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 Gynecology, published by the British Medical Association. The abstracts are divided into the following sections: syphilis (general, therapeutic, pathology); gonorrhoea (general, therapeutic, pathology); other venereal disease conditions; public health. 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.)

SYphilis (General)


This study of immunity is based on the concept that immunity may be relative and that degrees of immunity may exist which will be adequate to deal with minimum inocula but may be inadequate to overcome larger inocula.

The authors' investigation in the rabbit, in which a quantitative approach to the problem is used for the first time, is especially concerned with the duration of the original infection before treatment in relation to the degree of acquired immunity. The Nichols strain of Treponema pallidum was used throughout. The inoculum was prepared by injecting 10^7 organisms into both testes of normal rabbits; 14 days later the testes were removed and minced, and then ground with 4 ml of an equal mixture of normal rabbit serum and isotonic saline solution. After centrifuging, the treponemata in the supernatant fluid were enumerated. Suitable dilutions of the emulsion were prepared with 50% serum-salt to give the desired number of treponemata in 0.2 ml. The infectivity of the inoculum was checked on at least 3 normal rabbits before use. In the animals studied the original infection was produced by either single intra- or multiple intracutaneous inoculations; for the later secondary post-treatment inoculations the original route was used.

The 263 infected animals used were treated at either 3, 6, 12, or 24 weeks after inoculation. "Mapharsen" or penicillin was used. As controls on the efficacy of the treatment a certain number of animals in each group (total 51) were not re-inoculated. The expected immunity of the treated animals was challenged by re-inoculation 6 weeks after treatment. For re-inoculation purposes suitable dilutions of the emulsion, prepared as for the original inoculations, in 50% serum-salt were made so that the desired number of treponemata would be contained in 0.2 ml. Re-inoculations were made with ten-fold dilutions of the emulsion containing from 2 x 10^4 to 2 organisms. The rabbits were subsequently examined twice weekly for 3 months. If during this period of observation a dark-field positive lesion developed the animal was considered to have developed a symptomatic infection. If at the end of 3 months no lesions had appeared, both popliteal lymph nodes were removed and an emulsion of them was inoculated into the testis of 2 normal animals, which were subsequently examined twice weekly for 90 to 100 days. If a dark-field positive lesion developed in this test animal the original animal was classified as having an asymptomatic infection. If no lesions appeared in the node-transfer recipients their testes were removed, emulsified, and examined for T. pallidum. In the absence of treponemata and therefore of infection of the test animal the original animal was classified as having been immune to re-inoculation.

In general the type of response obtained depended upon the two varying factors—the duration of the original immunizing infection before treatment and the number of treponemata in the inoculum. As the duration of the original infection was increased from 3 to 24 weeks, before being cut short by treatment, a progressive increase in the number of treponemata was required to produce the symptomatic or asymptomatic state of infection. The gradual increase in the degree of immunity in the 3- to 24-week period of the untreated infection following intracutaneous inoculation is well portrayed in a figure, in which the decrease in the frequency of symptomatic infection and the increase in that of asymptomatic re-infection at 6 and at 12 weeks is clear, as is also the establishment of complete immunity to symptomatic re-infection (but not to asymptomatic re-infection) by the twenty-fourth week.

The authors point out that their data indicate that there is a minimal immunity demonstrable within 3 weeks of infection, and that there is an appreciable increase in the threshold required to produce symptomatic infection. The development of immunity is progressive through the 24-week period under study, and towards the end of this period the animal is completely immune to several thousand times the original infecting dose. The results after mapharsen or penicillin therapy are much the same. The authors discuss the pathogenesis of asymptomatic infection (which is a rarity in the infected but untreated rabbit) and presume that a few treponemata have evaded the local barriers and have reached the lymph nodes. They regard the ultimate fate of treponemata using these asymptomatic infections and their effect on the host as of the utmost importance, and regret that the course of experimental syphilis in the rabbit does not provide an answer to the problem.

In attempting to apply this work to the course of syphilis in man the authors consider that in patients treated early "re-infection" will tend to be of symp-
The Incidence of Infection in Contacts of Early Syphilis.

The author studied 3,383 contacts of syphilis who were divided into two groups: (a) contacts of patients with primary and secondary syphilis (1,250); (b) contacts of patients with early latent syphilis (2,133). Of the first group 271 were found to be already under treatment for syphilis. Apart from these, 656 were examined and 318 of this total were found to have syphilis. In the majority of these the disease was in the early stages. In the second group 363 were found to be already under treatment. In all 1,101 were examined and 446 had syphilis. In this group, as was expected, early latent and later stages predominated. In the first group 323 could either not be located or, if located, could not be examined; the figure for the second group was 669. Taking both groups together the author found that 48-5% of the patients examined had syphilis. He therefore considered that to treat contacts of early syphilis irrespective of the presence or absence of infection "would be not only medically and epidemiologically unsound but also rather costly."

G. W. Csonka

SYphilis (Therapeutic)

Bismuth Plus Penicillin in the Treatment of Experimental Syphilis.

Mapharsen and penicillin are known to have a synergistic action when combined in the treatment of experimental syphilis. The present article reports experiments which indicate that bismuth and penicillin are similarly synergistic. Rabbits of mixed breeds weighing between 2.5 and 3.5 kg. were inoculated intratesticularly with 10^7 Treponema pallidum (Nichols strain). After 6 weeks infection was confirmed by dark-field examination and treatment was started. Six schedules of treatment were followed, including one control schedule in which no bismuth was given. In the CD 50 of penicillin alone was 2,650 units per kilo and the CD 90 was 8,000 units per kilo. The addition of one-quarter of the CD 50 of bismuth subsalicylate (1.4 mg. metallic bismuth per kilo) at the beginning of penicillin therapy reduced the CD 50 and CD 90 respectively to 1,000 and 1,800 units per kilo. When the same dose of bismuth subsalicylate was not given until the completion of penicillin therapy so that simultaneous action was prevented, the reduction in the curative dose of penicillin was decreased (CD 50 and CD 90 of 500 and 1,300 units per kilo). Conversely, the use of a more soluble bismuth salt at the beginning of penicillin treatment produced a still greater reduction in the curative dose of penicillin (CD 50 and CD 90 of 1,000 and 1,800 units per kilo). When three-quarters of the CD 50 of bismuth was used even greater reduction in the curative dose of penicillin resulted. Further experiment showed that bismuth did not delay the excretion of penicillin or affect the level of penicillin in the blood, and it was therefore concluded that its action was truly synergistic. Comparison of the results of these experiments with those of comparable experiments combining mapharsen and penicillin, the authors conclude that bismuth is as effective as mapharsen in supplementing the action of penicillin in experimental syphilis.

