



JOURNAL OF CLINICAL PATHOLOGY

EDITED FOR

THE ASSOCIATION OF CLINICAL PATHOLOGISTS

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LONDON

BRITISH MEDICAL ASSOCIATION

TAVISTOCK SQUARE, W.C.1

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

Bacterial Meningitis. Results of Treatment in Seventeen Cases with a New Sulfonamide ("Gantrisin"). RHOADS, P. S., SVEC, F. A., and ROHR, J. H. (1950). *Arch. intern. Med.*, 85, 259.

After their previous work (*Quart. Bull. Nthwest. Univ. med. Sch.*, 1949, 23, 104) the authors studied the effects of "gantrisin" (3:4-methyl-5-sulphanilamido-iso-oxazole) in cases of bacterial meningitis.

Ten cases of meningococcal meningitis were treated with the drug alone, two cases of meningococcal meningitis with the drug and penicillin (30,000 units three-hourly), three cases of pneumococcal meningitis with the drug and penicillin, and two cases of *Haemophilus influenzae* meningitis with the drug and streptomycin (0.1 g. intramuscularly three-hourly). The initial intravenous dose of the drug was from 2 to 6 g., with a daily maintenance dose of 6 g. (given four-hourly orally or intravenously). The average level of the free drug in the blood was 9.5 mg. per 100 ml. and of the free and conjugated forms 12.5 mg. per 100 ml. The level in cerebrospinal fluid was one-third to one-half the corresponding blood level.

All 10 patients with meningococcal meningitis treated by the drug alone and both with meningococcal meningitis treated by the drug and penicillin recovered without complications due to disease or treatment. One of the three patients with pneumococcal meningitis treated with the drug and penicillin died of pneumococcal endocarditis; the remaining two recovered as also did the two with *H. influenzae* meningitis treated with the drug and streptomycin. Gantrisin can be given orally, intramuscularly, or intravenously, alone or in combination with penicillin and streptomycin without any toxic effects.

Malcolm Woodbine.

"Gantrisin" in the Treatment of Urinary Infections. CARROLL, G., ALLEN, H. N., and FLYNN, H. (1950). *J. Amer. med. Ass.*, 142, 85.

Tests *in vitro* and *in vivo* have shown that "gantrisin," (3:4-dimethyl-5-sulphanilamido-iso-oxazole), also known as "NU-445," is the drug of choice in the treatment of urinary infections due to *Proteus vulgaris*. It is also effective in infections caused by *Bacterium coli*, *Alcaligenes*, and certain intermediate organisms, and moderately effective in infections caused by the *Aerobacter aerogenes* and paracolon bacillus. Infections due to *Pseudomonas* and *Streptococcus faecalis* are resistant to treatment. If one of the organisms in a mixed infection is a resistant organism the value of the drug is greatly reduced. When "gantrisin" is given orally in doses of 2 g. every six hours or by intramuscular or intravenous injection of a 40% solution, no local or systemic toxic reactions occur. The use of alkalis or forcing fluids at the same time is not necessary.

Thomas Moore.

Pertussis Treated with Chloramphenicol.

PAYNE, E. H., LEVY, M., ZAMORA, G. M., VILARROEL, M. S., and CANELAS, E. Z. (1949). *J. Amer. med. Ass.*, 141, 1298.

In the department of Cochabamba, Bolivia, whooping-cough is a serious disease carrying a mortality of 20%, which does not appear to be related to social status. It has been found that penicillin and streptomycin prevent complications, but do not shorten the disease. *Haemophilus pertussis* and *H. parapertussis* are both sensitive to chloramphenicol *in vitro*. In this paper is described the treatment with chloramphenicol of 50 patients under 5 years of age seriously ill with whooping-cough, the diagnosis being confirmed either by cough-plate or by

swab culture. The clinical history of seven of these cases is given. The drug was given by mouth, as a rectal suppository, or intravenously, and dosage was calculated according to body weight. The therapeutic results are reported as excellent, fever disappearing by the second day and the frequency of paroxysms decreasing considerably. The only complication seemed to be a slight nausea. Cough-plate cultures were negative after seven days' treatment. It would appear that the drug is specific, as the authors mention neither mortality nor complications in the treated cases.

