in 1700, about 300 cases have been reported in the literature. It is most often a complication of toxic nephritis and renal tumour and only a small group of them are of polyarteritic origine — rather astonishing phenomenon if we remember that the renal vessels, too, are affected in 75 to 80 per cent of the cases of polyarteritis, and that, moreover, the lesions of renal vessels are generally of utmost gravity in periarteritis nodosa. GRAE reported in 1959 about 26 cases (including his own) registered in the Anglo-American literature as perirenal

haematoma of polyarteritic origin (three were bilateral cases). This number may have increased to about 30 since then.

In the Hungarian literature BALÓ has dealt with this topic but neither he publishes a single case of periarteric origin. So our case is the first observation in this country.

Magda Scholz, T. Marténvi

(Department of Histopathology, Municipal Hospital Uzsoki u. and Municipal Maternity Hospital XIVth District, Budapest)

Internal Adenomyosis

Opinions regarding the aetiology and pathogenesis of adenomyosis are conflicting. The nomenclature employed by the authors is not uniform either. A total of 305 cases has been worked up, of which 70 from a clinical and 235 from an anatomical and histological point of view. Their results have been compared with those of other authors, and the problems connected with internal uterine adenomyosis (81.7% in his material) have been discussed.

Adenomyosis was responsible for 17.11 per cent of all uterine diseases. The clinical diagnosis of the condition is difficult, since many a case (8.6%) elicits no complaints. Development and course of the disease are not decisively influenced by pregnancy or the menopause. Surgical intervention is necessary in every case.

The disease shows no characteristic gross changes from anatomical point of view. The muscles are, as a rule, not involved in the formation of the endometrial foci; the menstrual cycle undergoes no characteristic changes.

Adenomyosis hav been associated with fibromyomatosis in 43.4 per cent, and with mucosal hyperplasia in 64.6 per cent, of the cases. Stromal endometriosis cannot be regarded as a disease by itself; there is an essential difference in the histological structure of intrauterine and extrauterine endometrial foci.

All preferential sites of the condition originate from the coeloma epithelium and it is the multipotency of that epithelial tissue which under hormonal influences give rise to the formation of heterotopic endometrial islets. Adenomyosis is, therefore, regarded as an endophytic form of endometrial hyperplasia.

Anna Kádár, P. Tabák

(2nd Institute of Pathology, Medical University, Budapest)

Vascular Changes in Renal Tuberculosis

A total of 308 tuberculous kidneys removed by surgery in the course of 10 years was examined, 60 of them in detail, in specimens stained with haematoxylin-eosin, Van Gieson's, Azan, resorcinfuchsin, orcein, toluidine blue and Schiff's dye. The age of the patients was under 40 years and blood pressure was not higher than 140 mm Hg systolic and 95 mm Hg diastolic.

The changes were divided into specific and non-specific vascular changes.

The specific process spread invariably from the adventitia to the major renal blood vessels. Unlike in the cases of meningeal processes, no tubercles were found in the intima. The specific process causes a destruction of the blood vessel, a proliferation of the intima and within that the development of a new blood vessel.

With the non-specific changes in the small blood vessels the vascular wall is thickened and the lumen narrowed. An increase of hyaline connective tissue, of elastic fibres and of substances staining with elastic stains are responsible for the narrowing of the lumen. In larger vessels the internal elastic membrane becomes fibriated, multi-layered, at sites segmentally restricted to one portion of the vessel.

These changes closely resemble these seen in cases of hypertension, but are never so severe. As compared with them, they represent a plus merely quantitatively, qualitatively they are the same.

Julia Kiss

(Institute of Pathological Anatomy, Medical University, Szeged)

Endocardial Fibroelastosis

Ten cases of endocardial fibroelastosis have been examined, and the results compared with those obtained from 5 controls of the same age group. The age of the patients varied from 3 days to 5 years; five were males and five females. No maternal disease had been mentioned in any of the histories, and the delivery had been normal in every case. After a normal growth for some time, mostly suddenly dyspnoea, cyanosis and hepatomegaly had developed usually a few days before death.

Post-mortem examinations showed enlargement of the heart which has assumed a spherical shape in most cases. The myocardium (especially of the left ventricle) was thick, the endocardium appeared as a compact whitish layer 2 to 2.5 mm thick. In three cases, the fibroelastosis was especially on the valves conspicuous, with a simultaneous minimal thickening of the left ventricular endocardium. Histologically the thickened endocardium was observed to have invaded the myocardium at several points. This caused a separation of groups of muscle fibres. These fibres showed traces of degeneration and even necrosis and calcification, especially in the papillary muscles.

The aetiology of the disease is still uncertain. The majority of the investigators try to trace it back to a sole cause, while among others the author regards the appearance and the course of the disease as also its variable morphological picture as indicative of several factors being at play, suggesting that the heart is unable to respond to various injuries with an equal number of different tissue reactions; its only reaction is the accumulation of fibroelastic elements which gives rise to the fatal disease.

L. Nagy, J. Fehér

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Thrombosis of the Portal Vein

The cases of portal venous thrombosis have been examined in a material of 6800 autopsies. A comparison with data in the literature showed an increasing incidence of portal thrombosis which was observed in 33 cases of the examined material, mostly in association with liver cirrhosis. Portal thrombosis occurred in every second case of hepatic cancer, associated with cirrhosis. The initial site of the thrombosis was most frequently intrahepatic.

L. Megyeri

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Idiopathic Pulmonary Haemosiderosis in Adults

Idiopathic pulmonary haemosiderosis is a rare disease and occurs chiefly in young age. While more than a hundred cases have been described in children, the number of reported adult cases — verified by autopsy or biopsy — is not more than twenty.

The cases of seven adults and a child are reported in whom idiopathic pulmonary haemosiderosis was diagnosed post mortem. As a control, a few other cases are described who succumbed to pulmonary haemosiderosis of known aetiology.

Gross and microscopic observations are briefly compared. Most characteristic is the impregnation with iron of the elastic fibres and — in cases of long duration — the formation of foreign-body giant cells around the impregnated fibrous elements.

The histological character of the lungs is not specific, and it is only after a careful scrutiny and critical comparison of the general findings that one is justified to regard a haemosiderotic lesion of the lung as being idiopathic.

As to the pathomechanism, capillary dilatation and congestion play an important role in the development of haemorrhages. The inflammatory reaction goes usually hand in hand with haemorrhages in the pulmonary parenchyma.

I. Bartók, Gy. Domján, Éva Horváth

(Institutes of Pathological Anatomy, and of Biochemistry, Medical University, Szeged)

Changes in the Activity of Certain Enzymes in the Liver of Rats with Carbon Tetrachloride Cirrhosis. Histochemical Studies

After inducing hepatic cirrhosis in white rats by means of carbon tetrachloride, the activity of succinic dehydrogenase, cytochrome oxidase, lactic dehydrogenase, adenosine triphosphatase and alkaline phosphatase in the liver was compared with the activity of the same enzymes in healthy livers.

The two dehydrogenases and cytochrome oxidase were found to be of strong activity periportally and of moderate activity centrally in the lobules of intact livers. This characteristic intralobular activity was absent in cirrhosis, and in the pseudolobules of cirrhotic livers cell-groups with normal, reduced or increased activity seemed to alternate irregularly.

ATP-ase was found mostly in the bile canaliculi in intact livers; some activity was observable in the periportal connective tissue and in the wall of vessels and biliary ducts. The activity of the bile canaliculi was usually less or reduced to nil in the rats with cirrhosis, although sometimes it seemed to be more pronounced than in normal livers. A strong activity was found in the accumulated connective tissue.

Alkaline phosphatase in intact livers seemed to be present only in the wall of the vessels and biliary ducts, while, in cirrhosis, it appeared moreover in the connective tissue, in some Kupffer-cells and, rarely, in the bile canaliculi.

Éva Horváth, I. Bartók, Gy. Domján

(Institutes of Pathological Anatomy and of Biochemistry, Medical University, Szeged)

Histochemical Analysis of Different Enzymes in Subtotally Hepatectomized Rats with Carbon Tetrachloride Cirrhosis

Subtotal hepatectomy was performed on intact white rats and on white rats suffering from liver cirrhosis induced by carbon tetrachloride. The activity of succinic dehydrogenase, cytochrome oxidase, lactic dehydrogenase, adenosine triphosphatase and alkaline phosphatase was then studied histochemically in the rest liver at different intervals (1 to 20 days). The examined oxidative enzymes were found to have become less active after subtotal hepatectomy in both the normal and the cirrhotic animals. The rate of normalization seemed to be more rapid in the cirrhotic group. Alkaline phosphatase activity increased in both groups and reached its peak 48 hours after the operation; the increase was more marked in the cirrhotic animals. A significant increase in the activity of ATP-ase was, on the other hand, observable in connection with the hepatic regeneration in the non-cirrhotic animals only. In connection with the regeneration of cirrhotic livers, the normalization of the activity of succinic dehydrogenase, cytochrome oxidase and lactic dehydrogenase was accompanied by a re-establishment of the normal histochemical zonation when while the cirrhotic structure was maintained.

The role played in hepatic regeneration by oxidative enzymes, ATP-ase and alkaline phosphatase, as also the mechanism through which carbon tetrachloride produces its effect, have been discussed.

D. Bachrach, Gy. Baradnay, B. Korpássy

(Institute of Pathological Anatomy and Histology, Medical University, Szeged)

Histophysiological Changes of the Adrenal Cortex in Dehydration and Rehydration

The adrenal cortex of white rats has been studied at different times during water deprivation and the renewed administration of drinking water. The average nuclear volume in the cells of the zona glomerulosa was also determined. The study was complemented by determining haematocrit values and number of erythrocytes, as well as the sodium level of the serum.

Dehydration, due to thirsting, seems to be a particular type of stress, which exerts a stimulating effect on both external layers of the adrenal cortex alike. We found that, instead of a hypertrophy of the fasciculate and an inactivity of the glomerular zone, both phenomena characteristic of most stresses, a functional hypertrophy of both layers occurred. Rehydration brought a gradual decrease in the hypertrophy of the columnar layer, while the normalization of the zona glomerulosa was irregular, and was preceded in some instances by a renewed transitory increase of activity. We observed a considerable retention of sodium in the periods of water deprivation and a slight sodium retention at about the 12th day of renewed water supply. All this seemed to point to some specific function of the glomerular zone, a support of the theory regarding adrenocortical "functional zonation".

The histological symptoms of the hyperactivity of the glomerular layer may arise parallel with both hyperfunction and a state of rest of the antidiuretic centres of the hypothalamus. Changes in the fasciculate zone during dehydration and rehydration go parallel with the activity of the anterior hypothalamic nuclei.

K. Rajkovits

(Institute of Pathology, Medical University, Pécs)

Histochemistry of Lipids Deposited in Tay-Sachs' Disease

Post-mortem findings and the histochemistry of the nervous system are described in connection with a female child who died of amaurotic familial idiocy.

Only the nervous system seemed to be affected by the deposition of lipids which had led to macrogyria.

After extractions with various solvents (acetone, ether, chloroform-methanol), the properties of the remaining fat were studied. It appeared to be of a complex nature and formed a mixture of various lipids. Histochemical reactions revealed no difference between the different parts of the nervous system in respect of lipid storage.

The lipids gave maximal metachromasia on treatment with toluidine blue of pH 3.4; it remained unchanged after extractions with acetone and/or ether.

The lipids were not bound to protein but seemed to be stored in a free form.

G. Bencze, L. Lakatos

(1st Institute of Medicine, Medical University, Szeged)

Lupus Erythematosus (L. E.) Cell Phenomenon Induced in Dogs

Earlier attempts to induce the lupus erythematosus cell phenomenon were unsuccessful in lack of suitable model experiments. After a series of experiments with different species, it has now been possible to provoke the process in dogs by transfusion of plasma from patients, with systemic L. E., using the ZINKHAM-CONLEY method. Sixty minutes after the transfusion of plasma L. E. cells appeared sporadically; their number reached a maximum after 4 to 6 hours and began to diminish from the 24th hour, to persist for about ten days. After the transfer of thoracic fluid or plasma from L. E. positive patients it was equally possible to identify L. E. cells in the peripheral blood of dogs by the ZINKHAM-CONLEY method.

Experiments performed on humans and dogs have shown that there exist two different types of the L. E. plasma factor: a transferable and a non-transferable one. Each of them produces in humans and in dogs, the same result, namely the transferable factor invariably permits of being carried over the both subjects, and the non-transferable to neither of them. A closer inquiry has shown that the appearance of the L. E. phenomenon in human subjects and dogs depends solely on the donor's plasma, regardless of the recipient. Since the first experiments three years ago plasma from 14 L. E. positive patients was transferred into 100 dogs. Not once during this time did the plasma factor type of one and the same patient show any change. This constancy appears to be uninfluenced by the stage of the disease as well as by whether steroid or some other therapy has been applied.

A further observation which concerns the diaplacental transfer of the L. E. factor, merits attention. In the case of an L. E.-positive patient there occurred normal gestation and delivery. Repeated experiments with humans and dogs showed the patient's plasmafactor to be of the non-transferable type. Before and shortly after delivery, L. E. cells were found in the mother but were in the newborn examined immediately and again at intervals. It has been concluded that the non-transferable factor does not in the newborn induce the L. E. cell phenomenon.

I. Fodor, P. Forgács, E. Stark

(State Institute of Rheumatology and Balneology, Budapest)

Notes on the Morphogenesis of Trophic Changes in Denervated Rat Limbs

A portion of about 1 cm was excised from the sciatic and femoral nerve trunks of rats. The gross and microscopic changes observed fell into three categories. (1) Hyperaemia, oedema and cyanosis during the first 4 to 5 days constitute the acute phase. (2) Apart from muscle atrophy, hardly any gross change and only moderate histological changes occur during the second phase which may be termed a period of latency. (3) The third phase from the 12th to the 28th postoperative days, is that of trophic ulceration.

It is suggested that all these changes constitute consecutive phases of a single process, so that it is not necessary to postulate a secondary infection connected with the nerves resection. Circulation seemed to be disturbed in every case, and disturbances of this kind were a significant factor in the development of changes following neurectomy. Circulatory disorders presumably induce a disturbance of tissue metabolism, which may release further pathologic processes. That the phenomena induced by neurectomy occur in three phases points to the possibility of auto-immune mechanisms being involved in the development of trophic ulcers.

T. Neumark, I. Fodor

(State Institute of Rheumatology and Balneology, Budapest)

Recalcification of Bone in vitro

The physiological process of the calcification of cartilage and osteoid substance is still Not clear. The so-called ground substance and enzymatic systems are generally supposed to be involved in the process. Some authors attach more importance to the role of enzymes (That of phosphatase in the first place), while others seem to be more concerned with the ground substance.

The present investigations had the aim of studiing the role played by the ground substance and the sulphate-containing acid mucopolysaccharides in the process of calcification. Similar investigations, reported in the literature, were performed on rachitic epiphyseal cartilage. Sobel's method of recalcination (with slight modifications) was employed in the present experiments.

Some of the sections were treated with testicular hyaluronidase which is known to digest chondroitin sulphuric acid. Recalcination was not observed in vitro under these conditions and the cartilage so treated had lost its metachromatic property. Sulphation of the digested preparations was followed by renewed calcification. The metachromasia of the cartilage indicated the success of sulphatation.

The experimental results have confirmed the assumption that the sulphate-containing acid mucopolysaccharides of the ground substance constitute an important factor in the calcification of bone.

Edit Beregi

(2nd Institute of Pathology, Medical University, Budapest)

Investigations to Influence Experimental Glomerulonephritis

The role of the RES has been studied in the course of experimental glomerulonephritis induced by the author's method (Virchows Arch. path. Anat. **330,** 391 [1957]). Pilocarpine nephritis was inhibited when sensitisation of the animals had been preceded by splenectomy. When, however, sensitisation had prececed splenectomy, glomerulonephritis developed. The dose of colloidal copper blocking RES activity rapidly killed the rabbits. Smaller doses did not inhibit RES activity and acute glomerulonephritis developed.

K. Méhes, K. Jobst

(Institute of Pathology, Medical University, Pécs)

Variations of the Sex Chromatin Characteristics

In our earlier experiments it has been observed that in male rats subjected to androgen treatment only the "C" forms of leukocytary sex chromatins presented a shift in percentage.

To study the function of the hormonal mechanism, we removed the adrenals and the pituitary and observed the subsequent variations of the sex chromatin forms. According to our findings, the distribution of sex chromatin was unaffected only the subsequent androgen treatment gave rise to "C" forms resembling those of the intact animal and a simultaneous appearance of the so called "blackberry" forms.

Gy. Miklós

(Department of Pathology, János Hospital, Budapest)

Contributions to the Pathology of Foetal Infections: Intrauterine Enteritis Associated with Pneumonia

A premature infant weighing 1550 g had died 37 hours after delivery. Necropsy revealed a pseudomembranaceous ulcero-necrotic enteritis combined with organizing peritonitis in addition to interstitial pneumonia with ulcerous changes and hyaline membrane in the respiratory passage. The changes of the digestive and respiratory tracts pointed to intrauterine origin and seemed to have been due to ingestion and aspiration of amniotic fluid harbouring virus.

The inflammatory diseases in newborns died in the first three days of life are usually of intrauterine origin. — Although it is only in stillborns that such an origin can be established with certainty, some factors may still serve as indications, such as the history, the localization and intensty of the change and its probable duration. Most of the changes can be traced back to a prenatal infection due to early rupture of the amnion, protracted delivery, etc.

Intrauterine foetal infections may be conditioned by the mother's state of health, the pathogens, their port of entry and the time of attack. The transfer from mother to foetus may occur through the placenta or by ascension. From the fourth to fifth month of gestation it is normal for the foetus to ingest and aspire amniotic fluid. The intracanalicular appearance in the digestive and respiratory tracts of aminiotic fluid containing pathogens and pus-cells does not necessarily indicate an inflammatory disease (STAEMMLER), unless accompanied by reactive changes in the foetal tissues.

