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BY

A. GORDON SIGNY

LONDON
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TAVISTOCK SQUARE, W.C.1

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ABSTRACTS

This section of the JOURNAL *is published in collaboration with the two abstracting journals, Abstracts of World Medicine, ond 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

The Effective Concentrations of Penicillin *in vitro* and *in vivo* for Streptococci, Pneumococci, and *Treponema pallidum*. EAGLE, H., FLEISCHMAN, R., and MUSSELMAN, A. D. (1950). *J. Bact.*, **59**, 625.

The minimal effective concentration of procaine penicillin in the serum of mice sufficient to abort clinical infection following intramuscular injection of group A streptococci, group B streptococci, and types I and III pneumococci were found to be 0.012, 0.08, 0.08, 0.05, and 0.05 mg. per ml. In mice receiving group B streptococci by intramuscular, subcutaneous, or intratesticular injection and direct injection into the lung, the values were 0.12, 0.1, 0.07, and 0.1 mg. per 1 ml. respectively. In rabbits infected by the intratesticular injection of *Treponema pallidum*, the values varied from 0.005 to 0.01 mg. per ml. Approximately the same values were obtained with aqueous penicillin.

In *in vitro* tests, the levels necessary to kill the same organisms were regularly one-half to one-fifth of those given above. The discrepancy between the *in vivo* and *in vitro* values is accounted for partly by the fact that about half the penicillin in serum is bound to the serum proteins and partly because the concentration of penicillin in the tissues is probably lower than that in the serum. For these reasons, it is probable that the effective concentration of penicillin at the actual focus of infection is of the same order of magnitude as that which obtains *in vitro*.

Thus for the organisms studied, penicillin is effective *in vivo*, so long as its serum concentration is two to five times the minimal bactericidal level as determined by tests with the serum *in vitro*. *R. Hare.*

Prolongation of Penicillin Blood Level by Implantation of Procaine Penicillin Tablets. HUIDOBRO, F., CROXATTO, R., and LUCHINI, A. (1950). *Proc. Soc. exp. Biol., N.Y.*, **73**, 201.

The authors, working at the Catholic University of Chile, Santiago, found that the implantation of tablets of procaine penicillin (20,000 to 80,000 units per kg. body weight) subcutaneously in rabbits resulted in an effective concentration of penicillin in the blood for 7 days and gave no local reactions. When they were mixed with fat the period was prolonged to 11 days.

Chloromycetin in Surgical Infections. ALTEMEIER, W. A., and GIUSEFFI, J. (1950). *Surg. Gynec. Obstet.*, **90**, 583.

The authors give a brief survey of the main physical and chemical properties of chloramphenicol and include a list of the organisms known to be susceptible to its action. There follows a report on the treatment of 100 surgical patients selected at random. The daily dosage varied from 25 to 100 mg. per kg. body weight, single doses being given at intervals of 4 to 8 hours. There were 23 cases of infection with staphylococci, 4 with aerobic streptococci, 3 with anaerobic

streptococci, 43 with mixed Gram-negative and Gram-positive organisms, 8 with Gram-negative bacilli only, one with *Clostridium welchii*, and a miscellaneous group.

In the staphylococcal group the average duration of treatment was 6.7 days and the average total dose of chloramphenicol 8.6 g. In 21 of the 23 cases the results were classified as " excellent " or " good." Penicillin is still, however, the antibiotic of choice in these infections, although chloramphenicol is of value in penicillin-resistant cases. In the 43 cases of mixed infection the average duration of treatment was 12.44 days and the average total dose of chloramphenicol 17.82 g. " Excellent " or " good " results were obtained in 31 cases, " doubtful " results in 9, and there were 3 failures. [Figures are given for the other types of infection, but the numbers seem to be too small to be of any value.]

Bacterial resistance developed in 11 of the 100 cases, the infection in 5 being due to *Bacillus proteus*. The time taken for resistance to develop varied from 5 to 33 days. [No details are given of the degree of resistance encountered.]

The authors stress that the ordinary fundamental principles of surgical treatment are still as important as ever.

A. W. H. Foxell.

Chloramphenicol in Typhoid Fever. GOOD, R. A., and MACKENZIE, R. D. (1950). *Lancet*, **1**, 611.

