SYPHILIS (General)


The distinction between meningovascular and parenchymatous disease of the optic nerve has not been made sufficiently clear in the past, but is undoubtedly a very real one; the former type, described in this paper, has been somewhat neglected by neurologists, though it has been given a variety of names by ophthalmologists. Syphilitic optic neuritis, as opposed to the commoner primary optic atrophy, may occur as a manifestation of congenital syphilis, or in secondary or meningovascular syphilis. The author reports in detail five cases, one associated with secondary syphilis and the other four with tertiary syphilis. The patients' ages were 33, 37, 37, 44, and 61 respectively.

The condition of syphilitic optic neuritis resembles the common demyelinating optic neuritis in that the main symptom is unilateral visual failure, but differs from it in that (a) there is rarely ocular pain or headache, (b) although visual symptoms are unilateral the ocular signs are bilateral, and (c) there is no spontaneous recovery of visual acuity. Characteristically, the onset is abrupt, with blurred central vision in one eye progressing for days or weeks and then becoming stationary, vision declining to levels ranging from 6/12 to 6/60. There is concentric constriction of the smaller isopters, indicating a diffuse disturbance of the whole of the nerve; the field for colours is correspondingly diminished, sometimes with red-green blindness. The blind spot is enlarged. Involvement of the papillomacular bundle to a variable extent caused central scotomata in three of the cases reported. Sometimes a nerve-bundle defect, or a ring scotoma, is encountered. Four of the five had bilateral papillitis; one had secondary optic atrophy in one eye (affected 15 years previously) and intense swelling of the disk in the other, with some periphlebitis and choroiditis. The Wassermann reaction was positive in the blood in all cases, but in the cerebrospinal fluid only in the two cases in which other changes were found in the fluid. Three patients had no neurological abnormality other than the optic neuritis, one had minimal cord changes, and one had a multiple cranial neuropathy due to chronic basal meningitis.

The patients were treated with penicillin, with or without a later course of bismuth and arsenic. In marked contrast with parenchymatous syphilitic optic atrophy, treatment in cases of syphilitic optic neuritis reverses the visual changes, especially the central visual defects.

John Foley

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. The abstracts are divided into the following sections: syphilis (general, pathology, therapy); gonorrhoea (general, pathology, therapy); chemotherapy; other venereal disease conditions; public health; miscellaneous. After each subsection of abstracts follows a list of articles that have been noted but not abstracted. All subsections will not necessarily be represented in each issue.)


A married girl of 16 received a first injection of 0·3 g. nearsphenamine about 3 months after contracting syphilis. One week later a second injection, of 0·4 g., was given; the following day she was unwell and felt frightened; by the third day after the injection, when admitted to hospital, she was moderately atactic, terrified, and mute. There were gross twitchings of all limbs and, in the evening, a series of epileptic attacks occurred, beginning in the left arm and becoming generalized; they lasted for 4 hours, after which the patient was in coma, which continued for 4 to 5 days.

During this period the temperature and respiratory rate rose, respiration being of the Cheyne-Stokes type. The cerebrospinal fluid pressure was 300 mm. of water, the protein content 274 mg. per 100 ml., and the Lange reaction 555544333. From the sixth day of her illness she made a steady recovery, interrupted only by minor focal twitchings in the left arm and episodes of sensory disturbance on the left side, including hemianopia. At a later date the syphilis was treated with penicillin, and ultimate recovery was in all respects complete.

Serial electroencephalograms were of interest in that the high-voltage slow waves associated with coma persisted for at least 4 days after the return of consciousness. Focal slow waves and "slow spike" discharges occurred in the right occipito-temporal region before the onset of focal seizures.

W. A. Cobb


The Wechsler-Bellevue adult intelligence test was used for a study of psychological processes in 66 patients with
neurosyphilis. The purpose of the study was to evaluate the use of such tests in active neurosyphilis and to clarify such questions as the possibility of psychological correlates of specific pathological brain changes, the value of psychological tests in the preliminary study of the patient, as a prognostic aid, and as a measure of therapeutic efficacy. The group studied included cases of syphilis without neurosyphilis, of active asymptomatic neurosyphilis, of inactive neurosyphilis, of active symptomatic neurosyphilis, of tabes dorsalis and of psychosis.

On average, patients with early and latent syphilis without neurosyphilis were found to be of normal intelligence; those with inactive neurosyphilis were of borderline to dull normal intelligence; those with active symptomatic neurosyphilis were of a dull normal level; and those with active asymptomatic neurosyphilis were assessed at the borderline level of intelligence.

This is a preliminary report of an investigation in which the authors plan to use a battery of eight intelligence tests for the same purpose. The full report of the completed study may well reveal greater differences between the various types of neurosyphilis.

V. E. Lloyd


A psychometric procedure for the detection of mental deterioration in patients with neurosyphilis, and particularly of early simple dementing paresis, was applied to 72 patients. The Kohs block test and the Stanford-Binet vocabulary test were employed for this purpose. The results in cases of syphilis (1) without neurosyphilis, (2) with non-paretic neurosyphilis, (3) with paresis, and (4) with doubtful paresis are discussed. Evidence was obtained which suggests that the procedure indicates objectively the presence of mental deterioration and, roughly, its degree. The procedure is simple and consumes little time, and is considered to be of practical clinical value.

V. E. Lloyd

SYPHILIS (Pathology)


A new modification of Fontana’s stain for Treponema pallidum is described. After preliminary treatment with Ruge’s fixative solution followed by Fontana’s mordant fluid, the smears are placed in a solution of carbol-methyl violet (saturated solution of methyl violet, one part, and 5 per cent. aqueous carboxylic acid, ten parts) for a minimum of 2 minutes. The smears are then dipped in distilled water, drained on filter paper, dipped once in acetone, dried between filter papers and passed through a gentle flame. Finally they are placed in xylene and mounted in balsam or “permount.”

The treponemes are stained deep violet-purple and when viewed through gamma blue-green and amber glass filters, or “Kodak” filters B 68 and G 15 or E 22, the contrast is sufficient for photography. Excellent photomicrographs of T. pallidum and of mouth spirochaetes are reproduced, which show the capabilities of the method.

V. E. Lloyd


Employing the technique of Nelson and Mayer (J. exp. Med., 1949, 89, 369) the author demonstrated the presence of immobilizing antibody (I.A.) against Treponema pallidum in the serum of syphilitic patients. In order to obtain a supply of T. pallidum rabbits were given two injections of 0-5 ml. of a suspension of these organisms into the testicles; 24 hours after orchitis had developed the animals were killed and each testicle was cut into ten slices and washed with chilled 0.8 per cent. saline; the slices were then placed in 40 ml. Nelson’s medium in an atmosphere of 5 per cent. carbon dioxide in nitrogen at 35° C. for 2 hours. The number of spirochaetes in the medium was adjusted by dilution to 10 million per ml., and the suspension separated from the testicular debris by centrifugation at 1,000 r.p.m. for 10 minutes.

In carrying out the test, 0.05 ml. of the serum to be examined (inactivated) is mixed with 0.05 ml. of guineapig complement and 0.4 ml. of the suspension of spirochaetes; as a control the same mixture is prepared, but the complement is previously inactivated. The tubes are incubated for 18 hours at 25° C. in a Brewer’s anaerobic jar in an atmosphere of 5 per cent. carbon dioxide in nitrogen. A positive reaction is indicated if a large proportion of the organisms (at least 70 per cent.) are immobilized and a negative reaction if most of the organisms are still active. The difference between the two tubes should be at least 50 per cent. for a positive result, and a negative reaction should be confirmed by proving the presence of active complement by the addition of sensitized cells. The immobilized spirochaetes can be shown to have lost their virulence by injecting them into rabbits.

The immobilizing antibody differs from reagin; the latter is removed from syphilitic serum by absorption with Kahn or similar antigen, but the I.A. is not; also the serum reagin level can be shown to decrease under antisyphilitic treatment, though the I.A. does not. Thus it would appear that I.A. is closely associated with immunity.

The serum of most patients with syphilis beyond the primary stage gives a positive immobilization reaction, whereas that of normal persons and those suffering from diseases other than syphilis invariably gives negative reactions; this test may therefore be a valuable means of distinguishing true from biologically false positive reactions in the serum tests for syphilis. As yet the test cannot be used for the routine diagnosis of syphilis owing to technical difficulties, but if and when virulent T. pallidum can be cultured successfully it will have a wide clinical application.