As to the pathologic anatomy of intrauterine enteritis, there are 1. erosive, 2. ulcerous, 3. pseudomembranaceous, 4. necrotising, 5. intersitial and 6. mixed forms. Peritonitis as a frequent complication tends to take the characteristic form of meconium peritonitis when combined with perforation. Chronic inflammation may give rise to scarring with adhesions and atresia.

A brief review is given of the pathology of other intrauterine inflammations (pneumonia).

Aranka László, Anna Tószegi

(Institute of Pathological Anatomy, Medical University, Szeged)

The Causes of Death in Newborn Infants

The post-mortem findings in 1292 newborns in the 14 year material of the Institute have been analysed in order to ascertain the causes of death and their respective incidence. Autopsy revealed intracranial haemorrhage in 339 cases (26,6%); bronchopneumonia in 305 cases (23.6%); inadequate pulmonary ventilation due to immaturity of foetus in 104 cases (8%); aspiration in 100 cases (7.7%); intracranial haemorrhage combined with bronchopneumonia in 84 cases (6.5%); surviving inability in prematures of less than 1000 g. body weight in 54 cases (4.2%); hyaline membrane disease in 38 cases (2.9%); grave inflammations of the

digestive tract in 19 cases (1.5%); erythroblastosis in 18 cases (1.4%); grave inflammations of the respiratory tract, bronchopneumonia not included, in 16 cases (1.2%); pulmonary haemorrhage in 15 cases (1.1%); meningitis in 12 cases (0.9%); septicaemia in 12 cases (0.9%); miscellaneous causes in 30 cases (2.3%); unknown cause of death in 39 cases (3%).

Of the live-born infants, 82.04 per cent were premature and only 17.95 per cent mature. 66.25 per cent of the neonates died within three days after birth (during the so-called trihemeral period), most of them on account of intracranial haemorrhage, aspiration, inadequate ventilation of the lungs due to pulmonary immaturity, hyaline membrane disease.

Aetiology and pathomechanism of the most frequent causes of infantile mortality have been discussed, and comparisons were made between the above data and those in the literature.

Gizella Karácsony

(Institute of Pathological Anatomy, Medical University, Szeged)

Pancreatic Cyst with Hypersplenism

The author describes the case of a female patient of 60 years, who had before her death jaundice, splenomegaly, erythro- and thrombocytopenia. At necrospy the bone marrow was rich in cells and there was increased erythropoiesis. The haematological changes must have been due to an apple-sized pancreatic cyst which compressed the lienal vein and induced splenomegaly. In the pancreas, beside congestion a strong accumulation of reticulocytes, and erythrophagocytosis was observed.

Both the clinical data and the postmortem findings pointed to a case of hypersplenism.

J. Ormos, L. Veress, Gy. Gál, A. Németh

(Institute of Pathological Anatomy and Histology, Institute of Forensic Medicine and 1st Institute of Surgery, Medical University, Szeged)

Morphology of Acute Renal Insufficiency after Conservative Treatment and after Treatment with the Artificial Kidney

Out of 27 patients who had died of acute renal insufficiency (16 after having been subjected to dialysis), 7 showed at autopsy irreversible renal lesions. In 4 of these cases, such grave and advanced forms of subacute diffuse glomerulonephritis occurred as were never observable before the use of the artificial kidney. By means of dialysis it was possible to keep alive these patients up to 32 days, and the renal damage made further progress during such treatment. We regarded two further cases of symmetrical cortical necrosis and a case of nephroblaptosis combined with perirenal apoplexy as belonging to this group.

It is justified to suppose that regeneration and healing could have been achieved in 10 cases, had we succeeded to keep the patients alive longer. There were 9 cases of renal insufficiency in which death was caused by some complication without which recovery might have been achieved. These two groups included 16 cases of nephroblaptosis, and one each of acute diffuse glomerulonephritis, pyelonephritis and thrombosis of the renal artery. Autopsy revealed degenerative-necrotic lesions of the tubular epithelium and, especially in cases of long duration (2 to 4 weeks), casts in the convoluted tubules. The formation of casts reached its maximum earlier in the collecting tubules, in the peripheral zone in particular. Tubulorrhexis combined with granuloma occurred in a few cases of long duration. Already during the first days there were retrogressive changes and signs of regeneration of the tubular epithelium side by side. Two weeks later the regenerating epithelium had at some places either grown over the casts, forming a boundary towards the lumen, or grew round them giving thus rise to double-walled tubules.

We had one further case of nephroblaptosis due to incompatible transfusion, the patient recovered. Renal function became normal in 6 months, but death from other causes ensued nevertheless after 10 months. Autopsy revealed a practically intact renal parenchyma, and only a few interstitial scars were visible, presumably the consequence of interstitial oedema and inflammation.

A. Ábrahám

(University Institute for Zoology and Biology, Szeged)

Microscopic Innervation of the Human Palatine Tonsil

The palatine tonsil is surrounded by a dense nerve plexus readily visible with the conventional methods of impregnation on the part of the organ covered with epithelium as well as on the uncovered one. The nerve plexus, richer on the uncovered side, consists of some myelinated and a greater number of unmyelinated fibres. The nerve fibres extending from the plexus along the blood vessels and independently of them, enter into the lymphatic tissue wherein they form a very delicate network. To impregnate this network is very hard task due to the argyrophilia of the reticular fibres. This technical difficulty and the mode of interpretation gave the reason, that in our previous paper (1) figure Nr. 2 was objected by DAMIANI (2) and STÖHR (3). We should like stress — in both the Hungarian text and the German summary — it has been treated as a probability that the disputed fibres belong to the nervous system (-wahrscheinlich aus Nervenfasern besteht).

Nowadays, we have impregnated properly and quite separately nerve fibres in the lymphatic tissue especially at the edge of the tonsil. Here was found a real plexus and not reticulum. On the epithelium covered side of the tonsil, in the loose connective tissue there are terminal organs of sensory type. Some of them appear as papillary glomerule adhering to the basal layer of epithelium, the others are capsulated nerve endings. We did not see intraepithelial fibres in the tonsil epithelium. Sympathetic ganglia of different size are common in the connective tissue surrounding the tonsil, but never occurs in the lymphatic substance. Today the microscopic innervation of the palatine tonsil is well known. However there are questions to be elucidated: how the single fibres of the plexus in the lymphatic substance connected to the lymph-cells; are intraepithelial fibres present or absent in the epithelium and ganglia in the lymphatic tissue.

D. Szabó, Ilona Banga

(1st Institute of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest)

Binding of P^{32} by Collagen Fibres

Native collagen fibres, isolated from Achilles tendon, and its fractions free from procollagen and tropocollagen were tested for their ability to bind P^{32} (in sodium phosphate). Both the procollagen-free and the tropocollagen-free fractions were found to bind more P^{32} than the native collagenous fibres. The connection between the acid swelling of collagen and its P^{32} binding capacity, further the P^{32} binding capacity of metacollagen were likewise studied.

The results showed the exchange of P^{32} to be reversible in both the procollagen-free and tropocollagen-free fractions.

M. Németh—Csóka

(Central Laboratory, County Hospital, Pécs)

Chemical, Polarization- and Electron-Microscopic Investigations Concerning the Role of Chondroitin Sulphuric Acid in Fibrillogenesis

By adding different amounts of chondroitin sulphuric acid (in the following: ChSA) to acid collagen solution, fibres with different concentrations of ChSA (from 0.3 to 22%) were produced. Under the polarization microscope, the embedded sections were identical in phenol reaction (demonstration of the collagen fibrillar system); their reaction to rivanol and toluidine blue seemed to depend on the ChSA content (determination of acid mucopolysaccharides in the fibrillar ground substance as recommended by ROMHÁNYI). Electron microscopically the fibres with larger ChSA content generally showed crosstriated fibrils of 2000—

2500 Å periodicity. In further experiments, collagen fibres were precipitated by means of differently polymerized ChSA. While all these fibres gave an identical phenol reaction, fibres with a ground substance of depolymerized ChSA reacted neither to rivanol, nor to toluidin blue, not even in preparations of a chemical composition where we expected such reactions. Electron microscopically studied, only collagen fibres with long periods were observed to have been produced under the effect of depolymerized ChSA which were shorter and thicker than the fibres produced with polymer ChSA.

Thus, we may conclude as follows: *a)* ChSA affects merely the first of the two phases of fibrillogenesiis; *b)* the fine structure of the fibrils is determined by the polymerism of the ChSA.

J. Sugár, L. Holczinger

(Research Institute of Oncopathology, Budapest)

Histochemical Examination of the Polarization Optical Behaviour of Reticular Fibres

In the course of experiments on rat kidneys, it has been examined whether in the basement membrane the presence of lipids could be established by means of polarization microscopic and histochemical methods.

Under the polarization microscope, in formalin fixed sections the reticular fibres show a positive double refraction parallel with the long axis of the fibres. On imbibition with glycerol at increasing concentrations, parallel with the increase of the refraction index of glycerol instead of positive double refraction, transversal structures may be demonstrated, proved by the appearance of a negative double refraction. After pretreatment with lipid solvents this negative double refraction does not appear.

In sections embedded in paraffin and fixed in Bouin's or Flemming's fluid, the basement membranes stain instensively with fat stains.

In kidneys fixed in Flemming's solution, Baker's acid-heamatein test is positive; after extraction with pyridine the positivity disappears.

In unfixed frozen sections or sections treated with other fixatives lipids could not be demonstrated either by polarization or histochemically.

The results point to lipids being involved in the structure of the basement membrane in the rat kidney. The fact that their polarization and histochemical demonstration depends on certain circumstances, points to their "masked" nature and their close connection with the structural proteins which form the frame of the fibres.

G. Lelkes, F. Guba

(Institute of Histology and Embryology, Medical University, Debrecen, and Institute of Micromorphology of the Hungarian Academy of Sciences, Budapest)

Electron Microscopic Study of Elastic Fibre Development

The aorta from chicken and rat embryos of various ages have been studied. The intracellular filamentous structures seen in the arterial trunks of 70-hour chicken embryos are held to be the protofibrils of the myocardium under development. In older embryos the aortic cells do not present filamentous structure. On the transversal section of the thoracic aorta of a 20 mm rat embryo the fibres in the outer layers of the vessel wall enter into close contact with the cells and often cannot be differentiated from the cell membrane, whereas in the inner layers they are detached and lose their connection with the cell.

In fibre genesis a certain role is attributed to cellular activity but the existence of an intracellular preformation of the fibrous connective tissue structures is questioned. It remains to be established whether a differentiation of myoblasts, fibroblasts and elastoblasts can be made in the case of the aorta.

D. Tanka, B. Fiam, G. David

(State Institute of Rheumatology and Balneology, Budapest)

Morphological Changes in the Spleen after Nitrogen Mustard Poisoning and X-Ray Irradiation

Rats were subjected to X-ray irradiation with 800 r, equalling DL 50/30 days and their spleens were tested by histochemical methods for citochrome oxidase, succinic dehydrogenase, nonspecific esterase, alkaline and acid phospotase activity. The radiation effect was compared with that of an equale dose of nitrogen mustard. The animals were killed by stunning. From the spleen frozen sections were prepared in the fresh state or after cold formol fixation.

Cytochrome oxidase and succinic dehydrogenase activity showed no notheworthy changes. 24 and 48 hours after irradiation, the localization of alkaline phosphatase activity was indistinct, just a few active cells were seen around the follicle centres. After 120 hours the capillaries were the only parts to give a positive reaction. It was after 240 hours that the activity began to reappear and the localization of enzyme activity became perfect. Nitrogen mustard caused a marked decrease of alkaline phosphatosae activity and two days after the irradiation localization of enzyme activity was indistinct.

Acid phosphatase activity in response to irradiation for 48 hours rose and subsequently decreased with indistinct localization even after two days. Nitrogen mustard caused a considerable reduction of acid phosphatase activity in the first 48 hours, but restitution was complete after 120 hours.

Non-specific esterase activity responsed to both types of injury with the same rise of intensity, to diminish to the control level after some 240 hours.

Our results seem to furnish evidence that ionozing radiation as well as nitrogen mustard may produce either a drop or a rise in enzyme activity. The biochemical difference between the two effects is that the response provoked by radiation develops at a slower rate and under certain conditions lasts much longer than that of nitrogen mustard, which becomes effective soon after exposure and shows a shorter period of restitution.

D. Tanka, G. Dávid

(State Institute of Rheumatology and Balneology, Budapest)

Effect of Nitrogen Mustard Poisoning and Total Body X-Ray Irradiation on the Glycogen Level of the Liver

Rats were irradiated with 800 r, a dose equal to $DL_{50}/30$ days. A second group of animals was treated with nitrogen mustard in a dosage equivalent to $DL_{50}/30$ days. In formalin fixed livers the PAS reaction shoued the glycogen to have disappeared in 24 to 48 hours. Restitution sometimes took 30 days. Simultaneously a series of alcohol fixed livers was studied histochemically. The glycogen content was seen to decrease in 48 hours, with subsequent restitution generally taking 240 hours. The biochemical changes went parallel with the histochemical pattern in alcohol fixated livers.

To explain these observations it is suggested that the glycogen molecules in the liver, when exposed to the effect of radiation or nitrogen mustard, become less polymeric and thus more water soluble. A proof of this was furnished by ultracentrifugal molecular weight determination of the glycogen extracted from the livers of the irradiated or nitrogen mustard poisoned animals. The liver glycogen specimens were grouped according to the degree of PAS positivity, the samples with identical glycogen content were pooled and subjected to ultracentrifugation. The first results seem to support the above hypothesis.

J. Frezik

(Institute of Anatomy, Medical University, Pécs)

Distances Bridged by the Collaterals of the Purkinje Cells

The distance bridged by the collaterals of the Purkinje cells in the vermis and the hemispheres of the cerebellum has been found to be longer than it had been assumed on the strength of histological analyses. The distances in question are quite considerable especially

in the sagittal direction, and may reach the length of several lobes, so that the examined fibres significantly promote cerebellar association. The distance bridged in the transversal direction is considerably less, just a few mm, but still longer than usually supposed.

Mrs. Anna Horváth

(Institute of Pathology, Medical University, Pécs)

Some Notes on the Histochemistry of Unsaturated Lipids

A survey of the usual histochemical procedures has lead to the conclusion that the demonstration of unsaturated lipids depends on the appropriate manner of fixation. Autooxidation could be prevented by the use of a mixture of rongalite and formalin. If due attention is paid to the reactivity and solubility of the halogens, and interhaloids are added, the halogen atoms can be split off by means of alkaline silver solution, so that — after reduction — the site of unsaturated bonds can be demonstrated. This method, while taking the time factor into account, supplies a better picture of unsaturation than the usual methods, some of which are based on similar principles.

G. Csaba, Irén Bernád

(Institute of Histology and Embryology, Medical University, Budapest)

Histophysiology of the Thymus

Model experiments have been made to study the development of Hassall's corpuscles and the thymic cysts. Pieces of trachea or oesophagus from embryonic or newborn rats were implanted under the capsule of the spleen of adult rats and the changes taking place in them were studied. The oesophageal graft soon showed signs of cornification, then a PAS positive substance appeared on top of the epithelial layer and in the cells of the Malpighian layer. The graft is then similar in appearance to the corpuscles of Hassall. The tracheal graft forms cysts similar to the thymic cysts, the epithelial cells secrete a PAS positive substance. According to the morphological picture here the same mechanism as at work as with the thymic cysts. The experiments permit the conclusion that the thymic epithelium, just like the epithelium of the trachea and oesophagus possess potencies of the primitive gut and the appearance of the corpuscles of Hassall and of the cysts would be a manifestation of these potencies. Thus, in the course of functioning the thymic epithelium differentiates as an exocrine gland direction, but its excretion, not being able to leave the gland by some other way, is carried off by cellular transport; this phenomenon may be called cytocrinia. The cells that arise are mast cells, in the genesis of which the thymus plays an eminent role.

Katalin Mold, Gy. Csaba

(Institute of Histology and Embryology, Medical University, Budapest)

Heparin-Affinity of Lymphatic Organs

In tissue cultures of thymic tissue mast cells have been found to form in the area of the mother piece, while they do not or only rarely occur in cultures of lymph node and spleen. Pretreatment of rats with hormones especially cortisone and ACTH, induced intensive mast cell production. In response to cortisone, mast cells appear not only in the area of the mother piece, but in the zone of migration as well. This, too, takes place in the thymus, in the first place, while not in the splenic and lymph node tissue. According to the evidence obtained, cortisone has an important role to play in the formation of mast cells in the thymus, while it destroys other lymphatic organs.

I. Törő jr.

(Institute of Histology and Embryology, Medical University, Budapest)

Some Data to the Problem of the Relation between the Thymus and the Endocrine Glands

In a series of experiments performed on 100 albino rats weighing from 70 to 100 g each, we studied the functional correlation of the thymus and the neurosecretory activity of the hypothalamo-hypophyseal system, and character of the connection between the thymus as a presumptively endocrine organ and the parathyroids developing from the same branchial cleft. Following thymectomy the animals were killed with ether at 24, 48 and 72 hours furthermore after one and two weeks, the parathyroids were removed, fixed in Bouin, embedded in paraffin and 7 micron thick serial sections of them were stained with Gömöri's chromium haematoxylin-phloxin. Simultaneous sham-operations on control animals, inflicting heavy damage on the thymus without removing it, were intended to stimulate occasional effects of the surgical trauma, since the thymus is known to respond readily to any kind of stress.