An assessment of the action of chloramphenicol (" chloromycetin ") in typhoid fever was made in a group of 13 cases from the Crowthorne epidemic of 1949 (Vi-phage type E_1). The cases were first seen on the 8th to 14th day of the disease; 6 were treated with chloramphenicol and 7 were given general hospital treatment only. Later, relapses in 3 of the control patients were also treated with chloramphenicol. Positive stool cultures were obtained from all cases on admission, and frequent cultures of stools and blood were made during and after treatment. The dosage of drug given was that recommended by Woodward *et al.* (*Ann. intern. Med.*, 1948, **29**, 131), a loading-dose of 4 g. in the first hour being followed by 0.25 g. 2-hourly until the temperature was normal, and thereafter 4-hourly until the end of the 8-day course. The total dosage was 19 to 22 g.

In all treated cases the temperature fell to normal within 3 days; headache, toxaemia, and abdominal discomfort were relieved and the appetite returned. No haemorrhages or perforations occurred, and no toxic effects were observed during administration of the drug. Three of the 6 treated cases relapsed and 2 were given further chloramphenicol treatment with good results; no drug-resistance could be detected in the organisms isolated from these cases.

A single course of treatment had no significant effect upon the rate at which the stools were cleared of typhoid bacilli, but 2 of the patients who relapsed after the first course were rapidly cleared by a second course. In the third case of relapse a chronic carrier state developed and excretion of *Salmonella typhi* in the stools continued throughout the second course of treatment. Relapses in treated cases occurred about the 35th day of the disease, and in controls about the 25th day.

No variations in H, O, or Vi agglutination titres of the sera could be attributed to chloramphenicol treatment.

L. G. Goodwin.

The Effect of Aureomycin on the Bacterial Flora of the Intestinal Tract of Man. A Contribution to Pre-operative Preparation. DEARING, W. H. (1950). *Proc. Mayo Clin.*, **25**, 87.

The following regimen was used in the pre-operative preparation of 148 patients suffering from carcinoma of the colon, colitis, or enteritis (not all of whom were in fact operated upon): (1) low-residue diet and mild saline laxatives; (2) a series of saline enemata 1 to 2 days before operation; and (3) chemotherapy. This last consisted of aureomycin 250 to 750 mg. four times a day by mouth (80 patients), " sulphasuxidine " (succinylsulphathiazole) 4 g. six times in one day and 2 g. six times a day thereafter (32 patients), " sulphathalidine " (phthalylsul-

phathiazole) in the same dosage as sulphasuxidine (7 patients), dihydrostreptomycin orally 500 mg. four times daily (9 patients), or a combination of aureomycin and dihydrostreptomycin (20 patients). Medication was continued for varying periods, averaging 3 to 5 days but varying from 1½ to 10 days. A fresh specimen of stool was cultured each morning for aerobes, anaerobes, and (after heating) for spores.

In most cases all organisms initially present except *Proteus* and *Pseudomonas* were removed by the aureomycin. In 7 cases the growth of *Bacterium coli* was diminished but not eliminated, and *Streptococcus faecalis* persisted in 4 cases. The sulphonamides and dihydrostreptomycin were much less effective, although the latter combined with aureomycin gave good results when the type of case is taken into account. Bacteroides were not readily detected by the techniques used, but a separate investigation of 5 patients showed them to be removed by aureomycin therapy. Sterilization of the intestinal tract was hindered in cases of preexisting perforation with abscesses, fistulae, or obstruction, which probably interfered with access of the aureomycin to the organisms.

The authors recommend the administration of aureomycin orally, 750 mg. four times daily for 3 to 3½ days, for the preparation of patients for intestinal operations.

Aureomycin Treatment of Infantile Diarrhoea and Vomiting. MAGNUSSON, J. H., LAURELL, G., FRISELL, E., and WERNER, B. (1950). *Brit. med. J.*, **1**, 1398.

The investigations and treatment of two epidemics of infantile diarrhoea and vomiting in the Sachs Hospital for Children are described. The first occurred in 20 infants during July–September, the second in 14 infants during September–November. All the infants in the first epidemic and 10 of the 14 infants in the second became affected during their stay in hospital.

Bact. coli neapolitanum (B.C.N.) was demonstrated in 19 cases in the first epidemic and in all in the second. The organism was found in the respiratory tract of 15 cases, in the throat only in 3, in the nose and throat in 12. Out of a control series of 40 children in hospital at the same time, but without diarrhoea or vomiting, B.C.N. was found in the stools of one only.

The incubation period was from 4 to 17 days, most commonly between 8 and 12 days. The commonest symptom was diarrhoea, usually accompanied by vomiting. In the first epidemic 8 cases were mild and 12 moderately severe or severe; 5 children died. In the second epidemic, 2 cases were mild and 11 severe; no child died. All the infants were less than 1 year of age and 22 less than 1 month old; 12 were premature, 7 in the first epidemic and 5 in the second.