S. M. Laird
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From some available reports and an unspecified number of personal cases, the author suggests a plan of treatment for early syphilis in infants and children. He advises 50,000 units of sodium penicillin per lb. body weight at 3-hourly intervals over a period of 15 days and totalling 120 doses. In debilitated infants the initial dosage on the first day should be reduced by about half. A second course with double dosage is advised in cases in which there is clinical or serological relapse or in which the serological titre shows no reduction 6 months after treatment. After the first course the author expects patients to be serum-negative in from 3 months to 1 year (average period 7 to 8 months). Spinal fluid changes are present in 50 to 75% of young infants, but there is a tendency to spontaneous reversal without treatment. The majority of abnormal spinal fluids should respond to penicillin within 6 to 18 months. Reactions to penicillin treatment are usually mild, comprising initial fever, but in some cases there is gastrointestinal disturbance. Such reactions seldom call for cessation of treatment, but skilled paediatric care of syphilitic infants during and after treatment is most important.

The author emphasizes the fluid state of our knowledge of penicillin therapy in syphilitic infants and children; [it is considered that the dosage indicated should be considerably greater, especially if the penicillin is not supported by heavy metal chemotherapy.]

S. M. Laird


This report concerns the results of treatment of 109 children between the ages of 2 and 13 years suffering from late congenital syphilis; 81 had clinical signs and symptoms; 28 were asymptomatic. Serological tests were carried out in all cases by complement-fixation and flocculation techniques. The most frequent manifestations attributed to syphilis were abnormalities in the cerebrospinal fluid (36%), lymphadenopathy (35%), clinical neurological signs (18%), enlarged liver (15%), and bony changes (13%). Treatment was with sodium penicillin, given on the same lines as those recommended for cases of infantile congenital syphilis, namely, a course of 2-hourly or 3-hourly injections for 7 to 14 days in a dosage varying from 10,000 to 50,000 units per pound (0.45 g.). The authors finally recommended at least 50,000 units per pound.

There were no deaths. Benigo febrile reactions occurred in 39%. The authors classified their results as clinically satisfactory in 81-6%, uncertain in 9-2%, and unsatisfactory (either no change or actual progression) in 9-2%. Of 98 children who were followed up for 60 days or longer, 52 were under 6 years of age and 46 over 6 years. In the first group either the serum reaction became negative or the titre declined in 84-6%; in the second group only 58-7% showed such changes. Actual dosage of penicillin caused no significant difference, but in those who had received no previous anti-syphilitic treatment the results were much better than in those previously treated (and who might be considered particularly resistant). There were 37 such cases; in 27 treatment had been with the heavy metals and was judged inadequate in 24; in 10 penicillin had been given in adequate dosage. Of the 28 asymptomatic patients, 8 became serum-negative, the sera of 15 had progressively declining titres, and 6 were "fast." Improvement in the 20 neurological cases was disappointing. There were 8 cases of condylomata, which resolved within a fortnight; 6 cases of interstitial keratitis, 3 of which did well; 11 cases of malnutrition and anaemia, all of which improved, and 2 cases of Clutton's joints which were cured. A palatal perforation and a gumma responded well.

W. P. Galsford


The results of penicillin therapy in previously untreated cases of secondary syphilis are presented. The authors used 22 different treatment schedules. The numbers of cases followed up vary, and the assumption is made that the experiences of the patients who default are similar to the experiences of those who do not. With penicillin alone 1,200,000 to 2,800,000 units being given in doses of 20,000 to 80,000 units every 2 to 6 hours, the cumulative failure rate at 12 to 15 months in approximately 1,500 cases varied between 19-1 and 25-4%. In 61 patients given 40,000 units every 2 hours to 3,400,000 units the failure rate was only 4-3%. With penicillin in oil-beeswax the failure rates in 199 patients receiving 8 single daily injections to a total of 4,800,000 units and in 86 patients receiving the same total amount in 16 injections given twice daily were 16-5 and 11-4% respectively. If 300 to 320 mg. of arsenoxide was administered concurrently with 1,200,000 units of penicillin over 8 to 10 days the failure rates in 773 patients were 15-6 to 16-9%. The addition of bismuth did not improve these figures even if the dose of penicillin was increased to 2,800,000 units. Even if three sessions of fever of 3 hours' duration above 106°F. were combined with 2,400,000 units of penicillin over 7½ days, the cumulative failure rate was 14-7% in 57 cases. If 1,200,000 or 2,400,000 units were given over 28 to 50 hours with 6 hours of fever the failure rate in 135 cases varied between 25-8 and 35-6%.

Severe reactions were observed in 206 of 32,719 cases treated with aqueous penicillin alone, in 34 out of 11,015 receiving oil-beeswax preparations; there were no deaths. Of 88,202 patients receiving aqueous penicillin and arsenoxide 1,402 had severe reactions and 15 died.

