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PROCEEDINGS OF THE ANNUAL MEETING OF HUNGARIAN PATHOLOGISTS AND ANATOMISTS

Budapest, 1962

PLENARY SESSION

RELATOR

E. Rosnov: Text not received

P. Rácz

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The Experimental Pathology of Bacillary Dysentery

Bacillary dysentery is one of the most important infectious diseases in Hungary, the eradication of which is a task pursued with great vigour by the Health Administration.

The mortality rate of bacillary dysentery is low. Still, the elucidation of the pathogenesis of the disease requires further morphological investigations. As it has been emphasized by ANITCHKOV, it is impossible to clarify the pathogenesis of some infectious disease without studying its morphogenesis.

There are numerous unclarified features connected with dysentery. For instance, how the shigellae reach the distal areas of the large intestine without being destroyed by gastric acidity? Why is it that, except for a very small number of cases, the small intestinal mucosa is not affected? What role is played by the pathogenic organism, by the toxic substances excreted by or released from it, in bringing about the intestinal changes? Are these changes produced directly by the vital activities of the shigellae, or they arise indirectly, due to toxic effects or to circulatory disturbances?

Morphological studies in the human organism are rendered difficult by the fact that death very seldom ensues within the first few hours of the infection and therefore the early changes, so important from the point of view of pathogenesis, are examined only exceptionally. On the other hand, following death autolysis proceeds rapidly in the intestines and by the time autopsy is performed it is usually impossible to evaluate the finer mucosal changes.

The experimental, so-called model diseases serve to supplement the studies made in human material. The investigations aimed at studying the pathogenesis and pathology of dysenteric infection can be divided into two groups. To the first group belong the investigations involving infection of experimental animals by way of the gastrointestinal tract, to the second belong the experiments in which the animals are infected parenterally.

a) Experimental shigelloses induced enterally

Extensive pathological investigations have revealed that for the induction of dysenteric intestinal changes the best model is the monkey, followed by bear cubs and cats. In other animals only elements of the dysenteric process could be reproduced.

Summing up the results and evaluating the perspectives of work with the monkey as a model, highly important epidemiological, immunological and therapeutic results have been reached. Yet, monkeys are expensive and this is a serious obstacle, because large numbers of animals have to be killed in the various stages of infection if we want to study the experimental morphogenesis of the disease. The same applies to bear cubs.

By the end of the past century attempts were made to induce dysenteric infection in cats; then for a long time no such reports appeared in the literature and it was only quite recently that a series of reports confirmed that shigellosis can in fact be induced in cats by oral infection. However, the evidence presented makes it clear that enteral infection with shigellae did not always lead to the development of a true infectious disease.

In recent times the following additional factors have been introduced into the work concerned with the enteral infection with shigellae of cats.

1. The functional state of the nervous system was influenced by pretreatment with certain drugs.

2. By introducing orally large amounts of *Proteus*, or pathogenic staphylococci, or by feeding deficient diets, the intestinal flora of the experimental animals was altered.

3. The animals were orally sensitized in advance with filtrates, lysates or vaccines of *Shigella sonnei*. These investigations are significant, because they involved large numbers of animals and besides recording the clinical changes bacteriological and histological studies were also made. Unfortunately, the histological changes have been described, most briefly, and the value of the histological evidence presented has been reduced by the fact that most of the specimens originated from animals that had succumbed to the disease.

Experimental shigellosis of cats could be induced by the repeated administration of small numbers of shigellae, whereas no disease was produced if these doses had been given at once.

There is scarce evidence in the literature of successful infections in the dog.

In the rabbit some authors observed diseases similar to dysentery following infection with enormous doses of shigellae.

When different methods were employed to reduce systemic resistance, for example fasting, neutralization of gastric acid, paralysis of intestinal

movements by opiates, sensitisation with dysentery vaccine, a disease involving intestinal lesions and diarrhoea developed, which however, was not identical with a true infectious condition, because the bacteria did not multiply in the intestinal tract.

In 1960, a disease producing intestinal changes similar to those of dysentery could be induced in the rabbit by the intraduodenal administration of freshly cultured, highly virulent shigella strains, but the same authors could not reproduce their results.

It was only quite recently that reports have been published on the successful infection of small laboratory animals (guinea pig, rat, mouse).

In these experiments partly the above mentioned measures had been employed, partly, in the guinea pig, liver lesion had been induced by pretreatment with carbon tetrachloride. There are papers describing how infection was induced by changing the intestinal flora by streptomycin administration and that the shigellae disappeared from the intestinal contents after successful infection shortly after the introduction of antibiotic-resistant *E. coli*. By studying the morphology of the intestinal changes by means of fluorescent antibodies it has been shown that shortly after infection shigellae appeared in the submucosa of the small intestinal villi covered by intact endothelium. The investigations in which animals raised under aseptic conditions were involved are also interesting. These animals developed lethal bacteriaemia following the oral administration of shigellae. Previous oral administration of non-pathogenic *E. coli* prevented the development of shigellosis. In the intestinal tract of the animals raised under aseptic conditions the cells of the reticulo-endothelial system and the lymphoid elements are merely rudimentary. Administration of *E. coli* resulted in the development of those morphological representants of systemic defense.

Of the above, it is remarkable that in some experiments *E. coli*, this common inhabitant of the human gastrointestinal tract, should have prevented the development of dysenteric infection. It is also noteworthy that, similarly to human dysentery, the experimental intestinal infections were usually not accompanied by bacteriaemia. We attribute significance to the observation that the shigellae can enter the submucosa also through the intact mucosa.

It is to be emphasized, too, that in the experiments outlined above no full use has been made of all the possibilities morphological studies can offer in the elucidation of the phenomena involved. This applies in particular to the bacterioscopic examinations, although owing to the antigenic relationship existing between shigellae and other bacteria it is impossible to use fruitfully enough the fluorescent antibody method described by Coons.

Except for the experiments involving monkeys, the evidence obtained warrants caution as regards drawing conclusions concerning the pathogenesis of human dysentery, because the supplementary methods employed for diminishing

systemic resistance greatly differ from the effects observable in human pathology. The experiments on small laboratory animals are very attractive, but these correspond rather to carrier states than to true dysentery and thus it can be stated that the enteral induction of dysentery is not a solved problem.

b) Experimental shigellosis induced by parenteral infection

Following the intravenous or intraperitoneal administration of shigellae the experimental animals develop circulatory disturbance and non-specific dystrophic processes. Sometimes lesions are detectable in the intestines, too, and the changes may be similar to those occurring in man in the early phase of dysentery. As such intestinal changes may be brought about by the administration of the somatic antigen of shigellae, some authors have suggested that in the development of human dysenteric colitis the absorption and excretion of the somatic antigen of shigellae would play the decisive role. It has also been proved that for a time shigellae can multiply in blood and in the abdomen, but the phenomenon observed is not a true infectious disease, and its significance in the understanding of the pathogenesis of human dysentery is restricted, especially because bacteriaemia is not characteristic of the natural disease.

With subcutaneous infection a local inflammatory focus develops, accompanied by the symptoms of systemic intoxication. It has been shown recently that if immunized and non-immunized mice are infected subcutaneously in the thigh, in the immunized animals phagocytosis and lysis occur sooner than in the non-immunized ones. Moreover, in the immunized animals the agglutination of shigellae, too, was observable.

The results of rabbit experiments involving infection through the wall of the large intestine or coecum were comparable to those obtained with subcutaneous infection. The intestinal changes thus produced cannot be accepted as being a model of human dysentery, because some microorganisms might enter the abdominal cavity, as shown by the development of fibrinous suppurative peritonitis and abscesses in the area of operation. The administration of shigellae in this fashion gives rise to systemic infection and bacteriaemia.

True infectious disease could be produced *via* the urinary bladder of guinea pigs, the lung of mice, and the conjunctival fold of guinea pigs, as the portals of infection. In all three cases the shigellae multiply, and the experimental pneumonia thus induced makes it possible to study the quantitative changes in shigellae.

The histopathology of these experimental infections has been studied, but, following up the dynamics of the infection and observing the phenomena in large numbers of animals, detailed histological studies have been made in the field of experimental shigella pneumonia only. The three experimental models

agree in that museum strains, identical in every other respect with freshly isolated ones, have failed to produce the changes described. With every one of the three modes of infection the shigellae multiply also in the epithelial cells.

In our own investigations, in which we have been following up the morphogenesis of keratoconjunctivitis shigellosa, we have found this phenomenon of fundamental importance and, although in a slight measure shigellae can grow in the conjunctival exudate, intracellular multiplication is the decisive factor in the development of infection. In the development of corneal and conjunctival ulcers the intraepithelial growth of shigellae is the decisive factor. In the defense of the macroorganism the phagocytic activity of leucocytes plays an important role.

Although all three artificial infections produce diseases substantially different from human dysentery, they are suitable for studies of the interaction between the macroorganism and the microorganism. The phenomena observed in experimental shigellosis may presumably play a role of no small importance in the pathogenesis of human dysentery. Work should be continued in that direction and it is hoped that thereby we may get nearer to a better understanding of the pathogenesis of human dysentery, which may prove to be fruitful in prevention and therapy alike.

RELATOR

K. Rauss

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Recent Results in Bacteriology and Immune Biology of the Shigella

The Shigella genus, like other enteric bacteria, is classified according to biochemical properties. In recent years the Shigella group increased by a few species in the subgenera *Sh. dysenteriae* and *boydii*. Considering the rules which govern our present system of classification, it is open to discussion whether certain species presenting different fermentation properties can or cannot qe classified in the Shigella genus on account of their common mucosal pathogenicity. Obviously, the pathogenic properties are unsuited to form the sole basis of a classification which would upset the whole of our present system (cf. apathogenic Salmonellae). The opinion is even not uniform whether the Shigella group qualifies as a genus and the serotypes as distinct species.

As regards antigenic structure, the situation has been questioned of the recently described thermo-labile antigens which differ in properties from the types of such kind of antigens known before. Not until these antigens

and the corresponding anti-sera have been produced in a pure form, will it be possible to establish and place beyond dispute their very existence and function. Unsettled is also the question of fimbrial antigens.

Investigations into the antigenic variability in the *Sh. flexneri* subgenus have recently led, apart from disclosing the origin of the X and Y varieties, to the discovery of further antigenic variants (1b→3). It was possible to isolate the antigenic variant of type 3 under natural conditions.

Some authors regard the "phase change" of *Sh. sonnei* as a genuine process and consider phase II to be an S-form deprived of its thermo-labile antigen. In our opinion, what we deal with is an S→R mutation. In support of this we refer to the fact that highly sensitive serological methods have revealed a phase-II specificity in the isolated lipopolysaccharide of phase-I bacteria. We interpret this phenomenon as analogous to the biochemical change observed in connection with the Salmonella S→R mutation. The basis of the polysaccharide of the somatic S antigen is the R polysaccharide on which the secondary saccharide chains are build up carrying the S specificity.

A recent proof of the close genetic relation between the enteric bacteria is that some authors observed a conjugation between E. coli and Shigellae and succeeded in producing hybrids of Shigella antigenic structure with lactose positive stability.

There is increasing evidence of the Shigellae exerting a pathogenic effect on the *mucosa*. They not only attack the bladder *epithelium* and the *conjunctiva* in the guinea pig but multiply pathogenic strains intracellularly in tissue cultures. These strains are solely able to produce *kerato-conjunctivitis* in the guinea pig. This affinity of the *mucosa* probably is the decisive factor in the pathogenesis of human dysentery and the ulcer-producing effect of endotoxin on the locally injured mucosal surfaces is just a secondary one. The unexplored virulence factor of Shigella is probably identical with the one governing the organism's affinity to the *mucosa*.

The main obstacle in the study of Shigella immunity is the lack of suitable model animals. Nearly all we know about Shigella immunity derives from monkey experiments, these being the only animals in which infection takes the form resembling the human disease. Experiments to induce the disease in other animals have failed. It is true that mice, on elimination of the Gram-negative enteral flora by means of streptomycin, have been made Shigella-carriers for long periods, but this state was not accompanied by pathological changes in the intestines, except for one single experiment with *Sh. schmitzii*, and even this one has not been verified.

The attained immunity is type-specific and lasts only a few months. There seems to be increasing evidence that immunity depends much more on the copro-antibodies which arise and are traceable locally in the intestines, than on the considerable amounts of serum antibodies.

According to recent views, the process to be evolved for inducing artificial immunity must be one that favours the formation of copro-antibodies. Studies in that sense are in progress im our laboratory, and seem to promise some success.

The study of Shigella has led to important results in the last few years and research concerned with the problems of virulence, pathogenesis and immunity has called attention to more than one line of approach, with the reassuring promise to discover adequate ways of specific prevention of this widespread and so far hardly controllable disease.

RELATOR

L. Binder

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The Clinical Problems of Dysentery

Dysentery, once the cause of dreaded epidemics which — by the number of its victims — often decided the outcome of wars, has been reduced to a disease with a minimum rate of mortality, where nowadays apart from averting fatal terminations, the main task consists in solving minor problems. However, the editorial "More dysentery" in the British Medical Journal in 1960, shows that the problem of dysentery is still regarded as being of interest.

As stated in a study the present author wrote with Bodor and Mihályfi, the fundamental change in the clinical picture of dysentery was due to four factors: (1) the adaption of sulphonamides in the therapy; (2) the discovery of antibiotics affecting Shigellae; (3) the introduction of new efficient methods for the restoration of salt and water balance; (4) the practically complete disappearance of *Sh. krusei* strains from certain areas.

These statements have been supported by the examinations of Farkas and Kiss regarding the dysentery mortality rate in the Children's Department of our hospital. Treated with sulphonamides, 27.5 per cent of dysenteric infants died in 1947; this rate dropped to 10.3 per cent in 1952 when antibiotic therapy was adapted on a large scale; it went further down to 3.6 per cent in 1953 when modern fluid and electrolyte therapy was introduced; the rate was 1.3 and 1.2 per cent in the years 1954—1955, and the results are still more favourable at present, when the average mortality rate inclusive of old persons is below 0.5 per cent, although the number of dysenteric patients is high.

According to the statistics of the State Institute of Hygiene, the number of registered cases of dysentery between 1955 and 1960 varied between 10,000 and 12,500. It is, however, worthy of note that — according to the data of

FERENCZY, STOLL and VIRÁG — in 1955 not less than 69,951 cases of diarrhoea were seen by doctors in Budapest alone, and that this number increased to 88,117 in 1959. These figures are the more significant as the faeces were bacteriologically examined in 9 per cent of these cases only.

These facts raise two sets of problems, (a) the classification of acute enterocolitis, (b) the evaluation of the bacteriological results for faecal samples.

It is, we think, correct if we interpret dysentery to mean shigellosis. In this sense of the term, we diagnose as dysentery all acute diseases which start with or without fever and manifest themselves with abdominal pain, spasmus and frequent stools with mucus, blood and pus. They may appear in a grave or in a mild form, and may be accompanied or not by symptoms of intoxication. Vomiting does not exclude dysentery even in adult persons. Apart from Shigellae, the above-described type of stools, provided the disease is of bacterial origin, may be caused by *E. coli* 0.124 in adults, as observed by BORIÁN et al. and ourselves, whereas in infants they may occur also in diseases due to other pathogens, as stated by SCHMIDT.

A difficulty arises from the fact that the presently current Shigella strains may give rise to subclinical manifestations which are not severe enough to induce the majority of patients to consult a doctor. DUBOVSKY's data from 1958 are very instructive in this respect.

Let us now try to find out why there is such a striking difference between the number of patients treated for diarrhoea and that of the registered cases of dysentery. This phenomenon is no Hungarian speciality; it has been observed, among others, in Great Britain. Let us quote here ZHDANOV's apposite remark, that the proportion between the cases of dysentery and those of acute unclassified intestinal disorders constituted a qualitative index of dysentery diagnostics.

The diagnosis established on the history and the evidence of clinical manifestations, can always be checked in hospitals by means of a bacteriological study of the faeces. Our above-mentioned study made with BODOR and MIHÁLYFI, was based on the examination of 1805 cases, and it was in 30.5 per cent that the bacteriological result was positive. We have treated, since the October 1st, 1961, not less than 1500 patients whose illness had been diagnosed as dysentery on the strength of the clinical picture; bacteriology gave positive results in less than 15 per cent. The disparity between this figure and the statistical data concerning the incidence of bacteriologically positive cases over the whole country is striking. The explanation lies in the fact that there is no uniform acceptance of the term dystentery, so that a considerable number of patients who would qualify as dysenterics according to the wider interpretation of the term, are not classified under this head if their faeces do not contain microbiologically demonstrable shigella. Such statistical discrepancies due to differences in the definition of the disease are to be found in many countries.

The question arises whether the criteria and thus the interpretation of the term "dysentery" as applied by us are justified if, according to the culturing methods usual in most other institutes and parts of the country, not more than some 12 to 15 per cent of the cases regarded by us as dysentery are generally accepted as such. It may, we think, be taken for granted that the diseases regarded by us as dysentery cannot be of purely alimentary origin, *i.e.* exist without the agency of microorganisms. And yet, in a great number of cases it was impossible to isolate any kind of pathogenic bacterium.

This, of course, points to the possible agency of viruses. The reports of VERLINDE, GIOVANNARDI et al., and VOROSHILOVA, submitted to the 3rd International Congress of Infectious Pathology held in Bucharest in October, 1962, one of the main subjects of which were viral enteropathies, stated quite clearly that diarrhoeal diseases of viral origin occurred most frequently in childhood, and in the majority of cases in the age group under 5 years. The incidence of adults and children is practically equal in the material of our hospital, and some 40 per cent of the total consists of children under 6 years, from which it would follow that the viral origin is rather improbable in 60 per cent of the patients. It should be borne in mind that, while there may be blood in the faeces of infants suffering from viral enteritis, they contain neither mucus nor pus in the forms known as "viral gastro-enteritis", "summer diarrhoea" or "infantile diarrhoea". The situation is similar in non-bacterial apyretic infectious gastro-enteritis, a term applied by JORDAN and GORDON to a syndrome of uncertain aetiology which occurs also in adults. VERLINDE and several other authors consider the viral origin as probable in diseases which show pyrexia with pharyngeal-gastrointestinal symptoms, a concept supported by the results of WISNER et al. Of the enteroviruses, members of the ECHO-group have been shown by TIMBURY to be most frequently at play. GARDNER demonstrated the presence of adenoviruses in certain cases; when an enlarged lymph node provoked intussusception, there was passage of blood and mucus, but this was due to the invagination only.

Examinations of faecal samples of children and infants treated in our hospital for acute enterocolitis by bedside inoculation of the plates, combination with immune fluorescence microscopical investigation made by VOLTAY, OSVÁTH, GECK et al. in collaboration with the staff of the laboratory of our hospital, further the serological investigations of the same patients made by BACKHAUS has shown, that in 53% of the patients the disease could be guaranteed as Shigellosis. The results of these investigations were good enough to strengthen our opinion that the symptoms of our grown-up patients could be cheefly caused by Shigellae although the usual simple bacteriological examinations of the stools gave in high percentage negative results.

Let us now examine a few therapeutical problems. The favourable results achieved in this respect are in great part due to those profound pathophysio-

logical analyses which have been discussed by CSAPÓ et al. in connection with toxic dysentery and its various forms accompanied by dehydration, eclampsia, vasomotor paralysis and disorders of coronary circulation. Cases with fatal termination are practically limited to infants and old persons. Old people have little reserves, their vascular apparatus is usually damaged, their heart and pulmonary circulation are impaired, so that it is extremely difficult to counteract disturbances of the salt and water balance in serious cases. The resulting circulatory failure leads to a reduction of renal activity, and to anoxaemic lesions of the central nervous system.

When appreciating the results of controlling infectious diseases, therapeutical achievements have to be weighed not only from a clinical point of view, but must be judged from the angle of public hygiene as well.

A 3-day treatment with a daily dose of 2 g of chloramphenicol has been found by us to be equivalent to a treatment with sulphaguanidine as regards clinical improvement, and even more satisfactory in other respects. Chloramphenicol suppressed sulphaguanidine and the absorbable sulphonamides also, from the point of view of public hygiene; bacteriological negativity was obtained in more cases within the same space of time.

The results in respect of many thousands of non-hospitalized patients suffering from acute enterocolitis are completely obscure. It was for this reason that SKHORZEV opposed treatment in the patients' home. We agree with ZHDANOV that hospitalization should not extend over more than 7 days. It would be very useful if all discharged patients could be followed up. This problem still awaits solution in Hungary.

To make the duration of hospital treatment as short as possible is in the interest of both the community and the patient, and becomes particularly important at the time of epidemics when available accommodation in hospitals is usually far from sufficient. It was for this reason that we tried to find a treatment that would yield at least as good results as the current methods, but would do so in a shorter time. BODA et al. (1956) obtained in infants and children satisfactory results with chloramphenicol administered for two days. GARFINKEL et al. treated 1408 patients in a Korean P.O.W. camp in 1953 with sulphadiazine and several antibiotics, and observed the results during a considerable length of time. They registered the best results if the patient had received 4 g of a broad-spectrum antibiotic within 24 hours after having been admitted to the hospital. We have treated more than 1400 adult (mostly male) patients since October 1, 1961, by administering 2 g of chloramphenicol when the faeces were collected; a further dose of 1 g was given 12 hours later, and still another after another 12 hours. This treatment proved to be equivalent to the earlier ones as regards both clinical and bacteriological improvement whether results were referred to the total material or to Shigella-positive patients only.

We have recommended to prepare seasonal antibiograms of *Shigella* strains occurring in each regional unit. A comparison of certain data registered in 1960 with those collected in 1962 shows that 6.7 per cent of the examined Flexner strains and 2.7 per cent of the examined Sonne strains were resistant to chloramphenicol in 1960 against 19 and 17 per cent, respectively in 1962. A similar tendency has been observed in respect of sensitivity to oxytetracyclin. Of the orally administered antibiotics it is still to these two that sensitivity has remained highest.