Following thymectomy, the parathyroidal cells were seen to increase in size; enlargement was most marked after 72 hours. At the same time the basic substance was loosened, the cells displayed a high degree of vacuolization and large cells with a light cytoplasm appeared among the dark polygonal cells forming columns. The controls did not show any conspicuous changes.

In a second series of experiments, performed to study changes due to thymectomy in the paraventricular and supraoptic nuclei of the hypothalamus and the posterior lobe of the pituitary, the following observations were made. After 48 hours vacuoles appeared in the paraventricular nucleus, accompanied by incipient secretion and the granules of secretion, which in the controls were localized in the cytoplasm around the nuclear membrane, showed extracellular accumulation along the nerve fibres in the form of Hering corpuscles.

A high degree of secretion and vacuolization occurred 72 hours after thymectomy in the supraoptic nucleus, with no secretion observable.

Great amounts of colloid appeared in the posterior pituitary-lobe of the controls whereas 72 hours after thymectomy the secretion was completely voided. The same kinds of changes were seen one and two weeks after thymectomy, as an apparent proof of the constant effect of the absence of the thymus.

B. Aros, M. Ertl

(Institute of Histology and Embryology, Medical University, Budapest)

Connections of the Hypothalamus and the Juxtaglomerular Apparatus

The aim of the present study was to explore the endocrine function of the juxtaglomerular apparatus for its presumable correlation with the hypothalamus-hypophyseal system.

The existence of an interrelation between the hypothalamo-hypophyseal system and the juxtaglomerular apparatus has been based on experimental evidence which showed them both to play a certain part in the regulation of blood pressure and water houshold, furthermore in view of the fact that the peripheral endocrine organs appear to be under hypothalamo-hypophyseal control.

In our experiments hypotonic solutions were administered to mice intraperitoneally. The animals were killed at different interwals following treatment. The brains were stained with Gomori's chromium in haematoxylin phloxin Bargmann's modification, the various phases of the neurosecretory process were studied in the supraoptic and paraventricular nuclei and the posterior hypothalamic lobe. The juxtaglomerular apparatus was stained Mallory's haematoxylin dye by us modified. The amount of granular substance in the cytoplasm of juxtaglomerular cells was expressed by a quantitative index and from the changes a curve was plotted.

The amount of granules in the juxtaglomerular cells was found to increase following intraperitoneal administration of hypertonic NaCl, and to diminish, even to disappear, on the administration of hypertonic glucose.

The controls were injected with distilled water.

Observation of the simultaneous hypothalami, neurosecretory process pointed to the existence of an interrelation between neurosecretion and the function of the juxtaglomerular apparatus, as presumed on basis of the similarity between the two phenomena. Examination of the water houshold has failed to establish whether the connection is a direct one or some other factor, such as the function of the adrenal cortex, plays role in the phenomenon observed.

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Hypothalamic and Ependymal Neurosecretion

Earlier investigations into the secretion of the subcommissural organ, an ependymal organ situated below the posterior commissure in the third ventricle, revealed that structure to produce a Gomori-positive substance.

Led by the supposition that the modified ependymal cells of the subcommissural organ were not the only elements in the third ventricle capable of secreting a Gomori-positive substance, the other ependymal organ of the third ventricle, viz. the paraventricular organ has been studied, as also the ependyma lining the walls of the ventricles. It was the ependyma of the ventricular walls that contained a considerable amount of Gomori-positive substance in the fish and in amphibians, while the substance was more abundant in the paraventricular organ of birds and mammals. Secretion was found to be present in the ependyma of all ventricles.

These observations seem to justify the conclusion that the ependyma has the ability to produce a Gomori-positive substance for which the term "ependymal neurosecretion" is suggested. It is similar to, but presumably not identical with hypothalamic neurosecretion. The presumable role of the "ependymal neurosecretion" in the nervous system is discussed in detail.

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Angioarchitecture and Thermoregulation in the Testis

It is common knowledge that for testicular spermatogenesis and for the formation of spermatozoa of full value testicular temperature must be lower than body temperature. This is secured by the descent of the testes to the scrotum, as well as by the architecture of the scrotal wall. The scrotum has a thermoregulatory function, because it can become adjusted to changes in environmental temperature. Recorrelation between thermoregulation and the special vascularization of the testis has been studied.

The internal spermatic artery before entering the testis, forms in the funicle many closely packed loops, then runs from the cranial end of the testis in the tunica albuginea: where it again forms many loops and tendrils. Its end branches are directed at rectangles toward the mediastinum testis, where many loops are formed again. The large numbers of closely packed loops slow down the rate of blood flow and lessen the oscillations of blood pressure caused by pulsation. The small venous branches collecting in the testis reach at rectangles the veins running superficially in the tunica albuginea. These veins are wide, usually run a straight course and anastomose with one another. At the cranial end of the testis they reach the arterial loops, break up into fine rami, which in the form of a dense network sorround the arterial loops. This is the plexus pampiniformis. The plexus and the arterial loops together form the so-called vascular cylinder in the spermatic funicle.

From the point of view of thermoregulation the relation between artery and venous plexus in the vascular cylinder is as follows. In the veins of the plexus testicular blood of lower temperature is flowing, while in the artery blood of body temperature is flowing to the testis. The rate of flow is slow in either direction, because of the presence of the loops and plexuses. The colder blood of the veins cools the warmer blood of the artery; meanwhile, of course, the temperature of the venous blood increases proximally. The vascular cylinder acts in this way as a counter-flow cooler. As the rami of the artery run in the tunica albuginea, the blood in them may become still cooler through contact with the wall of the scrotum.

The conclusions drawn on grounds of the morphological pattern were controlled by a Biotherm type thermocouple. The measurements showed that for example in a bull having a body temperature of 38.7° C the temperature of the testis was 32.6° C, with a temperature difference of 4.2° C between the two ends of the plexus.

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Lymphatic Circulation of the Pancreas

The data published thus far in the literature concerning the lymphatic circulation of the pancreas are reviewed. In the present investigations the regional lymph nodes belonging to the pancreas and the intrapancreatic lymphatic pathways have been studied. The afferent lymphatics were studied experimentally.

1. The areas of the cauda and body of the pancreas form one segment on the basis of the (efferent) lymphatics. As regional lymph nodes the left and medial suprapancreatic lymph nodes belong to this area.

2. The cranial portion of the pancreatic head is the next segment, whence the lymphatics lead to the right suprapancreatic lymph nodes.

3. To the area of the caudal portion of the pancreatic head belong partly the right suprapancreatic, partly the mesenterial lymph nodes.

4. The fourth segment is that of the area of the uncinate process of the pancreas, from which the lymphatics drain into the mesenterial lymph nodes and into those along the inferior vena cava.

The lymphatics in the pancreas respect the segmental borders and it is only interlobularly that lymphatics with a wall of their own can be found.

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The Truncus Bicaroticosubclavius, a Frequent Variation of the Large Vessels Issuing from the Aortic Arch

In 4 cases out of a total of 42 examined the brachiocephalic trunk (innominate artery) and the left carotid artery have been found to originate together from the upper part of the aortic arch and to form, at their initial portion, a common trunk. The common origin appeared especially pronounced from the inner aspect of the aorta, since the wall which normally separates the two vessels was defective. The museum of the Institute possesses a number of similar preparations. All of the four cases in question had been aged persons, and the said anomaly was invariably associated with an anomalous course of the brachiocephalic trunk, which after an upward run, took a high transversal course to the right before the trachea. This anomaly may lead to pathological consequences and prove to be important in surgery.

The said common origin of the two vessels was encountered in 4 month-old human foetuses as well without, however, being associated with the above-described course of the large vessels.

The anomaly at issue, called *truncus bicaroticosubclavius*, occurs, according to literature, in about 10 per cent of human cases, and the space devoted to it in the existing textbooks is certainly insufficient.

Ontogenetically, the existence of the bicaroticosubclavic trunk can be explained by the height of that point at which the arterious trunk passes into the two embryonic ventral aortas. It is from a T-shaped "aortic sac" that this ramification starts; its height becomes less with advancing development, according to the branchial arteries. It is then bent asymmetrically laterally and comes to be exposed to various hydrodynamic influences, so that variations in this area are understandably frequent.

Viewed from a phylogenetic angle, the bicaroticosubclavic trunk is a typical trait in certain lower monkeys. Its greater length makes it the normal configuration in dogs and cats, while the normal human arrangement occurs as a variation in the dog. In the pig, the left common carotid artery becomes detached at a still higher level (bicarotic trunk). No straight phylogenetic line is observable in respect of the configuration of the large vessels.

FORENSIC MEDICINE

Recent Trends in the Medico-Legal Investigation of Traffic Accidents

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Traffic accidents have become a highly actual world problem since the growth of transport has given rise to an alarming increase in their number.

Not less than 40,000 persons die in the U. S. A. every year as the victims of traffic accidents. In other words one person is killed on the road every 15 minutes. Accidents are caused by vehicles every 40 seconds in the German Federal Republic, and there occurs a death from injuries so sustained every 6 minutes. Injuries due to traffic accidents have made an alarming advance in mortality statistics; they have come to occupy the third place after the fatalities due to diseases of the circulatory apparatus and malignant tumours in the statistics of the United States, Austria, Holland, the Soviet Union, Switzerland and a number of other countries. The situation is more favourable in Hungary, although a rising tendency in the frequency of traffic accidents has become unmistakable during the last five years. Notwithstanding the stepping up of preventive measures, the number of traffic accidents with fatal outcome is 15 per cent higher than 3 years ago. Vehicular traffic, with an average mortality rate of 36 per cent, claims nowadays as many victims as tuberculosis, and a further deterioriation of the situation must be reckoned with during the next decades.

Protection from and the prevention of traffic accidents and casualties have acquired primary importance and become a decisive problem of public safety and public health. Economic damage, loss of production and manpower due to traffic accidents, as well as the sum total of individual problems, psychic and bodily harms is inestimable.

Each traffic accident is a complex of many components so that its investigation and the analysis of its origin may be approached from many angles. Since this presentation cannot aspire to completeness, we will content ourselves with discussing a few important and actual questions.

Factors responsible for traffic accidents are usually divided in two categories.

(1) Technical factors, from the part of the vehicles.

(2) Subjective factors, i.e. accidents due to personal elements. They constitute the overwhelming majority, since of the road casualties are mostly caused by the behaviour of the pedestrians, passengers or drivers. According to international statistics, some 75 per cent of the traffic accidents are due

to the drivers, 7 per cent to pedestrians, 14 per cent to road conditions and 3 per cent to climatic factors.

Personal elements (i.e. factors of the second category) may be rooted in the human organism or arise in connection with the momentary situation occasioned by diverse conditions, such as fatigue, alcoholic affection and various diseases.

Fatigue is a complex phenomenon, and it is not easy to define it objectively and accurately for practical purposes. PATRICI distinguishes subjective and objective components. To the first category belong indisposition, weakness and a desire to quit working, while symptoms characteristic of the second category are a reduced oxygen supply, an accumulation of metabolic products (lactic acid, phosphoric acid, creatine, etc.), rise of temperature, and a disturbance of electrolyte equilibrium. The said author distinguishes between local fatigue due to the overstraining of a particular organ, and general fatigue of the entire organism. LEONHARD regards relaxation of the attention in certain situations as the cause of most traffic accidents. It has been proved that a reduction in concentration capacity lies at the base of the major part of casualties. Concentration means attention activated and governed by reason, and manifests itself through reactive readiness and reliability in traffic. Attention may be increased by the exertion of will power, but up to a certain limit only. The faculty of stepping up concentration is not fully developed in youth, and is mostly weakened in old age. These two age classes are, therefore, especially susceptible to risks. MIRKE goes as far as speaking of an accident affinity of young and old persons. There necessarily exists an upper limit to efficiency in middle age as well; if it is approached, the susceptibility to being influenced by disturbing factors will become more pronounced, while panic or a weakening of the impulse to activity will ensue if the mark is overstepped.

Drivers of vehicles must be constantly ready to meet dangerous or unexpected situations with the maximum of attention, and it is only natural that permanent preparedness must be tiring. A particularly intense concentration may be required from the driver on account of the negligence of other persons or any sudden breakdown of the vehicle. Power of concentration is decidedly influenced by traits of character, the actual somatic condition, a sudden loss of self-confidence, and any psycho-physical disorder or stress.

A systematic training is apt to enhance the faculty of concentration and so to counteract fatigue and afford a certain degree of protection from disturbing influences. Practice, besides conferring technical skill and thus enhancing public safety, stregthens concentration capacity and increases reactive readiness. Trained actions become, according to the Pavlovian terminology, dynamically stereotyped, i.e. automatic. The vigilance of a practised driver is relieved by such automatisms. He has an intuitive assurance, and, if necessary, his actions will be governed by automatisms operating at the threshold of consciousness.

It should, however, be noted that in cases of sudden surprise, automatic actions of the said type may prove harmful and even become the causative agents of accidents. While disburdening the driver, they may impair the elasticity of his attention. Vehicular traffic presents so many surprising moments that, as pointed out by LEONHARD, empirically acquired assurance is not always sufficient for coping with them. Permanent stresses undermine the elasticity of concentrating power, it is deprived of its last reserves so that the driver no longer possesses the necessary presence of mind, and his actions will lack purposefulness in emergencies. He will become too active or too passive. He may, for example, drive the car against a tree, turn it into a ditch or lose hold of the steering wheel.

The safety of traffic requires, therefore, that stresses to which drivers are exposed be reduced to the lowest possible limit. It is necessary to analyse past accidents in the light of these considerations, and to establish, on a scientific basis, those norms which must not be violated, e.g. the permissible maximum of mileage, the working hours of professional drivers, etc.

The influence of alcohol is universally recognized as a causative factor of traffic accidents. Statistics in this respect show wide fluctuations so that the known percentage of accidents due to alcoholic influences varies between 6.4 and 74.0 per cent. Statistics for Hungary show, according to OROVECZ, BUDVÁRI and GYÖNGYÖSI, the following figures. Alcoholic involvement was established in 38 per cent of the fatal and in 65 per cent of all traffic accidents in the years 1948 to 1950. In 1958 and 1959, 24.4 per cent of the accidents were due to the negligence of intoxicated drivers and 12.1 per cent to that of inebriated pedestrians.

Both the above data and those reported by other authors are based on determinations concerning the concentration of alcohol in serum. The number of such determinations made in drivers who were not involved in accidents is very low. VÁMOSI examined a number of such drivers and found alcoholic symptoms in 50 per cent. According to NELKER's report, out of the clientele of a Swedish insurance company, which accepted only teetotallers for insurance, only 7.7 per cent had fallen victim to traffic accidents against 11.4 per cent in the simultaneous case of other insurance companies. HOLCOM conducted researches in this respect in Chicago, and found that while 87.9 per cent of 1750 drivers who had caused no accident had no trace of alcohol in their blood, the corresponding figure was 53.37 per cent for 260 drivers who had been involved in accidents.

Let us now see a few interesting figures concerning the serum level of alcohol determined after accidents. Analysing 850 traffic accidents in France, JEAN found a level exceeding 0.25 per cent in 60.36 cent and one exceeding 0.11 per cent in 74.3 per cent of the cases. According to DÉROBERT, the concentration of alcohol in blood was higher than 0.15 per cent in 46 per cent

of patients hospitalized on account of traffic accidents. The Bucharest Institute of Forensic Medicine found the blood-level of alcohol to exceed 0.1 per cent in 70 per cent of the persons involved in traffic accidents. VÁMOSI affirms that, compared with the alcohol-free condition, the risk of accidents is 7 times higher if the serum level of the alcohol is at or below 0.1 per cent; the corresponding figures being 31 times at 0.15 per cent and 128 times above this level.

Laboratory determination of the alcohol concentration in blood does not yield reliable information on the effect of alcohol in each individual case. The blood concentration itself and the time coordinate of the serum-alcohol curve are determined by numerous factors. For example, distilled spiritus yield a higher concentration of alcohol in the blood and induce a higher degree of intoxication than other beverages containing the same amount of alcohol. The effect of alcoholic drinks ingested on an empty stomach is strong and rapid, while consumption of alcohol together with fat results in a lower blood level. The blood level is comparatively low and lasting if the alcohol has been consumed slowly and together with food. ELBEL and others found that habitual drinkers split and excrete alcohol three times as rapidly as persons who are unaccustomed to it. The breakdown of alcohol is, on the other hand, diminished in inveterate alcoholists or persons with hepatic lesion. Vomiting and nausea temporarily inhibit absorption. The interval is followed by an increase of the alcohol level but there occurs no change in the trend of the curve. It has been claimed that the serum level of alcohol is influenced by insignificant losses of blood, e.g. one of 50 ml in a person of 60 kg body weight. After serious loss of blood the serum alcohol level undergoes a double change, the curve descends, then ascends deeply, to descend once more; this second descent is followed by another slight ascent. On the other hand, not even blood losses of 200 to 500 ml seemed to affect the value of serum alcohol in HUMBREL's experiments.

The opinions concerning the connections between blood curve and clinical symptoms are likewise contradictory.

It has been shown that neuro-vegetative manifestations and ataxia belong to the ascending branch of the curve, i.e. occur mostly before the concentration of blood alcohol has reached its peak, while neuro-vascular manifestations characterize the descending branch, i.e. occur during the phase of elimination. This significant observation justifies the conclusion that it is not during the first hour after the consumption of alcohol, i.e. during the most vigorous clinical manifestations, that the danger of accidents is the most imminent, nor 60 to 90 minutes later when the curve of blood alcohol reaches its peak, but during the 3rd to 4th hour, at a time when the persons already feel, or impress others as being, perfectly sober.