Chloromycetin in the Treatment of Salmonella Enteritis. ROSS, S., BURKE, F. G., RICE, E. C., WASHINGTON, J. A., and STEVENS, S. (1950). *New Engl. J. Med.*, **242**, 173.

Nine cases of salmonella enteritis in infants were treated with "chloromycetin." The chloromycetin sensitivities of the various strains of salmonella isolated from these patients ranged from 2 to 5 μ g. per ml.

In spite of the ready susceptibility of the organism to the drug, only two of the nine patients in this series became permanently free of the pathogen after treatment. In the other seven cases a transitory inhibitory effect on both the salmonella organism and the normal stool flora was observed; however, within five to 40 days after chloromycetin was discontinued the pathogen reappeared in the stools. No increase in chloromycetin resistance was observed in any case after bacteriologic relapse.—(Authors' summary.)

Chloramphenicol in Treatment of Infantile Gastro-enteritis. A Preliminary Report. ROGERS, K. B., KOEGLER, S. J., and GERRARD, J. (1949). *Brit. med. J.*, **2**, 1501.

A serologically specific type of *Bacterium coli* was found in the stools of 86 infants under the age of 1 year admitted to the Birmingham Children's Hospital during a 10-month period. In 25 of the 86 cases reported the appearance of this organism was followed by no untoward symptoms during one month's observation. In the remaining 61 cases a gastro-intestinal disturbance developed, varying from severe gastro-enteritis to mild diarrhoea, from which 13 of the patients died. All severe cases were treated with intravenous alimentionation until the diarrhoea and dehydration were controlled, when oral feeding was gradually resumed. Initially, penicillin and sulphonamides were administered,

but although they helped to control parenteral infections they had little or no effect on the gastro-enteritis. Twelve patients were treated with streptomycin with disappointing results.

Treatment with chloramphenicol in 15 cases was much more satisfactory. All strains of *Bact. coli* B.G.T. tested were sensitive to this drug and also to aureomycin, but the former was chosen for therapeutic trial because of its relative stability. In most cases, the diarrhoea ceased and the organism disappeared from the faeces within two to eight days of starting treatment. In two cases, it reappeared one and seven days respectively after stopping treatment, but the organisms were still sensitive to chloramphenicol. Three children became carriers and in two of them chloramphenicol failed to eradicate the organism from the faeces. Apart from sore buttocks in four cases no other possible toxic reactions were observed.

Treatment of Typhoid Fever with Chloromycetin. Results in Four Cases and in a Chronic Carrier. COLLINS, H. S., and FINLAND, M. (1949). *New Engl. J. Med.*, **241**, 556.

From their limited experience the authors consider that, except for a lesser incidence of toxic effects, chloramphenicol is not strikingly more effective in this disease than aureomycin. It is suggested that earlier diagnosis, and possibly the use of maximal doses from the start, might give better results in some cases, but they are evidently disappointed with the drug.

Aureomycin Treatment of Herpes Zoster. FINLAND, M., FINNERTY, E. F., COLLINS, H. S., BAIRD, J. W., GOCKE, T. M., and KASS, E. H. (1949). *New Engl. J. Med.*, **241**, 1037.

This paper records the results of aureomycin treatment in 24 cases of herpes zoster. Administration was oral in 22 and the optimum dosage was found to be 1 g. four times a day, reduced to 0.5 g. for each dose after definite improvement or if there was nausea and vomiting. This was continued until the lesions showed signs of healing. The total dosage varied from 7.5 to 54 g. over 3 to 17 days, with an average of 19 g. in six and half days. Two patients who refused oral therapy were given 500 mg. in 500 or 1,000 ml. of 5% dextrose by slow intravenous drip, about one hour being taken for each dose.

Rapid healing usually began within about 24 hours and was complete in the majority of patients by the seventh or eighth day. In four

cases new lesions appeared during the first two days of therapy. In all cases pain was dramatically reduced in four or five days, but post-herpetic pain was not prevented in six cases and lasted for from two weeks up to three months. The authors believe that aureomycin has a definite beneficial effect on the course of herpes zoster.
A. W. H. Foxell.