T. E. Osmond

The treponemal immobilization test described by Nelson and Mayer (J. exp. Med., 1949, 89, 369) has been made more sensitive by increasing the final concentration of guinea-pig serum from 5-6 to 22-2 per cent. It is suggested that the immobilization test can be rendered even more sensitive by increasing at the same time the final concentration of the patient's inactivated serum from 11-1 to 22-2 per cent. The reliability and significance of the test still need further evaluation.

G. M. Findlay


Rabbit's testicles infected with the Nichols strain of Treponema pallidum were used to prepare a suspension of spirochaetes which was treated with 0-1 per cent. formalin. An intradermal injection of 0-1 ml. was made into the flexor surface of one forearm, while into the corresponding area of the other arm was injected the same amount of a suspension from normal rabbit testicles. Normal persons and those with secondary syphilis gave negative results, but in those with tertiary or congenital syphilis there was a tuberculin-like reaction. The term "treponem test" is suggested for this reaction.

G. M. Findlay


It would seem obvious that the narrowing of the lumen of the cerebral vessels which occurs in meningovascular neurosyphilis and general paralysis must lead to a decrease in the flow of blood through these vessels as compared with normal subjects. In the experiments described in this paper cerebral blood flow was determined by the nitrous oxide technique of Kety and Schmidt (J. clin. Invest., 1948, 27, 476) on 26 patients with general paralysis, nine with meningovascular syphilis, and 23 with asymptomatic neurosyphilis, and on a control group of sixteen non-syphilitic patients. The cerebral oxygen consumption was estimated from the product of the cerebral blood flow and the difference in oxygen content between arterial and venous blood.

In the group of patients with meningovascular syphilis the cerebral blood flow was, on the average, only 66 per cent. of normal, but there was no correlation between the reduction in blood flow in particular cases and the severity of the clinical symptoms. There was also a diminished oxygen consumption (77 per cent. of that of the normal group).

In patients with general paralysis the cerebral blood flow was reduced to 72 per cent. of normal, and a corresponding diminution in oxygen consumption was found. In some patients with general paralysis the oxygen consumption was extremely low—in one case only 24 per cent. of normal—and there was a definite relationship between the degree of dementia and the reduction in oxygen consumption. Any improvement in the mental state after treatment with penicillin or pyrexia was accompanied by an increase in cerebral oxygen consumption. In patients with asymptomatic neurosyphilis normal values were obtained for both cerebral blood flow and oxygen consumption.

Ruby O. Stern


Of the patients referred to in the previous abstract, fourteen with general paralysis and thirteen with asymptomatic neurosyphilis were treated with induced pyrexia, two being inoculated with malarial parasites, and the remainder given an intravenous injection of 0-1 ml. of a suspension of heat-killed typhoid bacilli. The maximum temperature ranged from 101° to 104° F. (33°-3° to 40° C.). The cerebral blood flow was determined when the temperature was normal and again at the height of the fever. In the patients with asymptomatic neurosyphilis values for both cerebral blood flow and cerebral oxygen consumption were normal when afebrile and showed only very slight variations during the febrile period. In those with general paralysis cerebral blood flow and oxygen consumption were abnormally low when afebrile, but increased during the period of the fever by 30 per cent. and 24 per cent. respectively. The authors suggest that the good effects of pyrexial therapy in general paralysis are due, at least in part, to dilatation of the cerebral vessels and the subsequent increase in cerebral blood flow.

Ruby O. Stern


Foci of osteoperiostitis and small osteolytic processes are described in a patient with sero-positive primary syphilis. The lesions were situated on the forehead and the left sternoclavicular joint. During the initial phases of antisyphilitic treatment a Herxheimer reaction occurred, and at the same time new foci appeared. Clinical cure was eventually obtained but radiological evidence of bone involvement was still present 2 weeks after the conclusion of treatment. G. W. Csonka


Histological studies were carried out on 75 syphilisitics with liver damage. Clinically the patients comprised cases of late (62) and early (7) jaundice after arsenotherapy, three cases of "icterus syphiliticus praecox";
and three of hepatitis without jaundice. Three of the early arsphenamine-jaundiced cases were distinct from the other four clinically and histologically, the jaundice being apparently obstructive in origin. In all other cases the histological picture was of the same type; details depended on the period of the illness at which the specimen was collected. The picture was that of a diffuse, chiefly central, zonal, necrotizing hepatitis which was essentially similar to that seen in infective hepatitis. Clear and careful descriptions are given in the text of the various stages, acute, regressive, and healing of the process. The authors conclude that the late jaundice of arsphenamine therapy clinically and epidemiologically resembles that of homologous serum hepatitis and is probably caused by the same agent, whereas the early jaundice cases and those of icterus syphiliticus praecoex are more closely related to infective hepatitis. They regard the antisyphilitic drugs as additional and accessory factors in the promotion of such hepatitis.

Nine patients treated with arsphenamine died in coma after becoming jaundiced. Necropsy revealed a picture also suggestive of death from virus hepatitis. Recovery either resulted in restitution of hepatic tissue or central and periperitral sclerosis. Eleven cases of cirrhosis following arsphenamine jaundice were studied at various stages. Five had a history of alcoholic abuse, but in the others it appeared that the arsphenamine jaundice could be regarded as the forerunner of the cirrhosis.

[Those interested are advised to read the original.]
B. G. Maegraith


A group of 37 rabbits with infectious syphilis of 6 to 11 weeks' duration following scrotal inoculation with Nichols strain of Treponema pallidum was treated with 14,400 units of sodium penicillin per kg. body weight, given in 48 two-hourly doses. Ten days later the immunity was challenged by a second similar inoculation and it was noted that 27 per cent. of the animals developed new chancres, while the remainder had asymptomatic infections, as proved by node-transfer experiments. Immunity was challenged in a like manner in 22 other animals, but on this occasion 6 months after treatment. None of these developed chancres and, although 36 per cent. were shown to have asymptomatic infections, no less than 64 per cent. were immune. This apparently indicates that immune bodies are formed after clinical cure.

A further group of 34 rabbits with latent syphilis of 8 months' duration was also treated with penicillin and the immunity challenged 10 days later; 53 per cent. developed asymptomatic infections and 47 per cent. were immune. When 25 more animals with latent syphilis of 8 months' duration were treated with penicillin and the immunity likewise challenged 6 months later, node-transfer studies made 4 months after this showed that 57 per cent. had a symptomless infection. After a further 2 months (6 months after the spirochaetal challenge) the same animals were re-treated with penicillin and the immunity was given a second challenge 6 months later. Lymph-node transfers made 4 months after this indicated that, by this time, only 31 per cent. had become asymptotically infected. R. R. Willcox


Full details are given of an experiment designed to determine the relationship of the spirochaeticidal antibody, capable of rendering suspensions of Treponema pallidum non-infective for rabbits when inoculated intradermally, to the immobilizing antibody, demonstrable in the serum in vitro. When the suspension of spirochaetes was treated with a pooled syphilitic serum in the presence of complement, infectivity was lost as the organism became non-motile, the loss of infectivity appearing to occur slightly before the loss of motility. A period of incubation in vitro of the mixture of immune serum, spirochaetes, and complement was necessary before the loss of motility and infectivity could be demonstrated.

D. G. Jf. Edward

SYPHILIS (Therapy)

A series of 127 syphilitic mothers received, during pregnancy, penicillin, arsenic and bismuth, or no treatment. In the penicillin series (66) all children were apparently normal at birth, but one showed a weak sero-positive reaction, the mother having been first treated at 9 months for secondary syphilis. Among 21 mothers receiving arsenic and bismuth, three bore clinically syphilitic children and the babies of two others were sero-positive at birth. In the untreated series (40), nine children were clinically affected and 21 were sero-positive. It is concluded that all pregnant women who have ever had syphilis should be retreated and the authors favour giving a combination of heavy metal, arsenic, and penicillin throughout the second half of pregnancy.

[From the figures given one could argue that penicillin alone is an adequate drug for the prevention of congenital syphilis. It is not mentioned whether a sero-positive reaction at birth without clinical or radiological support is taken as prima facie evidence of congenital syphilis. If the mother is sero-positive but was treated during pregnancy, such infants need only serological observation; the majority will be sero-negative within 3 months, thus showing it to be a harmless transient phenomenon.]