Rectoscopy is the best clinical method of checking recovery, but the method should not be performed without the indication and the patient's consent. Rectoscopy is especially useful in differential diagnosis; since it involves the risk of perforation, complaints in connection with which appear some hours after the examination, we are decidedly against rectoscopy being performed in out-patients.

Our textbooks are discussing acute dysentery side by side with its chronic form. Since, according to our definition as given earlier in this paper, dysentery means shigellosis, we have to decide whether these patterns (or part of them) satisfy the criteria of chronic shigellosis. We think that shigella carriers are inseparably mixed with other subjects suffering from intestinal disease and probably with some suffering from chronic shigellosis. No clear picture can yet be obtained in this respect. We have studied the aetiology in 116 cases of chronic enterocolitis. 2 to 3 bacteriological studies failed in all cases to isolate shigellae. It must, of course, be noted that in the history of only four cases was there dysentery mentioned and even that 5 to 15 years before the present investigation. Among them numerous patients were suffering from ulcerative colitis or carcinoma. We are, of course, not ignorant of the significance of the possibility that an incomplete healing of acute shigellosis may lead to the development of chronic intestinal disease. Postshigellosis and chronic shigellosis are nevertheless different categories in our opinion; the problem requires in any case additional detailed and large-scale microbiological investigations which should be supplemented by serological studies.

L. Csontos, E. Florián, A. Széky

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Generalized Cryptococcosis in a Dog

Nodous changes reminiscent of tumour tissue and extending to the skin, muscles, lungs and meninges, were found in the cadaver of a 2 years old dog. Histopathological and bacteriological as well as mycological examinations have proved the process to be one of cryptococcosis (torulosis). A detailed description of the morphological, histological and mycological changes is given.

S. Keresztury, F. Weiss

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Pathology of Listeriosis

The post mortem findings in 23 bacteriologically identified cases of listeriosis, observed between 1955 and 1962, are reported. Three cases occurred in adults (2 complicated with encephalomyelomeningitis, one with general infection) and twenty in stillborns or perinatally diseased prematures or newborns up to the 8th day of life. In a few cases there was granulomatosis infantiseptica, in others there were hardly any pathologic changes present. The importance is stressed to identify the disease bacteriologically. A closer cooperation between clinicians and microbiologists is desirable to clear many still open questions.

V. Augustin

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Pathologic Changes of the Bones in Enteral Infections

The bone complications attaching sometimes to infectious enteral diseases are involvements of a non-lethal character wherefore they reveal themselves to the clinician or the radiologist rather than to the pathologist.

Shigella dysenteriae may provoke purulent arthritis, *Sh. flexneri* and *Sh. sonnei* a toxico-allergic process, leading to exudative arthritis without destruction, which some writers identify with REITER's syndrome.

Bone changes associated with typhoid fever are seen usually in the period of convalescence or after recovery. Radiologically they appear for the most part in the form of osteoperiostitis, being discernible from the haematogenous osteomyelitis caused by *Staphylococcus aureus*. They occurred before the introduction of antibiotics with a frequency of 1.1 per cent and occur, though rarely, even today. Their place of predilection is in the ribs, the clavicle, the ankle and the vertebrae. They heal spontaneously under proper ossification.

The pathologic processes relased by other Salmonella species show bone involvement in 0.76 per cent. In contrast to staphylococcol osteomyelitis, they usually destroy the epiphyseal cartilage and assume the form of suppurative osteo-arthritis. The sole localization of salmonella in nearly one third of the observed cases appeared to be in the joints; intestinal processes were not observed and faecal cultures yielded negative results. The pathogens were mostly *S. suipestifer* and *S. typhimurium* : the usual localization was in the spine and the ribs, among joints in the knee, the shoulder and the hips.

Bone complications due to *Escherichia coli* usually arise as a sequal of bacteriaemia, in the form of destructive suppurative osteo-arthritis. The localization is mainly in the knee, the shoulder and the hips, frequently in several joints at once.

The use of wide-spectrum antibiotics has greatly reduced the mortality in infectious enteral diseases but the occurrence, especially in Salmonella and Escherichia infections, of bone lesions which may lead to deformation, joint rigidity or a retardation in growth, must still be taken into consideration.

Magda Frank

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Fatal Cases of Enterocolitis in Connection with Tetracycline Treatment

The noxious side effects of tetracycline on the gastro-intestinal tract are well-known, although the mechanism of the effect has not been fully elucidated. It is universally recognized that tetracycline produces dysbacteriosis in the intestines. Five patients suffering from different diseases were treated with the antibiotic. Four of them were more than 50 years old; the only young patient had undergone a grave pulmonary operation and tracheotomy. This young patient was the only one who received the drug intravenously, while it was administered orally to

the others. The primary disease was a neural lesion in two of the patients. Grave enterocolitis supervened shortly after the beginning of treatment in all patients but one, and led to death rapidly, despite all therapeutic efforts. Post-mortem examination revealed typical pseudomembranaceous enterocolitis in one case in both the large and the small intestine, and in the large intestine in the other cases.

The above cases should serve as a warning to pathologists that the harmful effects of broad-spectrum antibiotics, and especially those of the tetracycline should be taken into consideration in every case of pseudomembranaceous enterocolitis of unknown origin. It should be borne in mind that, notwithstanding the utmost care in the administration of these drugs and despite a thorough study of the pertinent complications, there still occur fatal cases of enterocolitis caused by tetracycline.

The study concludes with a comparative survey of tetracycline enterocolitis and other forms of pseudomembranaceous and necrotizing enterocolitis.

Magda Frank, I. Csillag, E. Lengyel

(Department of Pathology and Department of Surgery, János Hospital, Budapest)

Necrotizing Enteritis

The clinical diagnosis of necrotizing enteritis is difficult to be established. The disease is usually discovered at necropsy and the diagnosis confirmed by histologic examination. Both aetiologically and pathologically the disease is rather to be regarded as a morphological concept than a strictly defined morbid entity.

Our post-mortem examinations revealed six cases of necrotizing enteritis, 3 in males and 3 in females, the majority in patients over 60 years according to literary data. The process, except of one case, took an acute course. In four cases the process was a primary one. — Four patients had been operated on for acute abdomen, one for ileus; one aged patient could not be operated because of circulatory failure. In one patient the disease was limited to the descending colon and the sigmoid, in two to the small intestines, while in three it extended to both the small and the large intestines. The severest changes were always found at the lowest portion of the small and large intestines. Two cases were complicated by diffuse peritonitis due to perforation, two other cases with diffusionperitonitis. To the typical histologic changes a pseudomembranous process was associated in one case. As can be deduced from our observations and the literature necrotizing enteritis seems to have become a term of more extensive sense in the last decade than it had been interpreted before.

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Pathomechanism of Haemorrhage Associated with Certain Infectious Diseases

Investigations concerning disturbances of blood coagulation in hepatitis, scarlet fever and measles have led to the following conclusions.

1. Coagulatory disorders have been observed in the course of hepatitis. Frequently, such disorders do not manifest themselves clinically. They are due to a change in the factors which determine the type of plasma. Coagulopathy is partly of a haemorrhagic character (prolongation of thrombin time, increased heparin content and thrombin inactivation, reduced level of fibrinogen) and partly of a thrombotic nature (positive fibrinogen B, elevated level of prothrombin).

2. The coagulopathy shows a haemorrhagic character in scarlet fever and measles. The susceptibility to haemorrhage is partly due to an intoxication of the vascular and cellular elements and partly to a disorder of plasma factors.

3. Increased inactivation of thrombin and the protraction of thrombin time in scarlet fever are due beside hyperheparinaemia to other anticoagulants, while pronounced hyperheparinaemia has been observed in measles.

F. Szarvas, A. Macher

(1st Department of Internal Medicine, Medical University, Szeged)

Chronic Hepatitis and Liver Cirrhosis

In a total of 23,635 patients admitted in the last ten years, there occurred 536 cases of chronic liver disease. On a careful anamnestic review, 312 diagnoses were established undoubtedly (219 qualifying as chronic hepatitis and 93 as cirrhosis). Among physicians the said conditions occurred about twice as frequently as among patients of other professions. The average age was 40 years for chronic hepatitis and 58 years for cirrhosis. The original suspicion at admission of acute hepatitis proved to be chronic hepatitis in 38 per cent, and cirrhosis in 15 per cent. The development of cirrhosis within 10 years of the appearance of chronic hepatitis was observed in one single case only. Apart from its rapidly progressing form viral hepatitis does not greatly favour the development of cirrhosis. However, in combination with other liver injuring factors especially alcoholism, it carries a much greater likelihood of the danger. The general experience was that two or more concurrent liver injuring factors usually facilitate development of the cirrhotic process.

H. Meessen

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The Significance of Electron Microscopic Methods in Pathology

Electron microscopy has often proved of great value to the clinical pathologist in examining specimens obtained by biopsy or at surgery. The paper is concerned with the more significant observations made during the last ten years at author's institute.

In infectious mononucleosis it is possible to differentiate virocytes from basophilic monocytes. — The ultrastructure of the thrombocytes has been clarified. It has been established that they are capable of phagocytosis and that they contain drumstick granules not only in v. Willebrand-Jürgen's disease but also in thrombasthenia; the drumstick granules arise not in the megakaryocytes but in the separated thrombocytes in which they are an indication of a disorder of maturation. — In vaginal smears tumour cells can be differentiated from normal cells. In one case electron microscopy made it possible to diagnose pulmonary adenomatosis on the basis of cells discharged with the sputum.

Endometrial glands have been observed during both the proliferative and the secretory phase to contain ciliated cells and cytoplasmic components of which cilia are able to develop. — In the cells of the myocardium obtained surgically no changes were seen one minute after an anoxic cardiac arrest, but 45 minutes later changes of a reversible character, such as the disappearance of the glycogen granules accompanied by a swelling of the mitochondria and of the endoplasmic reticulum were observed. Anoxic cardiac arrest does not involve such a loosening of tissue structure as observed after injection of potassium citrate. — In mitral stenosis the air-blood diffusion distance is considerably prolonged due to pulmonary stagnation; in one case numerous centrioles were seen in the interstitial connective tissue cells. — The basement membrane of the renal glomeruli thickened in diabetes mellitus long before clinical data or light microscopy had revealed signs of renal injury.

In the well differentiated cells of bronchial carcinoids large cytosomes can be observed which are probably responsible for the positivity of the PAS and the thionine tartariate reactions, as opposed to intestinal carcinoids characterized by small granules which might contain catecholamines. Electron microscopy seems to have confirmed the view that intestinal carcinoids, in contrast to most of the bronchial ones, perform endocrine functions. — Granular cell myoblastomas have been found to be devoid of myofilaments; they are probably made up from Schwann-cells or from cells of different origin affected by irreversible metabolic disorders. — Laryngeal papilloma cells have been shown to contain a viroplasm similar to the mature Shope fibroma virus.

Electron microscopy yields good results mainly when the light microscope has come to the verge of its capacity. It is, however, of little value in the examination of supracellular structures but allows the analysis of cells and organelles which can be studied in all their relations to the environment, in contradistinction to biochemical methods. The electron microscope should always be used in combination with the light microscope and the tests should possibly be complemented by physiological and biochemical examinations.

L. Fruhling, A. Porte, E. Stoeckel

(Institute of Pathology, Strasbourg)

Ultrastructural Changes Associated with Dyproteinaemia in Waldenström's Disease

In Waldenström's disease the nature of the cells responsible for macroglobin secretion is still disputed. Electron microscopy of the sternal medulla has frequently shown the development of an ergastoplasmic structure in the majority of reticular cells. These cells can be so considered capable of plasmocytic transformation and protein secretion. The characteristic accumulation of glycoproteins on the wall of the plasmatocytes can be observed at an early point of time. The only changes in the studied cases were seen either in the distribution of young elements or in an incipient differentiation of the evolving plasmatocytes (transitory cells). Usually, the transitory cells predominate. In our view the macroglobulins are made up from plasmatocytic elements.

L. Cossel

(Institute of Pathology, Karl-Marx University, Leipzig)

A Contribution to the Problem of Submicroscopic Connections Between Intercellular Spaces and Sinusoids in the Liver

PAVEL, a Roumanian internist, was the first to suggest in 1949, on the evidence of light-microscopic investigations, that in the normal liver a direct communication exists between the bile canaliculi and Disse's spaces. It was then ROUILLER who, having experimentally produced cholostasis in the rat liver, obtained in 1956 an electron-microscopic picture showing the connections of the bile canaliculi with the Disse spaces. ROUILLER claims the existence of this phenomenon in the normal rat liver as well, and assumes accordingly that the bile canaliculi are connected not only with Disse's space but — through the endothelial pores — with the sinusoids also. ROUILLER's electron-microscopical findings have not been confirmed, all the authors who have investigated this problem by means of electron microscopy are unanimous in denying the existence of the said connections in the normal liver. The present author has examined many human and animal livers under the electron microscope in the course of 4 years, and found that — in certain functional states at least — a communication does exist between bile canaliculi, Disse's spaces and sinusoids, even in unimpaired livers.

J. Ormos, H. G. Solbach

(Institute of Pathology, Medical University, Szeged and Institute of Pathology and 2nd Department of Medicine, Medical Academy, Düsseldorf)

The Ultrastructure of Renal Vessels in Diabetes Mellitus

Kidney tissue specimens, taken by needle biopsy from 18 diabetic patients, have been subjected to electron and light microscopy and compared with the renal biopsies from 14 patients who suffered from other diseases. Apart from glomerulocapillary changes (which are beyond the scope of the present paper), there were changes of the arteries and the veins, less severe in the smooth muscles and the endothelium and most marked in the basement membrane. Conspicuous features were the general thickening of the basement membranes and the more than usual difference in thickness between the single membranes of the basement membrane network. The basement membranes themselves, moreover, became more loose or fibrillary and contained different deposits of apparently lipoid-nature. Similar deposits were sometimes seen in the smooth muscle cells and the endothelium. The lesion was most marked in the afferent arteriolae. Here the substance of the swollen basement membrane network gradually spread over the entire thickness of the vessel wall, displacing other tissue elements, except the endothelial cells which survived for a long time. This manifested itself under the light

microscope with a homogenous PAS positivity of the vessel wall. The absence of Hale-positivity pointed to an increase of neutral mucopolysaccharides. The observed changes in the vessels are thought to be part of the general diabetic lesions, extending to the kidneys if not over the whole organism.

H. Zschoch

(Institute of Pathology, Karl-Marx University, Leipzig)

Changes of the Intrahepatic Branches of the Hepatic Artery in Diabetes

The livers of 100 autopsied diabetics and 50 non-diabetics were examined light-microscopically and histochemically. The small-and medium-sized arteries in the livers of 22 diabetics showed a thick and hyalinized wall and a narrowed lumen. The arteries stained red with haematoxylin and eosin, yellow with van Gieson's and red with azan. There were no elastic and argyrophile fibres present. In the artery walls various histochemical stainings revealed proteins, mucopolysaccharides (especially neutral ones) and various lipids. This histochemical spectrum is similar to that found by GEILER in diabetic glomerulosclerosis. Some of the larger vessels had a hypertrophic media and many elastic fibres in the intima, like in hypertensive vascular disease. The same changes were noted in 2 non-diabetics, one of whom suffered from renal hypertension and the other from severe arteriosclerosis. There were no changes in the capillaries and the liver parenchyma.

Statistical analysis revealed a coincidence of the cases with changes of the hepatic arteries and arteriosclerosis, hypertension, diabetic angiopathy of the kidneys and eyes, and long-term diabetes.

We believe the above changes of the intrahepatic vessels to be non-specific for diabetes, but we assume that diabetes and hypertension — apart from or in connection with each other — might be able to produce the vascular disease.

P. Endes, I. Dévényi, Sz. Gomba, Gy. Dauda

(Institute of Pathology, Medical University, Debrecen)

Response of the Juxtaglomerular Apparatus to Salt-Load, Hydration and Dehydration in Acute Experiments

The so-called granulation index of the granular cells of the juxtaglomerular apparatus is inversely related to the sodium level of the serum, and directly related to the serum potassium level. Animals kept for several weeks or several months on a diet poor in salt have generally been used for experiments of this kind. The effect of a 4 per cent solution of NaCl (group I) and 2.55 per cent KCl (group II), intraperitoneally administered to rats in doses of 3 ml over 24 and 48 hours, has been studied in the present experiments. Members of group III received a 23.2 per cent solution of saccharose which, thus, had the same molar concentration as the 4 per cent salt solution. Members of group IV received an excessive amount of physiological saline, while those of group V were kept on a diet free from water during two weeks.

The administration of KCl induced the expected hypergranulation which occurred in 24 or 48 hours. In contrast to chronic saline treatment, 48-hour NaCl treatment induced likewise marked hypergranulation. It is well possible that degranulation, as observed in chronic experiments, is a phenomenon of exhaustion which is preceded by hypergranulation in the acute phase. However the almost similar hypergranulation following the administration of saccharose points to the possibility that the effect may be partly due to the hyperosmotic nature of the administered fluid. Acute hydration had no effect on the cells, while dehydration provoked intensive hypergranulation. There seems to exist some correlation between the salt and water balance of the organism on the one side, and the granular cells of the juxtaglomerular apparatus on the other.

Sz. Gomba, Margit Soltész, P. Endes

(Institute of Pathology, Medical University, Debrecen)

Histochemical Examination of Amino Acids in the Granulated Cells of the Juxtaglomerular Apparatus

The aim of the present detailed histochemical analyses was to find a criterion for distinguishing the granules in the juxtaglomerular apparatus from mitochondria, the size of the two structures being of the same order of magnitude. The amino acid composition of the granules of the juxtaglomerular cells seemed to allow such a differentiation. Further investigations are in progress with a view to supporting the histochemical findings by the behaviour of the histochemical findings by the behaviour of the granular cells in UV light, the withdrawal of certain essential amino acids, as also by biochemical methods.

J. Simárszky, K. Benkő, P. Endes

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Electron-Microscopic Examination of Kosugi's Granuloid

The intravital development of Kosugi's granuloid was demonstrated in earlier investigations by means of unilateral ureteral ligature. Granuloid was found in the lumen of the primary convoluted tubules of the ligated kidney 8 hours after the intervention, whereas none appeared in the contralateral kidney.

The ureter of albino rats was ligated for 24 hours in the present experiments. Fragments of 1 mm^3 were excised from the cortex of the ligated kidney, fixed in osmium tetroxide and potassium permanganate, embedded in metacrylate, and sectioned for electron microscopic examination. It appears from the preliminary results that the granuloid arises from the cytoplasm of tubular epithelial cells. The structure and possible cellular organelles of Kosugi's granuloid are under investigation.

P. Endes, I. Dévényi, Sz. Gomba

(Institute of Pathology, Medical University, Debrecen)

Experimental Transplantation of Renal Tissue

While literature contains numerous reports on the transplantation of the entire kidney, those on the transplantation of renal-tissue fragments are comparatively rare. The present investigations had the aim to ascertain the behaviour of the granular cells of the juxtaglomerular apparatus in connection with the transplantation of thin fragments of autologous renal tissue in albino rats. The fragments were first implanted to the mesotestis, as recommended by KNAKE. These experiments were unsuccessful because the implants disappeared after 16 days; they were presumably absorbed. Implantation in the second group was made to a pouch formed of the skin of the back. The implants were investigated after 3 to 90 days, 3 animals having been sacrificed at each investigation. The removed transplants were sectioned serially, and every fifth section was stained with combined trichrome; 15 to 80 sections were examined of each case.

Signs of regression predominated in the 3 to 14 day-old transplants. The granular cells were degenerated and poor in granules. Regression had ceased, new vessels had developed, and some surviving renal tissue was found in 30, 60 and 90 day-old transplants. The tubular epithelium seemed to be dedifferentiated, all fine structural differences had disappeared. Scarred glomeruli were frequent, well-preserved ones — with erythrocytes in the loops — were rare. It was only in the afferent arterioles of the surviving glomeruli that granular cells could be observed. In contradistinction to fresh transplants, groups of richly granulated cells appeared in the older ones, with index numbers 4, 6 and even 8.

The transplants were incapable of normal function. This is in contradiction to McMANUS's theory that substances passing through the macula densa are involved in the formation of the granules. No signs of a neural connection with the surrounding tissues were observed so that a development of normal innervation could hardly be supposed. It was evident that, by means of the vascularization required for survival, a humoral connection with the host tissues had developed. After an initial destruction, the granular cells reappeared in great numbers in the heterotopic surviving but not functioning renal tissue. Their accumulation in older transplants and the increase in the number of their granules may have been due to a change of the circulation and the low blood pressure in the graft.

K. Kovács, Margit A. Dávid

(First Department of Medicine, Medical University, Szeged)

Renal Cortical Necrosis Induced by Means of Posterior-Pituitary Extract in Rats Pretreated with Oestrone and Progesterone

After severe postpartum haemorrhage extensive necrosis of the anterior pituitary and hypopituitarism may result (Sheehan's syndrome). With a view to producing this syndrome, large doses of oestrone and progesterone, further, for eliciting vasoconstriction, posterior pituitary extract were administered to rats.

Pituitary necrosis was not observed in any of the cases, whereas necrosed areas could be seen with the naked eye in the kidneys. Histologically, the lesions were similar to tubular necroses suggestive of infarction. Posterior pituitary extract produced no effect without the administration of oestrone and progesterone. In the renal cortex of rats pretreated with oestrone and progesterone no necrosis could be induced by rat's hypothalamic and pituitary extracts, nicotine (which liberates ADH) or other vasoactive substances (serotonin, noradrenaline). Administration of prednisolone or reserpine did not prevent the appearance of renal lesions. The results suggest that hormonal factors seem to be involved in the pathogenesis of renal cortical necrosis.