The Association of Certain Types (α and β) of *Bact. Coli* with Infantile Gastro-enteritis.
SMITH, J. (1949). *J. Hyg., Camb.*, **47**, 221.

A particular variety of coliform bacillus had been found to be associated with cases of infantile gastro-enteritis. This organism has been variously named the neapolitanum variation, D 433 (Taylor, Powell, and Wright), and type α (author's laboratory). During 1947 the α type was found to be associated with 94.7% of 207 cases of gastro-enteritis. In November, 1947, it was noted that the α type was less frequently isolated in specimens from clinical cases of gastro-enteritis. By the use of antisera for the "O," "H," and "K" (Kauffmann) antigens another fairly frequently occurring type was identified and was named by the author for convenience the β organism. Up to the end of 1947 the β type was found in 21 cases of infantile diarrhoea. The β variety has no distinctive features when grown on agar or blood-agar plates. (The original article should be consulted for full technical details.)

During 1948, 75 cases were classified definitely as cases of gastro-enteritis. The α type was recovered from 25 cases (six deaths) and the β type from 35 cases (11 deaths). In 14 cases (six deaths), clinically of gastro-enteritis, neither type was isolated. One patient died before bacteriological examination could be made. The α and β organisms are easily identified by specific slide-agglutination tests, but there are considerable technical difficulties in recovering the types from faecal cultures, particularly if the agglutinable types are scanty. Either organism can be readily isolated during the acute phase of the disease, becomes increasingly scanty in the sub-phase, and usually tends to disappear from the intestinal contents as convalescence is established. A certain number of convalescent carriers were observed.

The author considers that while the actual significance of the association of the α and β types with gastro-enteritis has not been determined, their isolation points to a diagnosis of infantile gastro-enteritis, and also provides a means of controlling nursing technique and

determining whether or not intestinal cross-infection has occurred in cubicles or open wards.

The Relation of *Staphylococcus Pyogenes* to Infantile Diarrhoea and Vomiting. MARTYN, G. (1949). *Brit. med. J.*, **2**, 1146.

The following three groups of infants aged 2 weeks to 1 year were studied: (1) 119 infants in hospital suffering from diarrhoea and vomiting; (2) 78 infants in hospital, but without gastro-intestinal symptoms; and (3) 44 healthy infants attending a welfare centre.

Rectal swabs were taken in each case and were plated on to horse-blood agar plates and inoculated into 10% sodium chloride meat medium (see Maitland and Martyn, *J. Path. Bact.*, 1948, **60**, 553). All staphylococci grown were tested for coagulase production and positive strains referred to as *Staphylococcus pyogenes*; staphylococci were also tested for sensitivity to penicillin (40 units per ml.) and streptomycin (1,000 units per ml.). The frequency of isolation of *Staph. pyogenes* in each group was as follows: (1) 44.5%, 28.3% of these organisms being penicillin-resistant and 3.8% streptomycin-resistant. (2) 52.5%, 31.9% being penicillin-resistant and 4.9% streptomycin-resistant. (3) 34%, 60% being penicillin-resistant and none streptomycin-resistant. Twenty strains were not typable.

Distribution of bacteriophage types in the strains isolated was strikingly similar in patients (group 1) and controls (groups (1) and (2)); 19 in each (out of 53 and 56 strains respectively) being of type 47 (nomenclature of Central Public Health Laboratory). Of these 38, 26 were penicillin-resistant. In each series, five strains were of type 6/47 which has been shown by Allison (*Proc. R. Soc. Med.*, 1949, **42**, 216) to be associated with food poisoning.

In only four cases were staphylococci isolated direct on blood agar, suggesting that the number present was small; the selective medium, on the other hand, gave a high incidence of the organism from a sparse inoculum. In only four out of 13 fatal cases was *Staphylococcus pyogenes* isolated on selective medium. There was no blood or pus in the stools in any of the cases of group (1). The conclusion is drawn from the closely corresponding incidence of the organism in patients and controls and the similarity of phage-type distribution and sensitivity to penicillin and streptomycin that *Streptococcus pyogenes* is not the cause of infantile diarrhoea and vomiting.