G. W. Csonka


The authors have now treated 603 patients with
neurosyphilis with penicillin at the University of Pennsylvania School of Medicine, 124 of whom had paresis, 122 meningovascular syphilis, 229 tabs dorsalis, and 128 asymptomatic neurosyphilis. An analysis of their increasing experience has been made almost annually since the first patient was treated in 1943, and 207 patients have now been observed for 3 years or more. Before treatment 74 per cent. of patients had a type-III, 13-6 per cent. type-II, 3-8 per cent. type-I, and 8-6 per cent. a normal cerebrospinal fluid. The dose of penicillin was 5,000,000 units or less in 259 cases, and more than this amount in the remainder; 389 patients had only one course and 214 more than one course, while 473 received aqueous penicillin and 130 were given slowly absorbed preparations.

At 1 to 2 years after treatment the spinal fluid was normal or near-normal in 52 per cent. of cases, which figure had increased to 72 per cent. at 4 to 5 years. The rate of spinal-fluid improvement tended to level off by the third to fourth year and only about 5 per cent. of relapses were noted after this time. Increasing the total dose of penicillin or repeating the course did not seem greatly to influence the result. The desired maximum dose which should be given in one course appeared to be in the region of 5,000,000 units, and repetition of the penicillin course only brought about a further 3 to 5 per cent. improvement. Procaine penicillin G proved quite as effective as aqueous penicillin G. The results obtained with metal chemotherapy in pre-penicillin days in 146 patients are also presented. It is considered that a similar type of spinal-fluid response was obtained in these cases, but that the maximum effect occurred 2 years later than when penicillin is used.

R. R. Willcox

The Spirochaetidal Value of Soviet Penicillin. 

Russian-made penicillin was used in the treatment of twenty-four women with primary, and thirty with secondary, syphilis, 40,000 units being given 3-hourly by intramuscular injection. Smears were made and examined for spirochaetes at hourly intervals after beginning penicillin treatment. Spirochaetes disappeared after an average interval of 10-6 hours; there was no essential difference from the results of the treatment of 45 cases with American penicillin, in which spirochaetes disappeared after 10-9 hours. Disappearance was noted after an average of 10-8 hours in thirteen patients treated with American crystalline penicillin G. The time taken for spirochaetes to disappear depends also upon the nature of the lesion, being longer in ulcerative lesions and in the presence of much infiltration; it also depends upon the age of the patient, the shortest times being found in those below 20 years of age. A Herxheimer reaction occurred in 74 per cent. of patients treated with Russian penicillin; its occurrence was usually associated with an acceleration of the rate of disappearance of spirochaetes. During the course of penicillin treatment the spirochaetes showed abnormalities of form and motility.

D. J. Bauer


Bismuth penicillin is a whitish, crystalline substance consisting of three molecules of penicillin combined with one atom of trivalent bismuth; its correct chemical name is therefore bismuth tripencillinate or tripencillate. Its molecular weight is approximately 1,209 and it has a theoretical bismuth content of 17-29 per cent. The preparation used by the authors was a suspension in 2 per cent. aluminium monostearate gelled in sesame oil, and contained 0-255 mg. bismuth per 1,000 units penicillin. For clinical trials it is suggested that doses of 400,000 to 600,000 units, containing approximately 0-1 to 0-15 g. bismuth, be used.

Rabbits were inoculated intra-testicularly with the Nichols-Hough strain of Treponema pallidum, and treatment was instituted 6 weeks later in those which had acquired a dark-field-positive orbitis. Dark-field examinations were later made on eleven occasions at intervals ranging from 1 to 70 days after treatment, at which time lymph-node transfer was made into fresh rabbits which were observed for a further 4 months. Ten rabbits were given single graded doses of 5,000 to 100,000 units of bismuth penicillin per kg. body weight, and the minimum curative dose was found to be in the region of 5,000 units per kg., while in a similar series treated with a single dose of sodium penicillin G in oil and wax the minimum curative dose was 10,000 units per kg. Two further groups, each of ten rabbits, were treated with the two preparations, this time 800 to 16,000 units per kg. being given in eight daily injections. With penicillin in oil and wax the minimum curative dose was approximately 8,000 units per kg., but with bismuth penicillin it was reduced to 4,000 units per kg.

R. R. Willcox


A total of 639 patients with neurosyphilis have been treated during the 5 years since the introduction of penicillin therapy at the University Hospital, Ann Arbor, Michigan. A report is now issued on its effect on 430 of these patients who have been adequately observed. One-half of the number were treated with penicillin and malaria, and one-half with penicillin alone, and 30 per cent. of the patients have been observed over a period of 4 to 5 years. The series includes cases of meningovascular syphilis, asymptomatic neurosyphilis, paresis, and tabs dorsalis, with a preponderance of the last two types. Penicillin therapy consisted of a total dose of 4,000,000 units, given over 12½ days; malaria therapy consisted of 50 or more hours of fever above 103-5° F. (39-7° C.).

Details of the type and degree of improvement observed in the cerebrospinal fluid are set out in graphic form. The cell count and protein content, when increased, returned to normal figures within 3 to 9
months. The colloidal gold reaction became normal in 18 to 36 months. The Kahn test, however, remained positive in many instances for a longer period, and at the end of 4 to 5 years only 40 per cent. of patients had achieved a negative result. In general the attainment of a normal C.S.F. was not necessarily related to clinical recovery. There appeared to be little difference between the efficacy of penicillin with and without malaria except in the group of paretics, in which penicillin-malaria therapy gave superior results.

Necropsy observations on the brain were made in four cases [type of neurosyphilis not stated]. In two patients who died during treatment ample evidence of active neurosyphilis was found. Two patients died 2 years after treatment, and the brain in these cases showed little or no histological evidence of neurosyphilis.

The authors conclude that penicillin alone is adequate for all types of neurosyphilis except, possibly, severe paresis and primary optic atrophy.

V. E. Lloyd

Results of Penicillin Treatment in Congenital Syphilis.


This report concerns 142 previously untreated cases of congenital syphilis in patients ranging in age from 1 month to 31 years, who were treated, in the case of infants with 100,000 to 600,000 units of penicillin per kg. body weight, and in the case of children over 11 and adults, with 2-4 to 8-0 mega units, given in individual doses of 15,000 to 50,000 units every 2 to 3 hours for 5 to 32 days. Of the 142, 75 were subsequently followed up for more than 2 years.

Of 37 patients under 2 years of age at the time of treatment, all were free of symptoms and serologically negative 2 years later and none had relapsed. On the other hand, of the 38 who were over 2 years of age, 91-3 per cent. were sero-positive at 2 years, and two patients, both over 10 years of age, required re-treatment on account of a recurrence of interstitial keratitis. The first of these was successfully re-treated with penicillin, but the second, in spite of receiving a further 8 mega units of penicillin plus 33 hours of fever over 104° F. (40° C.), relapsed a second time 6 months later. Five patients had an abnormal spinal fluid before treatment, but when tested again 6 months to 2 years after treatment a normal fluid was found in two and a near-normal fluid (with a positive Kolmer reaction) in the remainder.

R. R. Willcox

The Effect of Previous Antisyphilitic Treatment on Present Treatment, as Indicated by the Records from the Nation-wide Study of Penicillin in Syphilis. RIDER, R. V. (1950). Amer. J. Syph., 34, 581. 5 figs.

An attempt was made to determine, by the examination of existing records at the Central Statistical Unit at the Johns Hopkins University, Baltimore, whether treatment for syphilis with inadequate dosage makes subsequent treatment with standard dosage less effective. Graphs are presented of cumulative clinical and total failure rates amongst coloured and white patients treated with amorphous and crystalline penicillins, classified according to whether previous treatment had or had not been given. In the group treated with amorphous penicillin, there were 1,056 Negroes and 333 whites who had previous treatment, and 2,128 Negroes and 671 whites who had not. Of those treated with crystalline penicillin G, 444 had had previous treatment and 1,828 had not. In the latter group no difference was noted between those previously treated and the others, the cumulative failure rate being in the region of 15 per cent. at 2 years and under 20 per cent. at 30 months. In those treated with amorphous penicillin, however, there was a slight tendency for those treated for the second time not to do as well as those treated for the first time, the difference in cumulative failure rates amounting to 5 to 10 per cent. at 2 years. When the figure of those treated a second time was adjusted to include only those treated for the same syphilitic infection this difference became much more noticeable.