I. Furka

(Institute of Surgical Anatomy and Operative Surgery, Medical University, Debrecen)

Covering of Experimental Kidney Injuries with Polyamine Netting

According to the literature, the incidence of urogenital injuries amounts to 0.1 per cent of all injuries, and 40 per cent of such cases have involved the kidneys. Since before the injury the organ had mostly been intact, there is every reason for trying the utmost to save it. A proper covering of the injury is likely to prevent such complications as post-traumatic nephritis, hypertension, formation of abscesses and calculi, etc.

The surgical use of synthetic materials gains increasing ground. BORNEMISZA has attained favourable results by the application of polyamide netting in atypical liver resection, for covering vessel defects, in thoracic plombage, etc.

In the present experiments we afflicted extensive injuries to the lower pole of the kidney, applied a few catgut stitches and covered the whole injured area with polyamine (nylon) netting of suitable size and fixed the netting with stitches of a polyamine thread to the kidney. Apart from scarring, there were no consequences. From the synthetic material and the organal cells an "autoalloplastic" substance had formed and spread over the injured surface. There were no haemorrhages, urine infiltration, calculus, hydronephrosis or any other clinical symptoms.

The results seem to indicate that the described method promises satisfactory and reliable results.

Anna Tószegi, L. Pokorny, J. Pocsai, I. Bartók

(Institute of Pathology, Medical University, Szeged)

Effect of the Serum of Partially Hepatectomized Rats on Chronic Liver Injury Induced by Carbon Tetrachloride

Earlier research has revealed a mitosis-stimulating effect on the rat liver of the sera of partially hepatectomized rats. In the present series of experiments chronic liver injury was induced in Wistar rats by 0.1 ml doses of CCl_4, injected subcutaneously twice weekly. One group comprising 26 animals was treated intraperitoneally twice weekly with 2 ml doses of the serum of rats, which had been subjected to subtotal hepatectomy and killed 30 hours after the operation. Of the other group comprising 38 control animals, 14 were additionally injected intraperitoneally twice weekly with 2 ml of physiological NaCl solution, the remaining 24 were treated only with CCl_4. The animals were killed on the 30th, 60th, 90th and 120th day following the beginning of treatment. The hepatic lesions observed at the end of the experimental period (necrosis, structural deformation, fibrosis, proliferation of the bile ducts) were less marked in the serum-treated animals than in the controls. Changes induced by CCl_4 in the succinic dehydrogenase, cytochrome oxydase and alkaline phosphatase activity were unaffected by the sera, but the considerable drop in adenosine triphosphatase activity was fully inhibited by it.

The results seemed to indicate that chronic liver lesions induced by CCl_4 are partly inhibited by the sera of partially hepatectomized rats. It seems worth while to study that affect under different experimental conditions and in other types of liver lesions too.

I. Dévényi

(Institute of Pathology, Medical University, Debrecen)

Effect of Chronic Methylthiouracil Treatment on in situ and Transplanted Thyroid Glands

The right thyroid lobe was implanted in 57 white male rats under the skin of the back of the same animals, and after an interval of 2 weeks a daily dose of 10 mg of methylthiouracil was administered with the food. The animals were sacrificed between the 155th and 678th days. Fortyone rats were treated longer than 400 days.

The purpose of the investigation was to establish whether the thyroid tissue in situ or that transplanted to a heterotopic surrounding would more frequently respond with tumorous growth to TSH stimulation due to the inhibition of thyroxin synthesis by methylthiouracil treatment.

The tumours so induced were adenomas of different types; they were of the same nature at both sites, and none was malignant in nature. Tumorous growth started after 200 days in the normal, and after 400 days in the transplanted, lobe.

Owing to its adequate nervous and vascular supply the physiological surroundings seem to be more favourable for the rise of blastomatogenic effects, even if — as in the present case — neoplastic growth is released by humoral stimulation.

Magda Scholz, M. Székely

(Department of Histopathology, Municipal Hospital Uzsoki, Budapest)

Histochemical Studies of Endometrial Changes

After a review of the pertaining literature, comparisons are drawn between the histochemical patterns of the normal and the diseased endometrium. The purpose was to explain the regressive histological and histochemical changes seen in various pathological forms, and partly to interpret such regressive processes diagnostically. The homogeneous substances forming the by-products of uterine curettages were examined for their staining with haematoxylin-

eosin, van Gieson, Goldner, Gomori, Weigert's elastic fibre, mucicarmine, Best carmine, Schiff, McManus-Hotchkiss, acid and alkaline phosphatase and Feulgen reaction. A total of 800 curettages were examined, from cases of intrauterine and extrauterine gravidity, decidua of uncertain origin, glandular or polypous hyperplasia of the endometrium, myomatous fragments in the curettage, polypus of the cervix and the fundus uteri, atrophied climacteric uterine mucosa, chronic endometritis, interstitial endometritis, changes of the uterine mucosa accompanying hormonal disorders, tuberculous endometritis, adenocarcinoma of the fundus uteri, cancer of the portion, internal adenomyosis, placental retention, and rhabdomyosarcoma.

The results were classified according to the diagnoses. The changes were identified as disintegrated stroma portions, typical polypus, tumour stroma, organized blood clots, hyaline complexes, hyaline thrombus, stromal oedema, fibrinoid necrosis, inflammatory stromal changes, myomatous and tumoral necroses, changes of the vessel walls, haemorrhagic necroses, stromal collagenization, oedematous pools, etc.

It has been found that regressive changes occur frequently in the abrased substance, especially in cases of extrauterine and intrauterine pregnancy and that these two forms of pregnancy produce unequal staining conditions. There are certain regressive changes which defy identification by haematoxylin and eosin and require some other treatment, such as Goldner's reaction and Gomori's silver impregnation. The homogeneous substance of connective tissue origin is conspicuous for the emerald colour given with Goldner's stain. Disintegration of the fibrous network is a feature of hyperplastic processes. The fibrous structure of the endometrium varies according to the cycles of the uterine mucosa.

The tests for glycogen are strongly positive results, notably more so after abortions than after delivery. In the inflamed uterine mucosa the number of collagen and hyalin fibres is increased and that of the elastic ones decreased. Stromal oedema is a concomitant of hormonal disorders and inflammatory changes. Hyperplasia is frequently accompanied by oedematous pools, due to coalesced cystic glands or to secretion discharged into the stroma.

The examination of regressive changes is regarded as a complementary diagnostic tool of curettages.

Gy. Botár, D. Dimitrov-Szokodi

(National Institute of Neurology, J. Balassa Hospital, Budapest)

Changes of the Sympathetic Ganglia in Bronchial Asthma

Ganglia Nos 2 to 5 of the thoracic sympathetic trunk, removed in the course of surgical intervention for bronchial asthma, have been examined after Bielschowsky-Gros'silver impregnation. The pathological changes in the nerve cells of the ganglia were found to be of a secondary character, having arisen under the influence of fever, hypoxia, etc. caused by the primary disease, namely asthma. There seemed to be no difference in this respect between young and mature nerve cells. One-third of the nerve cells showed pathologic changes in mild, and two-thirds in grave cases. The range of changes was narrower in young cells (accumulation of lipoid granules), and wider in mature ones (accumulation of lipoid granules, axonal hypertrophy and hyperplasia, vacuolisation, cellular fenestration). The accumulation of lipoid granules cannot be regarded as an accumulation of pigment due to old age, and the unipolar, bipolar and tripolar glomeruli induced by axonal hypertrophy and hyperplasia must not be looked upon as higher forms of nervous conduction.

Gy. Miklós

(Department of Pathology, János Hospital, Budapest)

Cytomegalic Inclusion Disease

In the course of earlier studies cytomegalic inclusion disease (C.I.D.) has been observed in 12 out of 50 infantile cadavers. The frequent association of the condition with interstitial plasma-cell pneumonia was remarkable.

Additional studies of another 50 cases revealed C.I.D. in 19 more infants, of which 5 cases were generalized, while only the salivary glands had been affected in 14 instances. No signs of the disease were observed at the autopsy of 50 foetuses and newborn babies, and 20 adults.

In the generalized cases the C.I.D. had affected the kidney in 4 instances, the lungs in one, and the pancreas likewise in one case. During life the disease remained unrecognized in all cases, and only post-mortem examination led to the establishment of a correct diagnosis. The case of pancreatic C.I.D. manifested itself by grave acute haemorrhagic suppurative pancreatitis and the pulmonary C.I.D. with interstitial plasmacell pneumonia. Renal C.I.D. was accompanied by moderate interstitial infiltration. In some cases the C.I.D. of an organ was associated with interstitial infiltration (without giant cells) of another organ. As the examined material consisted of 1 to 7-month old babies, extramedullary haemopoiesis was rare.

The frequency of interstitial plasma-cell pneumonia was remarkable, 16 out of a total of 19 cases. The association of C.I.D. with other infectious diseases was less frequent; there were 2 cases of associated enterocolitis and one case each of staphylococcal pneumonia, of otitis media and of post-poliomyelitic state. Common bronchopneumonia — mostly a secondary terminal infection — occurred in 14 cases.

Another striking feature was the comparatively frequent association of C.I.D. with developmental anomalies (6 cases), such as malformations of the heart, the large vessels, the central nervous system and the digestive apparatus, further Down's disease. No other diseases, usually associated with C.I.D., e.g. blood dyscrasia, haematological systemic diseases, tumours or ulceration, were observed in the examined material.

The significance of C.I.D. is not fully clarified. The disease is mostly due to intrauterine and less frequently to postnatal infection. It promotes a further deterioration of premature and other damaged infants, raises the frequency of secondary infections, and may, thus, lead to death. Generalized C.I.D. may be fatal in itself.

Klára Szemenyei, H. Jellinek, L. Nagy

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

Vascular Changes Subsequent to Acid Treatment

The infrarenal portion of the abdominal aorta on guinea pigs, rats and rabbits has been painted with concentrated hydrochloric acid. Subsequently the animals were killed at different points of time and the changes were studied. It was found that in the acute phase not only the smooth muscle cells and collagenous fibres disappeared but also the endothelial cells and acid mucopolysaccharides. The elastic fibres, although altered in structure, persisted. They formed the basis for the regeneration of the vessel wall, beginning with an increase of acid mucopolysaccharides and of cells at the boundary between the intact and affected regions. The cells, invading the necrotic areas gave rise to elastic fibres, even to a new internal elastic membrane, thus letting the regeneration of the vessel wall to a certain degree.

I. Kádas, M. Németh-Csóka, Enikő Pintér, Mária Simon

(Department of Pathology and Central Laboratory, County Hospital, Pécs)

Chemical and Histological Postmortem Analysis of the Myocardium

Recent investigations have made it clear that the electrolyte balance is upset in the incompensated myocardium as also in the area of cardiac infarction, and that this phenomenon contributes to a deterioration of cardiac function. Relying on these observations, in autopsy material selected at random the sodium, potassium, in some instances the chlorine, lipid and water contents of the myocardium of both the right and left ventricles have been studied. The results were compared to the clinical picture with special regard to the degree of failure, the extent of clinically observable lesions and the values of the serum electrolytes. Apart from corroborating the literary data, the results furnished useful information concerning the fatty degeneration of the myocardium (interconnection of the positivity of fat staining and the quantitative values), the incongruence of changes in the electrolyte values in the serum and the tissues, further about the possibility to demonstrate myocardial lesions in infantile toxicosis.

Gy. Gorácz, Éva Konyár

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

Cardiac Changes in Experimental Hypertension

The myocardial and vascular changes developing in white rats under the effect of experimental hypertension of the malignant type have been examined for a period of 70 days. As regards the myocardium, changes presented themselves in both ventricles as early as the second day. Vascular changes were observed with light microscopy only on the 5th to 6th day. Early myocardial necrosis without preceding vascular change resulted in diffuse scarring and so did necroses due to a previous vascular change; these are distinguishable from the former type only on the basis of the site where they occur.

A. Potondi, Gy. Gorácz

(Insitute of Forensic Medicine, Medical University, and 2nd Institute of Pathology, Medical University, Budapest)

Coronary Aneurysm

Five cases of coronary artery aneurysm are discussed. One, each, of two arteriosclerotic aneurysms occurred in the left descendent and the right marginal branch, respectively. A congenital cirsoid aneurysm was encountered at the apex of the left ventricle. The right coronary artery originated with a funnel-like dilatation in two cases. All these anomalies were registered post-mortem. Death had not been due to the aneurysm. Coronary aneurysm is a rare conditon; although it is of a certain significance in pathology, patients so afflicted suffer no serious inconvenience.

J. Balogh

(Department of Pathologic Anatomy and Pathohistology, County Hospital, Szekszárd)

Argyrophilic Fibre Structure Changes of the Pulmonary Arteries in Hypertonia of the Minor Circulation

The paper is concerned with hypertonic pulmonary blood vessel changes due to a primary lesion of the lung parenchyma. It was found that the argyrophilic fibre system has undergone a typical transformation, incident to the characteristic and well known process of elastic hyperplasia.

Distinctive marks of the injury are found partly in the perielastically located argyrophilic fibre structures themselves, partly in their relationship to the subendothelial and endothelial layers.

It has been revealed that changes in the elastic fibre system are always concomitant and related with changes in the argyrophilic structure.

These changes are believed to result from an increased stress of the vessels rather than from advanced age.

J. Juhász, E. Szalay

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

Experimental Cholesterol Crystal Embolism in the Pulmonary Circulation

Pulmonary embolism in rabbits has been induced with material obtained from atheromatous plaques of human aorta. The animals were killed at different time intervals and the effects of cholesterol crystal embolism in the branches of the pulmonary arteries have been studied.

In the early period there was panarteritis and foreign body giant cell reaction around the cholesterol crystals. Recanalisation of the vessels with subintimal proliferation of connective tissue set in within 7 to 14 days. There was no sign to indicate an absorption of cholesterol crystals. During recanalisation many of the original vascular lumina have been observed to disintegrate into several parts and regular elastic membranes to form around the new lumina. There was one animal only to present a haemorrhagic infarction. The findings seem to be indicative of a rapid regenerating capacity and a high functional adaptability of the pulmonary arteries. The method seems to give a favourable possibility for experimental studies of pulmonary embolism.

Aleksandra Krygier, Aleksandra Tustanowska, K. Stojalowski

(Department of Morbid Anatomy of the Medical Academy, Szczecin)

Morphological, Histochemical and Chromatographic Investigations of the Subcutaneous Nodule in the Course of Rheumatoid Arthritis

Combined morphological, histochemical and chromatographic investigations have been carried out on the subcutaneous nodule of the elbow region. Standard preparations were produced of the skin taken from the ulnar region of persins not affected by rheumatoid arthritis. Morphological investigations were used for topographic orientation.

Staining of the ground substance for acid mucopolysaccharides was performed to provide a basis for histophotometric measurements. Their results were found to correspond to the relative acid mucopolysaccharide. Chromatographic studies were carried out in hydrolysates of the same nodules and of the same sections of normal skin. The object of these investigations was to determine the amount of hexosamines (glucosamine and galactosamine).

The level of hexosamines was invariably elevated in the rheumatoid nodules. The increase in the amount of glucosamine was pronounced. The histophotometric measurements revealed a marked increase of acid mucopolysaccharides with both the carboxyl and sulphate groups in the course of the node formation, while at the time of full nodular development a considerable decrease in the acid mucopolysaccharides with sulphate groups was noted.

The nodules, being characterized morphologically by a high number of fibrinoid deposits, scanty granulation and poor collagen fibre production, displayed a slight rise of the acid mucopolysaccharide level in the ground substance. Chromatography revealed a high glucosamine level, whereas histophotometry showed an increase of the acid mucopolysaccharides with sulphate groups in all nodular types. The comparison of these two facts implies, in the subcutaneous nodules, the appearance of acid mucopolysaccharides of heparine sulphate or heparin types along with the raised level of chondroitine sulphates and hyaluronic acid. This was further supported by the presence of a high number of mast cells in the subcutaneous nodule. The elevated acid mucopolysaccharide level allows an increased production of collagen fibres in the subcutaneous nodule.

J. Kövi

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

Nonreactive Generalized Tuberculosis in Cases of Leukaemia Treated with Corticosteroids and Cytostatics

SIEGMUND in 1939 introduced the name of nonreactive generalized tuberculosis for a fatal form of tuberculosis characterized by an extremely acute course, high fever and a multitude of millet-sized necroses in the internal organs without the least sign of a cellular reaction, mostly concomitant with a serious disorder of the haemopoietic system. Pathological changes corresponding to the picture of nonreactive generalized tuberculosis were found in three cases of leukaemia which had been treated with corticosteroid and cytostatic drugs. Histology confirmed the nonreactive character of the lesion. Ziehl-Neelsen'stain revealed a great number of acid and alcohol resistant rods in the necroses. In the discussed cases it seems to account for the nonreactive form of tuberculosis that the reticuloendothelial system which is the main guard to avert the tuberculosis bacillus, is also the principal object exposed to the destructive attack of leukaemic proliferation. An additional decrease of the cellular and humoral defense by the corticosteroid and cytostatic drugs may also contribute to the nonreactive character. Unless a biopsy (liver, spleen, medulla) is made, it is difficult to diagnose nonreactive generalized tuberculosis *in vivo* because of the non-specific progress, so that the disease is usually recognized post mortem only. The increasing use of corticosteroids and cytostatics, especially in the treatment of leukaemia, gives reason for fear that a multiplication of nonreactive generalized tuberculosis cases will have to be reckoned with.

J. T. Kelemen, Margit B. Soltész

(Institute of Pathology, Medical University, Debrecen)

Contribution to the Histochemistry of Sarcoidosis (Besnier-Boeck-Schaumann's Disease)

Histochemical investigations have been performed on granulation tissue in cases of Boeck's sarcoid. As a first step, protein-histochemical reaction were made on lymph nodes and skin showing spontaneous sarcoidotic changes, and on skin changes induced by the injection of Kveim-antigen. In all of the cases tuberculous granulation tissue of proliferative character served for control. The reaction was identical in all the three groups, *i.e.* there was no difference between the spontaneous granuloma and the artificially induced granulation, nor between the protein-histochemical reaction in sarcoidosis and tuberculosis. The largest quantities of the various protein components were present in the giant cells. Studies with carbohydrate and lipoid as well as enzyme histochemical methods are in progress.

I. Kiss

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

Cicatrization in the Hilus-Pulmonary

A history of thrombo-embolic disorders is a frequent feature in senile patients suffering from cor pulmonale. Less frequently, if ever, is there a mention of changes of the hilar lymph nodes. In a great proportion of subjects died between 70 and 90 years of age cartilaginous scars of the hilar lymph nodes accompanied by hilar constriction has been found, the cicatrized or anthracotic lymph nodes frequently penetrate the main bronchus and the pulmonary artery, leading to lethal haemorrhage. Most complications, however, result from the hypertrophy and dilatation of the right ventricle.

The process is a non-specific one, with anthracosis as the predominant cause. The often observed accumulation of cholesterol crystals points to a chronic state.

The pathologic picture ranks among those of senescence. Its high incidence in X-ray records perhaps accounts for its being sometimes mistaken for a tumour.

Gy. Regöly-Mérei

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

Microscopical Investigation of Ground Specimens and Decalcified Sections of Palaeopathologic Bones

Decalcified sections and ground specimens have been made from remains dating from various periods between the aeneolithic age and the 11th century. Picric acid has proved to be the best decalcifying agent. In acid soils, especially in those containing carbonic acid, the bones are greatly apt to decalcify. The osteon-structure appears most clearly in ground sections but in decalcified ones the lamellar system, too, is discernible, as well as traces of the bone composition and of the decomposition process. The microscopic picture revealed several types of pathologic change. There were marks indicative of signs to pathomorphosis.

Gy. Miklós

(Department of Pathology, János Hospital, Budapest)

Inflammations of Foetal Membranes and Foetuses under 800 g Weight

At the 1960 Congress of Hungarian Pathologists the author has reported on the association of intrauterine enteritis with pneumonia. The phenomenon was attributed to the swallowing and aspiration of amniotic fluid; on account of lacking adequate material, it was not possible to study the inflammation of the foetal membranes.

In the course of further investigations — made with a view to studying intrauterine infections and their frequency — the autopsy material of 50 still-born and their foetal adnexa was subjected to a detailed histological analysis. In 6 instances signs of intrauterine inflammation were encountered, with pneumonia in all of them, together with enteritis in one, and hepatic abscess in another case. The foetuses ranged in weight from 190 to 780 g. (Inflammatory changes of presumably prenatal origin found in living premature or full-term babies were disregarded).

These intrauterine inflammatory processes were accompanied by pathological changes in the foetal membranes; both the amnion and the chorion showed signs of inflammation in 5 instances. (The membranes were not examined in the 6th case). The membranes exhibited granulocytic infiltrations of a phlegmonous character which must have been derived from maternal leukocytes, and this the more so as the major part of foetuses of small weight did not produce granulocytes. Likewise, maternal leukocytes appeared in the bronchi and the intestines, and some of them had passed through the walls of these organs. Immature myeloid (haemopoietic) foci had developed around leukocytic accumulations in the foetal tissues; they represented the inflammatory defence of the foetal organism. Likewise, only myeloid elements were found in the wall of the hepatic abscesses, while neither the placenta nor the umbilical cord displayed pathological changes.

There was no chorioamnionitis or any other intrauterine inflammation in any of the controls. The occasional presence of leukocytes in the foetal membranes or in the lumen of the respiratory or digestive channels can be regarded as a physiological phenomenon, and the same applies to the aspiration or swallowing of amniotic fluid. Absorption of amniotic fluid occurs through the foetal lungs.