Penicillin, sulphonamides, and streptomycin were without effect. Aureomycin was given orally, 25 mg. six times a day, to 8 cases in the second epidemic after B.C.N. was found to be sensitive to this antibiotic; the micro-organism's resistance varied between 0.16 and 0.6 μg. per ml., in thioglycollate broth. The stools became firmer and the vomiting ceased, usually in 24 hours; by the 3rd to the 5th day the stools were normal and there was a satisfactory gain in weight.

Aureomycin in Soft Tissue Infections. LOGAN, M. A., METZGER, W. I., WRIGHT, L. T., PRIGOT, A., and ROBINSON, E. A. (1950). *Amer. J. Surg.*, **79**, 229.

A series of 82 cases, which included cases of most of the surgical infections commonly encountered, was treated with aureomycin. In mild cases a dosage of 250 mg. orally three times a day was employed. In severe cases an initial dose of 300 mg. in 500 ml. of 5% glucose in distilled water was given intravenously and this was repeated 12 hours later, after which oral administration was begun. Occasional nausea and vomiting were the only toxic reactions to oral administration. In 15 to 20% of cases in which the intravenous route was used a chemical phlebitis developed. The use of a leucine buffer as a diluent instead of distilled water reduced the frequency of this complication.

The conditions studied included cases of cellulitis, perirectal infection, peripheral ulcer, lymphadenitis, wound infections,

and gas gangrene. The commonest organisms were staphylococci or β-haemolytic streptococci. In most cases one or two species of bacteria were found initially and could still be isolated 3 or 4 days after the institution of aureomycin therapy. In open wounds under treatment, the secondary contaminant organisms commonly found were still present. No evidence was found of the development of drug resistance with prolonged administration.

A wide range of Gram-negative and Gram-positive organisms are sensitive to aureomycin. The level in blood obtained by oral administration is sufficient to control growth of most of these. Clinically results were comparable whether the drug was given intravenously or orally. In the reported cases the dramatic influence of aureomycin on severe and mixed infections is well shown. Cellulitis, for example, treated before necrosis and pus formation, subsided without going on to fluctuation. Out of 4 cases of gas gangrene reported, one elderly arteriosclerotic patient died. Two other patients developed gas gangrene in spite of penicillin therapy. In both of these cases after adequate operation and aureomycin therapy recovery was rapid.

[The satisfactory response of a wide variety of infections to aureomycin is well shown by this paper. If results quoted are supported by further clinical experience, this will unquestionably mean the replacement of the more troublesome penicillin therapy by oral administration of aureomycin.]

J. G. Bonnin.

The Susceptibility *in vitro* of Some Salmonella and Shigella Strains to Chloramphenicol and Aureomycin. ALIN, K., and WAILMARK, G. (1950). *Nord. Med.*, **43**, 663.

A total of 75 strains was tested for sensitivity including *Salmonella typhi*, *Salm. paratyphi B*, *Salm. typhi-murium*, *Salm. bareilly*, and *Salm. montevideo*, and *Shigella sonnei*.

Aureomycin was the most active compound, and inhibited all strains in a concentration of 8 μg. per ml.; chloramphenicol produced complete inhibition in a concentration of 16 μg. per ml., and several strains survived exposure to higher concentrations of streptomycin. The average level of aureomycin in blood is lower than the concentration required for complete inhibition of these strains *in vitro*, whereas that of chloramphenicol is considerably higher. Chloramphenicol is thus to be preferred in the treatment of salmonella infection, although the organisms are more sensitive to aureomycin.

Fatalities in Salmonella Infections. SAPHRA, I. (1950). *Amer. J. med. Sci.*, **220**, 74.

During a period of 10 years ending in April, 1949, nearly 5,000 salmonella cultures were identified at the New York Salmonella Centre. An examination of the records in the 3,279 cases of human infection revealed that 174 fatalities occurred, 26 salmonella types being isolated from these fatal cases. The most virulent types were *Salmonella typhi-murium*, *S. cholerae suis*, *S. oranienburg*, and *S. newport*. The infection was with *S. typhi-murium* in 63 of the fatal cases and with *S. cholerae suis* in 40. The fatality rate in cases of infection with the latter micro-organism was 21.3%; it was seldom isolated from the faeces or from healthy carriers. In most cases the cultures were derived from parenteral sources and from material obtained at necropsy. No deaths were due to *S. paratyphi A*, a type which is rarely found in the United States. Another rare type was *S. havana*, which was originally isolated in 1939 from material from 21 newborn babies in a maternity hospital in Havana. The infection produced the signs and symptoms of acute meningitis and every baby died.