R. R. Willcox


The difficult problem is discussed of assessing the merits of neoarsphenamine when combined with penicillin and bismuth in the treatment of early syphilis. Before the autumn of 1947, 561 patients were treated for primary and secondary syphilis with penicillin, neoarsphenamine and bismuth. After that date, 183 similar cases were treated with penicillin and bismuth alone. The results of the two series are presented.

The first series consisted of 336 men and 225 women, of whom 145 had sero-negative primary, 199 sero-positive primary, and 217 secondary syphilis. Of these, the first 275 were given a total dose of 2-4 to 4 million units in 7½ to 12½ days, and a course of neoarsphenamine and bismuth lasting from 6 to 10 weeks. One-third of the males and half the females were admitted to hospital and given 40,000 to 75,000 units of amorphous penicillin 3-hourly or 4-hourly for 7½ to 12½ days, while the rest were treated as outpatients with penicillin in oil-beeswax mixtures. The remaining 286 patients received 2-4 to 5 million units in 8 days (500,000 to 600,000 units in oil-wax daily) followed by 4-0 to 4-5 g. neoarsphenamine (0-45 g. every 4 days) and 2-0 g. bismuth (0-2 g. every 4 days). The toxic effects from bismuth and penicillin were unimportant, but those due to neoarsphenamine were comparatively numerous. These numbered 150, but this included seventeen men and one woman with jaundice, which the authors attribute to the virus of homologous serum jaundice although the syringes and needles were boiled for 15 minutes. In all, 39 patients defaulted and ten were reinjected. Among the remaining 512 cases there were twelve failures, four clinical and six serological relapses, and two doubtful neuro-failures. The successful 500 became sero-negative within a year.

The second series consisted of 123 men and sixty women, of whom 34 had sero-negative primary, 49 sero-positive primary, and 100 secondary syphilis.
Of these patients 172 received 4.8 million units (double the dosage given in some cases in the earlier series) of penicillin in oil-beeswax mixtures in eight daily injections of 600,000 units, followed by weekly or bi-weekly injections of 0.2 g. bismuth oxychloride, 151 patients being given 1.5 to 2.5 g., and 32 less than 1.5 g.

The remaining eleven patients received the same total dosage of penicillin and bismuth, but aqueous, instead of oil-wax, penicillin was injected 2-hourly. There were no adverse side-effects except a few cases of urticaria. In this series 55 patients defaulted in less than 3 months. The remainder (128) all became sera-negative within 12 months. The authors list twelve failures: seven potential serological failures (six defaulted within 10 months) and five potential clinical failures. These five patients all admitted re-exposure to infection and were probably re-infected, but the authors generously class three of them as relapses and only two as re-infections.

As only a little more than half of the total number of cases in both series were observed for 12 months or more, and as 7.5 per cent. of them defaulted while still sera-positive, the authors do not attempt to calculate a percentage failure-rate. They think, however, that the end of the arsenical era may be at hand if penicillin-resistant strains do not appear.


After summarizing the results reported in the literature by various authors of the treatment of early syphilis with arsenicals and heavy metals, the authors of this article record their own results in 771 patients treated during the period 1921–33. Of the 771 patients, 467 (60.6 per cent.) were followed up for less than 5 years, 98 (12.7 per cent) for 5 to 16 years, and 206 (26.7 per cent.) for more than 16 years; the total number followed up for more than 5 years was thus 304 (39.4 per cent.) and these patients form the basis of the report. The diagnoses in these cases were: sera-negative primary syphilis, 32 (10.6 per cent.); sera-positive primary syphilis, 71 (23.2 per cent.); secondary syphilis, 201 (66.1 per cent.). Treatment was 0.4 g. arsenamine weekly for 6 weeks, followed by 4 oz. (113 g.) mercurial ointment by inunction and 3 g. potassium iodide by mouth, daily for 8 weeks; then 3 weeks’ rest, after which the course was repeated until serum reactions became negative and remained so for a year, and clinical signs disappeared. During the latter half of the period under review arsenamine, 0.4 g. weekly, and bismuth subsalicylate, 0.15 g. weekly, were given in alternating courses of 8 weeks, and mercury and iodides were discarded.

At the end of 2 years, of 64 patients who had received fewer than six injections each of arsenic and bismuth, thirty were cured, and 32 had latent and two clinical syphilis; of 240 who had received more than six injections, 168 were cured, and 58 had latent and fourteen clinical syphilis. Of the 98 patients followed up for 5 to 16 years, 27 received fewer than six, and 71 more than six injections; of the former sixteen were cured, and ten had latent and one clinical syphilis, while for the latter the figures were 56, two and three respectively.

Of the 206 patients followed up for 16 to 29 years, 37 received fewer than six and 169 more than six injections. The results in the former were: cured 24, latent seven, clinical syphilis six. The results in the latter were: cured 153, latent seven, clinical syphilis nine. There were ten deaths in this group, one due to paresis. Of the 304 patients, nineteen had active clinical syphilis (three of the central nervous system, one of the skin, four of the aorta, and one of the eye) at the time of final observation—a total morbidity and mortality of 6.2 per cent. Of the ninety patients who had had early latent syphilis after 2 years’ observation, 47 were clinically cured, and 43 of these had a reversal of the serum reaction at the time of final observation.

Of the total of 771 patients treated, serious treatment reactions occurred in 38 (4.9 per cent.), including nitritoid reactions in 21 cases, exfoliative dermatitis in 9, and hepatitis in six (with two deaths). Of sixteen patients with early relapsing syphilis, four had mucocutaneous, and twelve early central nervous system, relapse; three of the former and six of the latter were cured with ten to 36 injections of arsphenamine and eighteen to 41 of bismuth. A comparison between this series and the well-known untreated series of Bruusgaard shows that treatment greatly reduces the incidence of lesions of the cardiovascular and central nervous systems, the figures being 1.3 and 12.8 per cent. respectively for cardiovascular syphils and 4.2 and 9.5 per cent. for syphilis of the central nervous system. The cure rate with treatment was 81.6 per cent. and without treatment 27.9 per cent. The above results suggest that it is worth while continuing therapy over long periods with modern agents in order to prevent relapse or progression of the disease.

**GONORRHOEA (General)**


Not more than half of 240 cases of vulvovaginitis in infants and children were found to be gonococcal in origin. As in adults, culture was found to be the most reliable method of diagnosis. The most common symptom was a sero-purulent vaginal discharge, occasionally bloodstained. Dysuria was also common and vulval irritation was a prominent symptom. Retcht symptoms were infrequently observed but they were a most important group, as hidden rectal infection was the most common cause of relapse or re-infection. Complications were uncommon, ophthalmia and arthritis being seen only occasionally. Troublesome associated trichomonad infection was sometimes encountered. By far the most satisfactory results were obtained by treatment with either sulphonamides or penicillin, the average duration of treatment in each case being 4 to 6 days. Resistance of the organism to either drug was dealt with satisfactorily in most cases by changing from one to the other and, if necessary, by giving oestrogens at the same
time. This hormone therapy, producing vaginal cornification and resistance to infection, has been found most useful in difficult cases or in relapse. Comparably good results were obtained with oral, parenteral, or local oestrogen treatment.

C. J. Dewhurst

Gonococcal Rheumatism as a Clinical Entity. (Le rhumatisme blennorragique n'est pas un vain mot.)


GONORRHOEA (Pathology)


The presence of non-pathogenic Neisseria in the urinary tract of healthy adults is described. Of 43 cultures, twelve were identified as Neisseria subflava and 31 as N. sicca. Most of the plates containing the organisms showed only a very small number of colonies per plate and with one exception every attempt to isolate them in subsequent cultures from the same patient failed. The non-pathogenic Neisseria showed larger, more pigmented, colonies and gave the oxidase reaction as a black ring at the periphery of the colonies. In stained smears the cocci showed great diversity of size and were often arranged in close packets. The colonies were easy to isolate as they were not overgrown by contaminants.