A New Haemorrhagic Ulcerative Disease and its Aetiology. CASTELLANI, A. (1949). *J. trop. Med. Hyg.*, 52, 204.

This paper records in detail observations on the clinical picture and bacteriology of two cases of a hitherto undescribed disease. The patients were seen late in the course of the disease. Bullae appeared, chiefly on the limbs and were filled with a haemorrhagic fluid. These ruptured leaving an ulcer which, on healing, produced a raised keloid scar. A low-grade fever was present and one patient had bouts of abdominal pain which were followed by the passage of haemorrhagic stools. A well marked hypochromic anaemia was present, the leucocytes being normal in number and distribution. X-ray and pathological examinations gave negative results. Treatment with sulphonamides and penicillin had little effect. The first patient was not followed up; the second showed slow improvement over the course of a year.

The same organism was isolated both from the ulcers and from the bullae in each case. It grew well on the usual laboratory media and its cultural characteristics are described. Mice were readily killed by intraperitoneal injection of the freshly isolated organism. Injection into the skin of rabbits, guinea-pigs, and monkeys resulted in lesions which resembled those seen in man—especially in the case of monkeys. The organism is rod-shaped, 1.5 to 3.5 μ (or more) in length, non-sporogenous, actively motile, and easily stained. It was Gram-negative and not acid-fast. It showed some features akin to those of *Malleomyces pseudomallei*, and also to those of the genus *Pseudomonas*. The author proposes the name *Bacterium haemorrhulcogenes*.

Q Fever in Great Britain. Clinical Account of Eight Cases. HARMAN, J. B. (1949). *Lancet*, 2, 1028.

A clinical description is given of eight cases of Q fever occurring at the Royal Cancer Hospital, London. This is the first time that Q fever has been detected in the active state in Great Britain, although it is known that many cases arose in Italy and the Balkans during the late war, where they were called "Balkan grippe" by the Germans and "atypical pneumonia" by the British. The clinical manifestations, although constant, do not serve to distinguish Q fever from other short-term fevers; it has usually drawn attention to itself by its epidemic character. Features of the clinical picture are high swinging temperature

with rigors and drenching sweats, intense headache, and, quite commonly, delirium. Within a week a tickling unproductive cough develops and tissue-paper crepitations and high-pitched bronchial breathing are to be heard usually at the base. Gastro-intestinal symptoms are rare. There is no rash or coryza. The radiological signs, which may persist for weeks, suggest lobular partial consolidation usually at the base, though any lobe may be affected; collapse and pleural effusions may be seen. Complications in this disease are hardly ever seen and the death rate seems to be in the neighbourhood of 1 in 500. Case-to-case spread is remarkably absent.

Diagnosis was confirmed in all the eight cases except one (probably the original one) by the complement fixation test for *Rickettsia burnetii*. Antibody titres as high as 1 in 640 were recorded. In one case *R. burnetii* was isolated from the blood. In treatment the sulphonamides, penicillin, and probably streptomycin are useless. Aureomycin, which has a powerful suppressive action on experimental infections of eggs and guinea-pigs with the rickettsia of typhus, scrub typhus, Rocky Mountain spotted fever, and Q fever, has been used clinically in cases of Q fever with promising results, though one notable failure was seen and in others cure was delayed. Chloramphenicol is very effective in other rickettsia diseases, but there are no published records of its use in Q fever.

J. V. Armstrong.

Antihistamines in the Treatment of the Common Cold. A Preliminary Report. MIDDLETON, J. W., and RIDER, J. A. (1949). *Dis. Chest*, 16, 879.

Random treatment of the common cold with antihistaminic drugs indicated that some improvement occurred, and a controlled experiment was therefore made, 63 cases being treated with antihistaminic drugs and 29 with placebos. The drugs used were pyranisamine and phenindamine, and these were given four times daily in 50 mg. and 25 mg. doses respectively. No patient knew what drug was being administered. Drugs were assigned alternately in the order in which patients appeared.

