
In the introduction to this book the author suggests that little attention has been paid to the problem of fat necrosis. The first chapter deals with the anatomy and physiology of adipose tissue and the second with experimental work on subcutaneous and intravenous injection of fats. Two chapters are then devoted to fat necrosis, both focal and diffuse, and the various disease syndromes which it produces. The fundamental local lesion progresses from necrosis and cyst formation to laminated hyalinization and perhaps calcification. Phagocytosis of the fat from the dead cell by histiocytes and its deposition at a distance, where it acts as a foreign body, is the mode of spread of the lesions. The author considers that humoral protein imbalance is a factor in the production of progressive liposclerosis. In the last chapter he discusses the interrelationship of all connective tissue diseases, and suggests that the pathological changes in liposclerosis are similar to those in amyloid disease and other disturbances of protein metabolism.

This is an exhaustive study of the pathology of fatty tissue, and much of the monograph is repetitive, particularly the chapters on fat necrosis. The photographs also tend to show the same repetitive quality. A long classification of fat necrosis is given, which the author considers incomplete, and descriptions of the lesions are repeated much too often. In some cases the description suggests that changes in the fatty tissue are merely part of a diffuse polyarteritis, and at one point the author admits the possibility of primary vascular disease followed by necrosis of the surrounding fat. A further criticism of this book is that, although the title is Syndromes Nouveaux de Pathologie Adipuse, most of the syndromes were described many years ago, some even last century.

M. Gillespie.


In this new book the author attempts to interrelate perinatal pathology and physiology. The limitations of our present knowledge on these subjects are well brought out in a critical review of the relevant literature. The author's personal experience is skilfully interwoven, usually in tabulated form. This is not a textbook of descriptive pathology, but the reader will find it a useful reference book which will render the search of the widely scattered literature a much easier task and this is particularly helped by emphasizing in capital letters the more valuable references in the bibliography.

It is to be hoped that this book will stimulate further research on many of its important subject matters: it may for instance help to guide into more useful fields such futile attempts as the study of prematurity in terms of a pathological entity. It is also hoped that the author may overcome in later editions his present difficulties in the classification of some conditions such as are evident when he includes "congenital short oesophagus" among "Hirschsprung's disease and allied disorders."

The publishers are to be congratulated on taking the initiative in this country with the production of a book on a much neglected subject.

Martin Bodian.

Cross Reference.—Dr. Fairfield Smith, who wrote a paper "Urea Clearance Tests" for this Journal (J. clin. Path., 1949, 2, 266), has published an amplification of his statistical appendix in Biometrics (1951, 7, 185).

Correction.—In "The Question of the Rh Hapten" (J. clin. Path., 1951, 4, 475), Table VIII, column 2, in the first two sera the upper line refers to the saline control and the second line in each pair refers to lecithin 1:4,000.

ABSTRACTS

This section of the JOURNAL is published in collaboration with the two abstracting journals, Abstracts of World Medicine, and Abstracts of World Surgery, Obstetrics and Gynaecology, published by the British Medical Association. In this JOURNAL some of the more important articles on subjects of interest to clinical pathologists are selected for abstract, and these are classified into four sections: bacteriology; biochemistry; haematology; and morbid anatomy and histology.

BACTERIOLOGY


Reactions in animal experiments are described. Similar experiments were repeated in 4 people previously immunized with fluid tetanus toxoid or A.P.T. who were given 0.5 ml. fluid toxoid and 1,500 units tetanus antitoxin (in different limbs) after they had suffered injuries liable to lead to tetanus. In 3 cases the antitoxin was given at the same time as the toxoid, but in the other case, 2 days later. Three out of the 4, including the one in whom administration of antitoxin was delayed, showed a well-marked secondary response to tetanus toxoid; the remaining subject was known from other evidence to give a poor response to tetanus toxoid.

The authors recommend the use of simultaneous active and passive immunization against tetanus for patients who have suffered shock, compound fractures, and massively contaminated wounds at any time after they have been immunized, and for patients suffering less severe wounds 4 years or more after immunization.

[This is an extremely important paper, with an obvious bearing on medical practice: it is to be hoped that the work will be repeated with methods of antitoxin titration that inspire greater confidence. Testing for tetanus antitoxin at the 0.001 unit (U.S.A.) level involves considerable error, and is very liable to give an overestimate of the antitoxin content of a sample. The results for the rabbit that received a mixture of 0.1 ml. fluid toxoid (whose strength is nowhere stated) and 150 units of tetanus antitoxin (stated to be heterologous, presumably refined horse antitoxin, but no information is given) seem to deserve more comment than is given them. Only if the tetanus toxoid contained 1,500 Lf per ml. would the mixture be neutral; if it contained less toxoid (as would ordinarily be expected (some rise in antitoxin titre should have occurred in the rabbit, and later some fall. In no case has an experiment been controlled by injection of antitoxin alone.)