G. M. Findlay

GONORHROEA (Therapy)


The effect of combining oral penicillin with oral sulphonamides was investigated on the cure rate of acute gonorrhoea. Over a 5-day period a total of 500,000 units of penicillin was given by mouth together with 16 g. of a sulphonamide mixture. The mixture was composed of 2 g. sodium citrate, 0.5 g. sulphadiazine, and 0.5 g. sulphamerazine in 10 ml. water. Of 47 patients receiving the mixture, 44 were cured. When a dose of 300,000 units penicillin was given together with the sulphonamides the cure rate was lowered. A similar result was obtained when a dose of 500,000 units was given alone. There is no evidence that the addition of the sulphonamides to the penicillin increases either the blood level of the antibiotic or the duration of the penicillin in the blood. It is concluded that the sulphonamides act synergistically with the penicillin.

[No mention is made of the sensitivity of the gonococci to sulphonamides.]

G. M. Findlay


Terramycin, an antibiotic prepared from Streptomyces rimosus, was given by mouth to 24 patients with gonorrhoea, all but one of whom were Negroes. After observation for one week there were three failures among six patients given a single dose of 1 g., but among the remaining eighteen, who were given 2 g., there were only four failures. Three patients vomited ½ to 4 hours after swallowing the drug; two of them were unable to retain a second dose and were treated again with penicillin.

R. R. Willeox

Treatment of Gonorrhea with Chloramphenicol (Chloromycetin).


A series of 96 male patients with acute gonorrhoea was treated with single doses of chloramphenicol. The criterion of cure was the finding of three negative smears and cultures taken during the comparatively brief post-treatment period of 7 to 10 days; seventy cases were followed up for this period.

Of four patients receiving a single dose of 250 mg., only one was considered cured; of sixteen given a single dose of 500 mg., twelve were considered cured; of fifty receiving 750 mg. the outcome was satisfactory in no less than 48.

The danger of masking syphilis by chloramphenicol treatment is considered to be about as great as with penicillin. A single dose of 250 mg. was found to be insufficient to banish Treponema pallidum from the positive lesions of primary and secondary syphilis in three patients, while the spirochaetes were still motile after 96 hours in one of two cases given 500 mg., but had disappeared after 48 hours in the other.

R. R. Willeox

The Treatment of Various Infections with Terramycin.


This paper reports the results of treating 171 patients with various infections with terramycin. In most of the adults terramycin hydrochloride was given in doses of 2-0 g. initially, followed by 0-5 g. every 4 hours. Children were given 50 mg. per kg. body weight per day. The treatment was successful in 46 out of 48 patients with pneumococcal pneumonia (two died), fourteen with streptococcal infections, seven with acute gonococcal urethritis, seven out of twelve with urinary-tract infections, three with Vincent’s infections, and one case of herpes zoster, out of a total of 59 cases of virus infections, and in 22 out of a group of 28 miscellaneous cases. No serious toxic reactions were observed, although 25 per cent. of the patients had gastro-intestinal symptoms, and one patient had transient vertigo. The drug had to be discontinued in seven cases because of vomiting.

A. W. H. Foxell

OTHER VENEREAL DISEASE CONDITIONS

Forms of Inclusion Urethritis and Their Pathological Relationships: the Syndrome of Reiter, Fliessinger and Leroy: Fanconis Syndrome and Atypical Pneumonia.

(Le uroturies à inclusions et leurs parents morbidés :
Inclusions simultaneously. Symptoms.

There were symptoms with diarrhoea and dysentery and also a vaginal discharge without cystitis. Gonococci were absent from the vaginal discharge but scrapings from the urethral mucosa contained cells with cytoplasmic inclusions.

In the third paper the case of a market-gardener with non-specific urethritis is discussed. He was accustomed to collect human faeces from the privies of his neighbour and to use these faeces, undiluted, for the intensive culture of vegetables. He developed fever (temperature 40°C.), sore throat, and cough, and when these had subsided a non-specific urethritis. [The only evidence in favour of the faecal source of his infection is the presence of pneumonialike organisms, non-pathogenic, have been found in soil and in manure.]

In the fourth paper a typical example of Reiter's syndrome is described in a man aged 42 years. Urethral discharge without gonococci, swollen joints, balanitis, and keratoderma were present but there was no eye involvement. There was no history of any diarrhoea or dysentery and no agglutinins for dysentery bacilli were present: the serological reactions for syphilis were negative and cold agglutinins were absent. The temperature was 37.5°C. to 38.0°C. and at the same time a cough developed with fine crepitations and rales scattered over the left lung. Radiography revealed first, thickening in the left hilar region and then, as the other clinical symptoms disappeared, a diffuse peribronchial infiltration of the left lower lobes unaccompanied by any clinical symptoms. These pulmonary signs cleared up spontaneously. Inclusions were found in the cytoplasm of mononuclear cells in urethral scrapings. Aureomycin failed to improve the symptoms, except the balanitis, in this patient but the symptoms began to clear up when dihydrostreptomycin was combined with p-aminosalicylic acid (PAS). Dihydrostreptomycin was given intramuscularly in doses of 1 g. daily, PAS daily by mouth in a dose of 10 g. sodium salt. A slight urethral discharge still persisted but this is said to have disappeared on administration of an antigen formed from the urethral pus.


Oral (but not parenteral) administration of aureomycin is very effective in granuloma inguinale. The minimum effective dose appears to be 20 g. over 10 days, but prolonged therapy is necessary for patients with extensive lesions.

In lymphogranuloma venereum aureomycin was more valuable in late cases than in relatively early cases with buboes. Proctitis responded well. Daily manual dilatation of rectal strictures during aureomycin treatment gave good results and reduced the need for colostomy. Ulcerative lesions responded poorly. The minimum effective dose for buboes was 20 to 30 g. given in 0.5-g. doses four times daily; in cases of proctitis and stricture 40 to 80 g. or more was required.


Good results are reported in the treatment of all stages of chancroid with 4 to 6 g. streptomycin (in doses of 0.5 g. twice daily) without other medication. Check examinations showed that Ducrey's bacillus disappeared in 3 to 6 hours.
Effectiveness of Antichancroidal Drugs Tested by Hetero-
inoculation of Bubo Fluid from Untreated Donor.

Antichancroidal drugs were tested in ninety volunteers by assessing their power of preventing experimental infection after inoculation with virulent bubo fluid. Of the preparations so tried, sulphathiazole, streptomycin, aureomycin, and chloramphenicol gave efficient protection (of 36 persons, 33 were completely protected, three showing doubtful reactions). Antimony, bismuth, and neoarsphenamine proved ineffective. Of the thirty controls, 27 developed a pustule at the site of inoculation. Penicillin was only effective if a high concentration was maintained in the serum. Thus, of those receiving a single injection of 2,400,000 units of procaine penicillin in aluminium monostearate, only 50 per cent were “protected”, as against 100 per cent. of those receiving a daily injection of 600,000 units of penicillin in oil and wax for 8 days. Penicillin (400,000 to 600,000 units over 3 to 4 days) given orally “protected” three out of four and appears to have some prophylactic value.

[This appears to be a novel way of testing antichancroidal drugs, and provides clear results in a short time.]

G. W. Csonka

Granuloma Inguinale and its Treatment with Oral

Granuloma inguinale was first described by Conger and Daniels in 1896 as occurring amongst the Negroes of British Guiana; since then reports have indicated that this troublesome condition is endemic throughout the entire Southern United States. This paper concerns seventeen Negro patients from South Carolina, in smears from whose lesions Donovania were demonstrated. They were treated with 25 g. aureomycin, given in doses of 500 mg. 6-hourly for 12 ½ days. (In three cases slightly less than this amount was given and in two the treatment time was extended to 15 to 16 days.) Nausea with or without vomiting occurred in eight cases. In four these symptoms were very slight, and they were minimized in the others by the ingestion of aluminium hydroxide. The follow-up period varied from 1 to 7 months. One relapse was noted 25 days after treatment: this patient was re-treated with the same dose and remained well 6 months later. One patient received a second course of aureomycin 1½ months after the first had been given, because the lesions had not completely healed, although no Donovan bodies could be demonstrated in the smears. The lesions healed and the patient was well when seen again a month later.

R. R. Willcox

New Antibiotics (Streptomycin and Aureomycin) in
Advanced Cases of Nicolas-Favre Disease. (Essai des nouveaux anti-biotiques (Streptomycine et Aureo-
mycine) dans les cas avancés de maladie de Nicolas-

The results of sulphonamide and penicillin treatment in lymphogranuloma venereum were disappointing. Streptomycin, 1 g. daily for 4 to 6 months, was given in four cases in which there were bilateral inguinal buboes, the average total dose being 180 g. The action of streptomycin is very slow, but sure. In two cases, after streptomycin had been given for about one month, aureomycin was substituted with remarkable results. Aureomycin alone was then given in seven long-standing cases with vaginitis, rectal stenosis, proctitis, and multiple fistulae. It was injected intramuscularly as a 1 per cent. solution in physiological saline. Injections containing 15 mg. were given once, twice, or even thrice daily. The results are said to have been remarkable. Total dosage was from 225 mg. to 3 g.