With equal blood levels alcoholic affection may be different according to the individual tolerance. Of primary significance from the viewpoint of

traffic accidents is the effect of alcohol on the central nervous system. The occurrence or avoidance of accidents depends to a great extent on the faculties of perception and estimation, as also on changes in the neuromuscular reactions. It has been demonstrated by HORVÁTH and PIRITYI-NAGY among others that the consumption of a moderate amount of alcohol increases the acuity of vision but reduces adaptability. A reduction of visual acuity is mostly associated with an impairment of hearing. The acoustic threshold is shifted upward, especially if the driver's attention is diverted (SCHWARZ, ERICH, GRÜNER).

The sensitivity of the skin and the conjunctiva plays an important role in estimating the velocity of motorcycles. GOLDBERG claims that — if unaffected by alcohol — the skin of the face is capable of sensing atmospheric changes of 30 mmHg, while differences of 60 mmHg and above are only perceived if the serum alcohol level reaches 0.12 per cent. IVÁNYI found that the consumption of only 1/3 litre of wine reduced the sensitivity of the skin very considerably.

These observations encourage us to define our standpoint by suggesting that it should be prohibited for the drivers of motor vehicles to consume, within 10 to 12 hours before taking their seat before the steering wheel, that amount of alcohol which results in a serum level of 0.12 to 0.15 per cent this would correspond to about 6/10 to 7/10 1 of 10 per cent wine. This means that nobody who wants to drive a motor vehicle should be allowed to have even the slightest trace of alcohol in the blood, an undoubtedly radical but necessary rule.

How far a driver is affected by alcohol in a particular case should not be ascertained on the sole evidence of laboratory data; clinical symptoms and individual factors have also to be considered.

Literature contains numerous recent reports dealing with the effect of various drugs in connection with the consumption of alcoholic drinks. In Hungary, FAZEKAS, HORVÁTH and J. NAGY have made investigations of this kind. Research work in this field is being conducted in two directions. The efforts of investigators have long been directed towards finding some agent which would promote the excretion of alcohol, cancel, or at least decrease, its effects. It was demonstrated by SMITH in 1960 that ACTH and cortisone were capable of arresting the manifestations of acute alcoholic intoxication, while — according to other authors — these drugs are effective only in cases of severe intoxication. STULFAUT and JUNGE claim that a single large dose of insulin facilitates the process of recovering sobriety. Their method cannot be applied on account of the danger of hypoglycaemic shock. Sugars, e.g. glucose, fructose or laevulose, were found to promote the decomposition of alcohol in animal experiments, while their action seemed to be negligible in human individuals. All this is to say that, as of this moment, there is no drug which would efficiently and reliably counteract the effects of alcohol.

The attention of other investigators has been directed towards drugs which enhance the effects of alcohol. This side of the problem must not be underestimated at a time when the use of pharmaceutical products is steadily increasing, when a veritable pharmacomania exists in certain respects. It should be borne in mind that the various sedatives and hypnotics, certain analgesics and anti-allergens, antihistamines and alcohol, render each other more active. Although few experiments have been made in this respect, the results of numerous empirical observations are nevertheless available. It was established by NIEDERMANN (1939) that the combined effect of barbiturate and alcohol was veritably dangerous. Drugs containing aminopyrine produce disulfisane-like effect. It is suggested by WAGNER — a surprising suggestion — that 0.2 g of caffeine, i.e. two cups of coffee, if taken by vegetatively labile persons, impair the uniformity and reliability of kinetic processes. That there exists a widespread misuse in respect of barbiturates is well-known. Their sedative effect increases the self-assurance of drivers but produces at the same time an untoward influence upon their driving efficiency. The absorption of larger doses results in fatigue and somnolence. Barbiturates are slowly excreted so that preparations containing them, if taken in the evening, may be still effective the next morning. The danger of habituation and accumulation should also be taken into account. The efficiency of drivers is further impaired by phenmetrazine and pyribenramine.

All these observations should be made known in wide medical circles, while information regarding the uses and abuses of drugs would seem desirable among the drivers of motor vehicles. Pharmaceutical works would do well to indicate the effects of the described nature on the packages or in the directions for the use of their preparations.

A sudden loss of consciousness or any disease which is accompanied by disturbances of consciousness, further certain defects of the perceptive faculty, may likewise be the cause of traffic accidents. Many a motor car is driven by persons afflicted with cardiac and circulatory disorders who are unaware of their illness. TAMÁSKA and SOLYMOSI analysed in 1959 the cause of the sudden death of 60 drivers and found that, in the last analysis, it was vascular disease in not less than 50 cases. They attributed (at least partly) the comparatively high incidence of cardiac and vascular diseases among drivers of motor cars to the chronic inhalation of carbon monoxide. These authors want to promote public safety by a more frequent and more thorough medicral examination of the drivers. Other authors, e.g. NORMANN and SCHWARZ, share this view. Yet, cardiac and vascular disorders are not the only factors that have to be examined in a systematic manner. Traffic accidents due to epileptic seizures, diabetes, myotonia, senile alterations or organoleptic and various somatic defects are comparatively rare, so that problems connected with them will be discussed together with the requirements and tests of fitness.

Altough literature contains many papers on the requirements to be prescribed for the drivers of motor vehicles, the precise formulation of these requirements, as also the kinds of test to which drivers should be subjected, are still under discussion. That these questions are unsolved is, to some extent at least, due to the rapid advance of technical science in its bearing upon transport. It has repeatedly happened that by the time the experts succeeded in fixing certain medical requirements under the existing technical conditions, the latter had changed so considerably as to render the whole arrangement anachronistic. Let us just remember the supersonic speed which suddenly made the hitherto usual speed of 120 kg/hr obsolete; let us also think of the suddenly emerged problem of graviationless fields.

Medical requirements which drivers of motor vehicles have to satisfy cover a wide range. Relying on the evidence of traffic accidents recorded by the Zurich Institute of Forensic Medicine during several of decades, SCHWARZ divides drivers into three categories, each category having to comply with a special set of requirements. So does NORMANN.

The drivers of heavy trucks, traction engines and autobuses belong to the first, those of taxis, lorries and tractors to the second, and drivers of motor cars and motorcycles to the third category. Although it seems justified to estimate the suitability for driving according to the vehicle to be driven, a rigid categorization may lead from the examination of individual features to a conventionalized judgement of suitability.

Since all aspects of the suitability for driving cannot be discussed in this paper, we must restrict ourselves to the treatment of those problems which are still controversial.

Views are contradictory as regards the lower and upper age limit of drivers. Of recent, LANGEN studied this problem in KRETSCHMER's institute. He refuses to accept the notion that aged drivers mean a special danger for traffic safety. He has shown that, as regards bodily injuries, the worst age group is that between 18 and 25 years, the members of which cause ten times as many accidents as the old age group. The fact that other authors are of a different opinion in this respect, and that their opinion has likewise been on statistical evidence, is due to errors in statistical methodology. The influence of the drivers' age cannot be estimated correctly unless the distribution of drivers involved in accidents over the different age groups is compared with the age distribution of all drivers. None of the available statistical data seems to have been so calculated. It is worthy of note that the number of pedestrian victims is especially high in the age group between 6 and 14 years; the curve goes down thereafter to ascend once more after 55 years. A study of traffic accidents induced the authorities in the German Federal Republic to raise the lower age limit of drivers from 18 to 20 years. The matter of age limit is no light problem, and it would be highly desirable

to establish universal rules in this respect. We do not advocate the establishment of an exclusive upper age limit but suggest, instead, that drivers above a certain age should be obliged to submit themselves to medical examination at short intervals. A rule of this nature would promote public safety and at the same time protect the ageing driver.

Diseases, apt to cause accidents, preclude or reduce the suitability for driving. This raises the controversial problem of epilepsy. Naturally, epileptics are ruled out by transport undertakings as unfit for employment, and the question whether persons susceptible to seizures are to be allowed to drive at all is important from both the medical and the legal standpoint. There are two sharply opposite views in this respect. Certain authors, representatives of the radical group, hold that anybody who has had even a single seizure remains epileptic as long as he or she lives, and no driving licence must be issued to such persons. Not even conditional licences should be allowed in these cases, since seizures cannot be expected to manifest themselves at regular intervals, nor can the appearance of aura be relied upon with absolute certainty. This is the attitude of SIMONS, HOLZBACH, GROSSJOHAN and the American authors. HOLZBACH points out that, as regards epileptic drivers, not only the safety of the general public but also that of the drivers is at stake, i.e. of persons who frequently lack discernment and ethical faculties. — TÖNNIS, NITTNER and the German EEG Society take a different attitude. It is emphasized by NITTNER that to foretell the possibility of a sudden seizure involving loss of consciousness requires the unanimous opinion of the physician, psychologist and traffic expert. The mere fact of a seizure does not suffice to make its victim irrevocably unfit for driving. TÖNNIS suggests that the medical expert should make the patient sign a declaration to the effect that he or she has been duly informed of the risks involved in his or her condition. According to the view of the German EEG Society, as summed up by MEYER and NICKELIST, persons whose EEG shows no irregularity and whose seizure invariably occurs at night, may be accepted as drivers.

Another controversial question concerns the required minimum length of time since the last attack. MIKES is of the opinion that a driving licence can be issued to an epileptic person who has had no seizure for at least three years. Such drivers must not take any form of alcohol within 24 hours before driving, nor should they be allowed to drive longer than 6 hours.

We regard the medicolegal aspect of the problem as of primary importance. According to judicial practice, seizure or loss of consciousness prevent the indictability of criminal acts on the plea of non compos mentis. It follows that it must always be on the favourable evidence of a certificate, jointly issued by a neurologist-psychiatrist and a medical expert of transport psychology, that driving licences are issued or given back to epileptics.

As regards diabetics, OBERDIXE found not more than 72.000 such persons among 12 million individuals in possession of a driving licence. Only 3600 of the 72.000 diabetics used insulin, and the number of diabetics who had been involved in traffic accidents was quite negligible. The Zurich Institute of Forensic Medicine had likewise favourable experiences in this respect; SCHWARZ holds nevertheless that the visual acuity of diabetics should be examined at regular intervals. Opinion regarding diabetic drivers is almost unanimously favourable in Western literature. We, too, are of the opinion that diabetics cannot be flatly denied the right to drive motor cars: if the sugar tolerance of a diabetic can be maintained at a normal level without insulin, by the diet alone, he is entitled to hold a driving licence.

Optic functions are of decisive significance in the matter of suitability. Traffic is nowadays almost exclusively regulated by means of optical signs. Requirements concerning vision and colour perception have long been established, and a regular control of these faculties is universal. It is for this reason that the number of traffic offences due to disturbances in colour perception is fairly low. We cannot subscribe to the view represented by SCHUBER and several other authors that a faultless distinction of colours is less important for motor-car drivers than for railwaymen or shipmen. Colour blindness may be of harmful influence upon the action of a driver at a moment of sudden peril.

Also auditory functions should be perfectly unimpaired in the case of professional drivers. Out of 3000 deaf drivers 0.14 per cent were repeatedly involved in accidents. Experts agree that deaf persons and those hard of hearing are entitled to receive driving licence if they are otherwise healthy, their visual power is unimpaired and if they produce a permit of an institute for the care of deaf-mutes. This view is shared by SCHUBER, PONSOLD and SCHWARZ.

We cannot dwell upon diseases of negligible practical significance, such as for instance myatonia: drivers suffering from this disease are practically unknown to literature. Hypertension, an extremely widespread phenomenon in our days, does not incapacitate for driving if it does not give rise to sequelae which, in themselves, preclude suitability.

A somatic and psychologic analysis of the examined individual must be performed, and the entire personality of the would-be driver has to be synthesized in the course of the suitability test. Its result must rely on the evaluation of the candidate's psychophysical condition and his ability to compensate bodily or mental defects. Bodily defects can be well-compensated, and need not necessarily preclude the issue of licence for drivers of private cars.

A report, published by MARKUS in 1956, shows the dominant position of cranio-cerebral injuries in the statistics of traffic accidents. Analysing the post mortem records made during the last 8 years in the First Department of Surgery of the Vienna Medical University concerning persons who had been killed in traffic accidents, the quoted author found that the cause of death was

cranial and cerebral injury in 60 per cent of the fatalities. WALTER and LŐW surveyed the case history of 497 victims of motor-car accidents, and found grave or slight cranio-cerebral injuries in 407 cases. Not less than 56 per cent of all cerebral injuries were due to traffic accidents, thus occupying the first place in the statistics.

In 1958, the present author, together with KOMÁROMY, examined 133 persons who had sustained injury of the skull; 49 per cent of them died at the scene of the accident or during transportation. One third of those who had reached the hospital alive died the very same day. Patients who survived for 2—3 weeks or longer had, as a rule, no secondary injuries; they had sustained nothing but cranio-cerebral trauma and received the most up-to-date treatment such as tracheotomy, positive pressure breathing, hibernation, etc. It was on 30 patients, out of a total of 87 cranio-cerebral cases examined by us, that tracheotomy was performed in the hospital, and the major part of such operations was done in the neurosurgical department which shows that many of our surgical and casualty wards still maintain an attitude of reserve towards tracheotomy. The number of patients who succumbed to their cranio-cerebral injuries in the hospital amounted to 87, and 37 of them had been operated upon. Autopsy findings failed to bear out the suitability of the surgical intervention in 10 cases.

Among the 50 non-operated cases there were 12 in which anatomical changes could have been remedied by surgical means (2 cases of epidural and 10 of extensive subdural haematoma).

Nearly half of the persons with brain injury examined by us had been the victims of traffic accidents. According to the statistics for 1959, cranial or cerebral injuries were sustained in 81.6 per cent of all motorcycle accidents in Hungary. A percentage of this height must serve as warning. ELGÁR is quite justified in declaring that the motorcycle is the most widespread instrument of suicide for the youth. Spinal injuries are often disregarded in such cases, as the picture is overwhelmingly dominated by the symptoms of other more serious traumata. It is worthy of note that, in Lob's clinical material, only 2.34 per cent of the spinal injuries had been sustained in motorcycle accidents against 13.1 per cent in respect of other vehicles. That the incidence of cervico-spinal injuries was lower in motorcycle accidents may be due to that most of the persons meeting with such accidents usually die on the spot and do not, therefore, figure in clinical or hospital statistics.

Cervico-spinal injury is likely to occur if the head suffers frontal impact, a frequent phenomenon in motorcar and motorcycle accidents; the forehead is knocked against the windscreen in the case of cars, and the driver or passenger is flung headlong from the seat in the case of cycles. Fracture of the dorsal and lumbar vertebrae is likely to occur if a person falls out of a motor car through an open door. It is imperative that the vertebrae should be carefully examined

and X-rays from several directions be made in such cases even if the injured person does not utter complaints pointing to spinal injury.

It often happens that a disregard of vertebral fractures gives rise to claims for damages and a lengthy civil action against the medical attendant.

LENKER encountered thoracic and pulmonary injuries in 45 per cent of the examined traffic accidents. Nonpenetrating thoracic injury and also sternal fracture may result from the impact of the chest on the steering wheel or the handle bar. The oesophagus, trachea and larynx are seldom damaged. According to Lob's figures, the mortality rate of thoracic, pulmonary and mediastinal injuries is 12 per cent.

The possibility of cardiac injuries should always be taken into account in connection with thoracic lesions. HALLERMANN, at the autopsy of 467 persons who had died of non-penetrating thoracic injuries, found a concomitant trauma of the heart in 26.5 per cent of these cases. MEESSEN observed heart injury in 6 per cent of the examined traffic accidents. Commotion and contusion of the heart are two separate affections. While commotion means a dysfunction of the heart, contusion may arise from any mechanical stress on the thoracic wall or any lesion of the anterior wall of the heart or the septum injury of the posterior wall may occur if the heart is knocked against the spine. All these may result in circumscribed epicardial, myocardial and subendocardial haemorrhages. According to DERRA, injury of the coronary vessels (with thrombosis and aneurysm as sequelae) is likewise frequent. A penetrating injury of the large vessels rarely requires medical care, since death mostly supervenes on the spot.

Abdominal injuries are comparatively rare. It is not always easy to diagnose and differentiate thoracic, visceral and renal lesions. Hepatic injuries are frequent in motorcycle accidents, and their mortality rate is high. BOCK observed subcutaneous renal trauma in 10 per cent of his autopsy material. The ratio of renal lesions has been given as 0.5 and 0.9 per cent, respectively, by HELLER and MORRIS, and 8.0 per cent by WILLSON and REXPORT. Contusion of the kidney is comparatively frequent in collisions of motorcar and motorcycle. Repeated urine examinations should be performed in every case, since this alone enables the physician to recognize mild renal contusion or the development of the crush syndrome in due time. Of course, all possible means of renal diagnostics have to be employed as early as possible.

According to the statistical data for Switzerland, published by BAUER, injuries of the extremities occurred in 44.2 per cent of the traffic accidents, of which 14.8 per cent involved the upper, and 29.4 per cent the lower extremities. Injury of the upper extremity is frequently associated with a lesion of the brachial plexus; this has a poor prognosis. In the descending order of frequency, bone fractures most commonly sustained in traffic accidents are those of the tibia, the base of the skull, the calvaria, the femur, and the

humerus. According to the statistical data published by COLLE, JORGANSEN et al., 3870 children under 7 years of age were injured in traffic accidents between 1954 and 1956 in Denmark, a country where, as is known, the number of cyclists is very high. Injuries of the lower extremities were sustained by 12.0 per cent, and a quarter of them suffered fracture of the bone as well. About three quarters of the fractures were those of the tibia. Statistical data, compiled by MILFORD and ANDERSON in Californian hospitals, show that the frequency of injuries affecting the lower extremities was 53 per cent higher than that in respect of the upper limbs. Let us note that a measure is now planned in Czechoslovakia which will forbid children under 8 years to ride a bicycle in public thoroughfares.