C. L. Oakley.


Penicillin, streptomycin, dihydrostreptomycin, chloramphenicol, aureomycin, and bacitracin were each tested against strains of haemolytic streptococci, Streptococcus viridans, Staphylococcus aureus, Klebsiella pneumoniae, Haemophilus influenzae, H. pertussis and pneumococci which were known not to have been in contact with antibiotic drugs. Bacterial sensitivity was measured by the size of the zone of inhibition produced on a seeded plate by a paper disk impregnated with a solution of the antibiotic, and also by determining the number of residual viable organisms to be obtained from the disk by washing with broth.

All antibiotics left a residuum of viable organisms and the number of such organisms was regarded as a better index of sensitivity than the size of the zones of inhibition. By its use, penicillin G was shown to be more potent than penicillin K (as found by clinical experience). Against Gram-positive organisms penicillin was the most effective, bacitracin the next, and aureomycin the least effective. Aureomycin was also the least effective against Gram-negative organisms. Chloramphenicol was the most effective against H. influenzae and H. pertussis, while streptomycin was the most
active against *K. pneumoniae*. In the case of penicillin, bacitracin, aureomycin, and chloramphenicol the residual organisms were still sensitive to the respective antibiotics, but in the case of streptomycin and dihydrostreptomycin they were resistant.

The effects of penicillin paired with chloramphenicol and aureomycin respectively, and of streptomycin paired with penicillin, chloramphenicol, and aureomycin respectively were determined on the test strains. When organisms were sensitive to both antibiotics, the combined response was additive, but if the organism was sensitive to one of the drugs only the effect of the other was impaired. The synergistic effect is explicable as due to each drug acting on the viable residuum left by the other, while it is suggested that the interfering action is due to the stimulating effect of the ineffective drug on the organism sensitive to the other drug.

M. Lubran.


Over 6,000 cases treated with sulphonamides in Frederiksberg Hospital, Copenhagen, are reviewed with reference to the incidence of haematuria. The newer sulphapyrimidine drugs such as sulfadiazine or sulfamerazine, which are excreted more slowly, have a slightly higher tendency to cause renal damage than the older more rapidly excreted types. The lowest incidence was found with "lucosil" (sulphamethyldiazole); out of 3,078 cases, haematuria was demonstrated chemically in 2.3%. Children tolerate sulphonamides much better than do adults; the incidence of haematuria increases with age. In no case was the damage to the kidneys permanent.

E. H. Johnson.


The problem of the diphtheria carrier is an old one, and the methods of treatment numerous. Tyrothricin is the latest effective agent. In the present investigation 3 ml. of a 1 in 2,000 solution was given twice daily as an aerosol spray. Throat swabs were taken at the end of 4 days and again as necessary until three negatives had been obtained. Of 100 patients only 2 remained refractory, and as many as 54 were rendered negative after only 4 days' treatment. In general, convalescent patients harboured the less virulent organisms, which were easier to remove, while the slower and refractory results occurred in the healthy carrier with highly virulent bacilli. The method is difficult to carry out in younger patients, but appears to be free from toxic effects.

A. Paton.


Neomycin is a new antibiotic obtained from *Streptomyces fradiae*. The authors have tested it in 6 cases of pylonephritis and 4 cases of cystitis, some with complications such as bacteraemia, at the Pennsylvania Hospital, Philadelphia. The causative organisms included *Aerobacter aerogenes*, *Bacterium coli*, paracolon bacilli, *Pseudomonas aeruginosa*, non-haemolytic streptococci, haemolytic staphylococci, and *Proteus*. All these organisms were shown to be completely or partially resistant in *vitro* to penicillin, aureomycin, chloramphenicol, and streptomycin, but in all but one case were sensitive to neomycin (200 units per ml.). Only in the case from which the resistant organism was isolated did the patient fail to improve on treatment, bacteriological evidence of cure being obtained in all the others. Serum and urine assays of the drug were carried out at frequent intervals. Sulphobromophthalein sodium retention tests, phenolsulphonphthalein excretion tests, electro-cardiography, blood and bone-marrow examinations, retinoscopy, audiography, blood urea nitrogen estimations, and urine examinations were carried out before and after treatment and showed evidence of toxicity in only one case. This patient had a persistent elevation of the blood urea nitrogen level, with transient nausea and vomiting and transient impairment of hearing as shown by the audiogram. Dosage varied from 4,498 units (for an infant) to 100,000 units every 6 hours for 4 doses, followed by 50,000 to 100,000 units every 12 hours for 5 to 7 days. In the blood a stable level of 4 to 10 units per ml was reached in 48 to 72 hours. Maximum urinary levels varied from 26 to 410 units per ml. No relapse has been recorded, the follow-up period ranging from 1 to 4 months. Most strains of *Proteus* and, more especially, of *Pseudomonas* exhibited properties suggesting the potential development of resistance to neomycin.