G. M. Findlay

Lymphogranuloma Venereum with Arthritis of the Hip-

Lymphogranuloma venereum is a generalized infection and the virus may on occasion involve the joints. In a case with a large bubo in the left inguinal region there was pain on moving the left hip-joint. X-ray examination showed decalcification of the epiphysis of the femur and changes in the acetabulum. The patient was cured by three courses of sulphadiazine by mouth.

G. M. Findlay

Terramycin and Aureomycin in Rectal Stricture Due to
Lymphogranuloma. (Influéncia da terramicina e da
aureomicina no aperto rectal de origem linfor-

Four patients with stricture of the rectum and positive Frei tests were given terramycin or aureomycin every 6 hours. The terramycin was given for 7 days to a total of 100 capsules [each of 250 mg.]. Both antibiotics caused remarkable improvement in the symptoms.

G. M. Findlay

Reiter's Disease : a Case Successfully Treated with

The case is reported of a man, aged 20, who first came under treatment at the Boston City Hospital in 1944 with urethritis, conjunctivitis, and arthritis of the left knee. He was treated with sulphadiazine, apparently with success. Later that year the urethral discharge, conjunctivitis, and arthritis recurred, and he was again admitted to hospital. Investigation showed a leucytosis of 12,000 per c.mm., but the condition responded to sulphadiazine as before. He was admitted for a third time in 1946 with urethritis and a swollen left knee, and, shortly afterwards, the conjunctivitis again became evident. This time he was treated with penicillin and was discharged from hospital 13 days later. The condition recurred, however, after 2 months, with urethritis, conjunctivitis, and a swollen left heel. He was then treated with aureomycin, 100 mg. per kg. body weight being given in the first 24 hours, followed by 75 mg. per kg. daily for one week, after which time the
daily dose was reduced to 50 mg. per kg. [total dose not stated]. Improvement was immediate and the urethral, eye, and joint symptoms cleared by the third day. When seen 25 days later he was apparently well.

It is claimed that this is the first recorded case of Reiter's disease treated with aureomycin. [No investigations for pleuro-pneumonia-like organisms are reported as having been undertaken either in the patient or his consort(s).]

[Reiter's disease is attracting increasing attention in the U.S.A. at a considerable interval after similar interest was aroused in Great Britain. It is noteworthy also that in the U.S.A. non-specific urethritis is regarded as much less of a problem than it is in Great Britain.]

R. R. Willcox


Five Negresses with granuloma inguinale of the vulva received 13 to 40 g. streptomycin intramuscularly in divided doses over a period of 4 to 6 days. There were no toxic symptoms and there was subjective improvement in each case within 48 hours, with evident healing by the sixth day. There were no recurrences in a follow-up period of 2 to 10 months. Two women became pregnant; one delivery was normal, although previously the granuloma inguinale had made intercourse impossible; the other was by Caesarean section to avoid injury to the scarred and fibrotic vagina.

Three women with granuloma inguinale of the cervix received 4 g. streptomycin daily for 5 days. Symptoms disappeared in 2 weeks, and the appearance of the cervix was much improved, although one was left with a small superficial ulcer, and in two a chronic non-specific cervicitis which responded to conization. Pathological examination of the two latter revealed no Donovan bodies. Margaret Paxson


MISCELLANEOUS

Genito-urinary Lesions in Schistosomiasis Mansoni. (Lesões geniturinárias na esquistossomose mansoni.) FREITAS ARMBRUST, A. de. (1950). Hospital, Rio de J., 38, 177. 9 figs, bibl.

Manson's schistosomiasis, in Brazil, usually affects the portal system and the liver, and is accompanied by splenomegaly. There is no doubt, however, that it frequently infects the genito-urinary tract as well. The kidney is very rarely attacked, but the lower third of the ureter is frequently involved to such a degree that the lumen may become completely blocked. The bladder is the organ most frequently attacked, specially around the trigone; the membranous urethra also suffers. Other organs involved are the prostate, seminal vesicles, spermatic cord and epididymis, testis, and penis; the female genital tract may sometimes also be affected.

Most of this article is devoted to a survey of the literature dealing with the various aspects of schistosomiasis in all these organs. The author then describes four cases. In the first encysted eggs were found in the cortex of the kidneys. The second patient complained of scrotal swellings of 20 years' duration; biopsy examination of the testicle showed cysts which were surrounded by lymphocytes, plasma cells, and eosinophils; the eggs were easily recognized as having lateral spines, and some were calcified. The third patient was a woman who underwent hysterectomy, eggs being found in the Fallopian tubes; these were surrounded by epithelioid cells, and there was giant-cell formation as well. The fourth case was one of infected seminal vesicles. The author thinks that the kidneys suffer little when infected with S. mansoni; the infection is almost certainly blood-borne, for one egg was found in the afferent artery to a glomerulus (compare the origin of pulmonary bilateral infection with S. haematobium). In severe cases a septicæmia must exist. Paul B. Woolley


Terramycin is a yellow crystalline substance obtained from Streptomyces rimosus, and used in the form of the hydrochloride. It can be given either by mouth or parenterally, and the only toxic symptoms seem to be diarrhoea and occasional nausea and vomiting. The dose is about 2 g. per day.

The present paper deals with its use in four cases of active and "infectious" yaws. The first two patients received the drug thrice daily by mouth, and the second two twice daily. It was considered wise to omit the nocturnal doses, in view of the possibility of using the drug on a large scale in the endemic rural areas. Within 24 hours there was less pain and inflammatory reaction, possibly due to the drug's action on intercurrent organisms. The active lesions were cured in from 6 to 16 days; as with other drugs, the cicatricial lesions took longer to disappear. Spirochaetes were found after 72 hours only in one case, but the reaction to the Wassermann test, as would be expected, remained positive 20 days after treatment.

The total doses used were 5 to 15 g. (ages 2 to 22 years) over a 10-day period. The therapeutic results were similar to those of penicillin, but the spirochaete does not disappear so rapidly as with the latter. The value of the drug is obvious, and its employment is being extended by the authors. Paul B. Woolley


A housewife, aged 33, complained of an eruption on the arms and trunk. At the age of 15 she had contracted syphilis and had received an intensive course of anti-syphilitic treatment; at the age of 20 she had had pleurisy with effusion. The eruption had started on the right
arm 18 months before she was seen. It spread to the other arm and to the trunk. It was an extensive, papulo-nodular, erythematous, and violaceous rash with grouped lesions. Extensive pathological investigations were undertaken, the findings being as follows: Wassermann reaction, 4 plus; Kline reaction, 4 plus; radiograph of chest, normal; intracutaneous tuberculin tests: 1 in 1,000,000, 1 plus; 1 in 100,000, 1 to 2 plus; 1 in 10,000, 2 to 3 plus; B.C.G. vaccination, visible reaction in 24 to 48 hours, proceeding rapidly through all stages to scarring. Histological examination revealed the picture of sarcoid without giant cells. Penicillin, 11,300,000 units in 4 weeks, was administered. The eruption cleared rapidly and, at the end of the course of treatment, only very slight erythema and pigmentation remained.

This case supports the view that sarcoid is a clinical and histological entity which may occur during, or as an expression of, several infectious diseases and some non-infectious disease mechanisms. E. Lipman Cohen


The action of penicillin, aureomycin, and terramycin, alone and in combination, on *Streptococcus pyogenes* and *Klebsiella pneumoniae* was examined by inoculating 1 ml. of an 18-hour broth culture of the test organism (10^7 to 10^4 cells) into 19 ml. broth containing the antibiotics in various concentrations and proportions. During incubation at 37°C. 0.5-ml quantities were removed at intervals and viable counts made.