The present investigations have confirmed the theory that intrauterine pneumonia is due to aspiration, and that the infection is spread to the respiratory and digestive apparatus by the amniotic fluid infected through the inflamed membranes. Another possible way of infection is the blood path (this seems to have been the process in the case of the hepatic abscess), and it is in this way that other specific processes, as viral infections, give rise to foetal lesions. Grave haematogenic infections in this agegroup may lead to developmental disorders belonging to the category of foetopathies.

Infection may occur with intact membranes in the case of an excessive width of the cervical canal or a weakness of the cervix, and give rise to abortion or premature delivery. Abor-

tion due to other causes may, on the other hand, promote a secondary inflammation of the foetal membranes. It is, however, questionable whether such intrauterine inflammations are always responsible for foetal death. Prolonged spontaneous abortions may also lead to an infection of the membranes or the amniotic fluid. The latter assumption seems to be confirmed by the fact that none of the examined foetuses had been macerated. Although macerated foetuses are hardly suitable for a histological study, pneumonia can nevertheless be recognized in most cases, since even long maceration does not considerably affect the lung pattern.

I. Schneider, F. Szarvas, S. Benkő

(Department of Dermatology and 1st Department of Medicine, Medical University, Szeged)

Effect of Serotonin in the Eearly Phase of Experimental Hepatic Lesion

Chronic administration of serotonin reduces the activity of certain enzymes in the liver. It was also observed that serotonin, if administered for a week or longer, reduced hepatic damage due to carbon tetrachloride. In the present study the effect of serotonin in the early phase of carbon tetrachloride-induced hepatic injury has been investigated. Carbon tetrachloride, 0.05 ml per 100 g was administered subcutaneously to white male rats with a body weight of about 200 g, and the animals were sacrificed 10 hours later. A second group of rats received, moreover 1.5 mg per 100 g of serotonin-creatinin sulphate, subcutaneously. A third group received only serotonin, and a fourth group only physiological saline. The serum level of transaminase and alkaline phosphatase was determined, the liver was studied histologically and histochemically (succinodehydrogenase and alkaline-phosphatase activity; periodic acid-Schiff reaction, Sudan black).

Serotonin failed to inhibit the early hepatic effect of carbon tetrachloride; it reduced the succinodehydrogenase activity of the liver even if it was administered alone, and induce ' nearly the same elevation of serum transaminase level as carbon tetrachloride.

A. László, L. Pokorny, D. Bara (Bachrach)

(Institute of Pathology, Medical University, Szeged)

Effects of Chronic Diencephalic Lesions on the Adenohypophyseal-Thyroid System

Small bilateral electrolytic diencephalic injuries were inflicted in white rats with a view to demarcate the most sensitive neural structure within the thyrotropic region of the hypothalamus. At the same time it has been studied what other nuclear regions are able to take over the thyrotropic control function when a hypothalamic injury has decreased the reactive capacity of the adenohypophyseal thyroid system.

For this purpose six to six and a half months were allowed to pass after the hypothalamic injury, before treatments such as thiouracil, hemithyreoidectomy, have been applied to stimulate TSH secretion.

It has been found that a bilateral lesion placed at least half a year earlier in that part of the hypothalamus which hemispherically covers the paraventricular nuclei, inhibited the compensatory hypertrophy of one lobe subsequent to hemithyreoidectomy. Probably of similar effect was the injury situated in the close vicinity of the upper margin of the hypothalamus, in the plane of the paraventricular nuclei. It seems unlikely that at a later point of time other nuclear regions should take over the control to stimulate thyroid function when the hypothalamic injury is situated in the "thyrotropic area".

Under the given experimental conditions a chronic lesion of the paraventricular region or the eminentia medialis region somewhat inhibited the goitrogenic influence of methylthiouracil, but was not able to eliminate it fully.

J. Balogh, L. Wallacher

(Department of Pathologic Anatomy and Pathohistology, County Hospital, Szekszárd)

Morphological Aspects Concerning the Accidental Involution of the Thymus in Infancy

Variations in the Hassal-corpuscles of the thymus have been studied post mortem in infants succumbed to infectious disease, lesion of the alimentary tract or toxicosis.

The histochemical changes typical for the state of "Hassal-corpuscle excitation" (HAMMAR) are described.

Some features are pointed out of the argyrophilic reticulum structure changes which are regarded as characteristic in such cases.

G. Kendrey, L. Cossel

(1st Department of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest and Institute of Pathology, Karl-Marx University, Leipzig)

The Electron-Microscopic Structure of a New Transplantable Mouse Ascites Sarcoma, Induced by Isonicotinic-Acid-Hydrazide

Except for the Ehrlich ascites carcinoma, the electron microscopic structure of ascites tumours is scarcely known.

The present study deals with the electronmicroscopic investigation of a new transplantable ascites sarcoma in the mouse, induced by JUHÁSZ, BALÓ and SZENDE by prolonged intraperitoneal administration of isonicotinic-acid hydrazide (INH). The animals were examined 7 to 8 days after their inoculation with the ascites tumour. The anaplastic and immature cells of the ascites sarcoma presented either very few mitochondria mostly of abnormal structure or none at all. The endoplasmic reticulum was poorly developed, in many cell portions fully absent, and there were only few free Palade granules in the cytoplasm. Extension of the Golgi apparatus was observed in many tumour cells. In the hyaloplasm there was a fairly great number of osmiophilic fat droplets and vacuoles of various sizes. The occurrence of microvilli inside the latter seems to prove that the vacuoles originated from folds of the cell membrane. Virus-like particles 450 to 2000 Å in diameter were detected in the cytoplasm and 500 to 800 Å in diameter in the nucleus of certain tumour cells. They corresponded in part to Bernhard's "A" and in part to Bernhard's "C" type. What may be regarded as the most significant finding is the intranuclear localization of virus-like particles, seen for the first time in a growth other than Ehrlich ascites carcinoma or tumours due to polyoma virus.

G. Kelényi, S. Orbán, E. Zombai

(Institute of Pathological Anatomy, Medical University, Pécs)

Electron Microscopic Observations on a Transplantable Chloroleukaemic Tumour of the Rat

The transplantable chloroleukaemic tumour of the rat is known to be of haematopoietic origin, is made up of myeloid cell elements and reticulum cells, containing porphyrin and myeloperoxidase.

Osmium tetroxide-fixed and methacrylate-embedded tissues of the tumour have been studied by the electron microscope. In ultrathin sections of the tumour the chloroleukaemic reticulum cells presented a great number of phagosomes (lysosomes) which are likely to have some relation with certain biological properties of the tumour. Elementary bodies reminding viruses were found neither in the reticulum cells, nor in the parenchyma cells. The specific, myeloperoxidase containing granulation of normal myeloid cell was absent in the chloroleukaemic myeloid cell elements.

M. Sellyei, D. Heinz

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

The Ultrastructure of Mouse-Mastocytoma

Furth's mastocytoma has been adapted to a non-registered albino mouse strain, though originally it could only be inoculated into mice of LAf_1 type. The tumour growing in the albino mice contained large quantities of heparin, serotonin and histamine. By means of light microscopy it was possible to observe in the cytoplasm of the tumour cells some slightly PAS positive granules which stained metachromatically with toluidine blue.

Electron microscopy of the tumour tissue, fixed in osmium and embedded in Vestopal revealed in the cytoplasm granules 0.8 to 1.4 μ in diameter, enclosed in a simple membrane 150 Å thick. The granules were made up of a material showing a filamentous or globular pattern. The density of the individual granules varied.In the cytoplasm, near the granules, mitochondria 0.6 to 1.2 μ long and 0.2 to 0.3 μ wide were seen. The cytoplasm contained many free RNP granules. In the cisterns of the scanty endoplasmic reticulum, and in a few instances in the granules of the most cells, there were virus-like particles 50 to 80 mμ in diameter. The nucleoids of varying electrodensity measured 30 to 45 mμ in diameter. They were enclosed by a double membrane. The virus-like particles corresponded to Bernhard's type "A".

In a tumour examined 24 hours after the subcutaneous application of protamine sulphate, most granules were shrunk and around the substance of increased electrodensity a light halo was observed. In the centre of some granules the substance was loose and in the marginal parts it formed round or oval clots 40 to 120 mμ in diameter.

I. Orbán, G. Kelényi, Á. Gogl

(Institute of Pathology, Medical University)

Electron Microscopic Investigation of Peculiarly Differentiated Tumours

Two hormonally active tumours are described. One occurred in a woman showing signs of virilization and was recognized as an adenoma originating from the zona reticularis of the adrenal cortex. The other tumour was found in a man showing signs of feminization. The neoplasm was a testicular Leydig-cell tumour. Under the light microscop both tumours presented well-known histological characteristics. Under the electron-microscope, however, the Leydig-cell tumour showed, in addition to a highly developed ergastoplasmic system, a smooth endoplasmic reticulum reminiscent of the so-called myelin pattern. In the adrenocortical tumour, apart from lipoid drops there were ergastoplasmic membranes and smooth endoplasmic reticulum. Data in the literature seem to support the hypothesis that the smooth endoplasmic reticulum systems observed in both cases have some connection with the hormonal (sexual-steroid) synthesis of the tumour cells.

K. Lapis, F. Guba

(Oncopathological Research Institute and Chemical Structural Research Laboratory, Hungarian Academy of Sciences, Budapest)

Ultrastructural Changes in Ascites Lymphoma Cells Caused by Different Chemotherapeutics

The ultrastructural changes caused by one single large dose of different chemotherapeutics (Degranol, Endoxan, Sarcolysin, Vinca alcaloid) in ascites lymphoma cells have been examined, at various points of time (1 to 120 hours) following treatment.

The early, degenerative changes produced by the various agents were essentially similar, the only differences noticeable being merely quantitative or chronological. An exception to this was Vinca, which produced a marked and early nuclear effect. Another difference was the appearance of virus-like corpuscles following Degranol and Endoxan treatment, this was not observed after treatment with the two other agents.

The changes produced by the various drugs were much more different in the later, so-called regenerative phase. Multinucleated cells appeared. It was particularly remarkable that in response to certain drugs cells of more differentiated ultrastructure than the original cells might appear. For example, following treatment with Sarcolysin, cell structures resembling protein synthesizing cells, very rich in endoplasmic reticulum were observable.

L. Nagy, J. Pintér, R. Thurzó

(2nd Institute of Pathology and Department of Urology, Medical University and Department of Surgery, City Hospital, Csepel)

Androblastoma

The pathology, clinical course and histology of three cases of androblastoma are discussed with reference to the pathohistological aspects of differential diagnosis, the disease being often mistaken for other forms of testicular tumour.

Margit Zombori, Gy. Gorácz

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

Mammary Sarcoma

One case of sarcoma phyllodes and one of polymorphous sarcoma are described, compared with the pertaining data from the literature and discussed from the angle of prognosis.

S. Braun, M. Erdélyi

(Department of Pathology, Péterfy Sándor Hospital, Budapest)

The Leukemogenic Effect of Janus Green B in Amytal Ascites Sarcoma of Mice Treated with O_2 and NO

The "O_2 and NO effect", first established as a result of ionizing radiation, was believed to be induced chemically solely by acridine orange. We have succeeded in inducing it in amytal ascites tumour cells with Janus Green B (JgB) under conditions excluding an ionizing radiation effect or photosensitization by visible light. JgB of the same M-concentration has been found to exert a different effect according to whether it was applied during N_2, the O_2, or the NO gas phase. As concerns the N_2 phase, when the ascites cell had been incubated for as long as 120 minutes, JgB gave rise to lethal ascites tumours and the mice died within 18 days of the inoculation. The same ascites-JgB mixture was incubated during 15 minutes in optimal O_2-gas phase and then injected into normal adult mice, the animals survived for from 31,6 to 412 days according to the molar concentration of the JgB. In a proportion between 10 and 80 per cent, depending again upon the M-concentration, the ascites character ceases in the tumours which had been inoculated in the ascites form. At the same time 25-to 60 per cent of the animals died with lymphatic leukemia after an average incubation period of 412 days.

During the NO phase, the life of inoculated mice was lengthened with 161.9 days. The tumour which had been transferred in the ascites form, assumed a solid character in 10 to 45 per cent, depending upon the M-concentration, but lymphatic leukemia we observed only in one per cent of the incubated animals.

It must be stressed that the appearance of spontaneous leukemia has not been observed in our inbred mouse strain, either after the transfer of untreated ascites tumour or JgB incubation during the N_2 gas phase. Lymphatic leukemia during the O_2 phase did not occur under incubation with NaCl instead of JgB, but was provoked in a high proportion by JgB-treated ascites tumour cells.

A long period of latency, preceding the transformation of ascites into solid tumour, as also the long latency before the outbreak of lymhatic leukemia, point to subcellular transfer. Energy transfer is influenced by the paramagnetic effect of O_2.

Depending on the M-concentration, the "O_2-effect" changes the characteristics of the transferred ascites tumour cells, resulting either in solid tumour or in lymphatic leukemia, the latter even in the progeny. Much the same changes in the ascites tumour cells are brought about by NO, a combination of oxigen-like paramagnetic effect, although so far, conversion to solid tumour has only been observed.

M. Kovács, J. Kövi

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

The Formation of Polynuclear Tumour Cells in JBK Ascites Sarcoma

Opinions differ as to the formation of polynuclear tumour cells. ATSUMI, LETTRÉ, KELLNER and others claim that such cells originate from amitotic cell divisions, while according to NAGATA, OBERLING, BERNHARD and others they would arise from irregular divisions.

The phenomenon has been studied in the JBK ascites tumour of the mouse. Using 70 white male and female mice between 18 and 25 g body weight, of our own breed, we inoculated each animal intraperitoneally with 0.20 ml tumorous ascites. For 14 days following inoculation we counted the polynuclear tumour cells in the smears taken each day from 5 different animals. We found in the early period of growth not more than 1 to 2 per cent polynuclear (binuclear) cells. The proportion increased considerably as the tumoral growth progressed. Similarly, the proportion of irregular cell divisions was low at the beginning and gradually higher in the later stage.

In numerous polynuclear (binuclear) tumour cells Feulgen staining revealed internuclear connection threads consisting of DNA, probably as remainders from the bridges of previous irregular divisions. The findings justify the assumption that polynuclear (binuclear) tumour cells arise from mitotic divisions rather than from amitoses.

G. A. Dombrádi

(Institute of Physiology, Medical University, Szeged)

Comparative Investigation of Succinic Transhydrogenase Inhibiting Action of Anti-Tumour Agents on Normal and Tumour Tissue

L. Barla-Szabó

(Department of Histopathology, Municipal Hospital Uzsoki, Budapest)

Symbiosis of Melanocytes with the Epidermis and the Hair Follicle

The studies by DuShane, Dorris, Eastlick, Ris, Lopashov, Newth and Rawles have led to the teaching about the neural crestic origin of the melanocytes. This holds for epidermal as well as follicular melanocytes, since it is the latter type that served Rawles to establish his results concerning melanocytogenesis. Except what is known as the "Mongolian spot", the melanocytes in the human skin are capable of a pigment production only in symbiosis with the epidermis and the hair follicle. Danneel and Clefmann has shown in the mouse embryo that the melanocytes which entered the hair follicles, first intrude the epidermis from where they pass along the follicle to the hair bulb. We obtained the same results with embryos of guinea pigs. As concerns migration along the hair follicle, however, our studies have revealed a great difference between the guinea-pig embryo and the Caucasian human embryo, while in the former the melanocytes were impregnated with the same intensity with Masson's method in paraffin sections, whether they just entered the epidermis or passed on along the follicle or settled in the hair bulb, whereas in humans it is only on their invasion of the hair bulb and in the lower third part of the hair follicle that impregnation is pronounced with this method and the identification of epidermal melanocytes is more complicated. Moreover, in the human embryo follicular melanocytes become visible on Masson's impregnation in paraffin sections only when the follicle is developed. Considering the common origin of the epidermal and the follicular melanocytes, in man the original cell form exhibits histochemical differences according to its actual localization but in the guinea pig such differences are absent. We have found the same differences to exist even in the adult, as revealed by the dopa-test and Masson's silver impregnation. These findings agree well with those of Fitzpatrick and Kukita who found the follicular melanocytes to be characterized by a permanent tyrosinase activity. On the contrary, the epidermal melanocytes, apart from certain regions, become tyrosinase-active under the effect of ultraviolet radiation. Our observations have shown that the epidermal pigmentation of the guinea pig is independent of ultraviolet rays but the colour spots correspond to those of the hair. In man, however, the pigment producing apparatus of the epidermis is a functionally separate one from that of the hair; this means that the follicular melanocytes are in permanent activity to supply pigments for the growing hair, whereas the activity of the epidermal ones greatly depend on ultraviolet radiation. For that reason the epidermal melanocyte in the white man embryo cannot differentiate as intensively as in the guinea pig to a rigid cell type of permanent activity, but persists in a labile state to respond readily to the effect of ultraviolet rays. Owing to its low activity, it is less easy to demonstrate. The phenomenon is a typical example of differentiation under the modifying effect of the environment and of functions conditioned by the environment, which lead to histochemical variations in the derivatives of one and the same type of cell.

The differentiation of the follicular and the epidermal pigment-forming apparatuses occurs prenatally in human beings. While, in the embryo of the guinea pig, both the epidermal and the follicular melanocytes (except the albinotic inactive cells) develop into cells that form and contain abundant melanin, our investigations have shown that, in the human embryo, only follicular melanocytes continue to contain native melanin. The epidermal melanocytes contain considerably less native melanin and even that disappears completely after the fifth month of pregnancy. This would mean that, as regards production of melanin, the epidermal melanocytes of human embryos remain indifferentiated.

The results are also illustrative of the fact that melanin formation in white man only takes its beginning when the skin and its ancillary organs have completely developed. This is the case for the follicular melanocytes in the embryo whereas the epidermis which attains its full development only after birth, there is but a premelanin activity and definitive native melanin production proper begins in the post-natal period only.

A. Porte, A. Brini, M. E. Stoeckel

(Institute of Pathology, Strasbourg)

Electron-Microscopic Studies Concerning some Embryologic Problems of the Eye

Differentiation of the lenticular fibres, formation of the capsule and appearance of the vitreous body has been studied in chick embryos. In the induction stage there was no evidence of a connection between lens and retina. The vitreous consists of a fibrous substance which precipitates in the vitreous cavity without any relation either to the adjacent or to the basal cells (capsule and basal nerve cells). This process gives rise to collagen formation of which the vitreous body only represents a peculiar manifestation. The differentiation of primary fibres coincides with the development of the capsule. The epithelium at the cortical part of the human cataract is able to regenerate, owing to a basal growth of capsular type. This, like the embryonal epithelium, may determine a capsule formation.

Sz. Virágh, A. Porte

(Institute of Pathology, Medical University, Szeged and Institute of Pathology, Medical University, Strasbourg)

Electron-Microscopic Studies of Myocardial Development in Embryos

Myocardial development of the rat embryo has been studied by light and electron microscopy. The examinations covered a period from the 10-day embryo till the 7-week old animal. The most significant cardiac changes were observed to occur till the 16th day after conception. In the wall of the simply twisted 10-day heart-tube the outer cells present a higher degree of maturity than the inner ones which have gradually taken shape from subendocardial connective tissue elements. Myofilaments, arranged in cloud-like groups and measuring about 100 to 120 Å in thickness, lend the young muscle cells their first distinctive feature. What first appears of the striated structure is the Z disk; other parts advancing towards the sarcomere centre become distinct at a later time. The sarcoplasmatic reticulum assumes the characteristic form of mature musculature at the time of the myofibrils' differentiation. In young cells the Golgi apparatus is more extended than in the more mature ones. The cell membranes are frequently interconnected by thick portions of the desmosome type, hardly distinguishable at first from intercalated disks. With the maturation of the embryonal myocardial tissue its complicated initial structure assumes a more simple and regular form. In ultrastructure there is little difference between the heart of a 17-day embryo and that of a 10 to 15-day old animal. Subsequently the differences in atrial and ventricular fibre development and some major points egarding the function and morphology have been discussed.

B. Benke, P. Röhlich

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

The Relation between the Spinal Meninges and the Peripheral Nerve Sheaths in the Rat

The relation between the spinal meninges and the peripheral nerve sheaths has been studied by electron microscopy. It has been found that the dura mater is continued in the epineurium, while the arachnoid is in close connection with the perineurium. At the region of the posterior root, the arachnoid is partly transformed into perineurium, and partly connected with the perineurium of the distal part of the root. The physiological significance of these structural connections is discussed.

P. Röhlich, B. Aros, B. Vigh

(Institute of Histology and Embryology, Medical University, and Morphological Department, Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest)

Electron Microscopic Studies of Neurosecretory Cells

Since neurosecretory cells of vertebrates are most difficult to examine electron microscopically, such cells of the cerebral ganglia of the earthworm have been examined for neurosecretion. The secretion granules in the ganglia are submicroscopic in size (280 mμ), dark, homogeneous, and usually possess osmiophilic limiting membranes. It has been attempted to elucidate the development of secretory granules by comparative studies of the cells in the various phases of secretory activity. It has been found that the dark homogeneous substance characteristic of the secretion appears in the Golgi apparatus. The Golgi vesicles gradually become secretion vesicles, then secretion granules. The development of secretion is usually accompanied by a decrease of the ergastoplasm. Besides the organelles of ganglionic cells, the submicroscopic structure of glial cells and capillaries is described, with special reference to neurosecretion.

B. Vigh, B. Aros, T. Wenger, Sára Koritsánszky, G. Ceglédi

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

Effect of Dehydration and Rehydration on the Hypothalamic Glial Cells Containing Gomori-positive Granules

The hypothalamus is known to contain numerous Gomori-positive glial cells. The cells can be divided in two groups. The one type is situated around the vessels, the other one can be found beneath the ventricular ependyma.

It has been assumed by some authors that the granules arise in the glial cells by phagocytosis of the neurosecretion, but it is quite possible that one is dealing with a kind of "glial secretion", i.e. that the granules are produced by the glial cells themselves.