J. Maclean Smith.

This paper records the results of treatment with terramycin of 15 patients with various infections. Terramycin hydrochloride was given orally in all cases. Various dosage schemes were employed, but treatment usually consisted of an initial dose of 1 g. repeated 4-hourly for 3 doses, followed by 3 to 6 g. a day at 3- or 4-hourly intervals. Among the conditions in which good results were obtained were pneumococcal lobar pneumonia and infections due to staphylococci, Streptococcus viridans, Strep. faecalis, some strains of Bacterium coli, Bacillus mucosus capsulatus, Proteus vulgaris and Vincent’s organisms. In 2 cases of subacute bacterial endocarditis the response was good, but relapse occurred as soon as treatment was stopped. The only toxic effects encountered were nausea, vomiting, and diarrhoea, which occurred in 12 of the 15 cases, but were troublesome in only 3.

A. W. H. Foxell.


The authors describe the experimental treatment of tuberculous lesions of the cornea in rabbits and mice with combinations of streptomycin and various other drugs, the results of which confirm the statement of Woody and Avery (Science, 1948, 108, 501), that the action of streptomycin against the tubercle bacillus can be enhanced by combining it with potassium iodide. They found that this enhancement was more definite in advanced caseous tuberculosis than in very early lesions. Their findings also confirm the work of Bavin (J. Pharm. Pharmacol., 1949, 1, 790), who showed that the effect of p-aminosalicylic acid (2% in the diet) was not enhanced by the addition of potassium iodide. They report that treatment with either streptomycin alone or with p-aminosalicylic acid alone was more effective than treatment with a streptomycin p-aminosalicylate compound.

A. W. H. Foxell.


This paper records observations on the administration, absorption, distribution, and excretion of aureomycin in 150 patients, ranging from newborn infants to adults. The authors’ conclusions may be summarized as follows. Aureomycin in doses of approximately 11 mg. per kg. body weight given orally at 4-hour intervals is well tolerated by the majority of infants and children. Satisfactory serum levels are obtained with this dosage. Single doses larger than 11 mg. per kg. body weight do not produce significantly higher serum levels. The incidence of vomiting among 48 children on such a dosage schedule was 19% (9 cases). Gastrointestinal tolerance was increased when aluminium hydroxide gel or 3 to 4 oz. (85 to 114 ml.) of milk were given following each dose. When the intravenous route is employed the recommended dosage is 6-6 mg. per kg. body weight every 12 hours. The intramuscular route is unsatisfactory as it causes intense local pain and frequent febrile reactions. Rectal administration was tried in 3 cases but was found to be unreliable and often painful.

The peak serum level is reached somewhere between 1 and 4 hours after ingestion. This level is low but is maintained until 6 to 8 hours after ingestion. On the other hand, after intravenous administration there is a rapid rise and fall of the aureomycin level in the serum. The authors suggest that aureomycin is distributed rather uniformly throughout the body, but that it does not enter the erythrocytes. The fact that carinamide does not seem to affect the slope of the aureomycin serum level curve suggests that tubular excretion plays a negligible role, and that renal excretion is glomerular alone.

A. W. H. Foxell.


The effect of chloramphenicol alone in the treatment of 12 cases of Haemophilus influenzae meningitis occurring in children whose ages ranged from 5 months to 5 years (mean 2-4 years) is described. Experiments on mice demonstrated that while streptomycin, aureomycin, and chloramphenicol varied but slightly in protective power, terramycin was inferior and penicillin ineffective against H. influenzae. Chloramphenicol was chosen for use because of ease in administration, low toxicity, and a stability which simplified bio-assay.

In the present series chloramphenicol was given orally with an initial dose of 750 mg.
ABSTRACTS

followed by 250 mg, 4-hourly. The average duration of fever after instituting therapy was 2-3 days. There was rapid improvement with return to consciousness in on the average 1-3 days. All patients recovered and in one only was there any neurological residue, a patient in whom treatment had begun only on the seventh day, after terramycin had failed. In 5 cases the concentration of chloramphenicol in the cerebrospinal fluid averaged 13-2 µg., roughly half that in the blood.

The authors state that they have insufficient facts on which to recommend an optimum concentration, but with the dosage here employed no toxic manifestations were encountered. Oral administration presented no serious difficulty but it is stated that rectal administration of 500 mg. aids in the oral treatment. The mean duration of treatment was 8 days and the total received by one patient 10-4 g. The authors express the opinion that at present chloramphenicol is the antibiotic best suited to deal with infection by any of the Gram-negative group of pathogens.

Joseph Ellison.