The mortality was about 2% in patients aged between 1 and 50 years, 5.8% in infants, and 15% in elderly patients. In about one-third of the fatal cases occurring in patients aged more than 50 years the infection was a terminal event in diseases such as hypertension, pneumonia, and cancer; as these patients had become debilitated it was possible for salmonellae to pass from the

intestinal tract into the blood stream. Although acute gastro-enteritis was a common cause of death, especially in infants, the clinical manifestations of salmonella infection included meningitis, pneumonia and pleurisy, septicaemia, and bacterial endocarditis. Other manifestations were cholecystitis, appendicitis, peritonitis, and typhoidal syndromes. *A. Garland.*

Clinical Observations on the Use of Terramycin Hydrochloride. KING, E. Q., LEWIS, C. N., WELCH, H., CLARK, E. A., JOHNSON, J. B., LYONS, J. B., SCOTT, R. B., and CORNELY, P. B. (1950). *J. Amer. med. Ass.*, **143**, 1.

Terramycin is an antibiotic isolated from *Streptomyces rimosus*. It is a crystalline substance which forms salts with both acids and bases. This preliminary communication reports the results of the oral administration of terramycin hydrochloride to 30 patients with various infections. In the majority of cases the following dosage schedule was employed: in patients 14 years of age and older, 500 to 750 mg. every 6 hours; in children 9 years of age and younger 500 mg. every 4 hours. Assayable amounts of terramycin were found in the blood and urine for a period of 1 to 5 hours following the administration of 750 mg. by mouth.

Fifteen of the patients had pneumococcal pneumonia or lung abscess and the remainder had bronchopneumonia, urinary infections due to *Aerobactes aerogenes*, *Bacterium coli*, streptococci, *Bacillus pyocyaneus*, or *Staphylococcus aureus*, or bacteraemia due to *Salmonella cholerae-suis*. There were also 2 cases of pertussis. One patient with lobar pneumonia died within 24 hours of admission and in one case treatment was abandoned owing to vomiting: of the remainder, the result in 24 cases is classified as " good " or " excellent " and in 4 as " fair." Six of the 12 children treated developed toxic reactions which included nausea, abdominal pain, vomiting, diarrhoea, and transient erythema, but in only 2 cases had the drug to be stopped. It is concluded that terramycin is a useful antibiotic with a wide bacterial spectrum. *A. W. H. Foxell.*

A Study of the Effect of Neomycin and Other Antibiotics on Bacteria, Viruses, and Protozoa. FELSENFELD, O., VOLINI, I. F., ISHIHARA, S. J., BACHMAN, M. C., and YOUNG, V. M. (1950). *J. Lab. clin. Med.*, **35**, 428.

The action of neomycin was tested on 370 organisms. It showed strong action *in vivo* and *in vitro* against Gram-negative bacilli, streptomycin-sensitive and resistant strains of tubercle bacilli, *Bacillus anthracis*, *Listeria* (*Listerella*) *monocytogenes*, *Proteus* and *Pseudomonas*, and intestinal protozoa. It was effective against *Entamœba histolytica* and the organism of rickettsialpox. Its action on Gram-positive cocci was variable. Its activity was compared with that of penicillin, streptomycin, chloramphenicol, aureomycin, polymyxin D, bacitracin, and enniatin III. It was more effective than streptomycin against salmonellae and *Vibrio cholerae*, but showed no activity against the viruses of herpes simplex, influenza, equine encephalitis, and lymphocytic choriomeningitis. Its toxicity is lower than that of polymyxin D. *A. W. H. Foxell.*

Use of Pituitary Adrenocorticotropic Hormone (ACTH) in Poliomyelitis. CORIELL, L. L., SIEGEL, A. C., COOK, C. D., MURPHY, L., and STOKES, J. (1950). *J. Amer. med. Ass.*, **142**, 1279.

The fact that so many instances of infection with the virus of poliomyelitis are not accompanied by any paralysis has suggested to some that in this disease resistance involves non-specific defence mechanisms and that host resistance may be more important than virulence in determining the outcome in any given case [granted that this statement has any real semantic importance]. For these reasons investigations were carried out to decide whether adrenocorticotrophic hormone (ACTH) given early in the course of poliomyelitis can stimulate effective resistance to the virus.