R. W. Wilcox


In the authors' experience of the penicillin treatment of over 10,000 cases of syphilis, no serious reactions to the drug were encountered. The complications which were seen are classified as follows:

(1) Urticaria appearing 6 to 12 days after the beginning of treatment, noted in 2.5% of cases treated. Such reactions varied from mild pruritus with a few urticarial lesions to very severe pruritus and marked angioneurotic edema; in some cases there was fever. Of 804 patients treated for 8 days with penicillin in beeswax and oil, only 2 failed to complete treatment on account of urticarial reaction; in most cases, including those treated for 18 or 19 days, interruption of treatment was not required, and usually the reactions lasted only for 4 to 6 days whether or not treatment was continued, but in a few
In 31 patients tested, "pyribenzamine" seemed to influence the onset or course of the urticaria in most cases, although exceptionally, there was marked subjective relief. Intra-dermal sensitivity reactions with 5,000 units and 20,000 units of penicillin in 0.1 ml. water were negative, both during and after the injection reactions, in those reacting patients tested [the number is not given].

(2) Exacerbation of secondary syphilitic lesions—a reaction seen only in secondary syphilis, occurring 6 to 10 days from the start of treatment, and lasting for 4 to 10 days, whether or not treatment was continued. The reaction may be associated with local edema, malaise, sore throat, and high fever, together with the appearances of relapse in the secondary lesions, but in no cases were spirochetes found on dark-ground examination of the serum from such lesions. The authors are unable to classify these phenomena as "delayed Herxheimer reactions" on account of their late onset and protracted course. Their nature is discussed.

(3) Erythematous and papular reactions developing in the first day or two, and lasting 1 to 3 days; noted in about 25 cases only. These reactions were always mild, and interruption of treatment was unnecessary. The authors believe that such reactions may be associated with fungus sensitivity; the question is discussed in the light of other published cases.

(4) Local dermatitis at the site of injection, symptomless and unimportant, though a marked eruption of papules or follicular papules was seen on rare occasions. This reaction appeared on the third or fourth day of treatment.

(5) Bullous dermatitis in 2 cases, in which bullae appeared on the exposed surfaces of the upper limb.

G. I. C. Ingram


As the seasonal agricultural workers who "follow the crops" comprise a large percentage of the population of San Joaquin County, California, and only 26-6% of patients completed the traditional course of arsenic-bismuth treatment, a 10-day out-patient penicillin course was adopted; its administrative advantages are compared with those of the old orthodox methods. Compared with the pre-war figure of 26-6%, 96-6% of patients complete the prescribed course of treatment; they welcome the new scheme because of avoidance of loss of income and the stigma attached to in-patient treatment. Daily doses of 300,000 units of penicillin for 10 days plus 5 injections of "mapharsen" (arsenoxide) and 3 of bismuth saved time, money, and effort. Later, increased economies were effected by eliminating arsenic and bismuth and doubling the dosage of penicillin.

T. Anwyll-Davies


In this paper the therapeutic values are compared of mechanical hyperthermy, malaria, and penicillin in neurosyphilis as measured by examination of the cerebrospinal fluid.

A total of 458 cases was observed for a minimum period of 6 months; 122 were treated in a Kettering hypertherm for 30 to 60 hours at 104°F; 196 patients were inoculated with quartan malaria, of whom 85% had 40 to 50 hours fever; and 140 patients were given 4°F 6 monthly examinations of 20,000 units of penicillin in oil and beeswax (400,000 units daily for 15 days) plus 8 injections of arsenoxide and 5 injections of bismuth.

After 24 months' observation, treatment had failed in 11-6% of the patients given penicillin, compared with 12-6% given malaria, and 14-3% receiving hyperthermy. Therefore on the basis of failure rates penicillin appears as effective as malaria or hyperthermy in the treatment of neurosyphilis. Before treatment, activity was shown in the cerebrospinal fluid of 69% of cases in the hyperthermy and malaria groups, and 83% in the penicillin group. After 24 months activity was still present in the spinal fluid of 10% of the malaria-treated patients, 15% of the penicillin group, and 26% of the hyperthermy group. It was significant that less than 0-1% of the spinal fluid for 2 years revealed that penicillin eliminates activity in the spinal fluid more rapidly than does malaria or hyperthermy. After 18 months, there is little difference as regards the spinal fluid grouping between results of malaria and of hyperthermy. However, of those treated by hyperthermy 30% of the spinal fluids remained unchanged and only 9% were negative, compared with 18% unchanged and 26% negative after penicillin therapy.

The charts show that penicillin is the most effective of the three types of therapy, that there is little difference in the respective effects of malaria and hyperthermy on the spinal fluid, and that penicillin achieves more rapid and greater changes than the other two methods of treatment.

T. Anwyll-Davies


Of 54 patients with tabes dorsalis who were treated with penicillin, 33 received penicillin alone in amounts ranging from 1,200,000 to 20,000,000 units in divided doses while the remaining 21 were given from 1,800,000 to 20,000,000 units of penicillin in divided doses concurrently with malarial fever. Patients with the tabetic form of dementia paralytica were excluded from the study.

Of the 33 patients receiving penicillin alone, 26 were men and 7 women, and the average age was 47 years; the youngest being 29 and the oldest 79. In 15 there had been symptoms for under 2 years, in 14 for 2 years or longer, and in 4 the duration was unknown. Metal chemotherapy had previously been given to 21 patients, 3 of whom had had fever in addition more than 2 years before, all without improvement. The spinal fluid was negative in 4 cases. Of the 29 abnormal fluids 14 were in "group II," 6 only being active, and 15 were in "group III." In 4 patients, all with "group III" spinal fluids, there were febrile Herxheimer reactions, and in 2 there was a transitory exacerbation of lightning pains. The incidence of febrile Herxheimer reactions (12%) was significantly lower than the 79% obtained by the same authors in dementia paralytica. The patients were divided into 3 groups: 1. Those who responded rapidly to treatment; cell count and total protein levels becoming normal, usually within a few weeks. This was followed by a more gradual but equally well-sustained improvement in the results of the colloid
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These authors devised the method of administration of massive doses of penicillin by continuous intramuscular infusion. The technique was as follows. The dose was given in 500,000 units of penicillin administered daily for a period of 3 to 19 days. The first 9 patients were given crude penicillin and the last 15 penicillin G. The penicillin was dissolved in 500 ml. of 5% glucose in water. A No. 20 gauge spinal needle was inserted in the lateral aspect of the thigh after infiltration of the latter with 1% procaine hydrochloride. Ten ml. of 1% procaine hydrochloride was added to the penicillin solution and slow continuous infusion was started, 500 ml. of the solution being administered each 24 hours—an average of 4 to 6 drops per minute. It was found advantageous to insert the needle into the opposite thigh every 3 to 4 days. It was necessary to discard the spinal needle after an average of 2 to 3 courses of penicillin because the needle became rusty and broke easily. The authors found this method useful when massive dosage was indicated, when nurses were busy and scarce, when hospital admission was not feasible, when the patient objected to multiple injections, and when veins were not available for intravenous therapy.