Although typhoid fever usually runs a benign course in infants, the mortality before the days of modern antibiotics was certainly not zero. The authors treated 40 cases of typhoid or paratyphoid B between September, 1949, and September, 1950, with chloramphenicol. All these patients recovered rapidly. Convalescence was established always within a week and generally in 4 days. No complications occurred after the inception of treatment, but 2 cases of typhoid encephalitis and one of typhoid osteomyelitis were cured completely when the antibiotic was employed. Only one patient suffered relapse, the symptoms returning twice, with positive blood cultures, after apyrexial intervals of a fortnight; both relapses responded rapidly to renewed chemotherapy. It is suggested that these episodes were due to the release of organisms from the gall-bladder where they had been shielded from the impact of the antibiotic. On the second occasion an attempt at medical drainage was made with posterior pituitary extract and adrenaline. Small infants received 50 to 100 mg. per kg. body weight, and larger infants 1-5 to 2 g. of chloramphenicol daily by mouth. No difficulty was found in getting the capsules swallowed. They were softened in boiled water and then placed on the tongue immediately before the presentation of a feed. The authors deprecate the use of a "loading dose" and, indeed, recommend the use of half doses for the first 2 days of treatment. It is to this routine that they attribute the freedom from side effects in the series. The chemotherapy must be maintained for an adequate period which is considered to be between 1 and 2 weeks. No evidence was found to support the suggestion that the use of chloramphenicol interferes with the proper development of antibodies to the infection.

T. A. A. Hunter.


From Indochina the authors report 12 cases of typhoid treated with chloramphenicol: 4 fever patients were treated with the orthodox initial dose of 50 mg. per kg. body weight, followed by similar daily maintenance doses: they died with signs of vascular collapse or cerebral irritation. In further cases where the length of the history or the hypertoxic state of the patient appeared to warrant it, a much lower initial dosage scheme was employed, 15 mg. per kg. in four divided doses during the first day, with a gradual daily increase of 0.5 to 1 g. until the patient became afibrile, followed by maintenance of this dosage, usually about 50 to 60 mg. per kg. for 7 days. Symptomatic treatment with analeptics and deoxycortone was given when indicated. This regimen did not, in the cases reported, delay defervescence, which occurred on the 6th or 7th day of treatment.

W. G. Harding.


Shigella sonnei was isolated from the faeces of 5 patients in a children's hospital who had become acutely ill with fever and diarrhoea. The source of infection was traced to a symptomless carrier among the nursing staff who had had a mild attack of diarrhoea 3 months before the outbreak: 4 of the children and the carrier were treated initially with sulphadiazine by mouth. The therapeutic response to this drug was poor and Sh. sonnei persisted in the faeces for an average of 12 days. The other child was given chloramphenicol by mouth and rectally, and after 2 days' therapy the faeces were clear of shigella. In vitro sensitivity tests revealed that
the infecting strains were highly resistant to sulphadiazine and sensitive to chloramphenicol. Accordingly, the cases which were refractory to sulphadiazine were treated with chloramphenicol, and within 4 days of the change in therapy Sh. sonnei was eliminated permanently from the faeces.

Groups of mice were infected with two of the epidemic strains and were treated with sulphadiazine, sulphapyrazine, or chloramphenicol. The mortality rate was high in the groups treated with the sulphonamide drugs, and was negligible in those given chloramphenicol. G. B. Forbes.


A case is reported of a patient who was treated for 3 months for pyuria by administration of 0.25 g. of chloramphenicol every 8 hours. He developed a severe anaemia and decrease of blood platelets with an extensive purpuric rash. After death the main pathological changes were found in the lungs which were very oedematous, the bronchi being filled with coagulated protein and erythrocytes. Focal necroses were present round many bronchi and bronchioles. There was a marked reduction of haemopoietic elements in the sternal marrow. Only small amounts of other drugs were given and these were not of a kind likely to cause such a condition, which the authors attribute to the nitro-benzene group in the chloramphenicol molecule.

V. J. Woolley.


The authors, after reviewing briefly the antibiotics and chemotherapeutic agents which have been used, either singly or in combination, for the treatment of human brucellosis and the experimental disease in mice, give a detailed account of 35 cases in which the patient was given, concurrently, aureomycin hydrochloride and dihydrostreptomycin sulphate. The diagnosis in 21 cases was confirmed by blood culture, the organisms identified being: Brucella abortus (9), Br. melitensis (7), and Br. suis (4), with one unclassified organism. In 4 cases only localized lesions were present, from which Br. abortus was grown, once (spine) and Br. suis three times (thigh sinus, inguinal lymph node, lung tissues). Ten cases were diagnosed on the basis of the symptomatology and presence of high agglutinin titres. Scheduled treatment was: aureomycin orally 1 g. daily in 6-hourly doses, and dihydrostreptomycin 1 g. intramuscularly morning and evening, for 12 to 14 days; in cases with localized lesions the treatment was continued for 28 days, the dose of streptomycin being halved after the 14th day.