In a carefully controlled experiment, 35 patients, whose condition was diagnosed as poliomyelitis, received the hormone (dose not stated) while 35 others, selected a

random, were given a placebo. Activity of the hormone was controlled by eosinophil counts, which clearly demonstrated that the desired response was in fact elicited. The result of this investigation proved entirely negative, statistical analysis showing that ACTH is without either beneficial or deleterious effect on the course of poliomyelitis when it is given after the first onset of symptoms. *Jos. B. Ellison.*

HAEMATOLOGY

Effect of Thymine Desoxyriboside (Thymidine) on Human Pernicious Anemia. REISNER, E. H., and WEST, R. (1949). *Proc. Soc. exp. Biol., N.Y.*, **71**, 651.

Thymidine given to patients with pernicious anaemia provoked a slight reticulocytosis but was without effect on the erythrocyte count. Although the replacement ratio of thymidine to vitamin B_{12} is about 300 : 1 for the growth of *Lactobacillus acidophilus*, it does not appear to be able to replace vitamin B_{12} in the treatment of pernicious anaemia in man.

Observations of the Hemopoietic Factors in Hog Stomach and Duodenum, and the Treatment of Pernicious Anemia by Orally Administered Vitamin B_{12} in Combination with Extracts of Duodenal Mucosa. BETHELL, F. H., SWENDSIED, M. E., MEYERS, M. C., NELIGH, R. B., and RICHARDS, H. G. (1949). *Univ. Hosp. Bull., Ann Arbor*, **15**, 49.

The vitamin B_{12} content in 2 samples of desiccated hog stomach was assayed using *Lactobacillus lactis Dorner* and found to be 0.23 and 0.31 μg. per g. of material. Daily doses equivalent to 4.6 and 12.4 μg. vitamin B_{12} administered to patients with pernicious anaemia caused satisfactory responses but not if the preparations had been heated to 100° C. for 30 minutes. Evidence was obtained that hog stomach contains intrinsic factor as well as vitamin B_{12}. Neither factor was effective when administered singly by mouth in doses which together caused prompt responses.

Haemolytic Disease of the Newborn due to Anti-A Antibodies. BOORMAN, K. E., DODD, B. E., and TRINICK, R. H. (1949). *Lancet*, **1**, 1088.

The authors describe two cases of haemolytic disease of the newborn and present evidence indicating that this was due to anti-A antibodies. In the first case it was demonstrated that group A, but not group O, erythrocytes were rapidly eliminated from the infant's circulation; in the second (fatal) case anti-A antibodies were recovered from the infant's liver, kidney, and spleen.

Urethane (Ethyl Carbamate) Therapy in Multiple Myeloma. LOGE, J. P., and RUNDLES, R. W. (1949). *Blood*, **4**, 201.

Four patients were treated with doses of 4–6 g. urethane daily for periods up to 2 months. Transient leucopenia developed in three of them. There was some clinical improvement, usually commencing after 2–3 weeks, and two of the patients were able to do light work after 4–6 months. There was also objective improvement; e.g., a rise in the haemoglobin and a reduction in the numbers of abnormal cells in the peripheral blood, a diminution in the number of plasma cells in the marrow, and a reversion towards normal of the serum proteins.

Change in Tendency to Aggregate as an Expression of Disease of Erythrocytes. MLCZOCH, F., WUNDERLY, C., and WUHRMANN, F. (1949). *Acta med. scand.*, **134**, 260.

The erythrocyte sedimentation rate depends on the production of aggregates of erythrocytes, and the rate is increased when such clumps are larger than normal. Factors in the plasma producing clumping include fibrinogen and certain globulins, but the tendency to form aggregates varies in different species of animals.

Erythrocytes were washed several times in normal saline, and after re-suspension in a solution of pectin, a colloid substance, the sedimentation rate was estimated for 2 hours by Westergren's method. Certain variations were noted in different concentrations of pectin, and therefore the ordinary sedimen-

tation rate was estimated also. Erythrocytes from patients with pernicious anaemia showed more rapid sedimentation, but the rate approached the normal in remission. The presence of post-haemorrhagic anaemia did not influence sedimentation. In leukaemia and other disorders of the bone marrow sedimentation in pectin was more rapid, but in a few cases of epidemic hepatitis and of obstructive jaundice it was slower, a unique finding. The authors believe that by their test they can distinguish between disorders of erythrocytes and disorders in which erythrocytes are affected only secondarily.

E. Neumark.

Generalized Blood Platelet Thrombosis. Report of Three Cases with Necropsy Findings. GREEN, M. A., and ROSENTHAL, S. (1949). *J. Mt. Sinai Hosp.*, **16**, 110.