A few local complications were observed, including cellulitis of the thigh, abscess formation at the site of injection, and subcutaneous emphysema. General reactions included urticaria, chills, anorexia, and in one case a Herxheimer reaction.

[On the whole the small series represents an interesting piece of enterprise not without dangers and disadvantages.]

G. F. Walker


Twenty-six patients suffering from syphilis of the central nervous system (paresis) were treated with 100,000 units of penicillin intramuscularly every 3 hours for 3 days, followed by the same dose of penicillin together with 3 g. of caronamide (4-carboxyphenylmethyl-sulphonamide) orally every 3 hours for a further 5 days. Caronamide was given since it inhibits the excretion of penicillin by the renal tubules, yielding higher concentrations of penicillin in the plasma. After the 5 days of the penicillin therapy alone, in 15 patients the levels in the cerebrospinal fluid ranged from 0.019 to 0.052 unit per ml. At the end of the further period of 5 days (during which caronamide was given as well), in 20 patients concentrations of penicillin in the cerebrospinal fluid ranged from 0.026 to 2.5 unit per ml. The levels obtained were considered to be therapeutically significant since a concentration of 0.03 unit per ml. is usually sufficient to inhibit the growth of organisms such as streptococci, meningococci, and staphylococci. A lengthy discussion is given on the penetration of penicillin through the blood-brain barrier.

R. W.ien


Of 3,056 cases of peptic ulcer observed in 16 years 52 (1.7%) were of syphilitic origin. The incidence was...
much higher among cases of gastric ulcer—41 out of 826 (4.9%)—than among cases of duodenal ulcer—11 out of 2,240 (0.5%). All 52 patients admitted syphilitic infection, but only 23 had received regular treatment. The serum reactions were positive in all cases, and in a few positive specific reactions were given by the gastric juice and cerebrospinal fluid. The symptoms were not distinctly different from those usual in ulcer, but there was no response to the ordinary treatment. There was gastric hypoacidity or anacidity in 42 patients, and occult blood in 12. Radiologically, there was evidence of increased peristalsis and tendency to spasm. Gastroscopy revealed shallow ulcers with irregular edges and smooth pink bases. The mucosa in the area surrounding the ulcer appeared hyperaemic; the folds were not so broad and were less stiff; oedema, such as surrounds the simple peptic ulcer, was not observed in these cases. Erosions were often seen at the lesser curve, and occasionally were the source of profuse haemorrhage. Treatment with arsphenamine produced considerable improvement, even after 1:5 to 2:0 g. had been given. Increased acidity was a striking feature. In 3 patients treatment had to be interrupted when a profuse haemorrhage necessitated operation. The ulcers were situated in the antrum in all 3 cases; they were shallow and had a hard smooth base and irregular edges. Surrounding the ulcers were several erosions which had, previously been detected by gastroscopy. Histologically the submucosa was thickened by granulation tissue, and the infiltration spread both into the muscularis and the mucosa. There were numerous lymphocytes and plasma cells in the peri-vascular spaces, and the vessels, particularly the veins, showed marked thickening of the intima. Apart from these 3 patients, no evidence of ulcer was present radiologically or gastroscopically after the conclusion of the specific treatment.

**SYPHILIS (Pathology)**


From the Departments of Radiology and Pediatrics of Genoa University the authors report on 5 cases of defects of the cranial bones in infancy, demonstrated by radiological examination of the skull, and caused by congenital syphilis. The 5 cases came from a series of 13 syphilitic infants observed in 5 months. The patients studied were between 3 and 10 weeks old. In all cases the Wassermann reaction was positive, both in mother and child, and all but one of the infants (the exception being born prematurely) had osteochondritis and periostitic lesions of the long bones. The defects in the skull were multiple, and variable in size, some of them being clearly defined and others more indefinite, involving in all cases the outer as well as the inner table, except in the case of the premature baby, in whom the inner table only was involved. There was radiological evidence of peristitis of the cranial bones. The skull defects seemed to respond to anti-syphilitic treatment. It was possible to give a full course of treatment in only one case, and in this patient the lesions disappeared completely.

The authors' contribution to the subject of cranial lesions in early congenital syphilis is scanty and that such lesions are considered to be infrequent, which is contrary to their own experience. For the pathogenesis of the lesions described they suggest a multiple origin: an aspecific nutritional disturbance; a fibrous rarefying osteitis as described in the long bones and in other flat bones by Pick; a microgummatus process; and, finally, a true gummatous lesion. The authors think their findings confirm the suggestion that there is no hard and fast line dividing congenital syphilitic lesions of early infancy from lesions occurring in older children. They think that late congenital lesions are different from the tertiary lesions of acquired syphilis.

**P. E. Polani**


Plasma iron concentrations were measured following oral ferrous sulphate administration to patients with various manifestations of syphilis, with anemias, and with other chronic infections. No diagnostic or prognostic value could be attached to the tolerance curves in syphilis, and no correlation was noted between pathologic changes and iron concentration of the cerebrospinal fluid. Data are presented on the plasma iron concentration in a small number of syphilitic and normal rabbits.—(Author's summary.)