The results showed that concentrations up to 10 to 50 μg. aureomycin or terramycin per ml. interfered with the bactericidal action of penicillin on *S. pyogenes*. No interference could be shown if the first two substances were present in concentrations in which they were themselves bactericidal. The addition of a bacteriostatic concentration of aureomycin or terramycin to a bactericidal concentration of penicillin greatly decreased the death-rate for *K. pneumoniae* during the first 7 to 12 hours. After 27 hours, however, the organisms exposed to such a mixture were no longer viable, whereas organisms exposed for a similar period to the same concentration of aureomycin or terramycin alone were likely to multiply. A similar interference with the action of penicillin in vivo has been demonstrated in preliminary experiments with mice.

It is suggested that since penicillin acts mainly on dividing cells, its bactericidal power may be impaired if cell division is inhibited by bacteriostatic concentrations of the other two antibiotics.

[This paper presents yet another argument against “blunderbuss” antibiotic therapy.] J. E. M. Whitehead


A strain of *Bacterium coli* and a strain of *Staphylococcus pyogenes* were made resistant to chloramphenicol or aureomycin by subculture in increasing concentrations of the antibiotic. It was found that with the development of resistance to one, there was a small simultaneous increase in resistance to the other substance and also to terramycin. The mechanism of cross-resistance to antibiotics is discussed. J. E. M. Whitehead


Terramycin is a pure amphoteric compound obtained from a soil actinomycete, *Streptomycyes rimosus*. In contrast to aureomycin, it is relatively stable in solution, the sodium salt having an alkaline and the hydrochloride an acid reaction. Terramycin has a wide bacterial spectrum and is highly active in vitro against Gram-positive cocci and Gram-negative bacilli, inhibiting the growth of many of these organisms at concentrations of 0.25 to 0.5 μg. per ml. Most strains of *Pseudomonas pyocyanea* are relatively sensitive to concentrations as low as 5 to 15 μg. per ml., but *Proteus vulgaris* is highly resistant. The drug is administered orally in doses of about 50 to 70 mg. per kg. body weight daily. Therapeutic levels in the blood are usually maintained after such a dose for about 6 hours, and this is the recommended dosage interval for most purposes; it is, however, excreted in high concentration in the urine and adequate urinary levels can be maintained with a dose of 50 mg. daily. Therapeutic levels can be maintained in serious effusions, but penetration into the cerebrospinal fluid is very poor. On oral administration of 1 g. 6-hourly to eight patients, striking changes were seen in the intestinal flora, the normal picture being replaced by a heavy growth of *P. vulgaris*, *P. morganii*, or a yeast. After the first 24 hours concentration of the drug in the faeces ranged from 500 to 4,000 (average 1,250) μg. per g.

In a small clinical trial the authors treated thirteen cases of urinary infection, four cases of superficial skin infection, and four patients with post-operative infective complications, all of which responded well. A satisfactory response was also obtained in one of two cases of ulcerative colitis. Toxic symptoms occurring among the 33 patients who received the drug for 5 or more days, included gastro-intestinal disturbances in thirteen cases (severe in one only), an erythematous rash in one, and possibly a sore throat in one case. Terramycin was better tolerated when given with milk.

[This is the first report on terramycin that has been published in this country and should be read in the original by all those interested in antibiotics. Terramycin should prove to be a useful addition to the drugs available for treatment of a wide variety of conditions, but supplies are certain to be very limited for some time to come.] A. W. H. Foxell


Urinary tract infections in 32 women with obstetrical or gynaecological conditions were treated with terramycin.
Results were classified as "good" if the patient was afebrile and symptomless and the urine pus-free and sterile within 72 hours of starting treatment, "equivocal" if more than 72 hours was required or bacilluria with minor symptoms persisted, and "poor" if the course of the infection was unaltered. Of 27 cases without obstructive or other predisposing renal-tract lesions, results were good in 24 and equivocal in three; of five with such lesions, they were good in two, equivocal in one, and poor in two. Good results were obtained in nineteen of twenty-two infections due to *Bacterium coli* or *Aerobacter aerogenes*, but in only one out of four due to *Pseudomonas aeruginosa* (the other infections were due to: *Proteus vulgaris*, 1; *Staphylococcus albus*, 2; aerobic diphtheroids, 3; aerobic non-haemolytic streptococci, 2). Sensitivity tests were carried out *in vitro* on forty organisms isolated from urine; only two out of twenty strains of *B. coli* and *A. aerogenes* were resistant to 50 μg. per ml. terramycin, as compared with nine out of eighteen strains of *P. aeruginosa*. Comparative tests on nineteen organisms showed no gross disparity between individual sensitivities to aureomycin, chloramphenicol, and terramycin. The authors give no details of the doses of terramycin used in the present investigation, but suggest the following schemes: (1) for uncomplicated cases infected with *B. coli* or *A. aerogenes*, 250 mg. 6-hourly for 5 days, then twice daily for 5 days; (2) for cases infected with *P. vulgaris* or *P. aeruginosa*, or having other urinary-tract lesions, 500 mg. 6-hourly for 5 days, then 250 mg. 6-hourly for 5 days.

[It seems scarcely justifiable to base a recommendation for the treatment of *P. vulgaris* infections on experience with a single case.]

H. McC. Giles

**Clinical Observations in Gynaecological Infections with *Bacillus funduliformis*.** (Klinische Beobachtungen bei Funduliformis-Infektionen in der Gynäkologie.)


Since the isolation of *Bacillus funduliformis* by Halle in 1898 few cases of disease due to the organism have been reported. Most cases have been described by French observers, and the few cases of infection in the genital tract lack clinical detail. The present author describes cases which have been observed in the last 2 years. It was found that the organism was saprophytic in the vagina in health and disease. He examined 540 vaginal smears—many being taken from cases of abortion—and found the organism in 38 (7 per cent.). It was present in two cases of septic abortion, in one of which there was an abscess in the pouch of Douglas. In four cases of pyosalpinx it was in pure culture; in one of these there was marked pyrexia. In two others there was no pyrexia; the diagnosis in both these cases before operation was of fibroids. The fourth patient had remittent fever for 2 months and eventually tubercle bacilli were found.

In five cases the *Bacillus funduliformis* was present in association with other organisms, generally streptococci. In three of these there was prolonged pyrexia and pus formation. In one case in which the organism was recovered from the blood stream the illness was prolonged and severe, and there were numerous metastatic abscesses.

Gladys Dodds

**Survival of *Trichomonas vaginalis* in Vaginal Discharge.**


Earlier workers have established the fact that *Trichomonas vaginalis* can survive for a few hours at room temperature in dried specimens of vaginal discharge, and that most trichomonads survive for 24 hours in vaginal discharge kept at room temperature in cover-slip preparations sealed with paraffin, a few remaining active after


Of 1,014 female children at the Austin State School, Texas, 262 (25.8 per cent.) were found to have some degree of genital infection and the bacteriology of this was studied. In twelve of these children there was vulvo-vaginitis from which gram-negative diplococci were obtained, but these organisms proved to be *Nesseria sica* and not the gonococcus, though the gross findings in the tissues, as well as the stained smears, appeared the same as those in gonorrhoea.

The distinction between these two gram-negative intra- and extra-cellular diplococci depends on their cultural peculiarities and on fermentation tests, not on staining properties. The author therefore suggests that these methods of bacteriological diagnosis should be used in all suspected cases of gonorrhoea, but particularly in juvenile vulvovaginitis.

Donald Beaton


A standard medium for the isolation of pleuropneumonia-like organisms is described. It consists of "50 g. ‘bacto-beef’ heart for infusion in 1,000 ml. distilled water, to which is added 1 per cent. ‘bacto-peptone’, 0.5 per cent. sodium chloride, and 1.5 per cent. agar". The pH is adjusted to 7-8 per cent. before sterilization in the autoclave. Before the medium is poured into plates, 25 per cent. sterile human ascitic fluid or 10 per cent. mammalian serum is added to the cooled (50°C) melted basal medium; crystal violet 1 in 100,000 and potassium tellurite 1 in 50,000 are inhibitory to most bacterial contaminants. A total of 85 patients, fourteen females and 71 males, were examined, and seven women and fourteen men yielded positive cultures. There was arthritis associated with conjunctivitis, urethritis, or prostatitis in ten patients; prostatitis associated with iritis in two, and urethritis associated with iritis in two. Of these fourteen patients seven gave positive cultures. The possible venereal transmission of pleuropneumonia-like organisms is discussed. A husband and wife were cured with streptomycin.