Temperature and symptoms subsided in every case 48 to 72 hours after starting treatment, and no relapse was observed on following-up for 9 to 19 months, with the exception of one patient taking aluminium hydroxide gel (which apparently interferes with the absorption of aureomycin). There were no signs of toxicity or of 8th nerve involvement. The symptomatology, diagnosis, and treatment are clearly and thoroughly described, one case resembling primary atypical pneumonia closely. All varieties of brucellosis seemed to respond equally well.

[These remarkably successful results will no doubt lead to further trials of combinations of antibiotics in infections so far resistant. It would have been of interest to know the method of culture employed, but this is not stated.]

L. J. M. Laurent.


The incidence of toxoplasmosis in north-west England was investigated by testing 12 children with clinical signs (chorio-retinitis and cerebral calcification), 88 with doubtful signs, and a control series of 350 cases (150 blood donors, 100 normal children under 10 years, and 100 other adults serologically).

In 10 of the 12 clinically diagnosed cases, 6 of the 88 doubtful cases and 13 of the controls, the complement-fixation reaction for toxoplasmosis was positive. Among the 100 normal children under 10 years there were no positive reactions, so that the incidence of symptomless infection in the adults in the control series was 5%. This means that it is impossible to diagnose congenital toxoplastic infection in a child solely by examination of the maternal blood.

Re-examination of mothers' sera at intervals showed no detectable loss of complement-fixing antibody during periods of as long as 12 months, but whether this was due to continued infection or merely to a continuing stimulus to antibody formation is not known. The findings of Sabin and Feldman were confirmed; these workers had shown that antibodies from mothers who had given birth to infected infants were transferred in subsequent
pregnancies to infants who remained uninfected and whose transferred antibodies disappeared after 4 to 5 months.

It is suggested that possibly maternal antibody is protective to the foetus, and that only those mothers infected during pregnancy are likely to give birth to infected infants. This would mean that subsequent children are likely to be born uninfected.

Wilfrid Galsford.


Two strains of Rickettsia burnetii isolated in Great Britain, one from a patient with Q fever, the other from milk, were compared in the laboratory with a standard Italian strain. The British strains were similar in shape, size, and pathogenicity for the guinea-pig. The milk strain was more readily adapted to growth in the yolk-sac of fertile hens' eggs, and appeared more pathogenic for guinea-pigs than the human strain. There was complete cross-protection with all three strains in guinea-pigs. Antisera against the British strains reacted with antigens from the Italian strain, but antigens from the British strains would not react until they were prepared from strains which had become adapted to the egg. A change in antigenic structure during egg adaptation is suggested as the explanation.

J. E. M. Whitehead.


In this disease the nucleus of the cell is enlarged and the cytoplasm increased in amount. Large intranuclear inclusions surrounded by a clear halo and lying within a distinct nuclear membrane, containing one or more dense chromatin masses, are pathognomic of the disease. These lesions, for the most part, occur in the viscera and particularly in the lungs. They have also been seen in the kidney, liver, spleen, and other organs, and are accompanied by symptoms of blood dyscrasia or hepatic damage: in about one-third of the known cases there was an association with a previous attack of whooping-cough. In all, 69 instances of the disease have been reported, occurring, for the most part, in the newborn or very young, although one instance of the disease in a child of 13 years is known.

It is probable that the disease is a virus infection because the characteristic lesions closely resemble those seen in salivary gland virus infections in rodents.

R. Hare.


During an epidemic of acute pleurodynia which occurred in Massachusetts in the summer of 1947 attempts to isolate the causal agent were unsuccessful. Since then the isolation of strains of a virus pathogenic to infant mice from cases diagnosed as "non-paralytic poliomyelitis" has been reported, and laboratory infections by these "Coxsackie" strains have been observed to be clinically similar to epidemic pleurodynia. The authors have therefore re-examined the material obtained during the 1947 pleurodynia epidemic in an attempt to define its relationship to the Coxsackie group of viruses.

Throat washings had been collected in horse-serum saline and stored on dry ice. Two of the 6 throat washings examined contained an agent pathogenic for suckling mice. Nine pairs of sera collected from patients during the 1947 epidemic were then selected at random and examined for neutralizing antibodies.

The results of these experiments suggest that a close antigenic relationship exists between the agents responsible for epidemic pleurodynia and the Coxsackie group of viruses, although their pathogenic potentialities differ widely, as do those of the various Coxsackie strains. (Reference is made, in an addendum, to the report by Findlay and Howard (Brit. med. J., 1950, 1, 1233; Abstracts of World Medicine, 1950, 8, 310), published after completion of the present work, in which similar conclusions were reached.)

BIOCHEMISTRY


The authors investigated the concentration of \(z\)-amino nitrogen and of individual amino-acids in the foetal and maternal blood of 9 parturient women at University College Hospital, London.