In the present experiments, after rehydration a change was found to be accompanied by a rise in the number of the perivasal glial cells. The periventricular glial cells seem to be in relation with the ependymosecretory system.

Ingeborg Teichmann, B. Vigh, B. Aros

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

Histochemical Analysis of a Gomori-positive Substance in the Membraneous Labyrinth of Different Vertebrates

It was demonstrated in one of our earlier studies that the membraneous labyrinth of lower vertebrates contained a neurosecretion-like, Gomori-positive material. This material seemed to accumulate in the endolymph and in the endolymphatic sac.

In our present examination we have studied the Gomori-positive material of the endolymphatic sac in fish, Amphibia and Mammels. On the basis of the used histochemical methods we think the substance to be a sulphated mucopolysaccharide. The Gomori-positive material of the sac is histochemically well to distinguish from the Gomori-positive neurosecretorical material.

I. Törő jr., Gy. Rappay

(Institute of Histology and Embryology, Medical University, and
Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest)

Quantitative Analysis of DNA in Erythrocytes from Healthy and Diseased Fowl

Experiments have been carried out in which the red blood cells of normal 12-day old chick embryos and those of hens suffering from viral erythroblastosis were examined and compared. Smears of chicken liver cell suspensions served as controls. Smears of venous blood were fixed in formalin and either hydrolyzed in n/HCl for 4, 6, 8, 12, 14, 18 or 22 minutes and then subjected to the Feulgen reaction, or subjected to the ninhydrin-Schiff-reaction. A modified Lison histophotometer was used at 560 mμ wavelength. The amount of bound dyes was expressed in relative units.

The first series of experiments, concerned with the DNA contents of the erythrocytes, has shown that (1) the amount of DNA in the nuclei of normal erythrocytes had a hypodiploid, (2) that in the nuclei of the erythrocytes of chick embryos and of erythroblastotic hens a diploid, value. The red blood cells of adult healthy and adult infected animals showed, thus, a considerable difference in DNA contents. (3) The resistance of nucleoproteins to hydrochloric acid was much weaker in cases of erythroblastosis as compared with normal cells.

Experiments with ninhydrin-Schiff-reaction made in the second series of experiments, showed that the nuclei of the erythroblastotic red blood cells contained considerably more free alpha-amino groups than normal ones.

K. Jobst

(Institute of Pathology, Medical University, Pécs)

Cytophotometric Determination of Nucleinproteins after Methylation

Diazomethane has been used for blocking the active acid-hydrogen-carrying groups of nucleoproteins. It has been observed that with alkylation of the desoxyribonucleic acid component, both nuclear basophilia and Feulgen positivity ceased. However, the elimination of the carboxyl groups of proteins was not accompanied by their hydrolytic decomposition. Under the experimental circumstances it was possible to study in situ the quantitative conditions of basic nucleoproteins.

An account is given on the results of the cytophotometric histone determinations after fast green FCF staining in diazomethane pretreated histologic sections. Comparisons are drawn with the results obtained by other methods described in the literature.

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Histophotometric Studies of the (Quantitative) Interrelations between Nuclear Basophilia and Nucleoproteins

Calf thymus sections and smears were methylated by different methods. With increasing methylation there was a decrease in nuclear basophilia; when the sections were subsequently subjected to trypsin digestion, basophilia again began to increase.

The explanation is suggested that the methylation process has the effect of blocking the primary phosphate groups sooner than the amino groups of proteins. If, therefore, after partial methylation the protein component is digested by trypsin, the freed (but formerly screened) phosphate groups give again rise to nuclear basophilia.

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Effect of Thymectomy on Testicular Phosphorus (P^{32}) Metabolism

In the course of studies concerning the correlation between thymus and gonads, the effect of thymectomy on phosphorus metabolism has been examined in young (50 to 70 g), sexually mature (140 to 150 g) and old (300 g) white rats, by means of P^{32} Davidson's modified technique.

Thymectomy produced the most striking changes in the group of sexually mature animals. A considerable rise of the specific activity of the DNA-P occurred after 12 hours, and the rise was still more pronounced 3,7 and 14 days after the operation. The specific activity of the acid-soluble (the ATP-containing) fraction rose likewise. No essential change in the specific activity of the RNA was observed. No significant changes occurred in young and old animals.

On the basis of the stages of spermatogenesis, the percentual distribution of testicular ducts was studied; it showed no change after thymectomy. It has been concluded that all phases of spermatogenesis are accelerated by thymectomy.

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Lymph Circulation in Bones

The study of lymph circulation in the bones is a difficult task and it is perhaps for this reason that literature contains few reports on this subject. In spite of the fact that BUDGE described perivascular lymph sinuses in the Haversian canals as long ago as 1876, and that since several publications have dealt with the lymphatic apparatus in the bone, the periosteum and the bone marrow, it is still a matter of controversy whether the bones contain lymph vessels. Lymphangiomas demonstrated in the bones, seem to argue in favour of their existence.

By injecting dyes into the bone of calves it was possible to detect next to the blood vessels large trunks deriving from the lymphatic vessels of the periosteum, and further an abundant anastomotic communication between these and blood vessels. The lymph vessels of the epiphysis and the diaphysis seemed to be independent of each other.

The peripheral portions of the superficial medullary sinuses are filled retrogradely from the lymph vessels of the periosteum.

China ink was injected into the femoral condyle of rabbits. While being slowly absorbed, the dye gained access to the vessels of the medullary cavity and also to the lymph vessels of the periosteum and the surrounding soft tissues.

Investigations concerning lymphatic system contribute to a better understanding of pathologic processes occurring in the bones.

B. Zolnai

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On the Corrosion-Anatomical Picture of the Normal Rabbit and Human Kidney

Casts, especially corrosion preparations of vessels, can be used with advantage for anatomical, physiological and pathological researches. Hungarian authors have published report s using such techniques in cases of acute and chronic nephritis and also in scleroderma.

The present work is intended to improve and extend such methods. With this end in view, the details of injection and corrosion techniques have been standardized so as to make their results comparable. The principal variables concerned were: the chemical identity of the injected plastic material, the pressure, the time between death and injection, and the duration of the latter.

The kidneys of persons of various age-groups occasionally killed have been studied under histological control. The different portions of the arterial system of both humans and rabbits have been demonstrated.

Corrosion preparations of the kidney of healthy individuals show wide fluctuations in respect of the number of filled vessels and glomeruli, a fact which has to be taken into account in determining the "normal" corrosion anatomical picture. The variable pattern of the corrosion preparations corresponds to the functional state at the moment of death and shows the sensitivity of the method. According to other examinations, the picture is much more uniform in pathological cases, a phenomenon attributable to restricted functional adaptation of the kidney

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Quantitative Histologic Methods for the Determination of Renal Glomerular Volume Ratio

Three methods are described which in thin sections allow to make quantitative estimations and comparisons between such typical changes in glomerular volume as are observable in human pathology and in experimental kidney diseases.

I. The glomerulus is regarded as having the form of a rotation ellipsoid. On the analogy of theoretical considerations regarding the statistical method of nuclear variations, two measurements are taken of the glomerular segment, the longest diameter appearing in the section and the diameter bisecting the former under right angles. These data are used for calculating the volumes corresponding to the glomerular segments.

II. A similar process is used for determining the diameter and the volume of the glomerular capsule. Then the volume ratio is established between the glomerulus and the capsule, as computed from the section.

III. The volume ratio of the glomeruli is determined in the renal cortex. A network of 10×10 lines is projected onto the section and at the points of intersection tissue elements are analyzed. The proportion is determined between the number of intersections falling on the glomeruli and those on other tissues.

A chart is set up for measurement and computation. The results are illustrated graphically. The question of juxtamedullar glomeruli and the changes subject to age in their size and density are demonstrated on human and animal materials.

FORENSIC MEDICINE

RELATOR

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Medico-Legal Aspects of Acute Ethyl Alcohol Poisoning

Ethyl alcohol (C_2H_5OH) is a colourless transparent fluid of characteristic odour. Its specific weight at 28° C is 0.798, its boiling point, 78.3° C. Ethyl alcohol is produced from sugar by the agency of Saccharomyces; it can also be prepared by synthesis. Alcoholic liquors contain from 3 to 70 per cent of the substance.

Natural wines do not contain more than 16 to 17 per cent of alcohol, for yeast cells are killed at this concentration. Alcoholic beverages of higher concentration are prepared by distillation or by the addition of concentrated alcohol. Certain alcoholic drinks contain traces of methyl alcohol (from the disintegration of pectin methoxy groups).

Minute amounts of ethyl alcohol (0.001 to 0.007 per cent) are contained in the body fluids and tissues even under physiological conditions. The concentration of this so-called endogenous alcohol is so low as to make it negligible from a medico-legal point of view. A rise in the concentration of endogenous alcohol occurs rarely.

Absorption and excretion. The ingested alcohol is absorbed, distributed over the tissues and body fluids in proportion to their water contents, and then either oxidized or excreted. About 90 to 95 per cent of the alcohol introduced into the organism is burnt up, while some 5 to 10 per cent are excreted in unchanged form.

The different phases of absorption and excretion are clearly shown by the blood-alcohol curve. If alcohol is taken by mouth, its absorption begins in the oral cavity, but the process of absorption is most vigorous in the stomach and the initial portions of the small intestine. Although the rate of absorption depends on the degree of gastric repletion in the first place, the degree of alcoholic concentration plays a certain role in this respect, since alcohol ingested at medium concentration is absorbed at a quicker rate than lower or higher concentrations of it. Absorption from a stomach full of food may take a longer time. Absorption is further influenced by the autonomic nervous system, mainly through the vasomotor nerves. The phase of absorption lasts from the intake of alcohol to the establishment of uniform distribution (equilibrium

of diffusion), and is characterized by a sudden increase of the blood alcohol level. Absorption usually takes 60 to 90 minutes, sometimes even 120 minutes. Alcohol absorbed from the gastrointestinal tract passes first into the venous blood, then into the right half of the heart to reach, after having passed through the lungs, the tissues by means of the arterial system. The arterial blood loses a certain amount of its alcoholic contents in the tissues. Only water can be regarded as a solvent of alcohol. The distribution of alcohol is a process of diffusion in which no cellular activity is involved.

The height of the blood alcohol curve is inversely related to the water contents of the organism. The serum alcohol level is higher in persons with lower, and lower in persons with higher, water contents after the consumption of a given amount of alcohol. It is for this reason that—given equal conditions—obese individuals have a higher level of alcohol in the blood than lean persons, and this also explains the relatively higher blood alcohol level of females. (Women have more adipose tissue than men.)

Diffusion is rapid in areas with a rich blood supply; in the brain, for instance, an equilibrium is reached much quicker than in the muscles which need about an hour as from the time of oral intake. Since muscles represent about 40 per cent of the body weight, delayed uptake of alcohol by the skeletal muscles induces, in cases of quick absorption, a relatively high concentration of alcohol in the arterial blood and the brain.

The blood alcohol level becomes uniform throughout the vascular system as soon as a state of equilibrium has been attained. This is not the case during the phase of absorption, when the concentration of alcohol is highest in the portal vein. Owing to the slower rate at which skeletal muscles take up alcohol, its concentration in the venous blood coming from the extremities is lower than in the arteries or in the heart. The simultaneously measured alcohol levels are in such cases equal in the capillaries and the arteries, but lower in the veins. This difference may amount to as much as 15 to 22 per cent. It follows that the level of alcohol in blood collected from the capillaries during the phase of absorption is closer to the true concentration of blood and brain alcohol levels than in the blood drawn from the veins. It is, therefore recommended to test capillary blood for medico-legal purposes.

There is 20 per cent more alcohol in urine than in blood. We found that in cases of injuries sustained, or in those of certain poisonings (barbiturates) undergone, in the alcoholic state, the urinary output of alcohol was much higher than the usual value if the injury or the poisoning had been followed by a longer loss of consciousness. The ratio of urinary and serum alcohol is about 1.20 in the phase of equilibrium, and we measured even a ratio of 2.0 in the said cases. Relying on these observations we regard unusually high quotients of urinary alcohol per serum alcohol as indicative of a protracted premortal unconsciousness.

The second leg of the blood-alcohol curve runs a practically straight course. It is the result of two components. About 90 to 95 per cent of the ingested alcohol are oxidized in the organism. The decomposition is effected by alcohol dehydrogenase, an enzyme that occurs practically in the liver only. It amounts to a total of approximately 1.5 g and is capable of decomposing 8 to 10 g of alcohol per hour. Oxidation as far as acetic acid takes place in the liver alone, while further oxidation may occur in the muscle tissues as well. Catalase is another enzyme which decomposes alcohol; it oxidizes about 20 per cent of the alcohol ingested. Methyl alcohol is decomposed by catalase but not by alcohol dehydrogenase, a phenomenon that explains why methyl alcohol is oxidized in the organism at a much slower rate than ethyl alcohol.

It is mainly through the kidneys and lungs that alcohol is excreted in an unchanged condition. A negligible amount may be excreted with perspiration, milk and the faeces. The amount of excreted alcohol depends on various factors but never exceeds 10 per cent of the ingested amount.

The analysis of blood-alcohol curves enabled WIDMARK to offer new data concerning the oxidation of alcohol in, and its excretion from, the human organism. The serum alcohol curves may differ in the height of the peak according to the amount of ingested alcohol, but their general course is much the same in all cases. Since the amount of excreted alcohol is negligible in comparison with that decomposed by oxidation, WIDMARK identified excretion with the degree of oxidative decomposition. He assumed the rate of oxidation to be equal in the phase of absorption and in that of excretion. If the blood-alcohol curve is known, it is possible to determine

1. the amount of alcohol present in the organism at a given time;
2. the amount of alcohol that had been excreted by the organism before the time of the analysis;
3. the total amount of ingested alcohol;
4. the amount of alcohol excreted per hour and kg of body weight;
5. the time needed for the elimination of the total amount of ingested alcohol.

WIDMARK gave the values of blood alcohol in per mille, and it is necessary to determine these values during the phase of excretion.

WIDMARK used the symbol β to denote the fall of concentration per mille and per minute. The mean value of β is, according to literary data, 0.0023 per mille per min., *i.e.* 0.14 per mille per hour. We determined the value of β in 19 males and found it to vary between 0.0019 and 0.0034. WIDMARK used the symbol r to denote the ratio between the concentration of alcohol in the organism and that in the blood,

$$r = \frac{\text{alcohol concentration in organism}}{\text{alcohol concentration in blood}}$$

so that r expresses the degree of diffusion of alcohol in the organism. Using this factor r, and knowing the body weight as also the concentration of alcohol in blood, we can determine the total amount of alcohol present in the organism at any given time, provided the values refer to the phase of excretion. The formula for determining the amount of alcohol present in the organism is

$$A_t = c_t \cdot p \cdot r$$

where A_t is the amount of alcohol to be determined,

c_t is the concentration of alcohol in blood in per mille, and p means the body weight in kg.

For example, if $c_t = 1$ per mille, $p = 100$ kg, and the mean value of $r = 0.7$, the amount of alcohol in the organism at the given time is $1 \times 100 \times 0.7 = 70$ g. Our investigations in 19 men yielded values for r from 0.56 to 0.89, which are in good agreement with those reported in the literature (0.55—0.80).

WIDMARK's figures refer, of course, to a single act of alcohol uptake under physiological conditions. Blood-alcohol curves with a regular course are, however, infrequent. We have observed curves with widely differing irregular courses, especially in the case of chronic alcoholists, although the other conditions were similar.

Factors affecting the blood alcohol curve. The effect of different drugs, hormones and vitamins has been tested in this respect. It has emerged from these tests that none of the known preparations, hormones or vitamins is capable of significantly influencing the serum level of alcohol. Nor have substances been found that would produce a sobering effect on intoxicated individuals. There have been reports on experiments in which certain hormones (insulin) or certain saccharides (laevulose) reduced the blood alcohol level, but the data are not quite convincing. The metabolism of alcohol is, of course, closely connected with the general metabolism, so that disturbances of, or changes in, the latter lead necessarily to disturbances of, and changes in, the former.

The rate at which alcohol is decomposed depends on hepatic activity. Liver function tests have, therefore, to be made in the given case, especially if it is important to establish the fact that a deceleration of the normal rate of alcohol decomposition has to be taken into account owing to disturbed hepatic activity. The alcohol tolerance test, too, has to be carried out in these cases; the subject receives an adequate quantity of alcohol (0.6 to 0.8 g per kg body weight) whereafter the curve of blood alcohol level is plotted on the evidence of serial blood samplings. A procedure of this kind has proved of great value in numerous instances.

Several workers have examined changes in the serum alcohol level produced by the inhalation of various volatile reducing substances. The results were negative in this respect. Not even the inhalation of alcohol vapour or

the ingestion of substances like garlic was capable of raising the concentration of alcohol in blood.

It should be noted for practical purposes that, if alcohol is determined with *Widmark*'s method, incereased "*alcohol values*" will result in ether (up to 1.52 per mille) or chloroform (up to 0.25 per mille) anaesthesia, as also after injections of camphor.

Alcohol and drugs. Barbiturates, phenothiazine derivatives or disulfiram, if administered simultaneously with the consumption of alcohol, may give rise to serious intoxication. This phenomenon is of practical importance because even comparatively insignificant quantities of ingested alcohol may provoke grave symptoms or cause the death of persons taking drugs of the said kind. Alcohol metabolism is not influenced by these drugs, so that they do not change the course of the alcohol curve. We could observe the synergism of barbiturates (amobarbital) and alcohol in both animals and humans. It is, therefore, necessary to ascertain the history of medication in a given case, and this the more so as the regular taking of analgetics and sedatives has become widespread in our days. Another practical conclusion to be drawn is that, when treating acute alcoholic intoxication, drugs of the said kind must not be prescribed before the ingested alcohol has not completely been excreted.

Fatal alcohol poisoning. Data regarding the lethal dose of ethyl alcohol are fairly contradictory owing to the fact that not always the poisoning itself is lethal, for also other factors may contribute to the fatal termination, *e.g.* temperature, the copresence of some other poison or drug, a disease, etc. In general, the limits of the lethal dose are 80 and 300 g. ELBEL claims that 6 to 8 g/kg of body weight is fatal for adults and 3 g/kg for children. It should, of course, be taken into consideration that the limit of alcohol tolerance varies with the individual. The alcohol concentration of the blood has been found to vary between 4 and 7 per mille in fatal cases. If, however, there is a longer stretch between the uptake of alcohol and the time of death, values may be much lower. It also happens that death caused by acute alcohol poisoning ensues at a time when the whole ingested amount of alcohol has already disappeared from the organism. (This applies to children in particular.) We have hardly ever observed higher lethal values than 4 per mille.

Autopsy findings are not characteristic. Although certain organs and body cavities emit the odour of alcohol. This may be due to a number of factors, *e. g.* putrefaction, the synchronous uptake of other substances such as a solution of crude nicotine, etc. Necropsy generally reveals meningeal and cerebral hyperaemia, cerebral oedema, pulmonary hyperaemia, and oedema, hepatic and renal hyperaemia, a full urinary bladder, and liquid blood. Petechiae are sometimes seen in the pia mater, in the brain substance and even in the lungs.

Histological study reveals non-specific symptoms of degeneration, further oedema, chiefly in the brain and liver. Even if there are no characteristic

gross changes, it is expedient to remove brain and liver specimens for histological inspection, since the microscopic picture will always tell that some premortal toxic factor was at play, especially in the case of children.

Collection of samples. Since alcohol poisoning is accurately reflected by the blood alcohol level, blood is the substance most frequently collected for the demonstration of alcohol. Also cerebrospinal fluid, urine and saliva may furnish useful information.

Blood can be drawn *in vivo* from the tip of a finger, from the ear-lobe or from a vein. Volatile reducing substances such as alcohol, iodine, ether, benzene, must not be used for the sterilization of the skin. The site of puncture should be wiped with a piece of cotton soaked in mercury bichloride solution. Neither the syringe nor the cannula must be kept in alcohol or any of the said antiseptics prior to the collection of blood. It is best to use instruments sterilized by heat or boiling. The tube in which the blood is taken up should be filled to $^4/_5$ of its capacity and provided with a label recording the necessary data including the time of collection. The label or a special register should record all observed clinical symptoms pointing to drunkenness.

Relying on our long experience, we are in favour of taking the blood from a vein. This allows the drawing of a greater quantity of blood, so that it can be used for several tests, and, besides, the possibility of errors is greatly reduced if venous blood is collected. In connection with the drawing of blood from the vein it must be borne in mind that, although the possible admixture of a small amount of foreign substances may lead to a distortion of the result, the distortion may not be apparent, so that any technical fault committed in connection with the drawing of blood may thus escape notice. It is, therefore, convenient to record all details of the operation, including the disinfectant employed, as also the technique used (*e.g.* whether only needle or needle and syringe were used, etc.). Blood samples obtained under sterile conditions, retain their level of alcohol for several weeks even at room temperature. The tubes used for the storage of blood have to be carefully stoppered; used rubber or cork stoppers should be discarded.

If it is from a cadaver that blood has to be collected, it should be drawn from a peripheral vein because the danger of putrefaction is less in the peripheral regions, and further because the possibility of a postmortal diffusion of alcohol from the adjacent tissues is lower in this area than, for instance, in the blood of the heart. We, too, have observed that there arise volatile reducing substances in the pulmonary tissue very soon after death, and that they tend to appear in the cardiac blood.