Injuries of the extremities, sustained in traffic accidents, do not essentially differ from other traumata; yet, the fact that certain types of injuries are more or less characteristic of certain types of vehicles, as also the conspicuous frequency of certain injuries, should be regarded as indicating the necessity of certain definite improvements in the construction of motor vehicles.

The unavoidable growth of the number of traffic accidents makes it imperative that increased attention be paid to the matter of first aid, the transportation of the victims and their hospital treatment. While the chief aim of the first-aid service to be the quick and careful conveyance of the patients, its task is nowadays regarded as including a quick and efficient medical and surgical care of traumatized persons. It is in recognition of this trend that the Hungarian National First-Aid Service has been provided with ambulance cars equipped for surgical interventions. The training of expert traumatologists and the establishment of casualty wards have yielded most satisfactory results. A detailed schedule for the medical and general hygienic care of the victims of traffic accidents has been elaborated by BOGATSCHEVSKY on the strength of the lessons drawn from accidents that had occurred on the high way between Kharkov and Simferopol.

The ratio of persons hospitalized on account of traffic accidents increased from 17.2 to 22.2 per cent in the German Federal Republic between 1954 and 1956. The average duration of hospital treatment was approximately 3 months, while BOGATCHEVSKY's data yield an average of 27.7 days.

The services concerned with the transportation and the hospitalization of injured persons are exposed to particular periodical stresses caused by a peculiar rhythmicity of traffic accidents; their number shows sudden peakes on certain days, in the rush hours, during week-ends, and according to meteorological factors. So far, Monday has proved to be the most dangerous day as regards traffic accidents in Budapest. Traumatological institutions, existing in large cities, have to prepare for such emergencies.

The medicolegal expert, in order to be able to give satisfactory answers to a great many — often contradictory — questions arising in connection with

traffic accidents, has to be familiar with the syndromes due to injuries, with the principles governing the transportation and hospital treatment of traumatized persons. Relying on the sole evidence of the post-mortem finding, he has to give an expert opinion regarding the cause of death, the mechanism and localization of the injuries and the quality of the medical care that had been given to the deceased person. Further tasks of the medicolegal expert include statements concerning the subsequent and expectable condition of the injured person, as also his present and future fitness for work; the expert is also expected to tell whether victims of traffic accidents are likely to recover full health. A correct estimation of post-traumatic syndromes in their bearing on the injured person's earning capacity is extremely important, and the task of the expert is essentially different from that of the common practitioner. The statements of medicolegal experts are usually based on documents, medical certificates, case histories, and the examination of the traumatized person (if the person is alive), and it is frequently many months and even years after the accident that this examination takes place. To give correct expert opinion based on late symptoms and written documents is fairly difficult. The difficulty of the task is considerably enhanced by the well-known fact that, as a rule, most available case histories, medical certificates, as also the evidence of eye witnesses are highly subjective and deficient.

The first-aid surgeon is concerned only with the momentarily predominant symptoms and the momentarily necessary treatment, while the house surgeon who receives the patient in the hospital is almost exclusively concerned with questions of diagnosis and long-term therapy. While recording his findings, he may easily disregard the possibility that they might later constitute the conclusive evidence in criminal proceedings or in a civil action. The history recorded at admission is seldom complete or sufficiently detailed. It is therefore necessary to add later such data as will facilitate a subsequent reconstruction of the circumstances in which the injury was suffered. The case record should always contain the statement that the injured person did or did not lose consciousness, and, if so, how long the patient was unconscious. It must contain furthermore a detailed pretraumatic history, as also data regarding the character and personality of the patient, the latter sometimes based on information gained from the patient's next of kin. Such data are of fundamental importance for a correct estimation of post-traumatic manifestations and a possible change in the nature of the traumatized person.

The medical expert performs his work by virtue of a judicial order, and it is often restricted to a perusal of the existing files and a single examination. If detailed information regarding the original injury is lacking and the expert is obliged to complete it by examining and listening to the patient who presents a varying picture of post-traumatic syndrome, he cannot expect to receive objective and reliable answers. It is seldom possible to ascertain the organic

cause of the manifest symptoms, and patients well cognizant of the pertinent symptoms and with a tendency towards exaggeration may mislead even the most casehardened medical expert. Ambulatory examination cannot suffice in such cases, and only careful observation in a hospital will yield reliable results. Any pathological changes due to earlier lesions and diseases must be ascertained so as to prevent the patient from ascribing everything to the recent accident. Of course, the courts are endeavoured to finish each case as soon as possible. It is not easy for the medical expert to foretell the probable duration of full recovery shortly after the accident, and such prediction is especially difficult in cases of cranial injuries which manifest themselves with a great variety of symptoms and require a long time for healing.

The discussion of cranio-cerebral injuries leads to the question of electroencephalography. Changes observed in the EEG are not specific and may be due to any organic disease of the brain, so that this finding alone does not suffice for a correct estimation of subsequent complaints. Traumatic epilepsy is an exception inasmuch as the EEG may supply conclusive evidence by enabling us to differentiate psychic and organic seizures. The EEG should be repeated in doubtful cases.

It is often asked by the courts whether the victim of the traffic accident had suffered commotion or contusion of the brain, and if his or her condition may be expected to improve. Commotion is — according to the German term that has found acceptance in Hungary — a reversible damage without morphological changes. Its principal criterion consists in a longer or shorter loss of consciousness followed by amnesia. On the other hand, cerebral contusion is always associated with anatomical changes and so accompanied by organic neurological symptoms. With the patient being unconscious, it is sometimes extremely difficult to distinguish between these two lesions. The courts usually want to know whether the actual state of the injured person is connected with the trauma sustained in the traffic accident. It is well-known, that the complaints of the patient and the neurologic manifestations in the organism are influenced by diverse individual factors, e.g. the age of the victim, his pretraumatic condition, the site of the injuries, the manner of treatment, various post-traumatic circumstances, etc. We know of patients who, after having suffered cerebral commotion, had developed no organic neural symptoms and yet did not cease to utter serious complaints for many months and even for years. There exist, on the other hand, persons in whom, although they had recovered without observable consequences and without any complaints, it was possible to demonstrate lesions in the brain. It is well-known to medical experts that persons without demonstrable organic lesions may be afflicted with a long-term post-traumatic neurosis. Persons with organic injuries have, as a rule, a strong will aimed at recovery, and their complete social rehabilitation is usually achieved in a short time. We suggest that, in submitting his

opinion to the court, the medical expert should refrain from making a sharp distinction between cerebral contusion and commotion by defining the consequences of the trauma as "concussion".

Measures for the prevention of technical and traffic accidents have the fundamental purpose to establish such technical, constructional and traffic regulations as can be expected to preclude all possibility of accidents. This goal is, of course, not attainable, since human errors and shortcomings cannot be eliminated altogether. What we can and must achieve is the largest possible reduction of the number of traffic accidents and their victims.

This desired end can be well approached by the achievements of technical science, e.g. well-planned constructions of new roads and towns, improvement of existing ways and thoroughfares, the building of flyovers, elimination of level crossings, a bright pavement of the roads and their adequate illumination. The safety of vehicular traffic is promoted by suitable propaganda and education, by an appeal to the sense of responsibility of the youth, by the introduction of up-to-date tests of suitability for would-be drivers, further by the establishment of lower and upper age limits even for cyclists. An overburdening of the roads and streets with superfluous and impractical traffic signs should be avoided. The technical safety of the vehicles has to be augmented. Of recent, numerous reports have been published on the advantages of a safety belt which would fix the shoulder as well, and prevent the occupants of cars from bumping forward in collisions. There exists a great resistance to the adoption of such belts both in Hungary and elsewhere. In Czechoslovakia, crash helmets are compulsory for motorcyclists in the extraurban traffic. Crash helmets are known to be widespread in the countries of the North and West.

It emphasized by SCHWARZ that, compared with other emergencies, representatives of the medical sciences devote too little attention to traffic accidents, although it is the doctor who gains the best insight into these brutal occurrences and their consequences. While fully agreeing with this criticism, we feel bound to add that medical work alone cannot yield satisfactory results in this respect. Publicity on a wide scale is needed, and we are glad to recognize that a campagne for the prevention of traffic accidents has been launched in Hungary. It is, however, to be regretted that, so far, no medical experts have been invited to co-operate. Problems arising in the sphere of forensic medicine are handled by medicolegal experts, so that no far-reaching results can be expected without their collaboration.

Traffic accidents constitute problems of many facets. Their prevention or a reduction of their number requires the co-operation of all experts concerned, and no improvement of the existing situation can be realized without the joint efforts of all those who are professionally interested in the problem of traffic accidents.

DISCUSSION

Gy. Szuchovszky, I. Kenyeres

(Institute of Forensic Medicine, Medical University, Budapest)

Statistical Data Concerning Fatal Accidents Registered at the Institute of Forensic Medicine of Budapest University Medical School in the Period 1945—1959

The post-mortem findings made during 15 years in connection with fatal accidents are analysed. It has been necessary slightly to modify that part of the VIth international nomenclature which refers to the causes of violent death. A total of 32963 autopsies were performed during the period under review, and 8544 thereof (27.5%) represented cases in which death had been due to accident. This is a high percentage, but the correctness of the figure is borne out by all other available data. The annual proportion of fatal accidents shows neither a definite upward nor a definite downward tendency although, according to the Central Bureau of Statistics, the proportion of accidents to other causes of death has decidedly risen during the last two decades. The percentage of the causes of death in the material at issue was as follows.

Traffic accidents	48,5
Death from violent impact not due to traffic accident	19.5
Suffocation	9.0
Poisoning	8.2
Burn	6.6
Electric shock, thunderstroke	2.7
Shot	1.1
Diverse or unknown causes	4.4

The distribution according to age approximately corresponded to the proportion of the affected age classes within the total population. Within such limits, it is noteworthy that certain kinds of accidents seemed to occur with especial frequency in certain age classes. For instance, nearly 50 per cent of the electric shocks were sustained by persons between 15 and 30 years of age; about 40 per cent of the suffocations occurred during the first year of life, while most of the victims of fatal burns and falls were old subjects.

I. Kenyeres, Gy. Szuchovszky

(Institute of Forensic Medicine, Medical University, Budapest)

Analysis of 4176 Traffic Accidents Registered in the Autopsy Records of the Budapest Institute of Forensic Medicine

The universal increase in the number of traffic accidents makes this problem highly important from a medico-legal point of view. It was on account of this consideration that our statistical data concerning fatal traffic accidents has been subjected to special analysis.

The number of necropsies performed in the Institute between 1945 and 1959 totalled 32963, and 30020 thereof have been evaluated. Death was due to traffic accidents in 4176 cases, an incidence of 13.4 per cent. Generally speaking, the frequency of traffic accidents showed no significant change during the examined period, and it was only from 1957—1958 that a certain increasing tendency could be observed. In view of the fact that all fatal cases of traffic accidents occurring in Budapest are autopsied at our Institute, it can be affirmed that it was only during the last 2 to 3 years of the 15-year period under review that the number of street accidents in Budapest took an upward trend. It is attributed to the fact that the number of motor cars and, in general, vehicular traffic began to increase at a rapid rate in those years. It has been found that, in contradiction to the data in the literature, one third of all accidents happened to persons in the age class between 40 and 60 years. About 75 per cent of the victims were men, but this discrepancy between the sexes tends to decrease with advancing age so that the ratio was actually 1 : 1 above 80 years. The vehicles causing death were motor vehicles in 33, tramways and similar vehicles in 49, and other kinds of vehicles in 18 per cent of the cases. Most accidents occurred in May, September and December.

A. Ács, L. Jegesi, L. Tolnay

(District Court of the Metropolitan Area and Institute of Forensic Medicine, Medical University, Budapest)

Causes of Public Road Accidents and their Social Aspects

A review of the criminal indictments regarding 534 cases of public road accidents has been made to study the individual culpability residing mainly in the vehicle driver's behaviour, and to point out some social aspects.

The offences qualified in 534 cases as imperilment to life or physical soundness, in 161 as violation of the traffic rules; 34 defendants were acquitted.

As to the kind of offence against traffic rules, there were 287 cases of driving under the influence of alcohol; next in the order of frequency followed improper overtaking, wrong turning, failure to grant priority and neglecting speed limit. Statistical tables are given to show variations in the occurrence of such accidents according to hour of day and day of week. Data regarding distribution of the perpetrators according to age and occupation showed the overwhelming majority to have been between 20 and 40 years of age and half of them professional drivers.

The social aspects to be considered in connection with these crimes cover such questions as individual injury (422 cases) and the extent of material loss. The claimed damages in social or private property amounted to 1300 forints for one defendant on the average.

L. Virág, Á. Szabó, I. Örményi

(Department of Pathology, County Hospital, Szombathely)

Interrelations between Meteorological Conditions and Accidents

A review of accidents in County Vas in 1958 furnished the opportunity to examine the eventual interrelation between changes in meteorological conditions and the occurrence of accidents. The following facts have been revealed.

1. The majority of accidents coincided with frontal passages and interrelations between the two groups of events could be demonstrated by mathematical means in terms of cause and effect.

2. More than two thirds of the accidents occurred during periods of intensive solar activity.

3. The frequency of accidents seemed to be enhanced by the break-through of subtropical air masses, particularly when these appeared in the higher atmosphere and were accompanied by frontal changes.

4. Considering overall meteorological conditions, it appears that both the cyclonic and the anticyclonic situation play some part as complex factors in the occurrence of accidents.

L. Jegesi, L. Tolnay, A. Ács

(Institute of Forensic Medicine, Medical University, Budapest and District Court of the Metropolitan Area)

Characteristics of Injuries in Public Road Accidents

The inquest papers, inspection minutes and medical reports in connection with 755 casualties due to public road accidents have been reviewed.

The data revealed that of the injured subjects 38.3 per cent rode motorcycles, 20.7 per cent motorcars of various description, 5.7 per cent horse waggons and 14.6 per cent bicycles. 20.7 per cent of the victims were pedestrians. More injuries of fatal or severe consequence occurred among the motorcyclists and pedestrians than among the other groups of victims.

The data further demonstrate for the motorcycle and car passengers the figures indicating the distribution of suffered injuries according to body areas and the period of restoration. The same particulars together with the type of the vehicle are given for cyclists and pedestrians.

About half of the injuries were due to collision with a motorcycle but more fatal or severe casualties were caused by motorcars than by the other vehicles.

Finally, the greater part of casualties occurred in connection with motorcycles as 431 out of 755 victims were either cyclists or pedestrians or rode themselves a motorcycle.

S. Lukács, I. Körmöczi, J. Rupnik

(Department of Pathology, County Hospital, Miskolc)

Skull and Chest Injuries due to Traffic Accidents

A statistical review of traffic accidents has shown a considerable proportion of skull and chest injuries. The data recorded by the Security Authorities of County Borsod, in agreement with the experience of our own Department, seems to indicate, contrary to KIRSCHNER's opinion, that the number of traffic accidents and injuries with lethal issue can be reduced by

1. administrative measures combined with enlightening propaganda, and
2. the introduction of modern therapeutical principles.

Re 1. The number of public road accidents in County Borsod was 331 in 1958 with 33 death; 515 in 1959 with 54 death; and 192 in 1960 (up to 1st October) with 20 death. Eighty per cent of the fatalities were due to driving under the influence of alcohol and the motorcycle of all highroad vehicle types was responsible for the majority. The decrease of casualties in 1960 was attributable to the greater emphasis laid on public road control and preventive propaganda on part of the communication authorities.

Re 2. As regards the treatment of thoracic injuries, it is the more complicated forms of rib fracture that require the greatest attention, since the cardio-respiratory disturbance accelerates the fatal issue. Apparently the most efficient treatment to prevent this pathological process is the intermittent positive pressure breathing.

Special importance for the success of treatment of head and brain injuries is attributed to tracheotomy and in diagnostically doubtful cases to the wider application of trephining.

In conclusion the following measures are emphasized.

1. Closer co-operation with the authorities to prevent accidents.
2. More intensive control of public roads with a view transfer injured persons to hospital in due time.
3. More extensive use of resuscitation, bilateral trephining, tracheotomy and intermittent positive pressure breathing.

L. Komáromy

(Institute of Traumatology, Budapest)

Factors Influencing the Survival of Patients with Cerebral Injuries

There are numerous, though not equivalent, factors on which the survival of patients with grave cerebral lesions depends. Morphological and functional changes induced by the injuring force constitute the first, and therapeutical procedures the second group of the decisive factors.

Statistical data are adduced to prove that the presence or absence of a fracture of the skull does not, in itself, indicate the gravity of the lesion or the probable course and termination of the disease. More important and almost decisive from this point of view is the nature of the brain-stem functions. This is well indicated by the degree of the disturbance of the consciousness as also by the extent to which vegetative functions are out of gear. The mortality rate of non-penetrating cranio-cerebral injuries grows with the increasing depth of coma. About half of the examined fatal cases consisted of polytraumatized patients, i.e. persons who had sustained also other injuries (thorac, abdomen, spinal column, extremities) the effect of which was added to that of the cerebral lesion or induced a vicious circle. Multiple injuries thus, mean a grave prognosis, especially if cerebral lesion is associated with thoracic or spinal injury.

Appropriate treatment covers the second category of factors influencing survival. Much progress has been made in this respect during the last years. Resort to up-to-date procedures (tracheotomy, neurosurgery, artificial hibernation, etc.) has undoubtedly increased the number of survivals.

B. Sőrés

(Hospital of the Hung. First Aid Service, Budapest)

Cranial and Cerebral Injuries conditioned by Alcoholic Intoxication

Out of 4678 alcohol intoxications at the Ambulance Hospital, 128 cases of brain commotion associated with skull and brain injury have been reviewed by statistical methods to determine how drunkenness had affected — either mitigating or aggraveting — the patients' state. The results were as follows.

1. Head injury owing to accident occurred in 22 per cent of intoxicated subjects as contrasted to 12.7 per cent of the non-intoxicated patients.

