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); gonorrhea (general, therapeutic, pathology); other venereal disease conditions; general 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)

Tertiary Syphilis of the Uterine Body and Adnexa.
A 23-year-old married woman complained of vague abdominal pain for 3 months. Her uterus was found to be enlarged to the size of a fetaler head at term; it was mobile, and irregular. At laparotomy the presence of multiple adhesions suggested that a uterine fibroid was undergoing malignant transformation. Subtotal hysterectomy, bilateral salpingectomy, and left ovariotomy were carried out. Postoperative progress was uneventful. Histological examination revealed numerous gummata in the myometrium and the ovary. The Wassermann reaction was strongly positive. This is stated to be the fourth authentic published case of tertiary syphilis of the uterus.

S. S. B. Gilder

Inguinal Adenitis in Primary Syphilis in the Male.
A series of 116 males with a syphilitic chancre of the genitals was examined. The patients were grouped according to the length of time that the chancre had been present, as estimated from the history, the appearance of the lesion, and the serological findings in the blood. In no case was the chancre thought to have been present for less than 7 days if the serum Wassermann reaction was positive or if there was more than slight induration of the sore. Significant inguinal adenitis was noted in 73% of 18 chancres present for 1 to 3 days, in 78% of 41 chancres present for 4 to 6 days, in 84% of 32 present for 7 to 14 days, and in all of 25 which were of 15 to 21 days' duration.
Of 100 patients with syphilitic genital chancres the adenitis was unilateral in 45. In 37 it was bilateral, the lymph nodes of the same side being larger than or as large as those of the opposite side; in 3 only was it bilateral but with greater enlargement on the opposite side, and in no less than 15 cases were the contralateral lymph nodes solely affected. Of 52 patients with non-specific genital lesions accompanied by adenitis, the lymph nodes of the same side were solely affected in 37 and in 15 the affection was bilateral, but in all cases the enlargement was greater on the same side as that of the lesion.

It is concluded that enlargement of the inguinal lymph nodes in primary syphilis usually occurs simultaneously with or shortly after the appearance of the chancre, and it is suggested that the combination of a penile sore and enlargement of the lymph nodes in the opposite inguinal region is strong presumptive evidence of syphilis.

R. R. Willecox

SYPHILIS (Pathology)

Protective Antibodies in the Serum of Syphilitic Patients.
Turner has already shown that serum from syphilitic rabbits, when combined with virulent Treponema pallidum and injected after incubation intradermally into normal rabbits exerts a protective action against the development of a syphilitic lesion. The same technique has been applied to human sera by mixing with virulent T. pallidum and incubating at 36°C for 6 hours before injecting intradermally into normal rabbits and, by observing the inoculation site, demonstrating the presence or absence of inhibiting antibodies.
The specimens tested were obtained from 13 patients with primary syphilis, 35 with secondary syphilis, 135 with previously untreated latent syphilis, 31 with treated latent syphilis, 29 with tertiary syphilis; 107 came from presumably non-syphilitic persons in addition to 95 from other controls. Sera from patients with secondary, latent, or tertiary syphilis exerted an inhibitory effect on the development of syphilis, compared with non-syphilitic sera. There was either a complete suppression of lesions, a smaller average size of the lesions, or a prolongation of the incubation period. Sera from patients with primary syphilis occupied a somewhat intermediate position but in general more closely resembled those taken from non-syphilitic persons.
It is considered that persons with secondary and tertiary syphilis possess humoral antibodies, which may play a significant part in acquired immunity. It is not certain whether these antibodies are those which produce a positive serum reaction for syphilis but it is considered that there are indications that they are not identical.

R. R. Willecox

The work described was carried out with American penicillin prepared in 1947. It has been noticed that crystalline penicillin yields results which differ from those obtained with less purified material. The present findings are not, therefore, strictly comparable with those of workers who used other types of penicillin. The effect of penicillin on Treponema pallidum was observed in the following way: Fluid from primary and secondary lesions was examined microscopically with dark-field illumination. The number of spirochetes per field was estimated, their motility noted, and the number of coils per spirochete counted. A preliminary examination was made before treatment; thereafter 4 doses of 250,000 units of penicillin were given...
at 3-hourly intervals, and fresh samples of fluid were examined hourly. The numbers usually began to fall after 1 hour, and spirochetes disappeared completely in 7 to 11 hours. One patient was still free of spirochetes at the end of 43 hours, but in another a single motile organism was seen after 48. [These experiments were not intended as curative treatment.]

Counts made on a number of organisms [total not stated, but percentages only] showed that the number of coils per spirochaete was unchanged after the administration of penicillin. The results are set out graphically.

The curve rises steeply to the mode which lies between 8 and 9 coils, and falls more slowly with a positive skewness. The group 8–9 coils contain nearly 50% of the observations. The curves for treated and untreated cases are almost identical. The findings differ from those of other workers, who noted that the number of long forms was reduced during treatment.