Generalized platelet thrombosis occurs especially in young females and is an acute disease lasting a few weeks from onset to fatal termination. Symptoms of thrombocytopenic purpura—petechiae, ecchymoses, melaena, haematuria—and anaemia occur, but in addition there are arthralgia, headache, nausea, and general malaise. In the course of the illness signs of affection of the central nervous system appear, such as mental changes and focal symptoms—cranial nerve palsies, localized pareses, and aphasia; these neurological signs are transitory and variable. There is a low platelet count and a variable anaemia, sometimes haemolytic in type, and the bone marrow is hyperplastic with a normal count of megakaryocytes. Cerebrospinal fluid is normal. Splenectomy was tried in 2 cases without effect. Microscopical examination of tissues at necropsy reveals numerous thrombi in the terminal arterioles and capillaries of many organs, including the cerebral cortex. These thrombi contain no erythrocytes or white cells and appear to consist of platelets; organization occurs quite early. The thrombi in the cerebral cortex cause little if any parenchymatous change. Fifteen cases have been recorded in the literature and the authors add 3 more. The aetiology remains unknown.

M. C. G. Israëls.

Thrombopathic Thrombocytopenia: Successful Transfusion of Blood Platelets. HIRSCH, E. O., FAVRE-GILLY, J., and DAMESHEK, W. (1950). *Blood*, **5**, 568.

A child 9½ years old had had a splenectomy for haemorrhagic phenomena when 2½ years old. When seen recently he had anaemia, a tendency to haemorrhage, particularly from the nose, a marked diminution in prothrombin consumption, and a prolonged bleeding time even when platelet levels were between 150,000 and 280,000 per c.mm. The platelets were, however, morphologically abnormal, being large, bizarre, lacking in granules, and staining poorly. Similar abnormalities were noticed in the megakaryocytes. The condition is described as one of "thrombopathic thrombocytopenia." Transfusion of stored or citrated blood was without effect. Direct transfusion of blood from a polycythaemic donor, whose platelet count was about eight times the normal, with silicone-lined syringes and no anticoagulant, resulted in the recovery of a detectable proportion of donor platelets from the patient and in improvement in prothrombin consumption and decrease in bleeding time. The authors conclude that their data suggest that the life span of the transfused platelets was 5 to 6 days.

Janet Vaughan.

Thrombocytopenic Purpura: The Prognostic and Therapeutic Value of the Eosinophil Index, an Analysis of 100 Cases. SCHWARTZ, S. O., and KAPLAN, S. R. (1950). *Amer. J. med. Sci.*, **219**, 528.

The authors review the experience of the last 10 years which has led them to attach importance to the finding of a high eosinophilic index in thrombocytopenic purpura. The latter, determined from bone-marrow smears stained by May–Grünwald and Giemsa, is the number of eosinophils per 1,000 neutrophils at the metamyelocyte stage or later. An index above 50 indicates a 50% chance of spontaneous recovery, and a 96% chance of cure by splenectomy. This eosinophilia was not demonstrable in the circulating blood. Splenectomy performed in 18 cases when the index was low resulted in 8 deaths,

and in 2 other cases there was no improvement. *E. T. Ruston.*

Observations on the Coagulation Defect in Thrombocytopenic Purpura. CARR, T. L., and FOWLER, W. M. (1949). *J. Lab. clin. Med.*, **34**, 1227.

The Waugh–Ruddick test for increased blood coagulability (*Canad. med. Ass. J.*, 1944, **50**, 547) was carried out on the blood of 30 normal subjects, the results being in agreement with those of the originators. The test was then carried out on 15 patients suffering from thrombocytopenic purpura, 9 of the cases being of the idiopathic type. It was found that the coagulation time was normal in the absence of heparin, but was markedly increased with even small amounts of heparin and that the blood was easily rendered incoagulable. In 4 cases of non-thrombocytopenic purpura the result of the test was normal. Protamine sulphate and toluidine blue (1 to 4 mg. per kg. body weight) were given to 7 patients with thrombocytopenic purpura and the test then carried out on samples of their blood. In 2 cases there was no demonstrable effect. In one case the coagulation time returned to normal after the injection of protamine sulphate, but this was thought to be due to a spontaneous remission. In the remaining cases the coagulation time was shortened in the tubes containing the lower concentrations of heparin. The test was also carried out in 5 cases of thrombocytopenia before and after splenectomy. In 4 cases the platelet count returned to normal, as did the result of the Waugh–Ruddick test. In the fifth case the platelet count and the test result became normal, but when, 2 months later, cutaneous haemorrhages reappeared and the platelet count fell to its previous low level the coagulation times in the Waugh–Ruddick test were even more prolonged than initially.