As to the kind of head injury, among the 22 per cent intoxicated subjects there was
7 per cent commotion
0.17 per cent intracranial lesion
14.83 per cent injury of soft parts.
In the 12.7 per cent of non-intoxicad patients, there was 2.2 per cent commotion 0.03 per cent intracranial lesion
10.47 per cent injury of soft parts.

The data show that twice as many cranial and cerebral cases occurred among the intoxicated, than among the non-intoxicated patients.

2. Sex distribution in the intoxicated group was 88 per cent and 12 per cent women, as against 51 and 49 per cent respectively in the non-intoxicated group.

3. More intoxicated subjects (41.6 per cent) were wounded in consequence of fall, than by assault (30.4 per cent) or traffic accident (35 per cent) in contrast to the non-intoxicated victims with 39.1 per cent due to traffic accidents, 36.3 per cent to fall and 18.2 per cent to assault. Not in a single case was there impact by a dropped object responsible for the accident among the drunken as against 6.4 per cent among the non-intoxicated. As to the place of occurrence, 84 per cent of the intoxicated groups were wounded in the street and 0.8 per cent only at their working places; of the non-intoxicated 70 per cent were overtaken in the street, 16.3 per cent in their homes and 13.7 per cent at work.

4. As to interrelations between blood alcohol level and time of treatment, the following table shows a conspicuous rise of the latter as the degree of intoxication grows from moderate to severe:

‰	days in hospital		
	1—4	4—8	8—12
below 0.03			
0.03—0.5	1		
0.5 —1	1	14	14
1 —2	19	15	15
2 —3.5	16	12	15
3.5 —5		1	5

The following conclusions can be drawn.

a) The diagnosis is difficult, because alcoholic intoxication disguises the early symptoms of cerebral injury or makes them uninterpretable. Consequently the objective methods of examination (such as skull X-ray CSF and neurological tests, EEG) are gaining significance in throwing light upon the neurological state. It is endeavoured, therefore, to perform these tests at an early point of time, by all means within 48 hours of the accident.

b) Acute alcoholic intoxication increases the effect of the associated cerebral injury and aggravates the pathological picture. This is proved by the frequency of their common occurrence and the prolonged period of treatment.

K. Lukács

(Hospital of the Hung. First Aid Service, Budapest)

Temporary Faintness of Drivers

Selecting from a material of more than 500 cases in which motor-car drivers brought from the streets to the hospital of the National First Aid Service, the author analyses those cases of passing faintness which, by arresting the purposeful and necessary movements required from drivers, may — under the effect of the stress preceding accidents — achieve pathological significance. The addition to a suitable frame of mind, the fine and precise coordination of unimpaired sensorymotor reactive readiness, perceptive faculty and purposeful motions is necessary to enable the driver to perform his task. Paroxysmal loss of these faculties in 27 cases of epilepsy and 2 cases of hypoglycaemia are analysed.

The conditions which ensure the required frame of mind were found to have disappeared in 3 cases of acute psychosis and 52 cases of so-called functional faintness associated with agitation. To the same category belonged the cases of 213 drivers who had been taken to hospital with alcoholic intoxication. When judging the fitness of such drivers after recovery, the after-effects of the intoxication must not be ignored, and it has to be borne in mind that the effect of carbon monoxide, inevitably inhaled during driving, and that of alcohol during the elimination phase, are synergistic. To an intermediate group of incapacitating factors belong cardiac and vascular diseases which affect the sensorymotor reactive readiness; potentiated by the effect of carbon monoxide and the effect of stress, they may provoke temporary incapacity of action. Noteworthy of the 18 cases of cardiac decompensation were 3 cases of myocardial infarct and a case of paroxysmal tachycardia; there were 23 cases of sudden hypertension, among them 5 cases of apoplexy. Ophthalmic disorders may have been due to a functional impairment of the ciliary muscle (caused by drugs or circulatory disorders, etc.). Drivers may further be temporarily incapacitated by anoxic myopia after looking at a TV program or, else, by micropsia or macropsia. The examined material included further 4 cases of cerebrovascular lesion, 2 cases of tetany and 41 cases of enteritis: the purposeful regularity of the drivers movements had been imperilled in all of them dehydration, muscle-metabolism.

It follows from these observations that drivers, after having once caused traffic accident, should be subjected to renewed medical examination and tested for symptoms of all of the above-mentioned disorders. It is further suggested that the level of carbon monoxide in the blood of drivers should be determined from time to time, and that pathologists should devote more interest to the problems here discussed. The present time is well suited for a solution of the problems under review: individual shortcomings have to be remedied by the society without socially degrading the individual.

Gy. Szuchovszky

(Institute of Forensic Medicine, Medical University, Budapest)

Sanction of Traffic Regulations in Criminal Law

The discipline and safety of traffic are important enough to be safeguarded by Criminal Law. Certain problems concerning the protection of traffic regulations are discussed because the steadily growing number of traffic incidents has induced the government to prepare the draft of a modified Criminal Code in which traffic regulations are afforded enhanced protection. A discussion of the existing and the intended measures is followed by a detailed comparison of the actual with the proposed code.

Although the number of definitions and punishments is less in the draft than in the present code, the draft seems to be well suited for a more efficaceous prevention of traffic offences, because their proposed definitions are such as to cover the whole range of foreseeable infringements of traffic rules. §. 181 of the draft contains the definition of complex offences so that the tribunals will be able to apply adequately severe measures if necessary. The new code will undoubtedly increase the number of criminal proceedings occasioned by traffic offences but cannot, on the other hand, fail to decrease their frequency in the long run.

L. Takácsy, O. Szűcs

(Institute of Forensic Medicine, Medical University, Budapest and Hospital of the Hungarian State Railways)

Cardiac Lesions due to Chest Injury in Traffic Accidents

Among 300 subjects suffering chest injury in traffic accidents 47.3 per cent presented gross cardiac lesion. The victim's chances to survive depend largely on his heart's general condition before the accident. Death occurred in half an hour after the event in 49.6 per cent and within one hour in 75.4 per cent. The most dangerous among these injuries were those when the force had acted at right angles to the sternal region. The parts most gravely damaged were the left ventricle and the right auricle. (37.3 per cent of the accidents occurred with cars, 20 per cent with trams, 12 per cent with local trains, 10 per cent with ordinary trains and 9 per cent with motorcycles.)

Sometimes the heart appears to be normal at first inspection, but microscopic changes may still be present. The object of our examinations was to reveal the earliest of these cardiac changes, with reference to the injured person's survival. The usual histochemical methods have failed to reveal traumatic changes in the heart muscle in those surviving for one hour (Zenker's degeneration, disk-like and granular dis-integration of the myofibrils).

After an injury to the heart the ECG is generally indicative of myocardial ischaemia. Attempts have been made to reveal traumatic myocardial anoxia at an early stage by means of the periodic acid Schiff reaction as described by YOKOYAMA et al. Ruling out the possibilities of decomposition and glycogen (saliva digestion), the one-hour survivors presented focal PAS positivity and early ischaemic necrosis in the myocardial fibres, probably owing to reflectory arterial spasm subsequent to the injury and the muscle contusion.

R. Budvári

(Institute of Forensic Medicine, Medical University, Budapest)

Spontaneous Pneumothorax in Connection with Skull Injury

A case is reported where the correlation of spontaneous pneumothorax with cerebral trauma seems to be proved. A child of 9 years had suffered a motorcycle accident, was brought in unconscious state to the hospital and died there under symptoms of respiration insufficiency. A downward protrusion in the left diaphragm vault at autopsy called attention to the presence of a pneumothorax which has been identified with the immersion test. A roundish aperture of pinhead size was found at the anterior surface of the left upper pulmonary lobe. No other traces of injury were found in the thorax. There were signs of cerebral contusion on the basilar surface of the right temporal lobe, and conspicuous anoxic changes in the basal ganglia on both sides. The white matter, cortex and other parts were free from haemorrhage. The described case seems to indicate that cranial trauma may occasionally lead to fatal pneumothorax. Some of the apparently mysterious cases discussed in the literature of "spontaneous" pneumothorax communicated in the literature without any obvious chest trauma, may have been due to cerebral lesion.

L. Buris

(Institute of Forensic Medicine, Medical University, Debrecen)

Histochemical Study of Injuries

The histochemical changes of keratin and connective tissue structures have been studied in 30 cutaneous injuries of 13 patients.

The injuries had arisen partly during life, partly after death. The deceased had survived injury from a few moments to 4 to 6 hours.

Control injuries were inflicted by mechanisms similar to those at play in the premortal injury.

It has been shown that the keratin and connective tissue structure of the injured skin area showed increased Schiff-positivity, independently of the time elapsed between sustaining the injury and death, even if death was instantaneous.

L. Tolnay, M. Csellár, Z. Szarvas

(Institute of Forensic Medicine, Medical University, Budapest)

Fatal Shots in a 10-Year Necropsy Material

In the 10-year material there were 242 cases of fatal shot, representing 0.96 per cent of the whole necropsy material.

The distribution of the cases was suicide, 152 (62.8 per cent); homicide, 54 (22.4 per cent); manslaughter due to negligence, 27 (11.1 per cent), and accidents, 9 (3.2 per cent).

Sex distribution among the cases of suicide was: males 143, females 9. In the suicides, shots in the head were most common (70.5 per cent), followed by shooting into the chest (29.8 per cent). Abdominal shots were rare. Most of the head shots (77.3 per cent) were directed to the right temple. With the chest shots the left side of the chest was the commonest target. In most cases of suicide just one shot was fired, more shots were fired in 7 cases. In the latter, one shot canal went superficially, or the shots were fired into different part of the body. In these cases mostly short-barrelled guns were used (in 88 per cent).

The victims of homicide were 33 males and 21 females. In 55 per cent of the cases one shot was fired, with the head the commonest target, followed by the chest and abdomen (30 and 15 per cent, respectively).

In the cases of manslaughter due to negligence the characteristic feature was the unusual site of entry and the course of the shot canal.

Unlike in the cases of homicide and manslaughter, in those of accidental shooting the shots were fired mostly from a very short distance.

G. Dallos

(Hungarian Army Medical Corps)

Entrance Holes in Synthetic Fibre Fabrics in the Case of Close-Range Shots

In contrast with wool and cotton cloth, synthetic fabrics present characteristic changes if bulletts discharged from a distance even greater than 5 cm are shot through them. Threads taken from the edges of entrance holes and examined by phasecontrast microscopy present traces of a scorched or fused appearance. When the fire-arm had been discharged in contact with the synthetic fabric, the fibres exhibited globular bulges at their rent ends; shots from a distance of a few centimetres caused elongated, spindle-shaped deformations at the thread terminals. No difference has been noted between dyed and undyed fibres.

S. Ökrös

(Institute of Forensic Medicine, Medical University, Budapest)

Areas of the Skin Unsuitable for Injections

When administering injections it is important to consider the properties of the substance to be employed as also the anatomy of the different regions of the body, superficial or deeper vessels and nerve trunks in particular, so as to avoid harming the patient, to give rise to grave or even lethal lesions. Three regions of the body should be legally forbidden as sites of injection.

(1) The inner aspect of the elbow, where the brachial artery runs immediately below the vein, so that substances intended for the vein may easily be injected into the artery.

(2) The posterolateral part of the upper arm, where the radial nerve runs. Injections into this area may cause lesion or paralysis of the nerve.

(3) The middle third of the gluteal region, i. e. the skin area in the projection of the greater ischiatic foramen. Solutions administered here, especially oily ones given to infants, may gain access to the iliae artery or vein and lead to pulmonary embolism or a necrosis of the lower extremities.

Illustrations of the forbidden areas and the lesions caused there by injections serve to support the suggestion that they should be prohibited legally. A measure of this kind would best serve the prevention of accidents damaging physicians and patients alike.

Ö. Szép

(Institute of Forensic Chemistry, Budapest)

Micro Melting-Point Determination of Barbiturates

Whenever the Stas-Otto method is used for the examination various organ extracts, the final purification of the extracts for barbiturate assay is usually performed by micro-sublimation. When it comes to determining the melting point, the product frequently shows a considerable depression in spite of previous thorough purification. Then it is necessary to continue purification until the depression is to small to interfere with the identifying of the melting point.

In the case of barbiturate determination in decayed organs from corpses the sublimate prepared for estimating the melting point, often displays a heavy depression.

In some amobarbital assays, while the melt was allowed to chill, crystals were observed to redevelop and were subsequently retested for their melting points. The material was melting in the second instance at a higher temperature and frequently there was need for repeated meltings to establish the true melting point.

This experience in connection with sublimates for micro-melting point determination has induced us to leave the substance on the heater desk and to subject it, instead of repeated micro sublimations, to repeated melting-point determinations till a constant critical temperature has been reached.

The phenomenon appears to find its explanation in that the impurities which attend the pure substance and melt at a much lower temperature, recede to sublime at the edge of the glass slide so that the material in the field of vision is entirely free from foreign matter and the crystals it displays are characterized by a minimum depression.

It is maintained that the crystal form obtained by micro-sublimation is not sufficiently characteristic of a particular substance, for one and the same substance may crystallize under different conditions in several forms, showing a certain polymorphism. It is however also possible that different compounds are isomorphous, exhibiting very similar forms of crystallization.

It follows for practical use the crystal shape does not in itself furnish an adequate ground to identify a substance, in the present case a barbiturate.

Nevertheless it seems desirable that the barbiturate which otherwise sublimates in drops should be induced to crystallize in some way since in this form only does it permit to determine the melting point which must be known for identification purposes.

Phenolbarbital of all barbiturates is known for the inconvenience that it frequently sublimates in drops. For that reason it was difficult to identify drop sublimates obtained from organ residues. This in connection with the frequent occurrence of phenolbarbital poisoning may justify our efforts to produce a residue in crystal form and subsequently to determine the melting point.

Indeed, we have succeded in obtaining an unambiguously and invariably characteristic form of phenolbarbital crystal which proved well suitable for the melting point to be determined, making use of the following method.

Above the matter to be sublimated we placed a sheet to serve as collector lid and spread on its bottom surface an extremely thin layer of high purity talc. Under such experimental conditions the phenolbarbital crystals take form of densely arranged stellate needles, extending upwards and always characteristic of the sublimate. The grains of talc make up the nuclei of crystallization, with the crystal needles growing out radially in every direction. The sublimate obtained in that way usually indicates the melting point of pure phenolbarbital.

The method has proved as a practicable microscopic procedure to demonstrate the presence of phenolbarbital and to identify it on the bases of its melting point.

Klára Zsigmond

(Institute of Forensic Medicine, Medical University, Debrecen)

Direct Extraction of Amobarbital from Different Body Fluids and Organs

It has been studied in cases of fatal amobarbital poisoning in human subjects and animals how the drug could be directly extracted with chloroform from different body fluids and viscera. Amobarbital was demonstrated by means of the cobalt nitrate reaction.

In model experiments involving the use of labelled amobarbital it has been shown that by chloroformic extraction 30 to 35 per cent of the administered dose can be recovered from the viscera and body fluids.

In these experiments it has also been shown that brain extracts give a slightly positive reaction without the administration of amobarbital and that muscle extracts inhibit development of the cobalt nitrate reaction.

Extractibility decreases after death, therefore it is suggested that in cases of amobarbital poisoning the material should be tested as soon as possible, or the specimens should be preserved in alcohol.

In order to detect the breakdown products, not demonstrable by the cobalt nitrate reaction, chromatographic analysis should also be performed in cases of amobarbital poisoning.

Klára Zsigmond, J. Nagy, I. Békéssy, J. Csongor, B. Csaba

(Institutes of Pharmacology, Pathophysiology and Forensic Medicine, Medical University, Debrecen)

Distribution of Labelled Amobarbital in the Organism

The distribution of 6 C^{14} amobarbital following oral or intramuscular administration has been studied in the dog.

Activity was found to be low in body fluids and viscera, while high in urine.

In spite of its high activity, the urine gave a negative cobalt nitrate reaction, or in a few cases a slightly positive one.

Chromatography of the urine revealed low Rf value breakdown products of the drug.

On the basis of the results it is suggested that in cases of amobarbital poisoning the urine should be tested in the first place.

The isotope method and the paper chromatographic technique employed are described in detail.

N. Kapusz, T. Jávor, I. Békéssy, J. Csongor

(Institutes of Pharmacology, Pathophysiology, Forensic Medicine and 2nd Institute of Medicine, Medical University, Debrecen)

Changes in the 6-C^{14} Amobarbital Level in Blood and Bile in the Different Phases of Poisoning

The concentration of labelled amobarbital (Dorlotin) in blood, bile und urine was studied in dog after a lethal dose, injected intramuscularly. Bile was obtained continously by the authors' own method (internal biliary fistula with intestinal cannula).

The barbiturate level remained low in both blood and bile in the course of poisoning. The largest amounts of breakdown products were found in the urine. The maximum rate of excretion occurred 4 to 5 hours after administration.

Éva Grusz, Ö. Szép

(Institute of Forensic Chemistry, Budapest)

Detection of Glutethimide in Cases of Poisoning

Toxicological practice has made it necessary to find a method for the identification of glutethimide in a more reliable and sensitive way than that offered by melting-point determination.

Experiments made with the pure substance and with organ extracts containing different amounts of the drug have shown that its presence can be determined on the basis of spectrophotometric absorption curves.

The absorption maxima of 200 μg glutethimide per cent in methylalcohol or ethylalcohol can be well measured at 252,258 and 263 mμ. If an adequately pure extract made from the corpse is dissolved in methylalcohol or ethylalcohol, a comparison of its absorption curve with that of the pure substance will allow determination of small amounts of glutethimide.

The measurements were performed by means of a Beckman DU type spectrophotometer containing of the drug at 1 cm layer thickness. The volume of the solution was from 3 to 4 ml under our experimental conditions.