The best criterion of motility is rotation, because lateral movement seen under the microscope may be the result of Brownian movement or of currents in the preparation. It was found that rotatory movement began to diminish regularly about 3 to 4 hours after the administration of penicillin. J. C. Broom


Rabbits were fed with 0.5 g. cholesterol per day for 119 days; at the end of this time their blood cholesterol content ranged from 0.648 to 3.438 g. per 100 ml., as compared with a normal of 0.032 to 0.216 g. before feeding. Atheromatous changes developed in the arteries, particularly the aorta, coronary arteries, and aortic cusps. In some animals xanthomatous deposits developed in the iris, encircling the organ and extending halfway across its width towards the pupillary margin. When these lesions were at their maximum, 116 days after discontinuing the cholesterol, the animals were inoculated intrathecally with the Nichols strain of Treponema pallidum: iritis developed in 4 of the cholesterol-fed albinos but not in those not so fed. The iritis appeared about 34 days after inoculation, and in one animal lasted for 209 days. In one rabbit which had been infected with T. pallidum 324 days previously and then fed with cholesterol, xanthomatous lesions appeared after 60 days, and 90 days later a severe iritis of both eyes occurred. It is considered that the iritis was syphilitic and that the xanthomatous lesions affected the response to syphilitic infection.

T. E. Osmond


Most of the steps in titration and standardization of Kahn antigen are also applicable to cardiolipin antigen. These consist of: (1) titration with saline to determine the titre; (2) comparative tests with syphilitic and non-syphilitic sera in parallel with a standard antigen to determine sensitivity and specificity; and (3) adjustment of the antigen if it is over-sensitive or under-sensitive. As a general rule lecithin 1% cardiolipin 0-1%, and cholesterol 0-025% produce a usable antigen. The titre of this is usually 1 of antigen +0-9 of 0-9% saline, and mixtures of 1+0-8 and 1+1 cannot be used, whereas, with a Kahn antigen of a titre of 1+1, proportions of 1+1 and 1+1-4 give very similar results; thus cardiolipin has a narrow titration range and Kahn antigen a relatively wide one. For a cardiolipin antigen with a ratio of 10 parts of lecithin to 1 part of cardiolipin appropriate concentration of reagents is needed; neither ratios of 0-5% to 0-05% nor of 2% to 0-2% are satisfactory. The dilutions do a 20 to 1 ratio produce a workable titre with any of the above 3 concentrations. As regards cholesterol, 0-025% is the optimum concentration; 0-05% may occasionally be satisfactory but 1% never is. Further tests showed that though certain (not approved) lots of lecithin gave satisfactory titration results they caused antigens to be under-sensitive. In order to bring all cardiolipin antigens to a 20 to 1 ratio these sensitivity different lecithin-cardiolipin ratios may be employed such as 9 to 1, 9-5 to 1, 10-5 to 1, and 11 to 1, or even smaller graduations than these, such as 10-7 to 1; it seems possible also that under-sensitivity of cardiolipin antigens may be corrected by a slight reduction in the amount of salt solution in making the suspension.

T. E. Osmond
ABSTRACTS


The author compared his "spot" test with the Wassermann and Meinicke (M.K.R.) tests for syphilis on 858 specimens of serum and 142 of cerebrospinal fluid (C.S.F.); the Harrison-Wyler technique was used for the Wassermann test (W.R.) and for W.R. the modification of Ford Robertson and Colquhoun for M.K.R. The antigen for the spot test is prepared by adding nine parts of 3% saline to one part of Meinicke antigen, both heated to 56° C., and pouring the mixture rapidly backwards and forwards. For the test proper, one drop of fresh serum (or C.S.F.) is placed in the well of a slide and one drop of prepared antigen added; the mixture is stirred with a glass rod and the slide is placed in an incubator at 56° C. for 10 minutes and then rocked with a rotary motion for one minute. Precipitation and agglutination indicate a positive reaction; granularity indicates a doubtful reaction and no change a negative reaction. All three tests were negative in 721 of 831 sera and positive in 62, while there was disagreement in 48. The spot test agreed with the W.R. in 97.5%, and the standard M.K.R. and W.R, agreed in 98% of 142 C.S.F. specimens there was agreement in 140 and disagreement (not in two). Of the 48 sera in which there was disagreement 25 were from syphilitic patients; omitting these, the number of cases in which there was disagreement is reduced to 23; in one case of G.P.I. the spot test alone was positive, and this case gave no false-positive reaction in 140 and disagreement in two. Of the 48 sera in which there was disagreement 25 were from syphilitic patients; omitting these, the number of cases in which there was disagreement is reduced to 23; in one case of G.P.I. the spot test alone was positive, and this case gave no false-positive reaction in 140 and disagreement in two. Of the 48 sera in which there was disagreement 25 were from syphilitic patients; omitting these, the number of cases in which there was disagreement is reduced to 23; in one case of G.P.I. the spot test alone was positive, and this case gave no false-positive reaction in 140 and disagreement in two. Of the 48 sera in which there was disagreement 25 were from syphilitic patients; omitting these, the number of cases in which there was disagreement is reduced to 23; in one case of G.P.I. the spot test alone was positive, and this case gave no false-positive reaction in 140 and disagreement in two. Of the 48 sera in which there was disagreement 25 were from syphilitic patients; omitting these, the number of cases in which there was disagreement is reduced to 23; in one case of G.P.I. the spot test alone was positive, and this case gave no false-positive reaction in 140 and disagreement in two.