The authors conclude that, while the blood of patients with thrombocytopenic purpura is more sensitive to heparin *in vitro* than is normal blood, the coagulation defect is not due to an excess of heparin in the circulating blood since injection of such agents as protamine sulphate and toluidine blue does not remedy the defect, as would be the case were excess of heparin the basis of the changes. *R. B. Lucas.*

Clinical Studies of the Heparin Cofactor. HOLDEN, W. D., COLE, J. W., and DAVIS, J. H. (1949). *Surg. Gynec. Obstet.*, **89**, 20.

An increase in the coagulability of the blood after operation may be an important factor in the causation of post-operative thrombosis. Such an increase would result from a reduction in the quantity of any of the thrombin-inactivating agents present in the blood. Heparin in itself is not an antithrombin but requires for its activation the presence in the plasma of a cofactor, the exact nature of which is not known, but which is closely associated with the protein fraction of the plasma. In order to carry out a quantitative estimation of the heparin cofactor in a given blood sample, the serum is heated to 56° C. for 10 minutes, which destroys the thrombin and prothrombin but leaves the cofactor unchanged. After the addition of a known quantity of heparin and of thrombin to the inactivated serum, it is then possible to determine the cofactor activity of the serum by adding fibrinogen and measuring the coagulation time.

The heparin cofactor activity of the blood was estimated in 67 normal fasting subjects and 22 patients undergoing major surgical operations, on whom tests were carried out before, and on alternate days after, operation. In 20 of the patients no thrombosis occurred and the average deviation from normal in cofactor activity of the blood was insignificant. In the other two cases, however, a marked reduction in cofactor activity (5.8 and 15% of normal respectively) was followed by the onset of clinical thrombosis. In a small group of 6 patients with low blood albumin levels, a direct relation was found between blood cofactor activity and blood protein concentration, the former being markedly reduced in all cases and returning to normal in those in which the hypoproteinaemia was eventually relieved.

H. Payling Wright.

Disturbances of Clotting in Acute Leukaemia. Biological and Therapeutic Study. SOULIER, J. P., and DAUSSET, J. (1950). *Sang*, **21**, 602.

This report is based upon a study of the blood-clotting mechanism in 21 cases of acute leukaemia. The authors found a constant reduction in platelet count which, they suggest, is responsible for the prolonged bleeding time, increased capillary fragility, incomplete utilization of prothrombin, failure of clot retraction, and increase in protamine index and prothrombin time in such cases. They could find no evidence of the presence of a heparin-like substance in the serum in any of the 6 cases in which it was sought. All forms of therapy are transient in their effect.

E. T. Ruston.

Refractoriness in Haemophilia to Coagulation-promoting Agents: Whole Blood and Plasma Derivatives. FROMMEYER, W. B., EPSTEIN, R. D., and TAYLOR, F. H. L. (1950). *Blood*, **5**, 401.

In this paper details are given of 22 cases of haemophilia which had been treated with blood and/or Cohn's fraction I (antihaemophilic globulin). Five of these patients were proved to be refractory to treatment, for the usual reduction in coagulation time following transfusions of blood or plasma fraction was not observed. Circulating anticoagulants were demonstrated in their blood, and evidence was obtained that in these cases antibodies had developed against an antihaemophilic substance present in prepared plasma fractions and normal whole blood.

MORBID ANATOMY AND HISTOLOGY

Granulomas of Large Size Caused by Implantation of Talcum (Talcum Sarcoids). GRUENFELD, G. E. (1949). *Arch. Surg., Chicago*, **59**, 917.

The author seeks to shake complacency about the inertness of glove powder introduced at operation by recalling the warnings in the literature of recent years. He adds a personal case report of a rapidly growing tumour developing in the deeper layers of the scar 12 years after appendicectomy. On section it appeared as a large conglomeration of giant-cell tubercles with no round-cell infiltration. Needle-like inclusions in the giant cells were proved by polarized-light study to consist of crystalline silicate known to be present in talcum powder.

This " sarcoid " tumour is the rarest and most severe form of reaction to surgical glove powder, the milder forms of which are also recapitulated by the author. Several theories are advanced, but the exact mechanism of this foreign-body reaction appears not to be known. No dependable substitute for talcum powder has as yet been advanced.

R. P. G. Sandon.

Pathogenesis of Atherosclerosis. DUGUID, J. B. (1949). *Lancet*, **2**, 925.