Foetal blood was taken from the placental side of the cut umbilical vein immediately after tying: maternal blood was obtained from the antecubital vein immediately afterwards. Heparin was used as anticoagulant.

Analysis of \(z\)-amino nitrogen was made on either plasma or plasma ultrafiltrate by the ninhydrin-CO₂ method of Hamilton and Van Slyke. The concentrations of individual
Amino-acids were determined chromatographically on solutions derived from plasma freed of protein by ultrafiltration and electrolytically desalted.

The concentration of \( \alpha \)-amino nitrogen was found to be raised in foetal blood compared with maternal blood, the ratios varying between 3:1 and 1.6:1 in non-toxaemic cases and between 1.4:1 and 1:1 in 4 cases of toxaemic pregnancy. Chromatographic analysis showed that individual amino-acids were all concentrated to approximately the same extent by the placenta, which thus appears to act in such a way as to aid foetal synthesis of protein.

**HAEMATOLOGY**

Activity of Plasma Labile Factor in Disease.  

The plasma labile factor is a necessary constituent of the mechanism for the proper formation of thrombin. It has been called by various workers "component A," "factor V," and "plasma Ac globulin". The labile factor has certain well defined characteristics which enable its concentration in the plasma to be determined. The author has devised a quantitative method of estimating the factor, and used it in studying the importance of depletion of the labile factor in determining the prolonged prothrombin time in various diseases.

Blood samples from 187 persons were examined, 20 being healthy subjects, the rest having a prolonged prothrombin time or active bleeding: 15 cases of hypoprothrombinaemia due to dicoumarol and 15 post-operative cases were also investigated. Prothrombin activity, prothrombin concentration, and labile-factor activity were determined in each case. (References to the methods used are given.) In hepatic disorders the labile-factor activity is normal in obstructive jaundice, but decreased in liver dysfunction. Large doses of vitamin K did not restore the activity of the factor even though the prothrombin activity returned to normal, suggesting that vitamin K is not required for the synthesis of the factor.

In the group of haemorrhagic conditions the labile-factor activity was normal in those which were due to a vascular abnormality and in idiopathic and allergic thrombocytopenia. But in all cases of symptomatic thrombocytopenia studied there was a striking depletion in labile-factor activity. Although no change in the activity of the factor was found in haemophilia it was noted that there was a prolonged clotting time and decreased prothrombin activity a week preceding and a week following a spontaneous haemorrhage. In hypoprothrombinaemia of the newborn labile-factor activity was normal, but the prothrombin activity was decreased significantly and was lower than the prothrombin concentration, suggesting a further plasma factor. No change in the activity of the labile factor was found during dicoumarol therapy, contrary to the findings of other workers: this may be explained by the different methods used. In terminal carcinoma the labile-factor activity and prothrombin activity and concentration all fell, the fall being roughly parallel with that in serum protein level, as in liver dysfunction. In the post-operative cases the labile-factor activity had decreased to about 40% of normal by the third day.

In his discussion the author points out that although it appears that the liver is the main source of the factor, it may not be the only source, as no liver dysfunction is demonstrable in those blood dyscrasias showing a low labile-factor activity. The importance of fresh blood in the treatment of haemorrhage in those conditions with a low labile-factory activity is obvious. A low labile-factor activity without diminished prothrombin activity is seldom found.

*R. F. Jennison.*

The Anemia of Thermal Injury. I. Studies of Pigment Excretion.  

The excretion of pigments in urine and faeces was studied in a series of patients with burns of varying severity. Haemolysis, as judged by increased faecal urobilinogen excretion compared with total circulating haemoglobin, was present in all cases in the first few days after injury. It was greatest in third-degree burns involving more than 20% of the body surface. A remarkable increase was noted in urinary urobilinogen on the third day after injury; this they consider an indication of early hepatic dysfunction. The anaemia associated with burns is thought to be due in part to haemolysis and in part to dyshaematopoiesis dependent on disordered liver function. Oral aureomycin reduces both the faecal and the urinary urobilinogen to small amounts owing to a sterilizing action on the faecal flora. The authors question whether the petroleum-ether-soluble, Ehrlich-reacting substances found after oral aureomycin administration are urobilinogens or whether they are entirely different compounds.

*Janet Vaughan.*

In a study of pigment excretion following severe thermal injury the authors found an increased excretion of urinary urobilinogen, which they interpreted as evidence of liver damage. They therefore undertook an investigation of certain liver-function tests in burned patients, none of whom received sulphonamides, tannic acid, or other escharotic therapy. They found that minor to extensive third-degree burns showed an early impairment of liver function as judged by changes in (1) bromsulphalein retention; (2) cephalin-cholesterol flocculation; (3) thymol turbidity; (4) prothrombin time; (5) total protein and albumin-globulin ratio; (6) serum bilirubin level; and (7) urinary urobilinogen content. The most constant changes were found in this last and in the albumin-globulin ratio. Necropsy material in 5 fatal cases showed no constant histopathological change, but there was evidence of fatty infiltration, cloudy swelling, increased pigments in the reticulo-endothelial cells, focal necrosis, and congestion in the liver substance.