B. Rengei

(Institute of Forensic Medicine, Medical University, Szeged)

The Use of Paper Chromatography in Toxicological Studies

A paper chromatographic method for the detection of intoxications most commonly encountered in medicolegal practice (barbiturate, pyrazolone derivative and alkaloid poisonings) is described. Prior to partitioning the material to be tested is extracted with chloroform at different pH. s according to a modified Stas-Otto method, to eliminate most of the compounds interfering with analysis, then the solvent is evaporated, the residue taken up in a minimum volume of chloroform and chromatographed on a 2.5 by 35 strip of Schleicher and Schüll's paper 2043/b Mgl. To secure efficient partitioning and identification, barbiturates are partitioned by the ascending method in amyl alcohol: ammonia (2 : 1), pyrazolone derivatives in n-butanol: acetic acid: water (4 : 1 : 5) and alkaloids in n-butanol: formic acid: water (12 : 1 : 7). In the case of barbiturates the chromatograms are developed with cobalt and mercuronitrate reagents, as well as with UV light; in the case of alkaloids with UV light, Dragendorff and Pauly's reagent. Identification is carried out by running control samples, as well as on the basis of the Rf values.

J. Antal

(Institute of Forensic Chemistry, Budapest)

Post Mortem Determination of Carbon Monoxide

In order to establish a reliable post-mortem diagnosis of carbon-monoxide poisoning it is necessary to determine the amount of CO contained in the blood of the corpse. This is important in forensic medicine, for the value so determined is a good indicator of the degree of intoxication.

Wolff's technique has proved suitable for this purpose. It is based on the fact that, if the prescribed temperature time and pH factors are carefully observed, oxyhaemoglobin and plasma proteins are precipitated from the blood earlier than the CO-Hb complex. The two fractions can be separated by means of filtration. The dark red CO-Hb complex remaining in the filtrate can be estimated colorimetrically or otherwise.

We estimated the CO-Hb complex in the filtrate not on the evidence of its colour but by determinig its iron content. Breakdown of the complex was effected by the Szép-Grusz acid mixture microtechnique which allowed to perform this operation in five minutes. The iron was determined as rhodanate in the mixture; this procedure is reliable even in strong acid solutions. The precautions pointed out by Mázor and Grusz were duly observed. The same method served for plotting the standard curve and for the determination from a special 0.2 ml blood sample of the haemoglobin contents. The values so obtained allow to express the degree of intoxication in per cents of the whole blood's haemoglobin content.

This procedure has made it possible to avoid saturating the examined blood with carbon monoxide. The whole determination takes not more then 25 minutes.

Z. Kertész

(Department of Medical Casualties "Korányi" Municipal Hospital, Budapest)

The Carboxyhaemoglobin Level in Gas Poisoning

Systematic observations showed that in patients with gas poisoning the concentration of carboxyhaemoglobin was considerably lower than expected on the evidence of data in textbooks on toxicologv. In order to clear this contradiction, in blood samples—taken every hour—the level of carboxyhaemoglobin was determined in the so called "Wolff-filtrate" with the method of Klein und Zell as modified by us, using a Pulfrich photometer. CO saturation at admission varied between 8 and 24 per cent in 36 of 38 patients, it was 28 and 34 per cent,

respectively, in two grave cases. As regards the rate of excretion, it seemed to be higher during the first hour in gravely poisoned persons (40 to 60 per cent) than in milder cases (20 to 40 per cent). The complete disappearance of CO took from 7 to 10 hours. No fatal cases occurred during the period of observation. The level of carboxyhaemoglobin was 4 per cent in the fetal blood of a gas-poisoned mother, that had died intrauterine.

An attempt to determine, for diagnostic purposes, the concentration of CO in the CSF has failed as the CSF seemed to contain no measurable amount of CO.

The present results have been based on the elimination segment of the carboxyhaemoglobin curve, while the data in literature mostly refer to its initial portion. A co-operation with the ambulance service has been established in order to be able to follow the level of carboxyhaemoglobin from the earliest possible moment.

P. Csiky

(Department of Medical Casualties, "Korányi" Municipal Hospital, Budapest)

Toxic Action of Tobacco Decoctions, with Special Regard to Attempted Suicides

Evidence has been collected for 11 years regarding the effect produced on the human organism by the decoction of tobacco introduced by mouth and by tobacco swallowed in the dry state.

The number of people attempting suicide by drinking a decoction of tobacco is fairly high: there occurs, on an average, one such case every week, and the total number in this Department has gone beyond the 500 mark.

Textbooks of toxicology and pharmacology affirm that the tobacco of 3 to 5 cigarettes contains a lethal dose of nicotine. A decoction of 20 to 75 cigarettes could, therefore, be expected to cause death without a doubt; yet, experience showed that the symptoms developed by persons who had drunk the decoction were not worse than those observable in young people after the "enjoyment" of their first cigar or cigarette: pallor, perspiration, nausea, sometimes vomiting, vertigo, headache, diarrhoea.

Experiments have been made to reproduce the procedure. While the nicotine content of the decoctions was in agreement with that described in the textbooks, their pH was 6.4, instead of the expected pH 9. On the other hand, simple solutions containing the same amount of nicotine behaved as expected, a phenomenon possibly due to that, in decoctions, nicotine is present in the form of salts with low toxicity.

Experiments are in progress to determine the kinds of nicotine salts present in decoctions and the changes they undergo in gastric juice. Further experiments have the purpose to establish the toxicity of tobacco dissolved in various spirits.

L. Veress

(Institute of Forensic Medicine, Medical University, Szeged)

Blood Picture Examinations after Nicotine Poisoning in the Rat

A conspicuously high number of lymphoid reticulocytes, lymphocytes and monocytes has been observed in the white blood picture of patients died with acute nicotine poisoning. Although the phenomenon has been known to occur during life in persons suffering from acute or chronic nicotine poisoning, no data could be found concerning its mechanism.

Experiments performed on rats have shown that the proportion of monocytes increases very markedly under the effect of nicotine. The changes in the white blood picture were not identical with those described by Selye as arising under the stress of various poisonings; while the number of neutrophil granulocytes increased and that of the eosinophils first decreased and then increased, the appearance of a great number of mononuclear cells prevented the occurrence of a relative lymphopenia.

A comparison of thymectomized with intact rats, both poisoned with nicotine, showed the appearance of mononuclear cells to be delayed and their number decreased by 50 per cent in the former group.

T. Kaszás, G. Papp

(Department of Paediatrics, Medical University, Debrecen)

Poisoning with Medicinal Herbs in Children

Between 1946 and 1960, 128 patients were admitted to the Paediatric Department of Debrecen Medical University School on account of poisoning caused by henbane (Hyoscyamus niger). Jimson weed (Datura stramonium) and deadly nightshade (Atropa belladonna). These 128 patients constituted 26.6 per cent of all poisoned cases treated at the Department during the mentioned period; this percentage ranks next to that of drug poisonings (25.6 per cent). After a detailed description of the three above-mentioned poisonous plants the different manners of intoxication, and the distribution of such poisonings according to seasons and age groups have been discussed. As regards clinical symptoms, ketonuria mostly without vomiting was observed in one third of the patients. The lack of reliable data in history and marked neural symptoms made it necessary to perform lumbar puncture in 23 cases in order to exclude encephalitis or meningitis. The comatose state did not last longer than 4 days in any of the cases. There was no fatal outcome, and all patients recovered without sequelae. The average stay in hospital was 3.3 days. Treatment consisted in gastric lavage and the administration of emetics; barbiturate was given in cases of motor excitement; prostigmine in those of persistent tachycardia, vesical and intestinal paralysis; pilocarpine in cases of grave xerophthalmia. Promotion of circulation and rehydration may be necessary in certain cases. For the sake of prevention, the eradication of poisonous plants, pertinent lectures and film propaganda are recommended.

L. Kiss, Klára Zsigmond, J. Nagy

(Institute of Forensic Medicine, Medical University, Debrecen)

Lethal Isonicotinic Acid Hydrazide (INH) Poisoning

A male patient 39 years of age died a few hours after taking 200 tablets of INH by mouth under the influence of alcohol. The distribution of INH in the organs was determined. The histological changes are described. The distribution of INH in ten organism agreed with the data in the literature.

Animal experiments revealed no synergism between alcohol and INH.

M. Vámosi

(Institute of Forensic Medicine, Komenský University, Bratislava)

Common Pattern of Statistical Control and Medico-Legal Interpretation of Alcoholic Influence in Traffic Accidents

The available statistics about drunkenness in connection with accidents do not furnish an adequate basis to estimate the extent of damage due to indulgence in alcohol. To establish a uniform pattern of registering the degree of intoxication in each accident, it is suggested that the presence of alcohol in the injured person's organism should be indicated by a numeral, preferably with zero as the fourth figure, as laid down for group E (causa externa), in the WHO system of international statistical classification of diseases, injuries and deaths. A system of that kind would introduce a conformity in records, terms and estimation, without need for the diversities in jurisdictional, technical and other aspects to be taken into account.

There is much reason to believe that some facts about alcohol have been established unambiguously enough to meet, at the present state of our knowledge, with general acknowledgment. The introduction of uniform methods with careful attention to all details is apt to yield dependable results. In this context it would be desirable to embark upon an exchange of experience and records on an international basis. We must also be able to discover evidence of a general character. Some facts about chemical analysis, blood alcohol level and medical findings are discussed.

I. Gy. Fazekas

(Institute of Forensic Medicine, Medical University, Szeged)

Elimination of Alcohol in Intact and Adrenalectomized Rats

Groups of 5 adult male rats each were treated subcutaneously with 0.10, 0.15 and 0.20 g per 100 g body weight ethylalcohol in a 20 per cent aqueous solution before adrenalectomy and 6 days after bilateral adrenalectomy. The animals were tested for blood alcohol level by the Widmark method before the administration of alcohol, then at 30 to 60 minute intervals following the injection of alcohol, over periods of from 6 to 10 hours.

I. The maximum blood level following the injection of 0.10 g/100 g alcohol (0.125 to 0.136 per cent) was reached in the intact animals 1 hours after the injection. Subsequently the blood alcohol concentration declined gradually, to reach the initial level 5 hours after the injection. The same dose injected into adrenalectomized rats caused a peak blood level (0.13 to 0.139 per cent after 1 to 2 hours, the level remained about the same for a further 1 to 2 hours, began to decrease after the third hour and returned to the initial level 6 hours following the injection. Thus, after adrenalectomy the blood alcohol curve showed a plateau lasting for about 2 to 3 hours. This means that after adrenalectomy it took one hour longer to eliminate 0.10 g/100 g of alcohol.

II. After injecting 0.15 g alcohol, the blood level reached to peak (0.182 to 0.19 per cent) in the intact animals 2 hours following injection, then declined gradually and was at the initial level after 6 hours. After adrenalectomy the same dose reached the peak (0.186 to 0.20 per cent) 1 hour following injection, to remain for about 3 hours at that level. An appreciable decrease did not begin until after the fourth hour and it took 2 hours more, i.e. about 8 hours, to reach the initial level. Thus, in this group the plateau in the blood alcohol curve was three hours in duration.

III. Following administration of 0.20 g/100 g of alcohol the peak (0.246 to 0.276 per cent) in intact animals was reached in 3 hours and the initial level in 8 hours. In adrenalectomized rats the same dose produced the maximum blood concentration (0.26 to 0.276 per cent) in 4 hours. After a gradual decrease the initial level was reached after 10 hours, i.e. 2 hours later than before adrenalectomy.

According to these investigations, adrenocortical function plays an important role in the elimination of alcohol. This is in harmony with the earlier observation that hypersensitivity to alcohol is correlated with adrenocortical hypofunction.

J. Antal

(Institute of Forensic Chemistry, Budapest)

The Value of Preliminary Silver-Nitrate Test in Suspected Methyl-Alcohol Intoxication

The silver-nitrate test has been widely recommended for the preliminary determination of formic acid in urine in cases of suspected methylalcohol intoxication. However, certain deficiencies which have been noticed to influence these tests made it necessary to develop an exact method and to determine its sensitivity under the new conditions.

According to my experience the silver-nitrate test should be performed in the following manner:

To 9 ml of a standard 0.1 N silver-nitrate solution is added 1 ml of fresh urine. The precipitated mixture is placed in a boiling-water bath for exactly 10 minutes. Then it is left to chill. The reaction is positive, if a lilacbrown to dark brown, occasionally to black colour develops, according to the amount of formic acid present. Subsequently a varying amount of black granular precipitate appears at the bottom of the test tube. The sensitivity of the method is 500 mg formic acid per 10 ml. Normal urine will show a pale brown colour at most.

The test is unreliable in the presence in urine of materials reducing the hot silver nitrate solution. These may either be drugs or substances ingested with the diet, such as vitamin C. In pathological cases the presence of protein and sugar in the urine is disturbing the test.

The following drugs are giving a positive silver-nitrate reaction:

1. Aminopyrine and all preparations containing it.
2. Ascorbic acid, pure or combined with acetyl-salicylic acid.
3. Meprobamate on a large dose or on protracted dosage.

4. Chlorpromazine as above.
5. Nicotinic acid as above.
6. Calcium hypophosphite.
7. High doses of penicillin and tetracyclin.

All these considerations indicate caution in the evaluation of the silver-nitrate reaction which cannot be recommended as a reliable preliminary test.

J. Nagy, L. Pusztai

(Institute of Forensic Medicine, Medical University, Debrecen)

Automatic Apparatus for the Determination of the Alcohol Content of Expired Air

A wholly automatic device has been constructed for the quantitative determination of the alcohol content of expired air, using as a reagent sulphuric acid ammonium bichromate. The apparatus allows rapid testing of several samples in succession.

L. Turai, E. Somogyi, E. Cserháti, J. Kelemen

(1st Institute of Paediatrics and Institute of Forensic Medicine, Medical University, Budapest)

Acute Alcoholic Intoxication in Childhood

The cases of acute alcoholic intoxication in childhood in the 5-year material of the First Institute of Paediatrics and in the 10-year material of the Institute of Forensic Medicine of Budapest Medical University are discussed, a total of 34 cases, of which 8 were lethal. The main contributing factor in the poisoning was the carelessness of the parents. The symptoms and course of alcoholic intoxication in childhood differ from those in adults; the tolerance to alcohol of the young organism is very low.

The non-specific pathological changes and forensic problems associated with alcoholic intoxication have also been discussed. The therapeutical possibilities have been reviewed and, in addition to the usual symptomatic treatment, administration of glucose + insulin and fructose is recommended.

V. Földes, I. Kenyeres, L. Harsányi

(Criminological Laboratory, State Police Headquarters, Ministry of the Interior, Budapest)

Evaluation of Criminalistical Investigations of the Criminological Laboratory

The criminalistical material collected in the period 1955—59 is discussed. The results of 3888 investigations are analysed statistically and their efficacy is appraised. It is pointed out that this work means that criminalistical laboratory methods, a special field of forensic medicine, are employed in an increasing number of the cases. Now, when proving by criminalistical laboratory methods, the evaluation of the results of such investigations and the fitting of the results into the pattern of proving a case, are gaining acceptance in wider and wider circles, the discussion of a material, large not only by Hungarian standards, indicates how essential an aid is offered in criminal investigation by modern medico-legal work.

W. Göhler, W. Dürwald

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Exclusion Expectancies and Effective Exclusions in Affiliation Tests by Modern Serological Methods

The exclusion expectancies in the various systems can be calculated from the gen frequency of each characteristic. For the classical blood groups (ABO), the A_1A_2 subdivisions, the MN-system, the Rh-system with its C/c, D, E/e features and its C^w factor, the Kell-system and

the P blood-cell characteristic, all taken together, there is an overall exclusion expectancy of about 75 per cent. Considering the probability of a male's multiple exclusion in the various systems, the expectancy ratio obtained by the HIRSZFELD formula is 54.42 per cent.

Our own investigations have been concerned with 100 blood group tests, involving 155 males. There were 61 exclusions found in 44 men (28.4 per cent). What follows herefrom is the empirical establishment of a 1.4 quotient of overlap, with the final result of a 54.1 per cent exclusion expectancy, as related to the overall value of 75 per cent in all systems together. This value agrees almost exactly with the purely mathematical result according to HIRSZFELD. The effective ratio of 28.4 per cent in our findings does not contradict the calculated percentage of exclusion expectancy, for the latter relates only to males sued under malicious charge, whereas in the group of 155 examined men there must surely be an unestimable proportion of actual begetters. This view finds a strong support in the evidence provided by double and multiple fatherhood test reports which allow a higher percentage of males to be excluded than those relating to one man. Exclusions in maintenance lawsuits on evidence of double and multiple paternity test reports were confined to 22.2 per cent of the defendants as against 77.8 per cent cases of multiple conjugation. In connection with matrimonial divorce suits, the petitioner (husband) could be excluded in 8 cases, but an interferer in none.

By distributing the 61 exclusions among the various systems and taking the overlaps into account, it was possible to establish the real exclusion increment under application of the new systems and factors. An additional increment of at least 8 per cent may be expected from the adoption of the haptoglobin test in routine examinations.

J. Kobiela

(Institute of Forensic Medicine, Medical University, Krakow)

The Significance of Haptoglobin Tests in Forensic Medicine

POLONOWSKI and JAYLE coined the term haptoglobin to designate a serum protein fraction binding haemoglobin. Somewhat later a close relationship has been detected to exist between haptoglobin and α_2-globulin. An essential further advance came when haptoglobins were determined by zonal electrophoresis and three genetically distinct haptoglobin groups were identified as Hp 1—1, Hp 2—1 and Hp 2—2. Observations concerned with electrophoretic behaviour have shown that haemoglobins, although in normal zonal electrophoresis they migrate together with α_2-globulin, are identifiable under certain conditions as separate components.