This is a preliminary communication on the cellular content of cerebral and spinal samples of cerebrospinal fluid. The spinal fluid was obtained by lumbar puncture, and the cerebral fluid, after its displacement by the procedure for pneumo-encephalography, was obtained by the same route. The cerebral fluid cell count was raised above that of the spinal fluid in cases of glioma or of recent trauma, in chronic encephalopathies of infancy, in some cases of epilepsy, in disseminated sclerosis, and especially in neurological syphilis. No significant difference was seen in cases of meningioma, in cerebrovascular disease of long standing, in Parkinsonism, in a few cases of Pick's disease, and in amyotrophic lateral sclerosis (apart from the bulbar form).

**J. Maclean Smith**

**Description of Gastroscopic Appearance of Late Gastric Lesions in Late Acquired Syphilis.** Patterson, C. O., and Rouse, M. O. (1948). *Gastroenterology*, 10, 474.

An account is given of the gastroscopical appearance of the lesions of presumed gastric syphilis. The diagnosis was confirmed either because of the disappearance of the lesions after anti-syphilitic treatment or as a result of examination of the specimen removed at operation. Some of the cases were followed up for 9 years. Three types of lesion were seen, ulcers, tumours, or an infiltrative process leading to a leather-bottle stomach. Attention is called to the livid, slightly brown or violaceous colour of the mucosal margins of the ulcers.

**Christopher Hardwick**


No previous reports on the neuropathological findings in paresis after penicillin therapy have appeared. The dosage in the 4 cases reported here ranged from 2,400,000 to 4,800,000 units. In 2 cases there was clinical as well as serological improvement; the 2 which did not
improve were of the juvenile type of general paresis, 1 of them a Lissauer type. Histological examination of the brain of the 2 patients who benefited revealed less intense inflammatory changes than in untreated cases. The iron reaction was positive in all 4 patients, but was less pronounced in the 2 who improved. No spirochetes were found in any of the brains. These findings resembled those obtained at comparable times after malaria treatment. The possibility that penicillin may produce an initial exacerbation of the process is suggested by the 2 unimproved cases. From the results it would appear that penicillin alone can influence the pathological progress of general paresis.  

E. W. Anderson


This follow-up of 213 cases of late symptomatic neurosyphilis treated with penicillin indicates that this antibiotic has not altered the position previously existing as regards serum-resistance. The patients were observed for from 6 to more than 24 months after penicillin treatment and less than 10% became serum-negative. Repeated courses of penicillin were no more effective than one course in reducing the titre. Small fluctuations in serological titre can be expected, and the result of a single test must accordingly be interpreted with this fact in mind.  

S. M. Laird


Cardiolipin antigen was compared with standard Kahn antigen in testing a number of sera: the former consisted of purified lecithin 1%, cardiolipin 0-1%, and cholesterol 0-025%. The titres of the two antigens compared were 1 plus 0-9 for cardiolipin, and 1 plus 1-3 for standard Kahn antigen. Of 1,910 routine examinations there was absolute agreement in 98-2%, relative agreement in 0-3%, and disagreement in 1-5%. When standard Kahn reactions were compared with microflocculation reactions in 1% v/v sera, standard cardiolipin antigen being used, the figures were 98-0%, relative agreement 0-3%, and disagreement 1-6%. When the Kahn standard test was compared with the New York cardiolipin flocculation and complement-fixation tests in just over 200 syphilitic and 130 non-syphilitic sera, all three were found to be 100% specific, but the sensitivity percentages were: Kahn standard, 81-6; New York cardiolipin flocculation, 75-0; and New York cardiolipin complement-fixation test, 73-3. In various evaluation studies over the past 10 years, the Kahn standard test has always been found 100% specific, which does not mean that it never gives a false positive reaction, but that it is less likely to do so than other tests which were not found to be 100% specific. Details are given of the special technique with cardiolipin antigen in the standard Kahn tests; most of these are the same as for the ordinary Kahn test, but after the tubes are shaken the salt solution, added before reading, should be 1-2% instead of 0-9%. Details are also given for the Kahn microflocculation test with cardiolipin antigen. It appears that tests with cardiolipin are less sensitive than tests with Kahn antigen, but perhaps slightly more specific, and it is recommended that for the present the two tests should be used in parallel.  

T. E. Osmond


The Kahn "optimal zone reaction" is a supplementary procedure applicable to known syphilitic sera giving negative reactions with the standard test, were submitted to the "optimal zone" test: patients included 14 with paresis or taboparesis, 7 with tabes, 4 with a symptomatic neurosyphilis, and 1 with transverse myelitis. Spinal fluid from 22 of these gave positive reactions with the standard test and from 2 with the presumptive test. The optimal zone reactions are divided into three zones: (1) serum-antigen ratios 1 : 1 and 2 : 1; (2) ratios 3 : 1, 6 : 1, and 12 : 1; (3) ratios from 24 : 1 to 200 : 1: 21 (3) the sera tested gave positive reactions in zone 3 were 50 non-syphilitic sera, used as controls, gave negative optimal zone reactions. All the 26 patients had received considerable amounts of antisyphilitic therapy. The technique of the optimal zone test is similar to that of the standard Kahn test: the antigen is measured with a 0-1 ml. pipette graduated in 0-001 ml.: the serum is measured in amounts up to 0-2 ml. with a 0-2 ml. pipette graduated in 0-001 ml and in amounts over 0-2 ml. with a 1 ml. pipette graduated in 0-01 ml. Tubes are shaken for 3 minutes, saline is added, and results are read at once and again after 24 hours in the water-bath at 37°C. Particulars of the 26 patients, diagnoses, duration of the disease, treatment, and results of blood and spinal fluid tests are given in one table, and the technique of the optimal zone procedure is described.  