The authors suggest that attention should be directed to the prevention as well as to treatment of liver dysfunction in severe burns.

Janet Vaughan.


This is one of a series of studies from the Ohio State University on the various phases of the hypersplenic mechanism. The reservoir function of the spleen may be pathologically increased and therapeutically decreased, with a reversal of the formed elements of the blood sequestered in its pulp-sinusoidal spaces. Figures were obtained from: (1) blood volume and peripheral blood cell differential studies before and after subcutaneous adrenaline injections. These, in cases of chronic myelogenous leukaemia, demonstrate that the degree of splenic enlargement is a direct function of the abnormal delivery and storage of the granulocytic cells. With treatment, as granulopoiesis in the marrow becomes less dominant, delivery of these cells to the circulation decreases, erythropoiesis increases reciprocally, normal delivery of erythrocytes to the blood is resumed, and the spleen again returns to normal size. In a case of thrombocytopenic purpura, following adrenaline the platelet count rose, transitorily, from 20,000 to 100,000 per c.mm. with no parallel erythrocyte or leucocyte increase. (2) Splenic arterial and venous blood obtained at laparotomy before and after adrenaline injection into the artery. The subjects were 19 patients with primary hypersplenism (thrombocytopenic purpura, hereditary spherocytosis, and splenic panhaematopenia) and 17 with some constitutional disease involving the spleen. The primarily involved blood-cell elements characteristically entered the spleen in larger numbers than were found leaving this organ. Further, the involved elements tended to be increased in the splenic venous blood after adrenaline-induced contraction. After the surgical removal of all splenic tissue in hypersplenic syndromes, the subcutaneous injection of adrenaline failed to affect significantly the re-established, relatively stable, circulating cellular equilibrium in the blood.

A comparison of the pre-operative adrenaline test with the adrenaline test at laparotomy, made in 2 selected cases, showed that effective cellular mobilization, as interpreted directly from several peripheral blood counts, paralleled closely the direct evidence from splenic venous blood samples.

These findings favour the hypothesis that spleen-withholding rather than bone-marrow suppression of blood cells plays the major part in many of the hypersplenic cytopenic states.

Harold Caplan.


The authors review 25 cases of aplastic anaemia seen during the last 10 years at the Royal Victoria Infirmary, Newcastle, and give detailed case histories of 6 which were cured by the repeated transfusion of packed erythrocytes. Neoaasphenamine had been given to one patient, gold injections to 2, but in the other 3 cases no drug was incriminated as the causative agent. Comment is made on the psychological strain of the repeated transfusions on the patient and the doctor; the frequency of reactions despite careful cross-matching; the value of polythene tubing in reducing phlebothromboses and venous spasm in restless nervous patients; and the routine use of antibiotics to prevent infective complications. In 2 cases intrasternal injections of bone marrow from donors of the same genotype were given with benefit.

Ernest T. Ruston.

This is a report of experience gained in treating 108 cases of polycythemia vera with radioactive phosphorus during a period of 10 years. The results are contrasted with those in a series of 30 cases treated by the ordinary conventional methods. The aetiology and therapeutic considerations in polycythemia are considered, and then the method of internal radiation therapy is described. The effect on the symptoms, signs, and haematological picture in this group of cases is described, and the causes of death are discussed. There is a detailed description of the method of using radioactive phosphorus in the treatment of polycythemia vera. The authors conclude that the method is haematologically sound, effective, inexpensive, and convenient for use. They think that with adequate controls this method of treatment is safe.

John F. Wilkinson.


The most important laboratory test for haemophilia is the prolongation of the clotting time, but there seems little doubt that the test may be normal in very mild haemophiliacs and in ordinary cases in remission. In haemophilia, prothrombin is not used up in normal amounts in the clotting process. Thus, haemophilic serum may contain as much prothrombin as does the plasma. [In the clotting of normal blood nearly all the prothrombin is turned into thrombin.] Antihaemophilic globulin, which is found in normal blood, will hasten the clotting of haemophilic blood. The latter does not, of course, contain this globulin, and its absence can be proved by adding the suspected blood in minute quantities to haemophilic blood; there is no shortening of the clotting time. These three tests can be used in the diagnosis of haemophilia.

This paper describes the clinical histories of 8 families in which cases occurred with normal or only mild prolongation of the clotting time. Symptoms might be mild or severe; patients with mild symptoms lead fairly normal lives. Most of the patients, however, had had at least one severe bleeding bout, especially when teeth were extracted. Minor scratches gave little trouble, and only followed severe injury; thus ankylosed joints were infrequent. The author rightly stresses that the finding of a normal coagulation time may give a false sense of security, especially with regard to operations. Cases linked by family connexions were similar as regards both the clinical picture and the laboratory findings.