In general, the spot test and the M.K.R. tended to remain positive in cases treated with penicillin. The clinical effects of the test were to be superior to those obtained with ordinary aqueous solutions of penicillin.

It was concluded that the daily intramuscular injection of 300,000 units of procaine penicillin suspension produced a definite therapeutic response. In certain cases, such as those of subacute bacterial endocarditis, the dose should be increased to 600,000 to 900,000 units. The preparation was exceedingly well tolerated, the injections were painless, and no untoward reactions were observed, except for some eosinophilia and small local compact infiltrated areas, which only appeared some weeks after repeated injections. Experiments on guinea-pigs showed that small cystic areas were produced with some necrosis of the muscle fibres.

T. E. Osmond

SYPHILIS (Therapeutic)


Various means of retarding the action of penicillin have been suggested, and Sullivan and others (Science, 1948, 107, 169) have described a procaine salt of penicillin which the present authors have employed in their work. Procaine penicillin is a crystalline compound consisting of equimolecular proportions of penicillin G and procaine. It is suspended in sesame oil so that 1 ml. contains 300,000 units of penicillin G and 124.5 mg. of procaine. Preliminary observations by Boger and others (Amer. J. med. Sci., 1948, 215, 250) showed that in 50 patients no local pain or other reactions were encountered, and that 18 of 23 patients suffering from pneumonia recovered without complications after a single intramuscular injection of 300,000 units.

The present report is that after the single intramuscular injection of 300,000 units of procaine penicillin into 59 subjects, serum levels of over 0.03 unit per ml. were usually obtained. In 20 healthy persons (afibrile and with normal kidney function) the penicillin levels were maintained for a mean period of 30 hours (variation from 15 to 36 hours). Increasing the dose to 400,000 units did not further increase the duration which was 14 normal subjects), but 600,000 units caused a definite increase from a mean period of 30 to 48 hours (in 8 normal subjects). In 10 febrile patients an injection of 300,000 units produced a mean penicillin level of 0.03 unit per ml. for over 36 hours, corresponding to the effect produced by 600,000 units in afebrile patients. Similar results were obtained in afebrile patients suffering from renal deficiency, showing that in this condition the elimination of penicillin is obviously delayed. Penicillin was estimated by a hemolytic titration method and by the agar plate method. The clinical effects of procaine penicillin suspension were observed in 44 patients—18 cases of pneumonia (12 primary and 6 secondary), 11 cases of pyelocystitis, 3 cases of furunculosis, 2 cases of post-pneumonic pleural empyema, 3 cases of tonsilitis, 4 cases of erysipelas, 2 cases of subacute bacterial endocarditis, and 1 case of staphylococcal septicemia. The patients with pneumonia received daily intramuscular injections of 300,000 to 600,000 units; the preparation was normally given for a further 2 to 3 days after lowering of the temperature. In empyema the same daily dose was given up to a total amount of 5,700,000 and 7,200,000 units. Two of the patients with erysipelas died, and at necropsy interstitial nephritis was evident, but this was considered to be in no way due to the action of procaine penicillin. The clinical effects were stated to be superior to those obtained with ordinary aqueous solutions of penicillin.

It was concluded that the daily intramuscular injection of 300,000 units of procaine penicillin suspension produced a definite therapeutic response. In certain cases, such as those of subacute bacterial endocarditis, the dose should be increased to 600,000 to 900,000 units. The preparation was exceedingly well tolerated, the injections were painless, and no untoward reactions were observed, except for some eosinophilia and small local compact infiltrated areas, which only appeared some weeks after repeated injections. Experiments on guinea-pigs showed that small cystic areas were produced with some necrosis of the muscle fibres.

R. Wien


An attempt was made to slow down the excretion of penicillin by the administration of caronamide (4'-carboxyphenylmethanesulphonanilide) and in this way to obtain higher and better maintained penicillin levels in plasma. Penicillin concentrations were assayed on citrated plasma by the serial dilution method of Rammekamp (Proc. Soc. exp. Biol., N. Y., 1942, 51, 93) modified by the use of 0.5 ml. of the plasma dilutions. As it is recognized that excretion of penicillin is slower in older people two groups of patients were investigated: (1) 7 patients over 60 years of age receiving 2 g. caronamide 4-hourly; (2) 10 patients under 60 receiving 4 g. 4-hourly. The dose of caronamide was given in both groups for 12 hours before the intramuscular injection of 1,000,000 units of penicillin G and was continued for 24 hours thereafter. The subjects were all male convalescent patients, none of whom was suffering from congestive heart failure or recognizable renal disease; all received ordinary hospital diet.