There was no significant difference in results from pyranisamine and phenindamine, though the former gave rise to a higher percentage of side-effects. None of these was severe. Patients with a history of allergy were tabulated separately. Colds were considered to be aborted

only if symptoms were entirely relieved within 12 hours after the start of therapy and remained absent after discontinuation of the latter. Of the total treated 76% were benefited, with partial or complete relief of symptoms, as compared with 45% of controls. In only seven cases was the cold aborted. Of those with a history of allergy 88% were benefited as compared with 72% of the non-allergic (though the former group was small and may have included cases of allergic rhinitis and not genuine colds).

The authors do not claim any altered response to viral or bacterial infection, but rather a modification of symptoms.

Treatment of Surgical Tuberculosis with the Thiosemicarbazone "TB I 698." HASCHÉ-KLÜNDER, R., and LEIMBACH, G. (1949). *Dtsch. med. Wschr.*, 74, 1135.

Thiosemicarbazone as a chemotherapeutic agent has been used mainly in the treatment of pulmonary tuberculosis, and there are few reports of its use in surgical tuberculosis. The authors report their experience in 70 cases of non-pulmonary tuberculosis treated with thiosemicarbazone. Although no response was obtained in some cases, there was often marked improvement in the general condition of the patient, with a quicker and better localization of the active process, so that surgery could be employed earlier and with more certain healing. The drug was given by mouth and also locally by instillation into fistulae or abscess cavities.

It was most effective in bladder, bone, and joint tuberculosis, and in fistula-in-ano, but no effect was observed on cases with lesions of the kidney, prostate, and epididymus.

The authors point out that very careful experiment and observation are required for the evaluation of these drugs and the assessment of the indications and contraindications for their use before they can be accepted and related to other substances, such as streptomycin, in the treatment of tuberculosis.

HAEMATOLOGY

Diagnosis and Mechanism of Hemolysis in Chronic Hemolytic Anemia with Nocturnal Hemoglobinuria. DACIE, J. V. (1949). *Blood*, 4, 1183.

The primary abnormality in nocturnal haemoglobinuria resides in the patient's erythrocytes. It is of such a nature as to cause

them to be haemolysed by thermolabile fraction(s) of normal serum, but only if the pH of the serum is adjusted to the physiological level or below by the addition of acid to compensate for the alkalinity which develops when serum is exposed to air and loses carbon dioxide. This is the basis of the "acid-serum test." The patients' corpuscles are *not* unusually sensitive to acid *per se*.

An increase in haemolysis as the result of acidification of serum is, however, not specific for the reaction in nocturnal haemoglobinuria; other types of haemolysins are affected by change in pH and may be a cause of confusion. The necessary controls are outlined.

The nature of the corpuscular abnormality and the haemolytic factor(s) present in normal serum is briefly considered.

Acquired Hemolytic Anemia. I. The Relation of Erythrocyte Antibody Production to Activity of the Disease. II. The Significance of Thrombocytopenia and Leukopenia. EVANS, R. S., and DUANE, R. T. (1949). *Blood*, 4, 1196.

The authors have studied patients with acquired haemolytic anaemia whose corpuscles give a positive Coombs test. They have attempted to equate the intensity of haemolysis as estimated clinically with the degree of sensitization of the corpuscles, as measured by ascertaining the highest dilution of antiglobulin serum which would give a positive reaction. In general low titres of antiglobulin serum were associated with clinical quiescence, both before and after splenectomy. In one case, however, this was not so, for the corpuscles remained strongly sensitized without there being clinical evidence of a return of haemolysis.

Sickle Cell Anaemia, a Molecular Disease. PAULING, L., ITANO, H. A., SINGER, S. J., and WELLS, I. C. (1949). *Science*, 110, 543.

The authors have studied the haemoglobin molecule by physical means and have found that there is a difference in electrophoretic behaviour between haemoglobin of normal subjects and that derived from patients suffering from sickle cell disease. Corpuscles from subjects with the sickle cell trait contain both types of haemoglobin. The molecular abnormality is believed to affect the globin part of haemoglobin and to be of such a nature as to allow alignment of complementary parts of the molecules when oxyhaemoglobin is changed to reduced haemoglobin.