The alcohol content of the blood and the tissues decreases after death. The approximate rate of decrease is 0.1 per mille per day. This rate is quicker at higher, and slower at lower, temperatures. Postmortem decrease in the level of alcohol goes hand in hand with the accumulation of volatile reducing sub-

stances which can be demonstrated by *Widmark*'s method. The process is partly due to bacterial activity. Enzymatic analyses have shown that, while alcohol is gradually disappearing from the cadaver, there arises beside volatile reducing substances also alcohol. The post-mortem values of alcohol represent the combined result of these two processes. Whether in any given case the one or the other prevails, i.e. whether it is the loss of alcohol or the production of new alcohol and other volatile reducing substances which gains the upper hand, depends on a number of unelucidated factors. Since it is impossible to foretell the direction and the rate of the post-mortem change in the level of alcohol, it is advisable to obtain blood and urine samples as soon as possible and to register the time and details of sampling. It may be indicated to subject the blood to bacteriological examination which should extend to the possible alcohol-producing biological properties of the observed bacterial strain.

Apart from blood, also urine, saliva, exhaled air and — in the case of cadavers — brain tissue and muscles may be tested for alcohol. Before collecting samples of saliva, the mouth has to be rinsed and the sample should be taken after an interval of 15 to 20 minutes. The saliva alcohol value exceeds that of serum alcohol by some 20 per cent. The usefulness of saliva has repeatedly been proved in our practice. When analyzing the alcohol contents of exhaled air, it should be remembered that approximately 2 litres of air contain the same amount of alcohol as 1 ml of blood. American investigators recommend sodium fluoride for the preservation of saliva-, urine- and blood-samples. Brain and muscle tissue removed from cadavers should be stored in the refrigator and examined within 48 hours.

Quantitative determination of ethyl alcohol. This is usually carried out in Hungary by the method of *Widmark*. The method is based on the principle that part of a given quantity of sulphuric acid-potassium bichromate is decomposed by alcohol, and the amount of unchanged bichromate can be determined by iodometry. Since also other volatile reducing substances than alcohol may gain access to the blood and so distort the result, their effect has to be eliminated. The enzymatic method eliminates this source of error. There exist also physical methods for the quantitative determination of alcohol, but these have failed to gain popularity in Hungary. Methods employed for the quantitative determination of exhaled alcohol are based on its reducing property.

Effect of alcohol on the organism. Even small doses of alcohol give rise to functional disturbances, especially in the central nervous system. The effect is of a paralyzing character. The increase in the blood sugar level, caused by adrenaline, is counteracted by alcohol. The increase in the blood sugar level induced by nicotine was also prevented in our rabbit experiments by the simultaneous administration of alcohol. Small doses of alcohol cause vasodilatation of central origin; the hyperaemia produces a sensation of heat although body temperature remains unchanged. Alcohol increases the gastric hydrochloric

acid output, likewise an effect of probably central origin. Alcohol furthermore increases diuresis and promotes sweating.

The typical form of acute alcoholic intoxication is chiefly characterized by a disturbance of mental functions caused by decreased inhibitions in the cerebral cortex. The intoxicated individual is incapable of forming a clear judgement concerning his actual situation; such person underrates threatening dangers; the power of normal discernment and the normal degree of self-discipline are diminished. This phase is followed by depression. Mental activity becomes sluggish, perception is reduced and movements are slowed down. The next phase is characterized by symptoms of paralysis, faltering speech and uncoordinated movements. Consciousness becomes more and more blurred, and terminal sleep ensues. Sleep becomes deeper and deeper and comatose; the skin of the subject assumes a pale colour, is covered with sweat, the pulse rate is accelerated and easily suppressible, respiration becomes superficial, the pupillary reflex sluggish and the musculature relaxes. The comatose person may discharge faeces and urine. Waking up after a sleep of 6 to 8 hours, the subject feels a general malaise, is depressed, has a headache, is giddy and may feel nausea. These symptoms last sometimes 24 hours. Memory of happenings during the time of intoxication is more or less faulty.

It has already been observed by WIDMARK that the degree of drunkenness at a given value of alcohol level varies from individual to individual. WIDMARK observed no clinical symptoms when the concentration of blood alcohol amounted to 0.6 per mille. A survey of the pertinent literature reveals that clinical symptoms of drunkenness are fairly rare with a blood alcohol level under 5 per mille, although functional disturbances of certain sense organs and muscle movements can be demonstrated by adequate methods even in such cases. Clinical manifestations of intoxication become apparent in most cases where the concentration is between 0.5 and 1 per mille, and such manifestations appear invariably if the concentration of alcohol in the blood rises above 2 per mille.

Medical expertise encounters no difficulty if the influence of alcohol can be diagnosed by clinical methods. However, also alcoholic states without clinical symptoms and with comparatively low blood alcohol values may attain significance. It is for this reason that the authors unanimously demand the elaboration of simple and precise tests that ought to be more reliable than the current clinical procedures.

It should always be borne in mind that the degree of alcohol tolerance varies from individual to individual, and varies even in the same individual. Traumatization, fatigue, infectious diseases and general debility lower the limit of tolerance. Its upper limit is relatively low in any case. It has been demonstrated experimentally that the deviations between the different degrees of intoxication in connection with a given blood alcohol level amount to about

±30—40 per cent. It is often important to decide whether the blood alcohol level determined in a given case refers to the phase of absorption or to that of excretion. A single blood sample cannot decide the question; blood has to be drawn repeatedly, at intervals of one hour. With the same serum alcohol level, the degree of intoxication is higher in the phase of absorption.

Considering the above arguments it is reasonable that not merely the blood alcohol level but also all other factors should be taken into account when the degree of alcoholic influence has to be determined. It is just for the purposes of general orientation that the following figures are quoted. A blood alcohol level varying between 0.20 and 1.5 per mille means a low degree, one between 1.5 and 2.5 per mille a moderate degree, and one between 2.5 and 3.4 per mille a grave degree of alcoholic intoxication, while a concentration beyond 3.5 per mille may lead to fatal outcome.

RELATOR

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Medico-Legal Interpretation of Psychopathologic Phenomena of Alcoholic Origin, with Regard to the New Penal Code

From the medico-legal point of view, it is Art. 22 of the new Hungarian Penal Code which embodies the most significant reform. It rules that, in cases of offences committed in a state of self-caused alcoholic intoxication or clouded state, the mental confusion of the offender does not exempt him from culpability. This is a radical deviation from earlier practice which regarded drunken persons as non compos mentis and punished the action which had led to drunkenness instead of the offence committed in the drunken state. Wagner-Jauregg was the first representative of this concept which meant a progress in comparison with the still earlier practice inasmuch as, before him, alcoholic intoxication and derangement of mind used to be regarded as equivalent. This notwithstanding, Wagner-Jauregg's concept failed to achieve wider popularity since it was not satisfactory for constraining delinquency under the influence of alcohol. The principle that drunkenness and not the crime perpetrated in the intoxicated condition is punishable is now in vigour in German-speaking areas only, while in most other parts of the globe, among them in Great Britain, the United States, the Scandinavian and the socialist countries, felonies perpetrated in alcoholic intoxication are punished as if the offender had been sober.

This does not, however, mean that the majority of the world has come to a definite agreement as to the definition of the alcoholic state or the criminal

responsibility of alcoholists. As a matter of fact, most medico-legal and psychiatric textbooks emphasize that the problem of crimes committed under the influence of alcohol is still a controversial one. This is partly due to the fact that the rules in respect of alcoholic offences are governed in most penal codes rather by social needs than biological considerations. The introductory motivation of the Hungarian code is explicit in this respect: "The effect of alcoholism on criminality is exceedingly great, and law has to protect society from this danger with the most efficient weapons at its disposal." Apart from the motivation, the very tenor of the code makes it clear that the consumption of alcohol may, according to the legislator, befog the sensorium to an extent at which the offender is hardly or not at all able to recognize the social danger of his action, or to act in a judicious manner even if he does recognize it. The stipulations contained in Art. 22 of the new code apply to just this possibility.

Art. 22 of the new code puts a stop to the earlier state of affairs in which the medico-legal expert was forced to declare delinquents compos mentis whose mental faculties were evidently deranged by alcohol. All the expert has to do under the new law is to state whether the mental confusion of the offender has to be regarded as drunkenness or alcoholic numbness. The still much discussed problem of how to evaluate the biological or psychological effect of alcoholic intoxication has, thus, ceased to be significant in Hungary since the enactment of the new code.

The 1958 conference of Soviet forensic psychiatrists made it evident that the problem under review was quite as controversial in the Soviet Union as in other parts of the world. Discussions were mainly centred on the question whether alcoholic inebriation was to be regarded as a pathological state. The leading members of the Central Scientific Research Institute of Forensic Psychiatry (named after SERBSKY) represented one of the two extreme attitudes. Their views are essentially the same as those of BUNEYEV who had several years earlier, formulated his thesis that simple drunkenness, however grave, could not be regarded as pathological,and that, consequently, individuals in this condition had the same power of discernment as sober persons, and were, therefore, criminally fully responsible. KALASHNIK and HALITSKY championed this theory most vigorously at the conference. The most radical representative of the opposite extreme theory was SLUTCHEVSKY from Leningrad. He adduced convincing arguments to show that there was no such thing as "normal" inebriation. It can be demonstrated with psychological, physiological and electrophysiological tests that the cerebral functions are disturbed even in a state of simple drunkenness. He disagrees with the view that a drunken person retains the power of discernment and the freedom of action. He stamped this theory as especially dangerous because indirectly it might lead to a wide extension of the scope of pathological drunkenness. He abhors the

expression "pathological drunkenness" because all forms of drunkenness are, according to him, pathologic. SLUTCHEVSKY classifies that particular psychotic condition which is usually called pathological drunkenness under the head of epileptic disorders, since it is an epileptic reaction released by alcohol.

These opposite views released an animated dispute which led to an intermediate concept that was defined by KERBIKOV (who concluded the debate) and adopted by the majority of the participants. They agreed with SLUTCHEVSKY that drunkenness was an essentially pathologic condition, but refused his allegation that alcoholic intoxication had invariably to be regarded as an extraordinary condition, so that there existed no simple drunkenness. Nor did the majority think it advisable to discard the expression "pathological drunkenness", a grammatically inaccurate but world-wide expression. The principal task to be solved in respect of criminal responsibility was precisely a clear distinction between simple and pathological drunkenness, and so the congress emphasized the necessity of continuing clinical and medico-legal investigations with a view to finding a more precise definition of pathological drunkenness.

Although four years have elapsed since the congress, the problem still constitutes a battleground of controversies, since — as is evident from communications published since then — none of the participants has accepted the arguments of the opposite school. The controversy is not without significance for us because the problem is regarded also in Hungary as a controversial one, a fact clearly manifested by the contradictory findings to be found in the practice of our medico-legal experts.

A brief summary of the psychopathologic phenomena connected with the consumption of alcohol may help in finding a better approach to the problem. Literature is unanimous in dividing the psychic changes, induced by alcohol into two main categories, acute and chronic intoxications.

Since the clinical manifestations of drunkenness are more variable, KALASHNIK's nomenclature seems to offer the starting point:

1. Simple alcoholic drunkenness.
2. Pathological drunkenness.
3. Chronic alcoholism.
4. Delirium tremens.
5. Alcoholic hallucinosis.
6. Alcoholic paranoia (including maniacal jealousy).

If we wish to ascertain the significance of these categories for the purposes of forensic psychiatry, it seems advisable to begin with the less complicated forms. The three last items of the list belong really to the sphere of mental disorders and are, thus, less interesting from a medico-legal point of view.

Delirium tremens, alcoholic hallucinosis and paranoia are all mental disorders of alcoholic origin, If, therefore, they are correctly diagnosed, they

evidently fall under the rules as stated in Art. 21 of the penal code. Diagnostic problems may, however, arise in connection with a recognition of the so-called predelirious state. Persons in this state have fluctuating consciousness, and it is possible that an individual behaves more or less normally at the time of the examination, but is so deranged mentally before or after that time, as to be non compos mentis. Functional disturbances of the vegetative nervous system (profuse perspiration, flushed face, tremor, tachycardia) may offer good clues in this respect; these symptoms may be present and point to the disease even if it is not manifest at the moment. Diagnostic errors are rare in cases of alcoholic hallucinosis because the signs of associated anxiety are conspicuous. The establishment of a correct diagnosis is more difficult in cases of paranoia, since patients suffering from various forms thereof usually retain their personality and do not lose their power of discernment. If, however, their delusion is connected with the wrongful act, a careful elucidation of the facts and the peculiar motive of the offence will help in tracing a background of insanity.

The problem of chronic alcoholics in connection with mental derangement of alcoholic origin is so intricate as to require a separate treatise. It cannot, therefore, be discussed here in extenso, and this the less so as even the very definition of chronic alcoholism is still unsettled. The principle that habitual or even passionate drinking (addiction) does not, in itself, exclude criminal responsibility, has nevertheless beenacc epted all over the world. It is still dubious whether, in the case of addicts, drinking bouts and the resulting drunkenness have to be regarded as self-caused. Of course, to exempt persons of this kind from criminal responsibility would mean to leave society unprotected from the misdeeds of the morally lowermost layer of the population, of habitual drunkards who are most disposed to commit criminal acts. This is why chronic alcoholics are severely treated even in countries where the forensic attitude is otherwise lenient toward alcoholism. For instance, Art. 42/c of the West-German penal code rules that, after having served their term, such individuals have to undergo in a closed institute withdrawal cure which often lasts several years.

To a special category belong those cases of chronic alcoholism in which organic cerebral damage leads to a grave degradation of personality. According to the Presidential Council, of the Supreme Court (leading case No. XXVIII) "As a rule, a disturbance in personality development does not exclude culpability even if it is associated with dipsomania. It may, however, lead to a degradation of personality to the extent of verging on insanity, so that criminal responsibility may be restricted and even cancelled." Of course, manifestations indicative of approaching dementia or the rare case of Korsakov's syndrome belong to this category.

Let us now discuss acute alcoholic intoxication, a category of highest importance for forensic medicine, one that is open to most controversies. There

is no uniform attitude concerning the division of acute alcoholic intoxication. Soviet authors distinguish, as a rule, two groups: simple and pathological drunkenness. Such division offers certain advantages from a legal point of view but disregards the great variety of clinical manifestations. BINDER's division, suggested in 1935, seems to be more accurate both clinically and medico-legally:

A. Simple drunkenness.

B. State of abnormal drunkenness with the following subdivisions:

1. Alcoholic condition associated with quantitative abnormal phenomena (complicated drunkenness).

2. Qualitative abnormal drunkenness (pathologic):

a) foggy form

b) delirious form.

There seems to be no doubt that, essentially, simple drunkenness is a pathologic condition. According to PONSOLD, alcohol induces a disturbance of mental function. This disturbance, being a pathologic disorder of the psyche caused by intoxication, has to be taken into account both legally and medically. PONSOLD is undeniably justified in affirming that it is theoretically wrong to separate alcohol from other neurotoxins and that, accordingly, poisoning is pathologic whether caused by alcohol or some other neurologically poisonous agent. It is stated in a treatise of TARISKA that alcohol belongs, according to up-to-date notions, to that group of poisons which affect the nervous system and provoke nervous reactions without harming the structural integrity of the nervous apparatus. Its toxic action is — in contradiction to earlier views — not due to a direct inhibition of oxidation but is mainly caused by a change in the permeability of biological membranes. Therefore, alcoholic poisoning gives rise to particular morphological changes, a phenomenon of significance for the estimation of the pathologic condition even if disturbances of transudation — due to increased permeability and present in the brain of every person suffering from acute alcoholic intoxication — are in themselves insufficient for explaining the great variety of neuropsychiatric symptoms of alcoholic origin.

That the consumption of alcohol leads to a pathological state is clear also from a physiological point of view. Alcohol paralyzes, according to PAVLOV, both fundamental nervous processes; small doses thereof paralyze first the inhibitory and then the excitatory process. Alcoholic excitement is, thus, provoked by a decrease in inhibition.

Although all these morphological and physiological phenomena leave no doubt as to that the alcoholic state being pathologic, it does not necessarily follow that it diminishes criminal responsibility. It is emphasized, among other, by PONSOLD that alcoholic intoxication must not constitute a safe conduct for felons, although he maintains that alcoholism is pathologic even from the legal point view.

BINDER's above-described division — one that has been accepted by WYSS in his book "Psychiatrie der Gegenwart" published in 1962 — offers a psychopathologically convincing explanation of the legal attitude towards drunkenness. Simple drunkenness means, according to this division, only a quantitative and no qualitative deviation from the normal condition. While the original mood is changed and may be stepped up to euphoria, the interconnections of psychic concepts, temporal and spatial orientation as also self-control and behaviour remain unimpaired.

Simple drunkenness is characterized by gradual development and the dependence on the amount of alcohol consumed. There exist several nomenclatures for the various degrees of drunkenness: that of BOGEN has the advantage of being accompanied by blood-alcohol values:

1. Subclinical phase (below 0.1 per cent).
2. Phase of excitement (0.1 to 0.2 per cent).
3. Mental confusion (accompanied by diminished activity) (0.3 per cent).
4. Numbness, general apathy, pallor (0.4 per cent).
5. Complete drunkenness, coma (0.5 per cent).

This division supports the statement of GRUHLE according to whom unconscious drunkenness, so frequently referred to by lawyers, hardly ever occurs and has no practical significance, since unconscious drunks are usually not capable of performing coordinated actions.

It is of significance that BINDER regards the so-called complicated drunkenness as a merely quantitative and not as a qualitative category, so that it belongs to the group of simple drunkenness. The development of excitement and paralysis constitute, according to him, the quantitative alteration. Although the condition may be called prenarcotic, mental coordination and orientation (even if impaired) are still present, so that behaviour is not blind and fully dissociated from reality. It follows that the actions of the individual are not as unreal, phantastic or dreamlike, his personality is not as disintegrated, as in the state of pathological drunkenness.

According to BINDER's concept, the quantitative weakening of psychic functions does not involve grave mental confusion. It is accompanied by numbness which is different from other forms of mental confusion chiefly inasmuch as it is not associated with desorientation. Delirious mental confusion means, in BINDER's theory, that disintegration of the consciousness which is called "zerfallendes Bewusstsein" in JASPER's terminology. It involves, according to JASPER, the breakdown of "Ganzheitgestaltung", it means, the fragmentation of function complexes and the dissociation of normal coordination. Desorientation, illusions and hallucination are the characteristics of delirium.

BINDER's concept has the advantage of offering a reliable theoretical foundation for drawing sharp boundary lines between the categories of simple

drunkenness, pathological drunkenness and those forms of atypical or abnormal drunkenness which must not be interpreted as insanity.

Distinctions of this kind are highly significant in connection with the new Hungarian penal code because offences committed by insane persons do not fall under the stipulations of Art. 22 even though the insanity be of alcoholic origin. According to the practice of the Supreme Court, the various forms of pathological drunkenness consist in a temporary cessation of consciousness, are different from common drunkenness and belong to the category of psychosis. Cases of this nature fall under Art. 21 of the criminal code. It follows that it is of decisive importance whether a state of acute alcoholic intoxication is qualified by the medico-legal expert as pathological or as simple drunkenness. Diagnosis in such cases is difficult. It should be remembered that the category of pathological drunkenness had no great significance before the enactment of the new code because grave alcoholic intoxication precluded culpability whether it was pathologic or simple drunkenness. Another difficulty is due to the necessity of establishing a retrospective diagnosis based on mostly subjective factors (contradictory depositions of witnesses, subjective affirmations of the culprit, etc.).

The greatest difficulty arises from the fact that an internationally accepted definition of drunkenness is still lacking. NYIRŐ distinguishes four, STRELTCHUK six types, while SLUTCHEVSKY rejects the concept of pathological drunkenness and classifies it under the head of epileptic disorders. The majority of the author agree that a cooperation of several factors is necessary for the development of pathological drunkenness, and that only a single one of these factors is invariably present, *i.e.* alcohol. Opinions are widely divergent as regards interpretation of the symptoms. We think it would facilitate the establishment of a definition of pathological drunkenness if a distinction were made between pathological drunkenness *sui generis* and pathological drunkenness associated with other pathological phenomena. It is clear that pathological drunkenness may occur sometimes even in the case of perfectly healthy persons: we would regard such cases as pathological drunkenness *sui generis*.

The following forms are known in the category of pathological drunkenness associated with complications.

1. Pathological drunkenness of epileptics.
2. Pathological drunkenness of schizophrenics.
3. Pathological drunkenness combined with encephalopathy.
4. Pathological drunkenness of oligophrenics and psychopaths.

Drunkenness in these cases may assume very different forms; they are largely determined by the nature of the primary disease. Consumption of alcohol may, for instance, release an epileptic seizure, obnubilation or schizophrenic reaction. If the pathological drunkenness is viewed separately from the associated complications (and this is the more necessary as the latter

belongs to different categories from the point of view of criminal culpability), the remaining pure form of pathological drunkenness will be much clearer in respect of symptomatology. Only three of the many criteria will thus remain, those described by THOMSON in the American Handbook of Psychiatry, *viz.* (1) pathological drunkenness is released by comparatively small doses of alcohol; (2) it is accompanied by sudden restlessness; (3) it involves complete amnesia. We would suggest a fourth criterion, that the duration of psychosis is not longer than the time needed by the organism to burn up the ingested alcohol.

It follows that Art. 22 of the criminal code does not make the measurement of blood-alcohol concentration unnecessary since the amount of ingested alcohol is a decisive factor in the diagnosis of pathological drunkenness. It should be noted that high blood alcohol values are not necessarily incompatible with pathological drunkenness. It may happen that the offender drinks much more alcohol than the amount which would have sufficed for the release of the pathologic condition. The surplus amount of alcohol does not prevent the development of pathological drunkenness, nor does make an existing pathologic condition to cease. What happens is that the symptoms of simple drunkenness are added to those of pathological drunkenness. A further analysis of this question leads to the problem of differential diagnosis which will form the subject of a later study.

Summary

The psychopathologic phenomena, that give most frequently rise to medico-legal problems in connection with alcoholic intoxication, have been briefly analyzed.