Paul B. Woolley.


The case is described of a young woman aged 24 whose parents belonged to haemophilic but unconnected families. Her father and his brother, and her mother’s brother, were known haemophiliacs. Her sister’s son was also a haemophiliac and was found by the authors to show the typical coagulation defect of this disease.

The patient had been known to bruise easily since childhood. She came under investigation on the present occasion as a primipara who had gone to full term but had developed severe post-partum haemorrhage. Repeated investigation over a period of about 9 months provided convincing laboratory evidence of the coagulation defect of haemophilia. The platelet count was uniformly normal; the coagulation time was invariably prolonged; the accelerated coagulation time (oxalated plasma) was always greatly increased; and prothrombin consumption was very much delayed. The plasma prothrombin time was normal, the labile factor was shown to be present, and there was no demonstrable anticoagulant in the patient’s plasma. Adequate controls were included at all stages in the investigation, and there is no doubt that the case described satisfies all the established requirements necessary for the diagnosis of haemophilia.

A. Brown.


Studies of sera from 2 patients with paroxysmal cold haemoglobinuria (PCH) have shown that large amounts of complement may be necessary for haemolysis in the Donath-Landsteiner reaction. By using an adequate amount of complement, the haemolysins from both patients were found to be stable at 62° C. An excess of complement is necessary for antibody titration, since a reciprocal relationship exists between the amount of complement present and the antibody titre. Agglutination by
antiglobulin serum of erythrocytes sensitized in dilutions of PCH serum provides another measure of antibody level, the titres obtained being comparable to those found by haemolysin titration in the Donath–Landsteiner reaction. Complement is essential in both the cold and warm phases of this reaction, and there is a reciprocal relationship between the amounts of intact complement required in these two phases. The erythrocyte–PCH antibody system is unique in that it requires complement for antibody fixation as well as for subsequent haemolysis.

The PCH haemolytic system is unusual in another respect, because all components of complement are not necessary for haemolysis. Haemolysis occurs in the absence of C1 and C3. Haemolysis does not occur when C4 is missing in the cold phase, or when C2 is missing in the warm phase.

Since only two components of complement are required for haemolysis in PCH, titration of complement in a serum by the sheep cell-amoceptor system, which requires all four components, may not measure the capacity of that serum to produce haemolysis with PCH antibody.—[Authors’ summary.]

MORBID ANATOMY AND HISTOLOGY


The present paper is an extension of an earlier publication (Davson, Ball, and Plant. Quart. J. Med., 1948, 17, 175) in which the authors described the renal lesions in cases of polyarteritis nodosa. They now record in detail the renal changes in 4 further cases of the disease and 2 probable cases, stressing in particular the morbid anatomy, which they consider to be distinctive. The kidneys were enlarged, smooth, and congested. The characteristic feature was the presence of visible glomeruli as opaque grey spots. Microscopically, the kidneys in all cases showed an “explosive” glomerulitis with necrosis, cellular infiltration, and pericapsular infiltration. Polyarteritis nodosa was found in 4 cases, but its extent varied from the involvement of many organs to that of a few arteries only. They feel justified in including their 2 further cases because of this variability and because in all other respects they were exactly similar. They suggest that, in middle-aged patients who die of a fulminating acute nephritis without hypertension and whose kidneys show the naked eye lesions which they describe, a presumptive diagnosis of polyarteritis nodosa can be made in the post-mortem room.


The authors examined necropsy specimens of the heart in 600 male subjects who had died from various causes at ages ranging from 30 to 89 years. 100 being examined in each decade. Cross-sections were made and carefully examined at 3-mm. intervals throughout the length of the main stem and the anterior descending and circumplex branches of the left coronary artery, and of the main stem and the marginal and posterior descending branches of the right. The degree of coronary arteriosclerosis present, if any, was assessed on a basis of four grades ranging from minimal (grade 1) to complete closure (grade 4) in each main stem and in the proximal, middle, and distal segment of each branch. It was found that the average degree of sclerosis present increased steadily with the subject’s age from 30 to 60 years, but decreased slightly in those over 60 years of age. Sclerosis was most marked in the proximal segment of the anterior descending branch, reaching grade 3 in 11%, of those dying between 50 and 60 years. Sclerosis was least marked in the small marginal branch of the right coronary: in the remaining arteries, including the right coronary and its posterior descending branch, the degree was approximately equal. Hypertension, as evidenced by cardiac enlargement, had little effect on the amount of sclerosis, which was only 10% greater in subjects with hearts which weighed 450 g., or more, than in those which weighed less.

C. W. C. Bain.


The scanty literature on primary pulmonary hypertension is here reviewed and 6 new cases are described. Details are provided of the changes in the main pulmonary arteries and in their ultimate muscular branches.