[TThe detection of minimal amounts of reagin in the sera of neurosyphilitic patients with positive spinal fluid does not appear to be of much practical value, but the optimal zone reaction might be helpful in testing sera from treated syphilitic patients which give negative reactions with routine tests and so in assessing progress and establishing cure.]  

T. E. Osmond


For the cardiolipin test the antigen emulsion is prepared as follows: 0-85 ml of double distilled water is pipetted into a glass stoppered bottle: 10 ml of a 1% solution of cholesterol is pipetted with continuous agitation down the side of the bottle; the bottle is rotated for 20 seconds; 0-1 ml of alcoholic solution containing 0-2 mg. cardiolipin and 1-6 mg. lecithin (ratio 1 : 8) is pipetted down the side of the bottle; the emulsion is shaken vigorously for 1 minute; 2-45 ml of 0-85% NaCl is added rapidly. For the test 0-05 ml inactivated serum is placed in the concave depression of an agglutination slide and one small drop of antigen is added with a 2 ml. syringe fitted with a No. 25 needle [it would appear that the size of this drop must vary with the bevel of the needle and the angle at which it is held]. The slide is rotated on a flat surface for 4 minutes and results are read with a lower-power objective (X 100). Sixty sera can be tested and read in 15 minutes [presumably it is one person]. Significant positive reactions and small clumps a doubtful one. The cardiolipin test (1 : 10) was carried out in parallel with the
Kahn test on 3,626 sera from non-syphilitic persons: the former showed a specificity of 97% compared with 98.4% for the Kahn test. In the case of 99 strongly positive syphilitic sera the cardiolipin (1 : 10) test had a sensitivity of 99%; tests on 56 weakly positive sera gave the following sensitivity percentages: cardiolipin 92.8, Kahn 73.2; with all the 155 sera percentages were: cardiolipin 96.8, Kolmer complement-fixation test 90.3, and Kahn 87.7. In order to discover the optimum cardiolipin: lecithin ratio, various combinations were tried out with strongly positive, weakly positive, and negative sera. In general it was found that increasing the amount of lecithin increases sensitivity and decreases specificity and that probably 1 : 8 is the optimum ratio: with this latter, specificity reached 97.8%. Sera from 23 patients with acute malaria were tested; 6 gave false positive Kahn reactions but all gave negative cardiolipin (1 : 10) reactions.

T. E. Osmond


Male volunteer prisoners, apparently free from syphilis, were infected with malaria and their sera tested before inoculation every 2 or 3 days and immediately after the attacks and later at weekly intervals. The tests included: Kahn-standard, Kline exclusion and Mazzini-microflocculation tests, and the standard Kolmer complement-fixation test (C.F.T.), with ordinary tissue extract; and the Rein-Bossak and V.D.R.L. microflocculation tests, Kolmer C.F.T., and the E.P. 50 test with cardiolipin antigen. There were 104 individuals; 6,403 sera were examined and 51,224 tests were carried out; 78 of the patients were inoculated with the Chessor strain of malaria, 17 with the St. Elizabeth strain, and 9 with both strains. Of the 104 patients 75 gave one or more false-positive reactions—51 of the Chessor strain group, 15 of the St. Elizabeth, and 9 of the group infected with both. These reactions appeared from 0 to 39 days (average 8.7) after the onset of parasitemia and lasted for 2 to 181 days. Of the tests with ordinary tissue extract the Kahn gave the highest number of positives and the Kolmer C.F.T. the lowest. In those tests in which cardiolipin antigen was used the number of positive reactions was much reduced with the microflocculation tests and almost eliminated with the C.F.T. It is clear that in general C.F.T. are less liable than flocculation tests to give false-positive reactions in malaria.

T. E. Osmond


Little seems to be known concerning the survival of Treponema pallidum under varying conditions; in citrated human blood and plasma at 3° C. all die within 72 hours, though at -76° C. they will survive for years; in the chick embryo they apparently survive for only 4 hours. In order to study factors which affect survival, the author inoculated the virulent Nichols strain into testes of rabbits and removed the latter within 24 to 48 hours after recognizable lesions had appeared. He used 2 techniques for extraction of spirochetes from the rabbit tissues; details of these cannot be given in full but the important points are the washing of the tissue with cold normal saline, making a suspension in a "basal medium" consisting of crystalline bovine albumin, phosphate buffer, sodium thioglycollate, cysteine, glutathione, sodium pyruvate, a mixture of vitamins, sodium bicarbonate, and sodium chloride, and rotary shaking in an atmosphere of 1 or 5% carbon dioxide followed by filtration to remove gross tissue and spermatozoa. The main factors in maintaining viability of spirochetes are: (1) maintenance of anaerobiosis by means of an atmosphere of 95% nitrogen and 5% carbon dioxide, and sodium thioglycollate, (2) albumin; (3) a concentration of 6.8; (4) a concentration of 7.0; (5) a temperature of 30° C.; (6) tissue extract; (7) glutathione and cysteine; (8) sodium pyruvate. Under the conditions of the experiment spirochetes did not multiply but did grow in length and tended to produce filamentous projections at one or both ends; half-life of the organisms was prolonged for 6 to 8 days and they retained their virulence. Various substances tended to reduce viability; for example, ascorbic acid and crystalline penicillin G caused immobility in the range from 0.001 to 0.1 μg. per ml. but did not cause more rapid immobilization beyond the latter figure. It is suggested that this method of prolonging the life of spirochetes may be a useful method of studying new antibiotics or chemotherapeutic agents.