G. M. Findlay
as long as 5 days. The authors of this paper collected vaginal discharge from fifty untreated patients with trichomonas vaginitis, *T. vaginalis* being found active in samples taken from a speculum immediately after its removal from the patient. Of these samples 0·1 ml. was inoculated immediately into 10 ml. Lash’s serum medium (Amer. J. trop. Med., 1948, 28, 111) to which 1·0 g. cysteine hydro-chloride per 1,000 ml. had been added in an attempt to diminish bacterial growth by reducing the oxygen tension. These cultures were incubated at 37° C. and examined after 48 hours, when subcultures were made. Another 0·5 ml. of the vaginal discharge was put on the emamelled surface of a wooden block, within a wax-pencil circle, and a small portion removed and examined for living trichomonas after 10, 20, 30, and 45 minutes, and 1, 2, 3, 4, 5, 6, and 7 hours. At each examination an equivalent amount was put in culture medium and examined after 48 hours’ incubation. For the first 5 hours the drops on the wooden block were moist enough to allow the making of smears, but at 6 and 7 hours the addition of saline was necessary for this purpose.

It was found that the trichomonads survived for 45 minutes in all of the 50 drops of vaginal discharge studied, and that they survived in 29 (58 per cent.) of these for 3 hours and in two (4 per cent.) for 6 hours. Although the authors did not transfer infection to volunteers from the vaginal discharges studied [they do not state whether this was actually attempted], such experimental infection has been shown to be possible with cultures, and they conclude from their results that *T. vaginalis* infection may be shown to be possible with cultures, and they therefore conclude from their results that *T. vaginalis* infection may be transmitted by fomites, such as towels, toilets, and washing cloths. 

G. Lapage


Continuing their studies of a hitherto undescribed type of lymphadenopathy (Pr. méd., 1950, 58, 282; Bull. Soc. méd. Hôp. Paris, 1950, 66, 424), the authors report their findings in 42 cases, of which 21 were due to scratching and biting by cats, while the other patients developed the condition after a prick with a thorn or a splinter. The result of these wounds was an intensive reaction in the lymph nodes nearest to the injury. The authors suggest that the condition be termed “benign lymphoreticulois”. In histological preparations they demonstrated a reticular proliferation associated with small abscesses. They suspect a virus to be the infective agent. On immunological examination of the pus they have distinguished six antigens producing an allergic reaction on intradermal injection in the affected patients, while in control patients, affected by an adenopathy of different origin, the reaction was completely negative. Serological investigation of thirteen patients with a complement-fixation test based on that used for lymphogranuloma venereum showed a deviation of complement in eleven cases. The authors are of the opinion that the agent of this benign lymphadenopathy belongs to the same virus family as those of lymphogranuloma venereum and psittacosis. They were, however, unable to identify the virus either by culture or by inoculation.

Franz Heimann


The fact that treatment of vaginal trichomoniasis by chemical means takes an average of 3 months decided the authors to perform laboratory tests, at the Institute of Parasitology of the Charles University, Prague, of the efficacy of ultra-violet irradiation in sterilizing cultures of vaginal flagellates in vitro. The apparatus used for the purpose consisted of a 300-watt quartz lamp placed inside a quartz cylinder 12 cm. long and 3·5 cm. in diameter, with water circulating between the lamp and the cylinder so that absolutely cold radiation was obtained. It was found that after a total irradiation time of 45 seconds no living flagellates were to be seen, and none could be cultured from a culture of *Trichomonas columbae* in which the lamp was immersed.

In subsequent clinical tests, thirteen patients were treated for vaginal trichomoniasis with ultra-violet contact irradiation, the apparatus described above being used, and in later cases being rotated inside the vagina to ensure even distribution. This dynamic method of irradiation was especially successful, all of six patients being cured after one irradiation of 55 sec. It is pointed out, however, that the length of irradiation is rather critical, and women between 20 and 40 years of age will not tolerate a treatment exceeding 50 sec. without developing serious lesions of the mucous membrane, while trials with periods of 80 and 90 sec. respectively produced very severe colpitis in two cases. Women immediately before and during the menopause will stand irradiation for up to 1 minute. In some cases improvement became manifest by a very rapid regeneration of Döderlein’s bacilli after the first menstrual period after the irradiation.

I. Bierer


Biocca, of Brazil, introduced this name in 1945 for the disease which has been known as pinta and under a wide variety of other, mostly local, designations. The condition is common amongst the inhabitants of hot, humid villages and small towns, generally situated along the river banks, in the equatorial territories of the American continent. In cases recorded from elsewhere the diagnosis is considered doubtful. The incidence is very heavy in some communities—60 to 70 per cent. on the island of Guadalupe. American Indians, Negroes, and half-castes are the races usually affected, possibly because of their low social and hygienic standards. Both sexes appear equally affected, mostly between the
ages of 30 and 40 years; susceptibility to the infection is most marked between the ages of 15 and 40 years.

The incubation period, averaging 10 to 15 days, may vary from 7 to 30 days. Onset is insidious and the primary sore, at the point of inoculation, generally a habitually exposed part of the body surface, is accompanied by itching, which continues into the secondary stage. This develops in 2 to 5 months after infection, with rash, pyrexial attacks, and lymph-node enlargement. By the end of 1 to 5 years the tertiary stage has set in with a characteristic range of discoloured patches on the skin. Spontaneous local healing may lead to scarring and white patches. Lymph-node enlargement is also common in this tertiary stage and the heart and blood vessels may be affected.

Treponema caratum (Brumpt, 1939) is the infective agent. The causal relationship has been confirmed by various Latin American workers inoculating themselves and a number of volunteers. Blood-sucking insects may play a part in transmission by biting the host, or by being eaten with food. A direct skin inoculation appears to be the more common mode of spread, and in this, ritual dancing (mutual flogging) as well as criminal practices have been found to play an important part in regions of the Rio Negro and Rio Igana, Brazil, which Biocca visited in 1944. Venereal spread has not been demonstrated. Arsenic, bismuth, mercury, the iodides, and penicillin, provide specific remedies and, in the absence of tertiary changes in the heart and blood-vessels, the prognosis is favourable.

J. Cauchi


Cervical erosion is a common and incapacitating lesion the "manifestations of which are not sufficiently recognized." A careful analysis of 128 out of 870 cases treated at the Royal Salop Infirmary, Shrewsbury, is submitted in support of this view. These 128 were selected cases, there being associated conditions in most of the remainder which clouded the issue.

The symptoms attributed to the cervical erosion and crevitis were as follows, the incidence (checked after follow-up) being given in brackets: leucorrhoea (90 per cent.); backache (60 per cent.); abdominal pain (56 per cent.); frequency of micturition (75 per cent.); menorrhagia (67 per cent.); pruritus vulvae (100 per cent.); dysmenorrhoea (71 per cent.); dyspareunia (73 per cent.); cervical haemorrhage (100 per cent.); sterility (33 per cent.—that is, three patients out of nine conceived 1, 5, and 6 months respectively after treatment of the cervix). Three patients complained of a sense of pelvic weakness and two of these were cured after cautérisation of the cervix without pelvic repair.

It is recorded that in 42 of the 75 patients who complained of abdominal pain for which no cause other than the cervicitis and erosion could be discovered, there was relief of pain after treatment of the cervix. One of these had undergone appendicectomy (the appendix removed was normal) without relief of the pain. In another, aged 44, repair of the pelvic floor was carried out, followed 2 years later by a subtotal hysterectomy, right oophorectomy, and appendicectomy without relief of the abdominal pain, which was subsequently cured by cautérisation of the cervix and its numerous Nabothian follicles. Four other patients had had laparotomy without relief of pain, which, however, disappeared after cautérisation and did not recur.

The cautérisation of the cervix was done in the outpatient department by electric thermocautery without dilatation and without an anaesthetic, except where the hymen was intact or the erosion very large, or an anaesthetic was required for some other reason. The canal was cautérised first, and then the erosion in lines radiating from the external os. During the operation there was little distress, though most patients experienced an aching lower-abdominal pain similar to that which they had previously suffered before operation.

The author advises against cautérisation in the presence of pelvic cellulitis and of chronic salpingitis; acute exacerbation of these conditions is likely if this precaution is not heeded. No evidence was found to suggest that the treatment caused subsequent dystocia from rigidity. Seven patients were confined from 10 to 17 months after the cautérisation and each had a normal first stage of labour.

E. W. Kirk