1. It is explained and supported by references to literature that, while all kinds of alcoholic intoxication are pathologic in the biological sense of the term, the idea — as embodied in the new Hungarian penal code — that simple drunkenness does not exempt from criminal responsibility, is not foreign to medical notions.

2. There is a psychopathological boundary between simple and pathological drunkenness because simple drunkenness does not provoke qualitative changes; it induces merely quantitative alterations which cannot be regarded as being equivalent to insanity.

3. The key problem of medico-legal practice in connection with Art. 22 of the new code concerning alcoholic intoxication is a clear distinction between simple and pathological drunkenness. It is therefore an important task in the field of forensic medicine to analyze the clinical forms, explore the aetiology, elucidate the pathogenesis and study the differential diagnosis of pathological drunkenness, an acute form of temporary dementia due to the ingestion of alcohol.

RELATOR

M. Vámosi

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Recent Trends Concerning the Influence of Alcohol on the Safety of Traffic

Public attitude concerning the influence of alcohol in connection with traffic accidents is now changing all over the world. Let us point to the new traffic regulations in Czechoslovakia, Hungary, the German Democratic Republic, Great Britain, Norway, France, Yugoslavia, Sweden and the German Federal Republic which have all revised the earlier indulgent attitude regarding driving under the influence of alcohol. This change is due to the pressure of public opinion among others. The fact that public opinion demands a revision of the earlier indulgence and has actually enforced a severer treatment of drivers, in some instances even prohibition, must in our opinion be regarded as a result of the antialcoholistic movement.

A statistical registration of all traffic accidents traceable to alcoholic influence is not yet possible, but the available last figures are by no means as unreliable as those published after 1945. The adoption of a uniform statistical system, although planned, is still just a desideratum of experts studying the role of alcoholic influence in traffic accidents.

It is regrettable that there is as yet no agreement regarding the definition of the concentration of alcohol contained in the biological tissues. For instance, no agreement has been reached in London as to whether the amount of alcohol contained in blood should be expressed in $^0/_{00}$, $g^0/_0$ or $mg^0/_0$. Most European countries express the level of blood alcohol in per mille, but it is given in $mg^0/_0$ in Great Britain and Belgium, and in $g^0/_0$ in the United States, a situation which is bound to give rise to misunderstandings. This aspect of the matter has been revealed here only in order to show that the problem we are dealing with is far more complicated than what it would seem to laymen.

It is only by means of reliable statistical data, collected on the basis of uniform principles, that the true proportion of traffic accidents due to alcoholic influence can be measured.

Tests have been made in the course of the last years to ascertain the significance of small doses of alcohol for the safety of traffic. The number of tests and experiments made in this respect is regrettably small: we can refer only to those conducted by DREW (Great Britain), LOOMIS and WEST (U.S.A.) and COHEN (Great Britain). A 0.05 per cent serum alcohol level suffices, according to these authors, to impair the physical and psychic faculties of certain drivers, while all drivers with a blood-alcohol level of 0.1 per cent are influenced.

These values were accepted as correct by most of the delegates assembled at the 1958 alcohol-symposium in Indiana, among them HARGER, GOLDBERG, NEWMAN, WARD SMITH and LOOMIS.

The British Medical Association announced in 1960 that 0.05 per cent was the highest limit of blood-alcohol concentration tolerable from the aspect of traffic safety. Even skilled drivers accustomed to alcohol are unquestionably unfit to drive if the level of alcohol reaches 0.1 per cent in their blood.

We hold that, considering the figures published by HOLCOMB in 1937, LUCAS et al. in 1952, and VÁMOSI in 1960, there is no completely reliable limit in this respect. That this is so can be seen from the example of Czechoslovakia.

Article 4 of the Czechoslovak Traffic Regulations, in vigour since the 1st of January, 1961, forbids the consumption of alcoholic beverages before and during the ride; beverages containing more than 0.75 vol per cent of alcohol qualify as alcoholic, so that even the cheapest sort of beer is included in this category. The same article obliges all drivers to submit to breath-alcohol and blood-alcohol tests. Drivers who refuse to be so tested forfeit their licence and are fined in addition.

Let us now see the effects of this rule.

Of 26,579 traffic accidents that occurred in 1959, 11.4 per cent were due to the influence of alcohol. The corresponding figures were 29,219 and 10 per cent for 1960, and 29,917 and 8.4 per cent for 1961. These data are especially convincing if we compare the years 1960 and 1961, and take only those figures into account which refer to accidents in respect of motorized vehicles. The total number of such accidents was 29,169 in 1960 of which 2733 were due to alcoholic influence. The corresponding figures for 1961 were 23,127 and 2086, from which it follows that the number of alcoholic accidents was 647 less in 1961 than before the enactment of the new regulations, a drop of 23.7 per cent. An analysis of the causes of all accidents that occurred in the motorized traffic during 1960 and 1961 shows that, coincidentally with the decrease in the alcoholic category, there was a rise varying from 2 to 9 per cent in all other categories.

Surveying the records of the Institute of Forensic Medicine of Komensky University, Bratislava, we compared the number of traffic accidents and that of injuries sustained in fights and brawls during the first half of 1959 and 1961. Alcoholic influence was diagnosed in 56.6 per cent of the traffic accidents that occurred in the first half of 1959, and the corresponding figure was 30.0 per cent in 1961. As regards fights and brawls, 89 per cent of the cases occurred between intoxicated parties in the first 6 months of 1959, and the figure for 1961 was almost unchanged, namely 88.2 per cent.

Czechoslovakia is not the only country in which no alcohol must be taken before and during the drive. We think the fundamental difference between Czechoslovakia and other countries is that this country has not con-

tented itself with having scientifically ascertained the danger of alcoholism for the safety of traffic; this fact has been recognized by the competent authorities, and — moreover — the general public, too, has been convinced of the advantages of prohibition in connection with the driving of motorized vehicles.

Austria presents another instructive example in this respect. Here the number of traffic accidents has, according to BREITENECKER, decreased by 20 per cent since the adoption of the 0.08 per cent limit.

These two cases of positive results are unfortunately counterbalanced by many negative results in other countries.

Public opinion regarding the danger of alcoholism for the safety of traffic has undergone a radical change, and the demand of prohibition for drivers is steadily gaining ground. CARNELID hit the nail on the head by saying that the problem is not how one drives but how one thinks one can drive. And it is indubitable that even minimum doses of alcohol produce untoward effects.

Apart from the meeting in Warsaw, also that held in London tried to establish international collaboration. Let us hope that results will constantly improve in the future.

I. Gy. Fazekas

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The Effect of a Lethal Dose of Alcohol on the Blood Alcohol Level, Survival, and Hepatic Alcohol Dehydrogenase Activity in Intact and in Adrenalectomized Rats

Following the administration of 0.8 g/100 g alcohol, intact rats survived for 4 to 31 hours, adrenalectomized rats for 1 to 8 hours. At the time of death the blood alcohol concentration was 0.516 to 0.03 per cent in the former, and 0.194 to 0.5 per cent in the latter group. In response to 0.5 g/100 g of alcohol, the blood alcohol level of the intact rats returned to the initial value in 11 to 12 hours and the animals survived, whereas the adrenalectomized rats succumbed in 9 to 25 hours, when the blood alcohol concentration was 0.098 to 0.030 per cent.

In response to a lethal dose of alcohol the alcohol dehydrogenase activity of the liver increased during the first 5 to 6 hours, then gradually decreased in both the intact and the adrenalectomized animals. In the intact animals the increase in enzymatic activity is ascribed to the adrenocortical function being enhanced by alcohol, and the decrease of enzyme activity to a diminution of adrenocortical activity. In the adrenalectomized animals the increase of enzyme activity is attributed to a mobilisation of corticosteroids stored in tissues (FAZEKAS), and the decrease of enzyme activity to a breakdown of the corticosteroids mobilized from the tissues. This dual response of the hepatic alcohol dehydrogenase activity might be used as a new test of adrenocortical activity.

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Alcohol Breakdown in the Human Organism

The breakdown of ethyl alcohol has been studied under normal conditions and under the effect of insulin, dextrose and fructose. An opposition to the claim made by other authors, the above agents were found to exert no influence on the rate of alcohol breakdown. On the other hand, the clinical symptoms of alcoholic intoxication were favourably influenced by fructose; dextrose plus insulin acted unfavourably in this respect. In the course of alcoholic intoxication a marked hypoglycaemic tendency is observable.

D. Horváth

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The Influence of Some Drugs on the Effect of Alcohol

The appearance of new pharmacological preparations day by day and the frightening increase in drug consumption make it necessary to analyze from many angles the taking of drugs as a pathological condition.

One of the points in such an analysis is in connection with forensic medicine, notably the correlation between the effect of alcohol and that of drugs.

The well-known interactions existing between alcohol, on the one hand, and barbiturates, opiates, synthetic morphinoids, phenacetine and pyrazolone derivatives etc., on the other, are not dealt with here.

The author wishes to call attention to certain "fashionable" drugs, which are taken extensively, usually without medical supervision.

The problems discussed in brief are

1. The interaction between alcohol and some minor tranquillizers (Meprobamate, Trioxazin, Methylpentinol).
2. The dangers of combined preparations (Chlorpromazine with Promethazine and Reserpine, Ridol).
3. The hazards of certain combinations, owing to their opiate ingredients (codeine, dionine, etc.).
4. The non-innocuous nature of the barbituratefree hypnotics (gluthetimide).
5. The problem of taking corticomedullary stimulants (amphetamine, methylphenidate, phenmetrazine, etc.) together with alcohol.
6. The hazards of the uncritical use of antihistaminic drugs.

B. Rengei

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Influence of Phenylmercuric Borate on the Blood Alcohol Level

In connexion with one case the effect of phenylmercuric borate $C_6H_5HgBO_2$ (Merfen) solution on Widmark's blood alcohol test has been examined. With an aqueous solution containing 0.2 per cent of the compound and 10 per cent sodium nitrite the measure of the reaction was found to be 0.013 per cent. When blood is taken with a cannula kept in phenylmercuric borate solution, the contamination of blood cannot amount to more than 20 to 30 per cent even in the case of taking as little as 1 or 2 ml, and thus the blood alcohol level is increased by not more than 0.002 to 0.004 per cent. This value is too low to have some practical significance, the blood alcohol concentration decreases rather than incerases owing to the dilution of blood. Therefore, the result of Widmark's alcohol test must be considered reliable even with the use of such solutions for sterilizing the cannula.

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Psychiatric Diagnosis of Pathologic Drunkenness

(Discussion of Gy. Pollner's paper on alcoholism)

In the voluminous literature on alcoholism few authors have dealt with the problem of pathological alcohol intoxication. The postulates and analyses of Nyirő serve as a guide in international literature.

It is often difficult to establish the occurrence of pathological alcohol intoxication. The psychiatric expert has a grave responsibility in stating his opinion, especially when it has to be voiced in cases of criminal acts causing death. The judge tends to sentence the culprit to death, and if the psychiatric expert diagnoses pathological alcohol intoxication meaning irresponsibility, the defendant cannot be punished. All criteria of the condition seldom occur together. Abortive forms and peculiar varieties of symptoms often are encountered.

It would be important to publish reports of the cases diagnosed for p a t h o l o g i c a l drunkenness. An adequate number of pertaining case reports would allow drawing conclusions of general validity and formulating a uniform criminal-psychologic view.

F. Kósa

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Estimation of the Alcohol Effect in the Rat by the Tilting Plane Method

Arvola, Sammalisto and Wallgren used a tilted plane to test the equilibrium disorders and motor incoordinations in alcohol intoxicated rats and found that they are able to climb at a lower angle of inclination than untreated animals. They recommend the method for studying the effect of drugs synergistic or antagonistic to alcohol.

Our own observations seem to confirm the results of Arvola et al.

The rat's ability to climb up the inclined plane varies in dependence on the blood alcohol level (correlation coefficient, 0.15 to 0.89).

On the basis of hourly determinations of the angle of inclination under which the animals were still able to climb the plane, it was possible to differentiate 2—3 degrees of alcohol effect after a dose of 2 g, and 4—5 degrees after 5 g per kg of body weight of alcohol.

Significant differences presented themselves in the surmounted angles of inclination between alcohol-synergistic and alcohol-antagonistic drugs, up to a blood alcohol level not higher than 0.3 per cent.

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Medico-Legal Aspects of Injuries Due to Falls in Alcoholic Intoxication

In a year's material of the Hospital of the National First Aid Service the injuries suffered in alcoholic intoxication have been studied. The number of patients, admitted during the year with injuries sustained in alcoholic intoxication, totalled 1910 of whom 1001 suffered the injury exclusively on account of a fall, without the intervention of other persons or vehicles. The head was traumatized in 89 per cent, the extremities or the trunk in 11 per cent, of the cases. In the first category, 51 per cent were facial and 38 per cent cranial injuries. Epithelial lesions were most frequent, and haematomas were second in rank in the category of facial injuries, but lacerated wounds were less frequent. Haematomas and lacerated wounds were predominant among the cranial lesions.

If we regard the head as a cylindrical body structure, 89 per cent of the injuries affected the cylindric surface and only 10 per cent the calvary. Injuries on the side of the head were mostly on the projecting parts, especially on the forehead, supraorbital arch or nose, but seldom on the chin. The present studies had the purpose to help medico-legal experts in ascertaining whether certain injuries, suffered in a state of intoxication, are due to spontaneous falls or to the agency of others — this question frequently occurring in the courts.

Gy. Dallos

(Hungarian Army Medical Corps)

Histochemical Studies in Acute Alcohol Poisoning

Organs of rabbits killed by alcohol poisoning have been studied by means of Feulgen's reaction. A comparison with the controls revealed no change except an increased positivity in the adrenal cortex. The reaction was vigorous after the administration of 1 to 2 g of alcohol per kg of body weight. Increased doses were followed by a decrease of the reaction. The reaction became negative after chronic alcohol administration. Feulgen's reaction gave the same results as control reactions with phenylhydrazine and dinitrophenylhydrazine. That adrenocortical activity is stimulated by alcohol has been proved histochemically in the present studies.

Ö. Sátori, Á. Szabó

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Cerebral Injury — Alcoholic Intoxication

The cases of cerebral injury treated during four years in the Institute of Traumatology, as also autopsy findings in connection with fatal accidents during the same time have been analyzed. Alcoholic intoxication had occurred in 21.8 per cent of the cerebral injuries, and in 25.7 per cent of fatally terminating isolated lesions of the skull or brain. The difficulties of differentiating alcoholic coma from the comatous state associated with cerebral injury are emphasized. The following precautionary measures are suggested in doubtful cases:

(1) A careful observation of the patients.

(2) The execution of all routine examinations (supplemented by a quick informative blood-alcohol test).

(3) Persons admitted in the drunken state without known antecedents should never be discharged without a careful neurological examination if their consciousness is still disturbed or if they express uncertain complaints.

(4) The diagnosis of alcoholic intoxication, established after an uncertain history, should always be followed by neurological control after the patient has become sober.

Gy. Monostori, Klára Zsigmond, J. Nagy

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Experience with the Alcohol Probe

Over one thousand tests were made to estimate the alcohol contents of the expired air by means of the Nagy—Zsigmond type alcohol probe.

The instrument has proved highly valuable in practical tests. It is easy to handle, hygienic, gives reliable indications and responds specifically to alcohol. It can be regarded as an efficient means for prevention, education and as an inducer of self-restraint. Factors prohibiting its use have not been noticed during the tests. Quantitative blood alcohol tests according to Widmark, whenever they were taken, confirmed the results achieved with the probe.

L. Tolnay, L. Danka

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Non-Regular Deaths of Alcoholics

The non-regular deaths of 200 alcoholics were analyzed. The records were completed with details obtained from the relatives whenever the history and necropsy data raised the suspicion of alcoholism.

The points taken into account were age, occupation, the period and degree of the subject's addiction to alcohol and the cause of death.

Six persons out of the 188 males and 12 females had been at some time subjected to withdrawal treatment.

The average age, 47.8 years, was below that of the total population, with 22 and 71 as the lower and upper limits. The greatest mortality was between 39 and 49 years, in contrast to between 49 and 59 or more in the average population.

Death occurred in 46 per cent within the first 10 years, in 26 per cent between 10 and 20 years, the rest beyond 20 years of alcoholism. 122 persons died a violent, 78 a natural, death. Out of 66 suicides 39 hanged, 18 poisoned themselves, 9 committed suicide in some other way.

Out of 51 accidents 36 were traffic accidents, mainly train or tram; the rest were occupational accidents, drowning, or foreign body aspiration. In 87 per cent, Widmark's blood alcohol test showed a level between 0.08 and 0.35 per cent.

Predominant among the 78 cases of natural death was some kind of cardiac injury (43), with moderate hypertrophy, dilatation and myocardial degeneration. In 35 cases death was due to respiratory disorders, liver or stomach changes or to their complications. The non-regular mortality of alcoholics shows distinct differences to that of the average population.

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(Institute of Forensic Medicine, Medical University, Budapest)

Suicide and Alcohol

From among the interrelations existing between alcoholism and different social phenomena, the role of alcoholism in fatal suicides has not been sufficiently analyzed. A total of 1115 cases of suicides committed between 1960 and 1961 have been surveyed with a view to determining

(1) the frequency of alcoholism among the direct and indirect motives that had led to the suicide;

(2) how many of the felones-de-se committed their fatal act under the influence of alcohol.

The incidence of (1) was 12.6 per cent and that of (2) 20.3 per cent in the examined material. Both percentages are analyzed according to sex and age, the manner in which the suicide had been committed, as also according to other indexes. It is concluded that alcoholism is especially decisive among males and middle-aged persons who commit suicide in category (1) and that likewise middle-aged males constitute the majority of category (2) in which also the manner of suicide is often brutal.

Gy. Szuchovszky

(Institute of Forensic Medicine, Medical University, Budapest)

Criminal Law in the Service of Antialcoholism

Since the number of criminal acts committed under the influence of alcohol is considerable in Hungary, a social movement on a wide scale has been launched against alcoholism, and it was in the frame thereof that the new Hungarian criminal code, enacted in 1961, established rigorous penalties for crimes perpetrated under the influence of alcohol. Treating the subject from the medico-legal angle, the new provisions of the criminal code bearing upon general responsibility for felonies committed in a state of alcoholic intoxication, as also those provisions which refer to specific criminal responsibility for each particular criminal act are enumerated and the problem of the compulsory cure of withdrawal as introduced by the new code and points to the dangers involved are discussed. Since an increase in the number of alcoholic crimes may be expected, a new uniform standard for medico-legal expert opinions is urged.

S. Ökrös

(Institute of Forensic Medicine, Medical University, Budapest)

Demonstration of Traumatic Structures Caused by Injury in Heart Muscle Fibres

The normal architecture of the heart muscle fibres undergoes fundamental changes in response to injury. The change is caused by the acting force, the spasm, and the ensuing anoxia. In the area of the lesion the fibres swell, contract, or eventually become so mented into discs. The cross striation disappears. Instead a longitudinal striation appears, eventually with coagula in the sarcoplasm. The myofibrils are shortened, swollen, homogenised, fragmented, rounded off. Similar changes are noted at the site of insertion of the fibrils. The affected parts of the fibres are metallophilic, and on this basis the traumatic changes can be demonstrated electively by means of the Prussian blue test in 5 to 10 μ thick sections of the material embedded in paraffin. The sections are treated with a 1 per cent aqueous solution of potassium ferric ferrocyanide acidified with hydrochloric acid and a 1 per cent aqueous solution of iron chloride or iron alum, then stained with Heidenhein's haematoxylin and differentiated sharply. The affected fibres stain a dark blue, the intact ones a light blue.

L. Takácsy, F. Guba, G. Pártay

(Institute of Forensic Medicine, Medical University,
Electron-Microscopic Laboratory of the Hungarican Academy of Sciences, Budapest)

Electron-Microscopic Studies of the Ultrastructure of the Aorta

The electron-microscopic structure of the mammalian aorta, and especially the structural elements of the media have been studied. As opposed to some data in the literature, the elastic fibres in the tunica media have been found to show not a longitudinal, but a marked transversal structural pattern, dividing the elastic fibre into segments of various lenghts.

This is thought to be explicable by the different measures of contraction or relaxation. There is divergence from earlier observations also in that the tunica media contains numerous collagen fibres of characteristic structure, which in close connexion with the elastic fibres, completely interweave that layer. The ultrastructural architecture of the intima and adventitia has been found to conform with the descriptions in the literature. The ultrastructural patterns now observed in the normal aorta will form the basis of subsequent studies of the diseased aorta.

L. Nagy, M. Szabó

(Institute of Forensic Medicine, Medical University, Debrecen)

Ostium Barrier in Sudden Cardiac Death

In normal and hypertrophic human hearts the number of capillaries and the total capillary surface area per unit of surface area has been estimated, and the latter correlated with the size of the coronary orifices.

The coronaries were filled up by the Seifert counter-pressure apparatus, as modified by authors. Following fixation in formalin, embedding in paraffin and staining according to van Gieson, the capillary area visible in the projected sections was measured by a planimetric method.

It has been found that in the hypertrophic hearts the number of capillaries per unit of myocardial area was decreased, while the ratio between total capillary area and ostium area increased. This latter is suggested to be a sign indicative of a tendency to sudden cardiac death.

L. Takácsy, E. Flórián

(Institute of Forensic Medicine, Medical University, Budapest)

Solar Phenomena and Sudden Cardiac Death

The correlation between solar activity and the time of 725 sudden cardiac deaths has been studied. Changes in the strength of the geomagnetic field, due decisively to chromospheric eruptions, proved to be suitable for these heliobiological studies. A correlation, confirmed also by statistical methods, could be demonstrated between the cases of sudden cardiac death and the monthly average or total of the geomagnetic figures. In the light of the evidence it may be stated that the changes in the geomagnetic field caused by chromospheric eruptions may be considered to be one of the factors promoting sudden cardiac death. The results seemed to justify future research in this direction.