In group (1) peak levels of penicillin in plasma were double those noted in control subjects given no caronamide. This concentration was maintained at a high level, being after 6 hours 10-fold and after 24 hours 20-fold that in control subjects. In group (2) patients the peak concentration was 3 times higher than in a control series and after 8 hours penicillin concentration
in plasma was still 0.4 unit, while the plasma of the control series contained little or no penicillin.

Apart from slight nausea in 4 patients, with vomiting in 2 of them, and occasional slight reduction of Benedict's solution by urine, no untoward effects were noted after caronamidé administration. To evaluate the effect of sodium benzoate in similar circumstances, the 4 patients, 2 in each group, in whom penicillin levels in plasma had been highest with caronamidé, were given moderately large doses (up to 4.5 g. 2-hourly) of sodium benzoate. No significant rise in the level of penicillin in plasma was noted in these cases, although 4 patients complained of nausea.

**J. B. Wilson**

### Plasma Penicillin Levels after Oral Penicillin with and without Oral Caronamidé


An attempt was made to delay the tubular excretion of penicillin by the administration of caronamidé. The penicillin (100,000 units) was buffered with 0.5 g. sodium citrate and given orally in tablet form 4-hourly for 4 days. For 24 hours between the second and third days caronamidé was given with the penicillin, also at 4-hour intervals. The patients were all convalescent males on an ordinary hospital diet and without evidence of congestive heart failure or renal disease such as might delay their excretion of penicillin. Group I consisted of 8 patients under 60 years of age who received 4 g. caronamidé every 4 hours. Group II contained 9 patients over 60 years of age given 2 g. caronamidé every 4 hours. In Group III, 7 patients over 60 years of age were given 3 g. caronamidé every 4 hours. In this latter group, opportunity was also taken to study the caronamidé levels in plasma. Special note was made of the penicillin levels in plasma 4 hours after injection, that is, at their lowest point. The authors conclude that the penicillin levels in plasma are increased while caronamidé is being administered but that this increase is small and variable, the main controlling factors being age and state of renal function, factors which are known to affect both penicillin and caronamidé excretion. The caronamidé excretion was slowest in those patients with a slight increase in non-protein nitrogen content in the blood. The detailed results show that the dosage of penicillin used alone could not be relied upon to maintain an adequate penicillin level in plasma, but that with the addition of caronamidé plasma penicillin levels of 0.03 unit per ml. could be maintained in Group II. In Groups I and III caronamidé enhanced and prolonged the plasma concentrations after oral penicillin.

**J. B. Wilson**

### A New Vehicle for Parenteral Repository Penicillin Therapy


Evidence is produced to show that a mixture of potassium penicillin, adrenaline, and oil is not only easy to inject but prolongs the duration of effective levels of penicillin in the blood. Experiments were carried out on normal human volunteers. The dosage of penicillin ranged from 150,000 to 600,000 units and of adrenaline from 0.1 to 1 mg. For control estimations penicillin in isotonic saline or in beeswax-oil was used. In subjects receiving the saline solution (300,000 units) there was an initial high level, but this level rapidly fell, reaching zero by the seventh to eighth hour. With doses of between 200,000 and 600,000 units of the penicillin-oil-adrenaline mixture, injected intramuscularly, there were effective concentrations in the blood from 12 to 18 hours after the injection. A dose of 150,000 units of penicillin with 0.15 mg. of adrenaline, injected subcutaneously, produced in some patients a demonstrable level 15 hours after the injection. Serial estimations of the blood pressure at periods up to 21 hours after injection showed that the vasoconstrictor substance had exerted no significant effect.

**T. Anderson**

### A Clinical Study of the Toxic Effects of Bismuth Treatment in Syphilis.

**Curtz, F. R. (1948).** *Acta dermat.-venereol.,* Stockh., 28, 446.

A series of 143 patients (74 male and 69 female) with primary and secondary syphilis, received a minimum of 3 combined courses each consisting of 6 injections of 0.6 to 0.75 g. of neoarsphenamine and 10 injections of bismuth subsalicylate in oil containing 0.1 g. of bismuth per ml. (3 ml. for men and 2 to 2.5 ml. for women). The courses were repeated after intervals of 6 weeks, 2 months, and 3 months. Thirty-three patients developed stomatitis, 10 during the first course, 3 in the subsequent interval, 17 during the second course and 3 during the third course. In 20 cases the condition was severe, necessitating rest in bed in 10 instances. Diphtheria was suspected in 2 cases, as was agranulocytosis in some cases, but no granulocytopenia was demonstrable.

Stomatitis was the sole complication in only 4 patients, for albuminuria, with or without cylindruria, was also present in 21 and articular pains in 8. Urinary abnormalities were noted in 37 patients but there were no other signs of renal involvement. Stomatitis was most likely to arise in the presence of dental caries and para-dentosis. The importance is stressed of attention to dental hygiene before antisyphilitic treatment with bismuth.