This discussion of the mechanism of formation of atheroma (atherosclerosis) is partly a resuscitation of Rokitansky's views. The author's thesis, which is based on a wide study, reported elsewhere, of frozen sections of the aorta and arteries, is that the atheromatous plaque is the result of thrombotic accretions on the vessel wall, with subsequent contraction, organization, and compression of the mass. The author believes that the commonly accepted conceptions of the pathogenesis of atheroma originated by Virchow are quite incompatible with the kinetic hydrostatic conditions which are presumed to exist within the arteries during life. He admits, however, that the amount of fatty and lipoid material in the base of the atheromatous plaque cannot all be attributed to the breakdown of the thrombus. The complexity of the relationship between fatty change, ulceration, and thrombosis is discussed and the question left open.

A. C. Lendrum.

Measles Encephalitis. APPELBAUM, E., DOLGOPOL, V. B., and DOLGIN, J. (1949). *Amer. J. Dis. Child.*, **77**, 25.

The problem of acute encephalitis associated with the exanthemata is discussed in relation to 74 cases of measles ence-

phalitis, observed over a 10-year period in one hospital. The chief interest of the study lies in the post-mortem findings in 7 fatal cases. The most pronounced feature in those with the shortest history of neurological symptoms before death (3 days or less) was the presence of scattered areas of cellular infiltration of the adventitia of the veins. When symptoms had been present for 3 days or longer, the better recognized sign of demyelination began to be obvious, accompanied or followed by increase of microglia in response to cell damage. The authors consider the condition primarily inflammatory. Certainly in cases where neurological signs precede or appear with the rash, perivascular infiltration or a haemorrhagic encephalitis is commonest. The nature of the association between the exanthem and the encephalitis remains unsolved.

Sequelae are common. In a follow-up study of 33 cases, only 13 appeared entirely normal. Minor or major signs of cerebral alterations were present in the remainder. In the acute stage, human measles immune serum and human pooled plasma were without effect. *W. G. Wyllie.*

The Pathology of Gaucher's Disease in Early Childhood (with Special Reference to the Neurological Form). GIAMPALMO, A. (1949). *Acta paediatr., Stockh.*, **37**, 6.

The author studied two siblings with Gaucher's disease beginning in the one case in infancy and in the other in early childhood and pursuing a rapidly fatal course. He collected from the literature another 28 cases of Gaucher's disease occurring in the first year of life, and on the basis of these 30 cases he describes the pathological features and the symptomatology of Gaucher's disease at this age. When the disease appears in infancy it differs from the same condition in older children and adults. The differences are that it runs a much more rapid course, death occurring always within the first two years of life, that superficial lymph nodes are usually enlarged, that skin changes are absent and blood changes slight, and that frequently neurological symptoms form a prominent part of the clinical picture.

[The details of the clinical picture, the pathological changes, and the author's views on the pathogenesis of the condition should be read in the original.]

S. A. Doxiadis.

Cystadenoma of the Pancreas. A Report of Two Cases Showing Calcification. HAUKOHL, R. S., and MELAMED, A. (1950). *Amer. J. Roentgenol.*, **63**, 234.

In the two cases reported the tumour occupied the head and tail of the pancreas respectively. Both occurred in women (53 and 75 years) who gave short histories of abdominal symptoms. Calcification has not previously been reported in this type of tumour, according to the author.

Cushing's Syndrome and Thymic Carcinoma. HUBBLE, D. (1949). *Quart. J Med.*, **18**, 133.

A detailed description is given of the symptoms and signs and necropsy findings in the case of a man aged 47 with Cushing's syndrome associated with a carcinoma of the thymus. The patient had a niece who was a pseudo-hermaphrodite and who died in infancy, and a nephew who had pubertas praecox and died in childhood. The patient himself died 8 hours after surgical removal of the thymic tumour, the blood pressure never rising above 58 mm. Hg. The cells of the tumour were epithelial-like. The suprarenal glands together weighed 28 g. and contained numerous small extracapsular adenomata 1 to 2 mm. in diameter; the anterior lobe of the pituitary gland contained typical hyaline basophil cells. After a review of the literature the author concludes that in Cushing's syndrome there is a tendency to carcinogenesis.

A. C. Crooke.

Correction.—Dr. Cumings writes that "on page 346 of the November issue under 'normal controls,' the third line of this paragraph reads '. . . blood creatinine was 0.5 mg./100 ml. or below. . . .' The word 'creatinine' should have been 'creatine.'"