Á. Szabó, V. Kovács

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

Injuries of the Papillary Muscle of the Heart

Injuries of the papillary muscle have been studied in four years necropsy material. Such injuries have been divided into three categories: spontaneous, traumatic and non-penetrating injuries. The history and the gross and microscopic findings were analyzed in each individual case. Both the frequency of the necrosis and the infrequency of the rupture of the papillary muscle were in agreement with literary data. As regards non-penetrating injuries, it is suggested that noxious processes causing damage in the papillary muscle give rise to necrosis in the damaged area and finally lead to a rupture of the muscle.

L. Kiss

(Institute of Forensic Medicine, Medical University, Debrecen)

Colloid Reaction (PTS, CRP, Latex) in the Serum After Sudden Death

In cases of sudden cardiac death the PTS,* CRP** and Latex tests have been carried out.

In 80 per cent of the cases of coronary sclerosis, coronary thrombosis, myocardial infarction, myodegeneration, etc. one reaction, but often two or all three showed strong positivity. Negative results were obtained in several cases of severe coronary sclerosis, coronary constriction and coronary thrombosis.

In the control cases, sudden deaths due to causes other than a cardiac change, all three reactions yielded negative results, or, at the most, one was positive.

The positivity of colloid reactions suggests the presence of a pathological condition and supports the post-mortem diagnosis of sudden cardiac death.

L. Buris, M. Szabó

(Institute of Forensic Medicine, Medical University, Debrecen)

Histochemical Examination of the Furrow of Hanging

The changes in epithelial and connective tissue structure have been studied in the furrow of hanging. The specimens were obtained from forensic cases. The furrow of hanging was partly vital, partly postmortal (experimental) in origin.

In the area of the furrow of hanging of vital origin the epithelium and connective tissue showed increased Schiff positivity. By means of the methylgreen-pyronine and the acridine-orange fluorescence methods an increased RNA reaction could be demonstrated in the affected area. Such changes did not occur in postmortal furrows, where the lesioned areas showed the same behaviour as intact tissues.

The reaction of the epithelium has been examined by the method of Kuriowa and Ogata. The results were positive in both the vital and the post-mortal furrows. Thus, the method does not lend itself to decide whether the furrow has been caused during life, it only reveals that epithelium has been exposed to mechanical force. At the same time, it is suitable for the demonstration of epithelial injuries invisible to the naked eye.

Klára Zsigmond

(Institute of Forensic Medicine, Medical University, Debrecen)

Demonstration of Phenothiazine Compounds

The demonstration of the phenothiazine compounds (chlorpromazine, promethazine, thioproparazine diethazine and mepazine) has been studied by paper chromatography.

The most sensitive developer was found to be palladium chloride by means of which the smallest demonstrable amount was 5 μg. The UV spectrum of the above phenothiazine compounds in 96 per cent alcohol was also determined.

The urinary excretion by human subjects of therapeutic doses was determined. The procedures have been described in some detail.

* para-toluen-sulfon-acid
** C-reactive-protein

R. Budvári

(Institute of Forensic Medicine, Medical University, Pécs)

Inheritable Serum Properties; New Forensic Methods of Blood Stain Identification

The first example of inheritable serum property, the haptoglobins, was soon followed by the discovery of a few others. The greatest advance was made in the study of gamma globulins. The Gm (a) property was detected in 1956 by Grubb and Laurell and reports about new inheritable Gm-type serum properties have appeared almost each year. To-day seven different types of them are known to be bound to the gamma globulins. The present studies were concerned with the laboratory determination of Gm (a) properties and their application as a basis for routine blood group tests. The occurrence of Gm (a+) was 37.1 per cent. The determination was performed according to Prokop and Brocteur, with anti-D serum to sensitize the red blood cells which were added on the slide to a mixture of the serum to be tested and an anti-Gm (a) serum. The specimens were left to stand in a refrigerator for one hour before reading the results.

Another series of experiments was concerned with new methods of blood stain identification. Attempts to trace haptoglobin groups in dried blood stains yielded unstable results. More reliable were the "absorption-elution" tests suggested by KIND and NICKOLLS. By thermal elution of the specific antibodies it was possible in more than 100 cases to determine ABO and MN type properties in blood stains of known blood groups. Sometimes even the D property could be ascertained.

A. Simon

(Institute of Forensic Medicine, Martin Luther University, Halle)

Effect of the Washing Powders "Fit" and "Persil" on the Group-Specificity of Exsiccated Bloodstains

Four samples of different textiles, containing traces of blood and washing powder were tested with the technique of HOLZER during a period of 43 days. The products "Fit" and "Persil" were found to cause a continuous change in the chemical pattern of the blood groups, a phenomenon evidently due to the strong alkaline reaction of the bleaching substances. Notwithstanding the use of fresh blood samples, no indirect blood-group determination was possible in any of the textile fabrics after the lapse of 43 days. When glass dishes had first been painted with "Fit" or "Persil" and then stained with blood, it was possible to ascertain the blood group quickly and reliably with the method of LATTES even after 43 days. Since a blending of the bleaching agent with the blood mark is prevented by hard, non-absorptive material, the anti-blood components of the washing substance affect but the basal parts of the bloodstains.

I. Gábor

(Institute of Forensic Medicine, Medical University, Budapest)

The Use of the Gm System in Forensic Medicine

In recent years serological diagnosis has developed certain new methods, which have revealed some formerly unknown properties of the blood serum. Among these the Gm property of serum is of a certain interest.

The characteristic physical, chemical and serological properties, and the laws governing the heredity of the material in question have been clarified.

With the use of an adequate anti-serum, the method offers advantages in the determination of paternal identity. By its use eliminability can be increased by 11 to 12 per cent.

P. Guth

(Institute of Forensic Medicine, Medical University, Pécs)

Demonstration of Haptoglobin Groups in Tissues and Organs

In connection with investigations concerning different systems of blood groups it is customary to prove the occurrence of newly-discovered blood-group properties in the various tissues and organs. The present paper is concerned with the demonstrability of haptoglobin groups in tissues and organs. Specimens of liver, kidney, arterial wall and bone marrow, obtained from fresh cadavers, were studied.

After determining the haptoglobin type of the cadaver's blood, extracts of the tissues and organs of the same cadaver were made with 0.3 per cent saline, haemoglobin was added, and the extracts were then examined in starch-gel electrophoresis.

A total of 29 cadavers were examined. The presence of haptoglobin groups belonging to the same type as the blood was demonstrated from the liver in 21, from the kidney in 22, from the vessel walls in 19, from the bone marrow in 20 cases. The technique of extraction was such as to preclude the possibility of having determined the groups of haptoglobin from the residual blood of the tissues themselves.

The results supported the hypothesis of JAYLE and BOUSSIER regarding the origin of haptoglobins in connective tissue, and proved to be well suited for the purposes of criminal investigations (e.g. identification in cases of dismembered corpses).

T. Kalóczkay, Klára Zsigmond, J. Nagy]

(Institute of Forensic Medicine, Medical University, Debrecen)

Blood Detection Tests

Two methods have been discussed.

1. *Phenolphthaleine test.* The preparation of phenolphthaleine and of the reagent, and the experience obtained by the use of the test are described.

2. *Takayma's reagent.* The preparation of the reagent and the experience obtained with the test are described.

It is emphasized that both methods have the advantage of being applicable also in the presence of chlorophyl.

N. Kapusz, S. Balázsy

(Institute of Forensic Medicine, Medical University, Debrecen)

Fat Embolism and Serum Lipase Activity

Samples of blood serum from subjects with different traumatic lesions have been tested for lipase, by the method of COMFORT.

The specimens originated partly from forensic, and partly from clinical material.

In agreement with data in the literature, the normal values have been found to range from 0.2 to 1.2 (expressed in ml of n/20 NaOH).

In the cases in which death had ensued immediately, or not later than two hours after, sustaining injury, no change could be noted in the serum lipase level, in spite of fat embolism in the lungs.

When the injured survived the injury by several hours or eventually by days, the serum lipase level was found to have increased to several times the normal.

J. Lesznyák

(Institute of Forensic Medicine, Medical University, Debrecen)

Changes in the Specific Gravity of the Brain After Injuries and Poisonings

The specific gravity of specimens taken at autopsy from different areas of the brain (frontal lobe, occipital lobe, cerebellum, pons, oblong medulla) has been determined by means of a special hydrostatic balance constructed by the author. The material included normal subjects, as well as patients who had died in consequence of cerebral injury or poisoning with carbon monoxide or barbiturate. The specific gravity of normal brain tissue has been found to vary between 1.037 and 1.149, with the lowest value obtained in the area of the cerebral hemispheres and the highest in that of the oblong medulla. In some cases of poisoning this relation was unchanged, whereas in others the differences disappeared, i.e. the specific gravity of the cerebellum, pons and oblong medulla became comparable to that of the cerebral hemispheres. This is indicative of a water uptake in the area of the cerebellum, pons and oblong medulla.

The results obtained explain the observations by ELBEL, MEYER and PROKOP, who found different concentrations of alcohol in different areas of the brain. These differences in alcohol content are ascribed to differences in water content.

D. Horváth, Katharine Barth

(Pharmacy of Medical University, Pécs)

Rapid Informative Identification of the Residues of Drug Mixtures

In cases of poisoning the rapid identification of the drug mixture residues makes it possible to begin causal therapy without delay. As in most cases some residue is in fact available a method for the identification of minute quantities has been developed.

The rapid identification of barbiturate derivatives and some alcaloid drugs is discussed.

L. Gát, J. Nagy, L. Pintér, L. Buris

(Institute of Forensic Medicine and Department of Physiology, Medical University, Debrecen)

Changes of the Ocular Fundus in Chronic Nicotine Poisoning

Dogs had been treated for more than one year with subcutaneous injection of sublethal doses of nicotine (average dose, 1 mg/kg body weight). The changes developing in the fundus were studied and recorded by colour photography. In every animal severe degenerative changes appeared in the retina from the third month on. The gross changes found are described in detail. The histological changes are also shown, together with those found in organs other than the retina.

D. Horváth, Katalin Held

(Pharmacy of Medical University, Pécs)

Identification of Drug Preparations

Poisonings, accidental or intentional, are mostly due to the taking or administering of officially registered commercial drug preparations. The residues found may play a decisive role in the elucidation of the nature of intoxication, either at the first medical aid or in the course of criminal investigation.

We have developed a system on the basis of which the drug residues found may be identified with a high measure of probability without requiring analysis, and therefore such materials can be spared for later investigations.

The characters of commercial preparations have been fitted into the system on grounds of the following features:

Oral preparations:
shape, weight, size, colour, characteristic commercial symbol on the tablets, the dye used for staining dragées.
Parenteral preparations:
Ampule volume (1, 2, 5, 10 ml), colour and viscosity of the solutions.
The above system has been discussed.

B. Rengei

(Institute of Forensic Medicine, Medical University, Szeged)

The Use of Paper Chromatography in Criminological Investigations

The components of various sorts of ink, China or India ink, ball-point pen dyes and lipsticks have been studied by means of paper chromatography. The substances examined have been manufactured in Hungary or were preparations available commercially in this country.

The inks, China inks, ball-point pen dyes dissolved in water or methanol were subjected to ascending chromatography on Schleicher and Schüll's paper No. 2043/b Mgl, in a system of n-butanol-acetic acid-water 5 : 1 : 4. Lipsticks were dissolved in petrol ether, then the dye was separated from the fatty ingredients by means of shaking out in methanol. After application to Schleicher and Schüll's 2043/b Mgl paper the material was run by the ascending technique in n-butanol-water-metanol-ammonia 100 : 44 : 20 : 1. On the basis of the Rf values obtained and the colour intensity it is possible to identify the above substances.

I. Szabó

(Institute of Forensic Medicine, Medical University, Debrecen)

Lethal Acute Gasoline Poisoning

Two cases of acute lethal poisoning with gasoline are described. Both subjects wer-children and had ingested the gasoline by mouth.

At autopsy hyperaemia of the pia mater, severe cerebral oedema, and in the lungs hyperaemia, patchy haemorrhages and oedema were the most conspicuous changes. In one case petechiae were visible subpericardially, in the other streaks of haemorrhage were found subendocardially in the left ventricle and in the myocardium. In the latter case punctate haemorrhages occurred in small numbers in the spleen, too.

Beside the gross changes, microscopic ones are also discussed, partly on the basis of animal experiments.

L. Harsányi, Erzsébet Bellus

(Institute of Forensic Medicine, Medical University, Budapest)

Diatomes in the Lungs of Non-Drowned Subjects

Four to five gram post-mortem specimens from the lungs of 28 non-drowned subjects between 2 months and 78 years of age were treated with acid, sedimented and washed in distilled water. Seven specimens, two of infants and 5 of adults, were negative, but 21 have shown 4 to 5 silicious algae, each. These must have penetrated the lungs during subjects life, apparently with inhaled dust. The results are in agreement with those of Otto (1961), presenting a new aspect for the view that the occurrence of diatomes in the lungs cannot be taken as a proof of drowning as the cause of death. Studies are carried on in the organs of the major circulation.

Gy. Nyirő, K. Irányi

(Department of Psychiatry, University Medical School, Budapest)

Evaluation of the Syndrome Ganser

The development of psychotic symptoms during criminal process arouses the suspicion of simulation. Under such conditions the development of the Ganser syndrome may be the expression of a pathological state and true simulation alike.

We have observed the development of the syndrome in 7 patients. Three cases had no criminal basis. One of them was under treatment for schizophrenia, the two others suffered from neurotic depression. The remaining four patients were under criminal procedure. Two showed the classic symptoms of pseudodementia and paralogia. The third was a hysteric psychopathic embezzler, the fourth showed initial symptoms of progressive paralysis. Two amoral psychopathic criminals made a clumsy attempt at simulating psychosis.

By analyzing the above cases it may be stated that *a)* pseudodementia and paralogia may be associated with reactive or psychogenic conditions, join the symptoms of psychosis or develop on grounds of organic cerebral changes. *b)* The conflict eliciting the syndrome may be correlated with some criminal act, or may be familial or existential in nature.

In forensic practice the presence of Ganser's symptoms raises the question of responsibility. When formulating the expert opinion, the above points of view should be borne in mind.

E. Somogyi, J. Irányi, B. Orovecz, K. Irányi

(Institute of Forensic Medicine, Medical University, Budapest)

Evaluation of Lightning Trauma in Forensic Practice

The 156 accidents caused by lightning in 1959—60 in Hungary have been analyzed. Of the survivors, 12 were examined hours or days, and 106 one or two years, after sustaining the injury. In addition to the data of hospital treatment, the report of the ambulance physician has been taken into account.

Expert medical opinion was sought late in most of the cases. The sources of error and conflicting opinions were the misinterpretations of acute symptoms and late lesions, the identification of the accident caused by lightning with that caused by high-voltage industrial currents.

1. Lightning elicits a characteristic organic functional symptom-complex in the survivors, which we have termed the lightning syndrome. Its components are syncope, peripheral nervous injury and the appearance of lightning arborisation on the skin. The characteristic syndrome may be complicated by diverse symptoms. "Functional superposition" and "emotional shock" are often erroneous diagnoses. The mortality rate was 30 per cent. Instantaneous death ensued without any demonstrable morphological changes.

2. Persisting defects, and even more so, organic neuropsychiatric processes are rare. In the 106 injured individuals the following late changes were observed: cerebrasthenic symptoms, not interfering with the patient's working ability, neurotic symptoms, pain in the limbs reminiscent of causalgia, impairment of hearing due to disturbances in the inner ear, cataract, skin scars and pigmentations as a result of burns. The medical expert must bear in mind that even severe acute symptoms have a tendency to disappear rapidly and completely.

3. Being struck by lightning is a special kind of accident. The factors active in conjunction with it, the pathomechanism, the symptomatology, prognosis, the rules of prevention, emergency treatment and thus also the evaluation by the medical expert differ from those occurring in any other kind of accident.

G. Paneth, Á. Szabó, A. Szende

(Metropolitan Tribunal, Budapest)

Sexual Manipulation — Suicide?

A man 40 years of age, clad in female apparel, female stockings on his legs and female sandals on his feet, was found hanged. Strange notes with fetishistic contents were near the corps. Analysis of the case led to the conclusion that it was a fantastic combination of fetishistic and travestite tendencies with sadistic phantasmagories. The deceased worked off part of his pathological fancies by way of fetishistic tendencies (interest in female feet in shoes with high heels). The transvestite inclinations manifested themselves partly in a socialized, larvated form (domestic chores performed in female negligée). All this satisfied him, however, but partially, so that he sought full satisfaction by means of autoerotic manipulations in a hypoxic state which caused his accidental death.

D. Schranz, M. Bartha

(Department of Oral Surgery, Medical University, Budapest)

Sexual Dimorphism of the Teeth

Many reports have been published on the sexual differences of the teeth, but the results are often controversial, owing to the small number of examined cases. Clinical and radiographical examinations of several thousand persons point out the special features permitting to determine the sex according to the teeth.

M. Fehér

(Institute of Forensic Medicine, Medical University, Budapest)

Utilization of Hereditary Characteristics in Affiliation Cases

The usefulness of hereditary characteristics for deciding problems of paternity depends on the following factors. (1) It should be precisely definable; (2) it should not be sensitive to environmental factors; (3) its genetic course should be clear; (4) it should be idependent of age; and (5) sex; (6) it should be comparatively rare. With the exception of (6), these requirements are satisfied by blood-group properties. Considering that haematological evidence suffices only to eliminate every second male falsely accused of paternity in affiliation suits, it has to be supplemented by anthropologic examinations. In a total of 3500 medico-legal examinations the most useful marks were found by observing the cutaneous pattern, the features of the mouth, chin, zygomatic area, the external ear, the general build of the face, the features of the temporal region, orbital area, nose, further the complexion. Also PTC and hereditary anomalies may be of use in certain cases.

Ö. Szedlák

(Medical Division, Health Department of the Ministry of Interior)

The Role of Police Surgeons in Medico-Legal Work

After a brief survey of the conditions prevailing before 1957 and the results achieved since then, it is pointed out that since 1957 the medical staff of the Police have been regularly engaged in nation-wide medical expert activities. The number of the tasks to be fulfilled has also increased considerably. The results achieved and the deficiencies still existing are discussed.

It is emphasized that such activities of the medical staff of the Police require close cooperation with the forensic medical experts (with the Institutes of Forensic Medicine of the universities, with the medical experts of the Law Courts, with the pathologists of the county hospitals, etc.).

An outline is presented of the conditions prevailing as regards post-graduate training and specialisation of forensic medical experts, and their significance.

L. Tolnay

(Institute of Forensic Medicine, Medical University, Budapest)

Suicide by Asphyxiation with a Nylon Sac Pulled Over the Head

A case is reported in which death by asphyxia occurred in an unprecedented manner.

A survey of the literature on deaths due to asphyxia is presented. Most of the reports describe accidents caused by auto-erotic manipulations, and it was only in one or two cases that suicide could reliably be ascertained.

The case in question was that of a man, 45 years of age, an electric welder by profession, with a normal sexual life, who had consumed alcohol regularly for 25 years, had repeatedly suffered cranial trauma, and had attempted suicide twice by means of hanging and drugs. He committed the third suicide in the following manner.

Fully dressed, he lay down in a supine position, drew a nylon sac of 5 litre capacity over his head and fixed it around his neck with a rubber ring. He placed in his mouth a rubber tube of 1.5 m length; this was led under the ring and connected to the cock of a cylinder containing propane-butane gas. On breaking into the closed flat, a strong smell of gas was felt, and a suicide note was found.

At necropsy ballooning inflated lungs, with dry cut surface and liquid blood were found. The bones of the skull were coarsely thickened. The Widmark blood alcohol test yielded 0.176 per cent. Wenezland's test revealed no CO in the blood, so that death was due to nothing but asphyxia, since the inhaled gas mixture has no toxic effect. A sharp distinction between accident and suicide is necessary, for most deaths of a similar nature are due to accidents caused by auto-erotic manipulations.

Gy. Farkas

(Institute of Forensic Medicine, Medical University, Pécs)

Splenic Haemorrhage in Two Stages

After a brief survey of the literature two cases are reported. Death occurred 9 hours after the fatal injury in one of the cases. The patient's condition seemed satisfactory for 24 hours after the injury in the other case, then death ensued. The autopsy confirmed the gross observations. The difficulties of correct diagnosis and medical expertise are discussed and the establishment of new traumatological institutes is urged.

V. Kovács

(Institute of Forensic Medicine, Medical University, Budapest)

Double Aneurysm of the Right Coronary Artery

After a survey of 67 cases of coronary aneurysm reported in the literature own case is discussed. In a male patient 59 years of age thin-walled aneurysms were found in the right coronary artery, one pea-nut sized 3 cm from the orifice and one bean-sized 5 cm from the orifice. The lumen of the artery between the two aneurysms was moderately wide, the vascular wall was thick and butter yellow plaques were visible on it. The case merits attention, since a double aneurysm of the right coronary artery is a rarity.

L. Danka, I. Gábor, A. Potondi

(Institute of Forensic Medicine, Medical University, Budapest)

Basilar Aneurysm of Unusual Size

The aneurysm under review had a size of $4 \times 5 \times 3.5$ cm and, lodged in the right anterior communicating artery, it extended to the right frontal lobe. It was diagnosed 2 years prior to death but had given rise to symptoms 10 years before. After having been recognized, the aneurysm was enveloped in a muscle flap as a palliative measure. The patient lost the senses of smell and taste, but displayed no other symptoms for 18 months after this intervention, when he suddenly died.

A survey of the literature showed reports on five cases of aneurysms of a similar size; most of them were recorded post mortem (KRAUS, DITTRICH, KRAYENBUHL, FEARNSIDES, WICHERN).

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