**R. R. Wilcox**

### Jarisch-Herxheimer Reaction in Early Syphilis Treated with Crystalline Penicillin G.


Herxheimer reactions have been recorded after intramuscular, intravenous, and oral administration of penicillin, in aqueous solutions, and in suspensions in peanut oil and wax, in early syphilis. The most consistent, most highly diagnostic, and most accurately measured manifestation is an elevation of temperature. With commercial penicillin, these febrile reactions occur in 30 to 70% of adults with early syphilis. The author has collected data from 20 clinics in the United States on 939 patients with early syphilis who were given 2,400,000 units of crystalline penicillin G. Of this group, 384 (41%) had pyrexia, but no significant racial or sex differences as regards its incidence or severity were observed; pyrexia developed with equal frequency and severity in serum-negative primary, serum-positive primary, and secondary syphilis. Temperatures were recorded rectally every 4 hours and a temperature above 100° F. (37.8° C.) was considered to represent a febrile reaction.

In a group of 121 patients the temperature was recorded every 2 hours to determine its relation to dosage. Within a wide range (10 to 120,000 units per kilogram body weight) the incidence of the temperature reaction was constant (40 to 50%) and the temporal pattern uniform and independent of the dosage. Febrile reactions were absent with very small doses (1 to 5 units per kilo body weight) but they occurred with single doses of penicillin.

In the author's experience what has been termed ninth-day erythema developed between the seventh and fourteenth days after the first injection of arsenic and was independent of the second injection. A rise in temperature preceded the rash, but occasionally the high temperature occurred alone. Some patients complained of "sore throat" and pharyngitis. Streptococci were demonstrated in some cases. The sore throat preceded the rash by one day. Two cases of hemorrhagic encephalopathy were included in this series, in both of which the symptoms started 9 days after the first neoarsphenamine injection; in one case the condition was accompanied by a morbilliform rash. As an explanation of ninth-day erythema it is thought that a latent infection—for example, streptococcal—is activated by the first injection of neoarsphenamine. [This paper is not very convincing, and it does not explain why the eruption should appear about the ninth day.]

G. W. Csonka


This is a study of 84 patients with early syphilis treated with daily injections of amorphous sodium penicillin in water-oil emulsion and of 12 patients receiving a daily dose in 2 equally divided injections at 12-hour intervals. Different brands of penicillin were used, the total dose varying from 2,000,000 to 5,000,000 units. The daily dose ranged from 400,000 to 1,000,000 units. The authors note that penicillin levels in serum were not constant either for the same patient or different patients and that frequently there was a complete absence of penicillin in the serum during the second half of the 24-hour period after single daily injections.

Of 66 patients followed up for periods of from 3 to 26 months, 55 showed satisfactory clinical and serological progress and there were 7 clinical and 2 serological relapses as well as 2 cases of serological failure. The ascertained failure rate was thus 16-6%. Spinal fluid of 49 patients was examined approximately 6 months after the end of treatment, with negative results in all but 3 cases. Out of these there was a slight increase in lymphocytes (5 and 8 cells respectively) with all other findings negative, while in the third serological reactions were positive in both blood and spinal fluid. Though the relapses appeared to be unconnected with the total amount of penicillin given, 10 out of the 11 occurred in patients who had been given one injection daily.

The authors consider that the administration of penicillin in water-oil emulsion prolongs its presence and probably its action beyond the time when assayable levels of penicillin are demonstrable in the serum. Comparable results were achieved by workers in the Royal Navy and the Royal Air Force during the war with daily aqueous injections of 300,000 and 500,000 units up to a total dose of 3,000,000 units.

G. L. M. McElligott


The authors give detailed case-reports of 9 patients suffering from intestinal keratitis treated with penicillin and fever induced by twice-daily injections of typhoid vaccine; the total dosage of penicillin ranged from 4 to 6 mega units, and the average number of daily fever reactions was twelve. [It is not stated what was the dose of the typhoid vaccine.] Most of the patients received arsenic and/or bismuth for varying periods after the penicillin-fever therapy. All had poor vision (less than 20/200) in one or both eyes before treatment, and in 8 of the patients the final visual acuity in the poorer eye was 20/100 or better. One patient relapsed 10 months after treatment; she had had higher fever than most of the others but did not follow treatment with arsenic and bismuth. It appears that most of the benefit must be attributed to the fever, since in one case lesions actually progressed during penicillin treatment and before fever therapy was started. The most striking observation was the lessening of pain and photophobia within 5 to 6 days of starting fever therapy. The ultimate results are not considered very satisfactory.

T. E. Osmond


This article describes the results of treating 76 patients suffering from various forms of comparatively severe neurosyphilis with penicillin plus malaria therapy. The patients included 19 with paraparesis, 13 with tabes, 7 with optic atrophy, 8 with meningocerebrospinal neurosyphilis, and 13 with asymptomatic neurosyphilis. The duration of the disease was unknown in 37, 5 years or less in 2, 6 to 10 years in 6, 11 to 15 years in 12, 16 to 20 years in 7, and more than 20 years in 12; 40 patients had had little or no previous treatment, and 30 had had 20 or more arsenical and heavy metal injections. [It is not stated in what form the arsenicals were given.]