In the present study the inheritance of haptoglobins has been examined. Among the observations, 2128 involved non-related persons, 420 families including a total of 456 children, and 678 mother-and-child combinations. It appears that the Hp-types may now furnish some information in cases of fatherhood tests.

In the Medico-Legal Institute of the Academy of Medicine, Krakow, the Hp-system has now been used in some disputed cases of affiliation. Owing to the comparatively high theoretical exclusion proportion (appr. 0.1800), the Hp method is regarded as a working complement to the conventional blood group systems. Paternity exclusions attained by its use may now be taken to be almost as important as those by means of the Rh and Kell systems.

J. Kobiela, W. Socha

(Institute of Forensic Medicine, Medical University, Krakow)

Paternity Blood Group Tests Made in the Medico-Legal Institute of Krakow

Blood group tests in connection with civil maintenance lawsuits have been introduced in the Krakow Institute in 1926 by Olbrycht. Such examinations have been carried on till the present day. On their evidence in the past ten years the paternity of the defendant was excluded in 1119 out of 9160 cases, i.e. in a proportion of 12.21 per cent. Routine tests in the last two years covered the following blood factors: ABO, MN, Rh-system: C^wCDE_{ce}, Kell and in extraordinary cases Haptoglobin, leading to a 19.10 per cent exclusion of paternity.

J. Kobiela, W. Socha, Z. Marek

(Institute of Forensic Medicine, Medical University, Krakow)

New Methods of Human Bloodstain Determination

The following methods have been used to check the efficacy of modern test procedures in determining human bloodstain:

a) Precipitation according to Uhlenhuth
b) Precipitation in agar gel according to Hartmann
c) Inactivation of the antiglobulin serum
d) Passive hemagglutination according to Ducos.

Human bloodstains varying in time of origin from eight years to one day have been subjected to examination under different conditions and in different control agents. The method has been checked for reability with stains from an additional variety of substances such as human biological fluids, extracts from human tissues, bloodstains from domestic and laboratory animals, and combined stains of human and animal origin. The discussed methods, apart from their experimental application, were used also for the analytical treatment of exhibits submitted for identification. The reliable precipitation test according to Uhlenhuth was used as a control to verify the results. A total number of 727 tests has been carried out.

According to the results, although in routine work the antiglobulin serum inactivation test can be used to some extent for referring human bloodstains to a specific origin, yet the efficacy of this method is rather limited.

The techniques outlined by us seem to be more or less equivalent, except in special cases when one or the other proves superior to the rest. But such chance occurrences have no real bearing on the final decision of preferring any particular method in medico-legal routine examinations.

The choice of the proper method must be left to rest with the examiner who should let himself be guided by the type of material and his own experience.

R. Budvári

(Institute of Forensic Medicine, Medical University, Budapest)

Mathematical Criteria and Critical Analysis of the Reliability of Blood Group Determinations

The reliability of blood-group determinations can be verified by statistical analysis. Essentially, such analysis consists in a comparison of the calculated (expected) and the observed percentage of the occurrence of the different blood-groups. Results in respect of 9469 examined persons were the following:

Incidence of blood-group M—	observed	32.67%
	expected	32.37%
Blood-group N—	observed	48.46%
	expected	18.58%
Blood-group MN—	observed	48.46%
	expected	49.05%
Incidence in the ABO system:		
Blood-group A—	observed	42.518%
	expected	42.519%
Blood-group B—	observed	18.366%
	expected	18.791%
Blood-group O—	observed	29.391%
	expected	29.391%
In the haptoglobin system:		
Type Hp 1—1—	observed	12.70%
	expected	11.97%
Type Hp 2—2—	observed	43.57%
	expected	42.77%
Type Hp 2—1—	observed	43.73%
	expected	45.36%

The differences between the calculated and observed frequency of the different blood groups not being significant statistically, the usual methods are fairly reliable. Another criterion of the reliability of blood-group determinations is the identity of results obtained from different (anthropological etc.) tests concerning hereditary characteristics namely that of the exclusion-frequency, with those obtained from blood-group determinations. Anthropological examinations showed 44 per cent as the actual frequency of exclusion, and both the corresponding calculated and observed percentages in the different blood-grouping systems were of the same magnitude.

In the ABO system:	calculated	17.729%
	observed	7.61% (43% of the former)
In the blood-group MN:	calculated	18.718%
	observed	9.07% (48% of the former)
In the haptoglobin system:	calculated	17.508%
	observed	8.29% (47% of the former).

The differences between the results of the two methods amount to about 2 per cent which is likewise insignificant statistically. The procedure in question should be utilized for the control of other methods, together with simultaneously performed blood-group determinations.

J. Nemeskéri, L. Harsányi, V. Földes

(Department of Anthropology Nat. Hist. Museum, and Institute of Forensic Medicine, Medical University, Budapest)

Establishment of Identity on Skeletal Evidence

When examining the skeleton of unknown persons it often does not suffice to determine sex and age. Expert opinion may be required also as to whether it is possible to identify the skeleton as having belonged to one of a number of given persons.

A method of identification has been elaborated. It consists, essentially, in the following.

The photograph of a missing person's face (preferably that on the identity card) and a photograph of the skull (taken in the same position as the face) are adjusted to the same enlargement, and one of the photographs is then projected upon the other. Identity or rather non-identity is then determined according to the coincidence or divergence of certain anatomical points, while due regard is of course paid to the usual anthropological measures and proportions.

A number of successful and also negative cases are described. It should be remembered that negative identification (i.e. the certainty that a skeleton is *not* that of this or that person) has, in certain cases, the same criminological value as a positive proof or at least probability. It is, therefore, emphasized that the method is based on the principle of elimination.

L. Harsányi, J. Nemeskéri

(Institute of Forensic Medicine, Medical University, Budapest)

Investigation of Age Changes in the Compact Substance of the Bone

The compact substance of the femur of 20 persons of different ages has been analysed histologically in order to ascertain whether the transversal diameter of the Haversian channels increases significantly with advancing age. Literature contains contradictory data in this respect.

No such changes in the mean value of the diameters were observed in the present observations as would allow inferences to age. It is claimed that there occur no qualitative changes in the tissues of aged persons and that it is merely their quantity which diminishes.

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Chronic Alcoholism and Legal Responsibility

Analysing the records of investigation of 100 cases of alcohol-addict criminals shows how many features there may be in chronic alcoholism. It is unjustified to say that alcoholism and psychopathy go together, because phychologically normal persons may also become alcohol-addicts under untoward circumstances. The toxic effects of alcohol may produce secondary cerebral lesions, which in turn may cause severe changes in personality. On the other hand, there are often pathologic mental processes in the background of alcohol addiction. In 26 per cent of the analysed cases organic nervous lesions were demonstrated, partly by EEG or PEG. In judging responsibility, the nature and way of execution of the crime are of decisive importance. 37% of the analysed subjects committed crime against property. In most of these cases chronic alcoholism was not considered to be a factor altering responsibility. Characteristic alcoholic crimes are those against life and physical integrity (17 per cent), disorderly conduct (16 per cent), subversion (9 per cent), and sexual crimes (6 per cent). In 41 per cent of the cases could the § 10 of the Criminal Code be applied, mostly in the form of restriction.

O. Kozáry

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Pulmonary-Gastric-Intestinal Air Test of Foetuses

The test is widely used in forensic medicine to determine whether or not foetus was born alive. The test, however, is of little use for determining the postnatal duration of life. Comparative data have been obtained for the three different steps of the pulmonary test (air test of the lungs together with the thoracic and cervical organs, detached from them and tested one by one, and air test on excised samples of lung tissue), as well as for the air content of the stomach and intestines, taking into consideration the factors that may influence the results. Considering that the air content of the lung may vary and that other changes, too, may occur, histological studies were also made. Premature infants and newborns who had died within two days after delivery were included in the material.

In 70 per cent of the cases both tests were positive. Both tests were negative in 4 per cent of the live-born newborns. Of the remaining 26 per cent, 6 per cent showed some pulmonary air with no air in the gastro-intestinal tract, and 20 per cent the opposite variation, which emphasizes the significance of the gastro-intestinal air test.

The importance of carrying out all the two tests is emphasized.

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Aspiration of Parturition Mucus, Amniotic Fluid, and Blood as the Cause of Death of Newborns

The incidence of fetal aspiration of parturition mucus, amniotic fluid and blood in the material necropsied during the period 1929—59 was analysed.

Of 370 newborns 115 (31.1 per cent) had died of suffocation or pneumonia due to perinatal aspiration. Of the total number of deliveries had taken place 36.5 per cent in the institute. In spite of the fact that in the last ten years 50 per cent of the children had been delivered in institutes, the incidence of deaths due to aspiration increased. Of the newborns 45.2 per cent were mature and 54.8 per cent were premature. In 61.1 per cent the cause of suffocation or pneumonia was aspiration of parturition mucus and in 36.5 per cent aspiration of amniotic fluid. In 41.7 per cent of the cases delivery was normal.

The data emphasize the importance of repeated removal of the mucus by suction in addition to the use of analeptics and attempts at resuscitation. Of the newborns 77.5 per cent died of suffocation and 22.5 per cent of pneumonia. A greater percentage of the mature new-

borns died because of aspiration of mucus, as compared with the premature infants. On the other hand, death due to suffocation caused by aspiration of amniotic fluid and pneumonia due to aspiration are more common with premature babies. Two-thirds of the newborns died in consequence of aspiration had been born alive and most of them died during the first 24 hours of postnatal life.

Clinicians have a tendency to ascribe the deaths following repeated episodes of asphyxia more often to intracranial haemorrhage than to aspiration, although just the opposite is true. Carelessness or lack of knowledge on the part of primiparae, as well as the secret delivery without assistance of unmarried women often led to the death of the newborns, as illustrated by the fact that in 23.5 per cent of the cases forensic autopsy was ordered by the authorities. In 40.8 per cent of the cases of death due to aspiration the cause of death could be determined only by microscopic examination. Attention is called to the dangers of perinatal aspiration and measures of its control are discussed.

T. Kaszás, G. Papp

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The Role of Foreign Bodies in the Accidents of Infants and Children

Accidents caused by foreign bodies in 82 infants and children and treated during the past 10 years are discussed. The circumstances preceding the accident are dealt with in detail and the difficulties of making the diagnosis are emphasized.

Most of the cases (59 children) belonged to the age group 1 to 3 years.

Swallowing of foreign bodies occurred in 33 cases. The objects most often swallowed were drawing pins, razor blades and hair pins. In 26 cases the swallowed object was spontaneously discharged, in 5 cases oesophagoscopy had to be employed and in 1 case the object had to be removed by jejunostomy. As complications, pneumonia occurred in 3 cases and mediastinitis in 1 case.

In 49 cases the foreign body was aspirated. Sunflower and melon seeds and beans were the objects most often aspirated. In 42 cases bronchoscopy was required and the prognosis was unfavourable, because complications (pneumonia, atelectasis, emphysema, pneumothorax, laryngeal oedema) occurred. In this group 8 children were lost.

After discussing the difficulties of differential diagnosis the details of prevention and treatment are dealt with.

V. Kovács, Á. Szabó

(Institute of Forensic Medicine, Medical University, and Metropolitan Tribunal, Budapest)

Cardiac Lesions Occurring at Resuscitation

Manual massage of the heart after cardiac arrest is liable to cause certain lesions, the anatomical manifestations of which are pericardial, endocardial and myocardial haemorrhage; contusion; rupture of muscle fibres or bundles; detachment of the papillary muscle; perforation of the ventricle. Such lesions usually occur in adipose, degenerated hearts. Massage should be performed with great circumspection.

L. Takácsy, F. Guba

(Institute of Forensic Medicine, Medical University and Electron-Microscopic Laboratory of the Hung. Acad. of Sciences, Budapest)

The Electronmicroscopic Ultrastructure of the Myocardium

The cellular architecture of the heart muscle is clearly discernable under the electromicroscope. The muscle cell is surrounded by a double sarcolemma of distinct contours. Arranged within the sarcoplasm are the myofibrils, the endoplasmatic reticulum, the rows of characteristically laminated numerous mitochondria, plasmosomes, Palade granulations, vacuoles and a variety of lamellae. The myofibrils and the sarcoplasm are not clearly demarcated; they are interconnected by lamella-stripes in the region of the Z-lines. The myofibril presents a

round or bandlike transversal section and is divided by the metameric sequence of Z-lines into anatomical and physiological units called sarcomaeres. In the myofibrils the myofilaments are arranged in parallel bundles presenting a hexagonal transversal pattern; the myofibrils extend without interruption through the different stripes and lines to the intercalated disks. These make up the specific structure of the myocardium, the cell membrane or sarcolemma, with the function to act as partition surface between two muscle cells. The parallel arrangement of intercalated disks and myofilaments seems to disprove the syncytial character of the heart muscle. The oval sometimes angular myocardial nucleus appears within the sarcolemma in the centre of the sarcoplasm amidst the myofibrils. The nuclear membrane shows sharp double contours and a parallel pattern, with the nucleoli arranged in its interior. The connective tissue elements of the heart are clearly discernible.

I. Gábor, A. Potondi

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Aneurysmal Ruptures at the Base of the Brain

A survey of the literature reveals the following aetiology of aneurysms at the base of the brain (1) injury; (2) arteriosclerosis; (3) hypoplasia and anomaly of the vessels; (4) syphilis; (5) infections; (6) inflammations. The significance of variations and anomalies of the cerebral vessels has been recognized. They must be accompanied by some endogenous or exogenous factor which actually induces formation of an aneurysm in the weakened arterial wall.

The mechanism of rupture has been studied in 20 cases of aneurysm at the base of the brain. Histology revealed the following lesions in the vicinity of the rupture.

(1) A change in the circulatory conditions of the so-called cushion arteries increases the permeability of the vascular endothelium; thus the plasma gains access into the vessel wall.

(2) Thickening of connective tissue fibres and oedematous swelling of the intima.

(3) Hypoxia caused by the oedema and the consequent precipitation of hyalin or a fibrinous substance.

(4) Subsequent haemorrhage and necrosis of the tunica media.

(5) The last phase consists in the rupture of the necrosed and dilated vessel wall.

G. Dallos

(Hungarian Army Medical Corps)

Sudden Death due to Abnormal Development of Coronary Artery

The medico-legal autopsy findings are discussed in a case of sudden death of a 20 years old, clinically asymptomatic man. Between the descending branch of the left coronary artery and the anterior interventricular vein there was an anastomotic opening 2 mm in diameter. In the dilated lumen of the vein there was a stonehard structure, greyish-white in colour and 26 by 16 by 14 mm in size. Other pathological changes did not appear neither in the heart nor elsewhere.

The finding seemed to indicate the presence of a congenital arteriovenous fistula between the left descendent coronary artery and the anterior interventricular vein. Increased pressure in the vein due to abnormal circulatory conditions led to phlebectasia. The whirl in the dilated vein section had given rise to a thrombus, wich organized in the course of time and was transformed into a phlebolith. The case deserves attention as an example of a rare anomaly

O. Szücs, L. Takácsy

(Hospital of the Hungarian State Railways and Institute of Forensic Medicine, Medical University, Budapest)

The Lipoid Contents of the Adrenal Cortex in Cases of Sudden Natural Death

The following histochemical reactions and staining methods have been used to study in frozen sections the lipoid contents of the adrenal cortex in fifty different cases:

1. Digitonin reaction — 2. Sudan III. — 3. Dinitrophenyl-hydrazine reaction — 4. Schiff reaction without pretreatment. The last two reactions failed to yield convincing results.

Heavy lipoid loss either in spots or all over the organ occurred in 18 cases; in 12 of these various lethal changes were associated with the exhaustion of the adrenal cortex.

The latter symptom suggested itself as the only cause of death in six cases. Two of them were accompanied by the clinical signs of adrenal hypofunction. In the third there was thyrotoxicosis subsequent to strumectomy. In three cases death was due to infantile salt loss and dehydration.

Finally the need for utmost precaution is emphasized in ascribing death to the disappearance of the adrenal lipoid, for only by consideration of the general necropsy report and all other circumstances is it possible to draw the right conclusion. This view is supported by evidence from the latest literature (*T. Symington et al Ciba Found. Coll.* Endocrinology, V. (1955) *8*, — *I. Carr.*, J. Path. Bact. (1959). *78*).

L. Nagy, Klára Zsigmond, J. Nagy, J. Lesznyák

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Estimation of Alcoholic Intoxication by the Use of Saliva Samples

The changes in the concentration of alcohol in samples of saliva have been studied at temperatures of +20°C and +4°C.

Saliva samples were obtained after the necessary precautions (prohibition of smoking, food and fluid intake) and to such samples ethyl alcohol was added to reach a concentration of 0.15 to 0.2 per cent. The alcohol content of the saliva was determined according to Widmark immediately after addition, then at 24, 48 and 72 hours.

It has been found that the alcohol values of the saliva samples did not change during the first 72 hours, either at room temperature or at +4°C. No preservatives had been added to the saliva samples.

Experiments with saliva containing no alcohol showed that during the first 72 hours no disturbing or reducing substances accumulated in the samples that would have interfered with the reliability of the Widmark test.

Considering that the salivary alcohol values change parallel to the blood alcohol level the salivary alcohol concentration may be used to determine the measure of alcoholic influence.

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Changes in the Audiogram in Experimental Ethylalcohol and Barbiturate Intoxication

The audiograms of normal individuals with intact auditory organ, aged 20 to 30 years have been studied following the administration of a small quantity of alcohol, amobarbital and the combination of both. The curve was plotted by means of Pedersen type audiometer.

The audiograms under the influence of both alcohol and amobarbital showed a loss in high frequencies. The effect was more marked following the combined administration of the two agents, causing in some cases a loss of hearing of 35 to 40 dB.

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