T. E. Osmond


Syphilitic rabbits, cured after having had the disease for 3 months, are usually resistant to infection. The authors carried out a series of experiments to see whether the injection of killed Treponema pallidum would protect rabbits against infection. They injected varying numbers of dead pathogenic spirochetes, obtained by mincing testicular chancre, intradermally, intraperitoneally, or intravenously, and found that these rabbits developed positive Wassermann and flocculation reactions, but no immunity against ordinary experimental infection. In the normal controls titres in serum averaged less than 1 in 2; in the experimental animals they were as high as 1 in 96, this antibody response reaching a maximum in 2 to 3 weeks and then remaining constant or falling. When cultured spirochetes (Reiter strain) were employed no rise in titre was noted. That the antibody was not due to the extract of testicular tissue is shown by the fact that control animals injected with this, with or without Reiter spirochetes, did not show an increase of titres. It was found that organism suspensions containing relatively small amounts of tissue extractives were just as antigenic as those containing large amounts. Antisera from the experimental rabbits did not agglutinate pathogenic T. pallidum, did not give specific complement fixation with spirochetal antigens, and failed to render spirochetes non-infective. It is considered that Wassermann reactivity induced by injection of dead spirochetes and the reaigen occurring in syphilitic infection represent an antibody response to the spirochetes and mammalian tissue apparently both containing an immunologically related antigen.

A particularly interesting observation was that some animals injected with organisms in a water-in-oil emulsion may have been sensitized by preceding aqueous injections, since the incubation period was reduced; the relation of this finding to the wide manifestations making a spirochetal tissue reaction, is clear.

T. E. Osmond
GONORRHOEA (General)

Experimental Gonococcal Infection of the Rabbit's Eye. 

This article is a report of an attempt to produce in some laboratory animal a local gonococcal infection suitable for the testing of prophylactic agents. The lack of susceptibility to gonococcal infection of the urethra or vagina of the laboratory rabbits led the authors to investigate the possibility of using the eye of the rabbit. It was found that the conjunctiva was susceptible to infection but only when large numbers of gonococci were placed in the conjunctival sac and the lids sealed up; secondary bacterial infection was frequent. The conjunctival sac method was abandoned in favour of direct infection of the anterior chamber of the eye which was effected by the introduction, after aspiration of the aqueous humour, of 0.2 ml. of a suspension of gonococci. A large series of rabbits was thus infected and kept under observation for periods of up to 14 weeks' duration. The frequency of successful infection was found to depend upon the number of gonococci introduced. The introduction of 20 million organisms produced infection, in 93% of cases, and of 200,000 to 2 million in 82 to 84%. Even with the introduction of only 200 organisms infection ensued in 45% of cases.

This method of experimental infection was then used for testing the efficiency of various prophylactic agents which were introduced directly into the anterior chamber of the infected eye within an hour after a standard inoculation of 20 million gonococci. The eyes were excised after 24 hours and the aqueous humour was aspirated and cultured; the ciliary body was removed and macerated, and cultures were taken from this material and from the surface of the lens. The substances tested were penicillin, mild and strong solutions of silver protein, and ointments of various bases containing sulphathiazole or calomel or both. Penicillin was uniformly effective in a dose as small as 2-5 units. Sulphathiazole (15%) and calomel (30%) were also highly effective, separately or together, but only when incorporated in a watery or vanishing-cream base. The most effective base of several under study contained propylene glycol 26%, starch glycérine 34%, stearic acid 4%, glycerol monostearate 2%, spermaceti 2%, and water 32%. 

V. E. Lloyd

GONORRHOEA (Therapeutic)

Single Injection Treatment of Gonorrhoea with Potassium Penicillin Suspension in Oil-containing Epinephrine. 

Acute gonorrhoea in adult males was treated with single intramuscular or subcutaneous injections of a penicillin-in-oil mixture containing 300,000 units of crystalline potassium penicillin and usually 0.3 mg. of adrenaline per ml. of vegetable oil. The aim of follow-up was to obtain three negative post-treatment prostatic cultures during a 3-week period, but only 154 patients were observed for over 2 or more weeks. Some 300 patients were treated. Single injections were given of 0-25, 0-5, 1, and 2 ml. of the penicillin-in-oil mixture and the adrenaline content was also varied so that the total dose was between 0.6 and 2.0 mg. A total of 99 patients received 150,000 units of penicillin and 0.15 mg. of adrenaline in 0.5 ml. of oil and were followed up for 2 to 3 weeks; there were only 3 failures, and all 3 responded to further treatment. Seven out of 9 were apparently cured with the 0.25-ml. injection containing 75,000 units and 0.075 to 2.0 mg. of adrenaline, but it is concluded that this dosage of penicillin is insufficient. All the 46 patients who received 1 to 2 ml. of the mixture containing from 200,000 to 600,000 units of penicillin with 0.1 to 2.0 mg. of adrenaline were apparently cured. There were 9 re-infections; 5 of these 9 patients were not delinquent and responded to further treatment.

Local pain lasting up to 5 minutes was sometimes noted, though it was apparently less when the injections were administered subcutaneously. Blood pressure was estimated repeatedly in 15 patients; in 8 there was no change, in 6 there was a fall, and in only 1 was there a rise, after treatment, of 14 mm. of mercury. There was no increase in the pulse rate. An exacerbation of pre-existing dermatophytosis was observed in 2 patients. No blood levels of penicillin are recorded, but a reference to unpublished data of other workers suggests that with this material the prolongation does not exceed 12 hours after injections.

[Trials with penicillin-adrenaline mixtures in Britain have not been so successful. The injections have proved more painful than penicillin-oil-beeswax mixtures and the prolongation of the blood levels and the clinical results have been less striking.] 

R. R. Willcox

GONORRHOEA (Pathology)

Alleged Penicillin-resistant Gonorrhoea. 