While 53% of patients had Grade III cerebrospinal fluids before treatment, only 1% had such a fluid after treatment; 5% had arrested fluids before and 63% after treatment; 88% had Grade I fluids or better after treatment. Of 13 patients with asymptomatic neurosyphilis, 70% had a satisfactory clinical result and 6% were worse; those with optic atrophy showed the poorest results. In general, improvement increased with lapse of time, though additional therapy did not appear to be very effective; crystalline penicillin G did not appear to be more effective than the amorphous form, and previous treatment did not seem to affect the results. It is concluded that malaria therapy with penicillin is the treatment of choice in severe parenchymatous neurosyphilis [though no figures are given to show that this combination is more effective than penicillin alone].

The authors consider that the administration of penicillin in water-oil emulsion prolongs its presence and probably its action beyond the time when assayable levels of penicillin are demonstrable in the serum. Comparable results were achieved by workers in the Royal Navy and the Royal Air Force during the war with daily aqueous injections of 300,000 and 500,000 units up to a total dose of 3,000,000 units.

G. L. M. McElligott
The usual total dosage of penicillin was 4 to 6 mega units, and of malaria (benign tertian) 8 to 10 paroxysms averaging more than 50 hours of fever over 103°F. [In both the text and in the tables actual and percentage figures are given but the numbers in each category are too small to be statistically significant and only general conclusions can be drawn. It seems not improbable that better results might have been obtained with a higher total dosage of penicillin, since the amount employed was little more than is now commonly used in early syphilis.]

**T. E. Osmond**


The authors observed 223 neurosyphilitic patients for at least one year after treatment: 108 of them were given penicillin alone and 115 combined penicillin and malaria therapy. In 104 of the 223 patients observation was continued for 2 years or more. The penicillin regimen consisted of 100 3-hourly injections of 40,000 units each (4 mega units), while 50 or more hours of fever at a rectal temperature of 103.5°F. or over constituted the malaria course. At the end of one year 97% of the group treated by penicillin alone showed clinical improvement, and in 82% better results were obtained on examination of the cerebrospinal fluid (C.S.F.). For the penicillin with malaria group the figures were 69 and 89%, respectively. At the end of 2 years 86% of the group given penicillin alone showed clinical and 85% C.S.F. improvement, while the comparable figures for the penicillin and malaria series were 66 and 98%. At the end of one year 21-5% of those receiving penicillin alone and 12-3% of those given the combined treatment had completely negative C.S.F., but at the end of 2 years the figures had risen to 37-2 and 14-5%. With few exceptions, clinical improvement was accompanied by improvement in the condition of the C.S.F.

It is concluded that patients with asymptomatic neurosyphilis, meningo-vascular syphilis, and tabes dorsalis respond as well to penicillin alone as to penicillin with malaria. In this series those with paresis and taboparesis responded clinically as well to penicillin alone as to the combined treatment, but at 2 years there was a slight superiority in the C.S.F. response in those treated by the latter method. It is considered that further observation is necessary before a final conclusion can be drawn, and that the long-term result may well be that penicillin alone is just as good: it is certainly less hazardous.

**R. R. Wilcox**


In the treatment of malaria induced therapeutically in cases of dementia paralytica some workers advocate quinacrine hydrochloride (mepacrine) while others favour the use of quinine. Though convulsive seizures rarely occur after normal doses of mepacrine, it has been noted that when similar doses are given to patients with advanced syphilis of the nervous system such effects are not uncommon. In this study 115 patients with dementia paralytica were given mepacrine, and 153 were given quinine. Convulsive episodes were 14 times as common after mepacrine as after quinine. In a series of 150 patients with less organic deterioration the convulsion rate after mepacrine was roughly similar to that after quinine. The authors conclude that mepacrine should not be used for the termination of induced malaria in patients suffering from dementia paralytica.

**G. L. M. McElligott**

**GONORRHEA (General)**


Many cases of Reiter's disease were observed after an epidemic of dysentery in 1944 on the Karelian isthmus in Finland. There were 344 patients but the records of 10 have been lost; 310 were men and 34 women; 288 were between the ages of 21 and 40 (extremes 2 and 55). In 97% joints were involved and in 89-2% the eyes; 79-3% had abnormalities of the urogenital system. In 69-1% the onset was monosymptomatic, involvement of the eyes and urogenital system being the common combination. In only 8% did the entire triad appear over a long period. All three signs were finally evident in 69-8%; in 71-4% of those showing all three signs the lesions appeared within the first 10 days, though occasionally a symptom was delayed for as long as 100 days after onset.