Pteroyl-polyglutamic Acids in the Treatment of Pernicious Anaemia. WILKINSON, J. F., and ISRAËLS, M. C. G. (1949). *Lancet*, **2**, 689.

Thirteen patients were treated with synthetic pteroyl- γ -triglutamic acid (teropterin) and/or pteroyl- α -diglutamic acid (diopterin) by the intravenous, intramuscular, and oral routes. In 8 patients treatment with teropterin alone produced satisfactory haematological responses, while in 3 patients treated with minimal doses of diopterin the response was less.

These results are held to indicate that patients with pernicious anaemia can hydrolyse and utilize synthetic folic acid.

Erythropoietic Effect of Cobalt in Patients With or Without Anemia. BERK, L., BURCHENAL, J. H., and CASTLE, W. B. (1949). *New Engl. J. Med.*, **240**, 754.

The results of cobalt administration to patients with a variety of anaemias proved disappointing. In none of 5 patients with refractory anaemia and hypocellular marrow, nor in patients with anaemia associated with nephritis or liver disease was there a significant response. A definite rise in the reticulocyte level and in the erythrocyte count was observed, however, in 2 of 5 patients with chronic infections, in 1 or 2 patients with inoperable carcinoma of the stomach and in one patient with Cooley's anaemia. A slight reticulocyte response was produced in 17 patients with a normal blood picture who were given 300 mg. cobaltous chloride daily.

Idiopathic Thrombocytopenic Purpura. ROBSON, H. N. (1949). *Quart. J. Med.*, **18**, 279.

Nineteen cases of thrombocytopenic purpura submitted to splenectomy were studied, as well as 14 patients undergoing splenectomy for other conditions. Seven patients with no blood abnormality who were undergoing abdominal operations served as controls.

In thrombocytopenic purpura the bleeding time was reduced as soon as the skin incision was made; it reached normal on an average 48 minutes after ligation of the splenic pedicle. Capillary resistance increased after ligation of the splenic pedicle and became normal about 4½ hours later. The platelet count also increased, reaching normal levels in ½-4 hours and maximum levels up to 22 days afterwards. Observations on the control group suggest that the changes in bleeding time and capillary

resistance and platelet counts are non-specific and due to the operation itself. Later changes are effected by the removal of the spleen. The megakaryocytes were also studied; lack of platelet formation was the most constant finding.

The Cause of Thrombocytopenia in Sedormid Purpura. ACKROYD, J. F. (1949). *Clin. Sci.*, **8**, 269.

One or two tablets of sedormid taken by mouth by patients who have recovered from purpura caused by this drug may precipitate another attack of thrombocytopenia. In such patients the drug causes agglutination and lysis of platelets *in vitro* and capillary damage if applied to the skin. The minimal concentration of sedormid required to cause lysis of platelets *in vitro* corresponds closely with that calculated to be present in the plasma after therapeutic doses of the drug.

The Control of Polycythemia by Marrow Inhibition. A Ten Year Study of 172 Patients. LAWRENCE, J. H. (1949). *J. Amer. med. Ass.*, **141**, 13.

One hundred and twenty-one patients with polycythaemia vera have been treated with P₃₂ during the past 12 years. They received as a rule 2 injections of 3 to 6 millicuries of radioactive phosphorus. This course was usually repeated after an average of 3 years, but many patients needed no further treatment for 4-8 years. Occasionally this regime has been supplemented by venesections. Twenty-one of the patients died, 5 of leukaemia, a recognized complication of polycythaemia (however treated). The incidence of thrombosis during treatment was small, and it is concluded that P₃₂ therapy is a satisfactory way of treating polycythaemia vera.

Homologous Serum Jaundice. LEHANE, D., KWANTES, C. M. S., UPWARD, M. G., and THOMSON, D. R. (1949). *Brit. med. J.*, **2**, 572.

The occurrence of jaundice following transfusions was ascertained in a series of 4,430 patients. The incidence after blood transfusion (0.8%) was not significantly different from that following transfusion of plasma obtained from small (10 donor) pools (1.3%). The incidence after transfusion of plasma prepared from large pools was much greater (11.9%).