On account of suspected penicillin-resistant gonorrhoea 216 men were evacuated from the Far East. A thorough clinical examination, including smears and cultures, was carried out. By the time the patients reached the base hospital 86 men were asymptomatic, 93 were suffering from non-gonococcal urethritis, 18 had other forms of disease of the urinary tract; only 19 were shown to have gonococci. All the last group responded satisfactorily to a single injection of 300,000 units of penicillin in oil and beeswax. It is concluded that penicillin-resistant gonorrhoea is not encountered at the present time and that suspected cases are in reality cases of non-gonococcal urethritis which have been misdiagnosed, often on account of overstaining by Gram's method. Staphylococci were isolated in 24% of these cases; these organisms are the most likely to cause confusion if incorrect staining techniques are employed.

R. R. Willcox

OTHER VENEREAL DISEASE CONDITIONS

Laboratory Diagnosis of Granuloma Inguinale and Studies on the Cultivation of the Donovan Body. 

A method of growing Donovan bodies in fresh non-incubated yolk medium is described; the medium is prepared as follows. Yolk is removed aseptically from fresh eggs and diluted with an equal part of sterile saline. A base medium of 1% "bacto" pentone, 0.3% "bacto" tryptone, 0.3% dextrose, and 0.2% sea salt [composition not stated] is adjusted to pH 7.3 and to it is added 0.12% agar; the mixture is sterilized and allowed to cool to 45° C. when an equal quantity of the diluted yolk is added. Tubes are inoculated with 0·1 ml. of recently
infected embryonic yolk and incubated at 37° C. for 4 days. Growth is free and dividing forms of Donovan bodies are often seen; these bodies remain viable for 8 to 10 days at room or refrigerator temperature. Apparently success depends on the addition of agar, and 0-12% was found to be the optimum concentration. [Donovan bodies from smears and cultures, including encapsulated forms, are well shown in four figures.]

T. E. Osmond

Cultural and Serologic Studies on Granuloma Inguinale.

After many unsuccessful attempts to grow Donovania granulomatis on artificial media, material from the ninety-second egg passage was successfully cultivated by incubation at 35° C. for 1 to 2 weeks after planting on slants consisting of 10 ml. of beef-heart infusion agar with 1 ml. of normal yolk from six-day embryos. Eight serial transfers were made with this medium and also to slants prepared from 5 ml. of 3% agar in tryptone beef-heart infusion broth and 5 ml. of modified Levinthal's stock broth. Colonies were irregular in outline, shiny, translucent, and grey. An antigen was prepared for serological studies by washing and suspending the material in 1/100 phosphate buffered physiological saline, shaking and centrifuging, and employing the supernatant fluid, which was preserved in 1 in 10,000 "merthiolate." When complement-fixation tests were carried out with this as the antigen, 30 positive reactions were obtained from 58 sera of patients with granuloma inguinale, from 1 of 32 with syphilis, from 2 of 18 with gonorrhea, from 2 of 7 with lymphogranuloma venereum, from 3 of 10 with chancre, and from 4 of 19 with varicose ulcers. No positive reactions were obtained from the sera of 10 patients with tuberculosis or of 4 normal persons.

R. R. Wilcox


In past investigations into the etiology of granuloma inguinale the Escherichiae have not infrequently been isolated as a possible cause of this condition. The evolution of a complement-fixation test, with cultures of Donovania granulomatis as an antigen, led to similar trials with material prepared from cultures of Friedlander's bacillus. The organism was cultured on 1% tryptone agar for 18 hours and then washed off with physiological saline buffered to pH 7-8. After centrifuging for 30 minutes the organisms were re-suspended in buffered saline, frozen and thawed 10 times in alcohol and dry ice, shaken, and once again centrifuged; the supernatant fluid was used as the antigen. Twenty out of 30 sera taken from patients with granuloma inguinale gave a positive reaction, compared with 25 with D. granulomatis antigen. When 14 sera from patients with known recent venereal exposure were tested positive reactions were obtained with one and three respectively. Of sera from 4 patients with varicose ulcers, 2 gave positive results with the antigen prepared from Friedlander's bacillus, and 4 with that from D. granulomatis. The almost complete reduplication of these tests suggests that Donovania might belong to the tribe Escherichiae, a hypothesis supported by their common susceptibility to streptomycin.

R. R. Wilcox


Of 21 negro patients, 11 of whom were male, 14 had granuloma inguinale for 1 to 18 months and 7 for 14 months to 12 years. Nine had received previous treatment with antimonials. All were given 1 g. of streptomycin a day by 4-hourly intramuscular injection, which was continued until the ulceration was healed. Healing was achieved in 5 to 47 days except in one patient who developed a squamous-celled carcinoma. A weekly biopsy was performed while the patients were in hospital, though some specimens still contained Donovania after one week, all were negative by the fourteenth day. Only one patient had a headache, dizziness, and tinnitus, but treatment was not discontinued. A follow-up of 7 to 10 months has revealed no relapse and a steady regression of granulomatous lesions.

R. R. Wilcox


Sixty-five coloured patients suffering from granuloma inguinale, in whom the diagnosis was confirmed by the identification of Donovan bodies in the biopsy smear, were treated with lithium stibiothiomalate ("antihomaline"). The drug was given by intramuscular injections in doses of 3 ml. (equivalent to 30 mg. antimony) twice weekly, the total number of injections varying from 5 to 42. The results were comparable with those obtained with staphoben and with antimony potassium tartrate. Rest in bed, a daily bath with soap and water, and a balanced diet with iron and vitamins are as necessary as drug therapy.

Geoffrey McComas


This paper amplifies an earlier report by the same authors on the use of chloromycetin in experimental infections with psittacosis virus (Science, 1947, 106, 418). For this work the 6-BC and F-4 strains of psittacosis virus were employed. The L.A. strain of lymphogranuloma venereum used in these experiments was obtained from an inguinal lymph node of a patient in 1943, and has since been maintained in the authors' laboratory.

Evidence is produced to show that chloromycetin possesses little or no direct virucidal action against the agent of psittacosis, though it has a suppressive effect on its growth. Chloromycetin has about the same degree of activity as that of penicillin and sulphadiazine in similar studies.

A. W. H. Foxell
Abstracts

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