Arthritis, present in 325 cases, involved more than one joint in 316. In 82-5% articular swelling was noted but in 17-5% only arthralgic pains were present. The most commonly involved joints were knee, ankle, toes, shoulder, wrist, fingers, metatarsals, sacro-iliac, elbow, vetræbrae, and hip, in that order. Exudate from the knee-joint was examined in 30 cases. It was greenish-yellow and viscous, and usually contained up to 90% neutrophil granulocytes, but sometimes lymphocytes predominated. Radiological examinations were made of 76 joints but in none were the findings abnormal.

Ocular involvement was noted in 298 patients—acute conjunctivitis in 239, kerato-conjunctivitis in 13, iritis in 11, corneal ulcer in 4, and iridocyclitis in 8; 20 others had mild ocular symptoms without any obvious lesions. In 80% of those with conjunctivitis both eyes were simultaneously involved. Smears and cultures of the ocular discharges were negative.

Nine patients had renal involvement; 29 out of 30 specimens of urine gave negative results on culture but Salmonella paratyphi B was found in 1 case. Although 103 had urethritis alone, in 63 others the urethritis was combined with a macular eczema of the penis, in 11 with a suppuration or ulceration of the penis, in 24 with a reddening of the mental margin, in 12 with dysuria, in 4 with hematuria, in 9 with nephropathy, and in 9 with involvement of the testis or epididymis. Ten others had a macular eczema of the penis, 14 dysuria, and 3 pain in the testes or penis without obvious urethritis. No bacteria were generally found in the urethral discharge which, in about half the cases, cleared up in the first week and in 87% by the fourth week. Twenty-two patients developed cystitis but cystoscopy revealed nothing abnormal. Penile skin lesions were observed in 87%.

Mild dry pleurisy was definitely diagnosed in 26 patients and was considered probable in 48 others; 23 patients had myocarditis and pericarditis, 16 myocardiitis alone, and 3 pericarditis alone. The electrocardiogram was abnormal in 2. The carditis lasted for up to 1½ months and might occur as early as the first week of the disease, though in one case it was delayed until the thirty-second month. Hyperkeratotic skin lesions re-
ABSTRACTS

GONORRHEA (Therapeutic)


To test the efficacy of penicillin tablets given by mouth in preventing gonorrhea 350 naval personnel were divided into two equal groups. In one group each man, on return to his ship after each shore leave, received a buffered tablet of 100,000 units of crystalline penicillin G (later in the experiment this dose was raised to 250,000 units); the men in the second (control) group received similar tablets, but containing no penicillin. The average shore leave was 6 to 8 hours. In 24 weeks there were 43 cases of gonorrhea in the control group, making 11.9 infections per 1,000 leaves. In the group given 100,000 units of oral penicillin there were 5 cases of gonorrhea in 16 weeks, equivalent to 1.8 infections per 1,000 leaves. Over the last 8 weeks, when 250,000 units were given, only one further case of gonorrhoea occurred, but this patient said he had not taken the tablet. Later the 250,000-unit tablets were made available to the entire station on a voluntary basis. Over 8 weeks, covering a total of 1,943 leaves, this prophylaxis was requested on 670 occasions; there was one question-able failure. In the 1,273 leaves where this prophylaxis was not asked for 6 cases of gonorrhoea developed.

It is considered that the oral penicillin in this experiment was highly effective in the prevention of gonorrhoea. The average frequency with which penicillin was taken during the first 16 weeks was 1:1 tablets weekly, and there has been to date no evidence of penicillin sensitization, no development of penicillin-fast strains of gonococci, and no instances of suppressed syphilitic infection. The maximum length of time after exposure for which a single 250,000-unit tablet is still effective remains to be determined. G. W. Csonka


The treatment of sulphamidine-resistant gonorrhoea with oral penicillin was investigated. In a pilot study on 35 cases, 200,000 units were given in 3 schedules: (1) 40,000 units 4-hourly by day cured 3 out of 10 infections; (2) 40,000 units 2-hourly by day cured 7 out of 11; (3) 40,000 units 2-hourly by night with the patient fasting cured 13 out of 14. The third schedule was then adopted in the treatment of 97 cases. Seven patients, penicillin being used in gelatin capsules containing 10,000 to 15,000 units and 0.5 g. sodium citrate; 47 patients received 200,000 and 53 had 300,000 units; 73 infections had already proved sulphamidine-resistant. Oral penicillin cured 79. Gonococci disappeared from discharge more slowly than after intramuscular penicillin. Discharge usually lasted for from 3 to 5 days, but in 7 cases for more than 7 days. In 8 out of 14 failures, a second course of 500,000 to 600,000 units orally cured the infection. S. S. B. Gilder


A single injection of procaine penicillin G in sesame oil, containing from 100 to 500 units per kilo body weight, was given to each of 50 patients with acute uncomplicated gonorrhoea. Cure was assumed if smears and cultures were negative 48 hours after treatment. At the end of the experiment all patients received 300,000 units of penicillin G in oil-beeswax, before they were discharged from hospital. Serial blood specimens for penicillin assay were examined by the Eagle modification of the Kirby-Rantz method for 4 hours after the injection; (the method consists of serial dilutions in which complete inhibition of hemolysis of human group O erythrocytes by the C-203 strain of Streptococcus pyogenes was the end point). In 4 male patients the total urine was similarly examined for penicillin content. It appears that the peak concentrations of penicillin in the blood are higher after the aqueous product, but that the levels are better sustained with procaine penicillin in corresponding doses, as tested over 4 hours after injection. The urine contained traces of penicillin, but this had no bearing on the therapeutic outcome. It was found that
100 units per kilo failed to cure; all patients receiving 250 units per kilo appeared to be cured. The authors recommend 500 units per kilo (36,000 units of procaine penicillin G for the average adult) as the routine dose in uncomplicated gonorrhea.

[The 48-hour period which was allowed to elapse before assessing "cure" appears very short; also the small volume—average 0.12 ml.—which makes up the dose might easily lead to inaccuracies.]

G. W. Csonka


It has been shown that the impurities in amorphous penicillin enhance its activity in vitro and in animal experiments. The effect of these impurities, which are heat-stable, was thus called "enhancement factor." A series of male patients with acute gonorrhea were divided into two groups: the one receiving 10,000 units of crystalline penicillin every hour for three doses, the other receiving the same dose of penicillin with a determined amount of enhancement factor (calculated to correspond with a 4- to 6-fold increase in the penicillin level in the blood of rabbits). In a second similar series a different enhancement factor was used, but its dosage had to be halved as its injection caused so much pain. In a few patients receiving the enhancement factor the penicillin level in the blood was estimated but showed no increase (although it did in rabbits). Clinically it was not possible to make claims for any added value of the amorphous penicillin—that is, penicillin with enhancement factor—over the crystalline penicillin. It was thought possible that the higher blood levels in rabbits may have been due to a difference in administration of the enhancement factor, which was given intravenously as against intramuscularly in man.

G. W. Csonka

OTHER VENEREAL DISEASE CONDITIONS


The histories of 3 cases of abacterial pyuria are presented in detail. This well recognized condition is also referred to in the literature under various other names, including "amicrobic pyuria," "sterile pyuria," and "acute interstitial cystitis." The condition has frequently been confused with tuberculosis of the urinary tract, because of the finding of marked pyuria, with absence of infective organisms either in the urine smear or in the culture. All investigations show, however, that "abacterial pyuria" is an entity quite distinct from tuberculosis. Since Wildbolz first demonstrated the dramatic efficacy of the arsphenamines in this disease, the compounds have been used as a therapeutic test as well as for the specific cure of the condition.

Of the 3 cases here reported, 1 was treated with penicillin alone and 2 patients received both penicillin and arsphenamine. In all cases the condition resolved completely, but in the case treated with penicillin alone resolution was slower. [No patient received arsphenamine alone, so that, apart from the small number of cases reported, no impression can be obtained whether these patients might not have been more effectively treated with the arsenical only.] The authors suggest that abacterial pyuria and Reiter's syndrome may be merely different manifestations of the same disease. Therapeutic trials of arsphenamine in a series of cases of Reiter's syndrome might elucidate this point.

James Kemble


Vaginal smears were examined and cultures made from 39 women. Döderlein's bacillus (Lactobacillus acidophilus) was usually recognized without difficulty in the former and was cultured from 21 individuals. The commonly observed organisms were however corynebacteria (isolated from 33 cultures). In direct films these were sometimes Gram-negative and of a curved shape, and hence might be mistaken for vibrios. The use of special media failed to produce any growth of vibrios. Coccii were usually not abundant in direct smears but 29 cultures were positive for staphylococci, and Diplococcus crassus (which could be mistaken for the gonococcus) was isolated from 10 persons. In two direct smears slender Gram-negative filaments, possibly of Streptobacillus moniliformis, were observed.

G. T. L. Archer


Evidence is accumulating of the beneficial effects of the use of streptomyacin in a variety of infections of the genito-urinary tract. Cases reported include many which have previously proved resistant to both penicillin and the sulphonamides. The results obtained in 51 cases here reported are encouraging. Streptomyacin has a bacteriostatic action against Gram-negative bacilli and is especially effective against Bacterium coli, Aerobacter aerogenes, Proteus vulgaris, the gonococcus, Pseudomonas aeruginosus, Klebsiella pneumoniae, Salmonella typhi, and Streptococcus fecalis. The cases reported included the following conditions: acute pyelonephritis and ureteric obstruction, urinary sinus tracts, chronic upper urinary tract infections, interstitial cystitis, epididymitis and prostatitis, gonorrheal urethritis, and tuberculosis of the genito-urinary tract. The benefit varied greatly, especially in relation to the location of the infection. The extent and severity of the toxic manifestations encountered call for a warning. The most serious were disturbance of auditory nerve function and a fall in the neutrophil count. The development of streptomyacin-resistant strains in the organisms not completely destroyed was also observed.

James Kemble