**ABSTRACTS**

**SYphilis (Clinical)**


**Misleading Effect of Treatment with Penicillin on the Diagnosis of Neurosyphilis.** (De misleidende invloed van behandeling met penicilline op de diagnostiek van neurololies.) **Mackenzie-Van der Noordaa, M. C., and Haagsma, F. M.** (1958). *Ned. T. Geneeskr.*, **102**, 1595.


**SYphilis (Therapy)**


The first part of this study relates to 2,954 inmates of Sing Sing prison, Ossining, New York, seen between 1939 and 1949, in whom a diagnosis of latent or asymptomatic syphilis was made. During that period the treatment was mainly with arsenical drugs and bismuth, and although these were later superseded by penicillin the results of this study are important in evaluation of recent therapeutic methods. Very careful studies of all syphilitic prisoners were made, and so far as possible information was obtained from institutions or individual physicians regarding previous treatment and the results of tests. Treatment in prison was carefully controlled and standardized on certain schedules, and diagnostic categories were clearly defined.

In 1953 a special study was made of a representative fraction of the original series, namely 277 persons who had had no other treatment for syphilis than that given in prison and who were still in prison and thus available for study. For 130 of these the time from the onset of the disease was known and up to the final examination in 1953 this averaged 25 years; for the entire group the average period of study and observation was 14 years. The records showed that out of the original 2,954 studied the cerebrospinal fluid (C.S.F.) findings were negative in 1,905 and that re-examination at a later date of 288 of them showed that only one was abnormal, while none developed clinical neurosyphilis. Of the group of 277 patients, 255 were given a full neurological examination; none had frank evidence of general paresis or tabes dorsalis but isolated neurological abnormalities were noted in a few. The frequency of such signs as altered patellar reflexes and papillary abnormalities was no greater than that in a comparable group of non-syphilitic persons. Thus no evidence of the development of neurological symptoms or signs of neurosyphilis was obtained. However, in regard to the cardiovascular system one man was found to have an aortic aneurysm, and nine others had an accentuated second aortic sound or some degree of aortic dilatation, but these findings are considered to be not necessarily or even probably due to syphilis. No correlation with persistently positive serological reactions was found. It is concluded that “adequate” treatment of latent syphilis with arsenical drugs and bismuth results in a very high degree of success.

Robert Lees

From the Institute of Venereology, Budapest, the author presents the results of treatment in 512 cases of neurosyphilis, these comprising 227 cases of meningovascular syphilis, 103 of asymptomatic neurosyphilis, 81 of tabes dorsalis, 40 of general paralysis, and 61 of taboparesis, all of which were discovered as a result of the examination of 5,000 syphilic cases. The importance of examining the cerebrospinal fluid (C.S.F.) in all cases of latent syphilis before treatment is instituted is stressed.

Findings in the C.S.F. are presented in tabular form, using the classification of Moore. In 35 per cent. of cases of tuberculous meningitis examination of the C.S.F. gave negative results, but in these the treponemal immobilization reaction was positive. Results are given for the entire group of 512 patients, including those treated by various methods before the advent of penicillin, and also for the 344 (67 per cent.) amongst them who received the antibiotic. Penicillin was used in the form of “supracillin” (procaine penicillin with aluminium monostearate in oil) or “bismocillin” (procaine penicillin with aluminium monostearate and bismuth subsalicylate). Patients first received two or three courses each of 6 to 9 mega units, and if after an interval [duration not stated] the C.S.F. still showed evidence of activity a further course of penicillin was given. If this, too, was unsuccessful it was repeated, with the addition of fever therapy. The authors conclude that penicillin is required in 67 per cent. of cases of neurosyphilis and that all cases in which there is clinical or serological activity should be treated initially with penicillin alone.

[It seems likely that the outcome, in terms of the reversion of changes in the C.S.F., has been assessed prematurely in this series. Hahn and co-workers (J. chron. Dis., 1957, 7, 209, and A.M.A. Arch. Derm., 1956, 74, 355, and 367; Abstr. Wild Med., 1957, 21, 249) have shown that changes in the C.S.F. may take a considerable time to subside following the successful treatment of neurosyphilis.] Eric Dunlop


SYphilis (Serology)


In experiments performed in the Venereal Disease Branch of the Communicable Disease Center, Chamblee, Georgia, anti-human and anti-rabbit sera were prepared in goats by Poom's method (J. Path. Bact., 1943, 55, 419) and the globulins separated by precipitation with ammonium sulphate followed by dialysis. The purified globulins were then conjugated with fluorescein and used in testing sera for the presence of antibodies to Treponema pallidum. The test was carried out by drying suspensions of treponemes obtained from infected rabbits' testes on slides, lightly fixing by heat, and then exposing the fixed organisms to the action of the serum suspected of containing antitreponemal antibodies for 30 minutes. The slide was then washed in buffered saline and the appropriate fluorescein-labelled antiserum preparation added and allowed to act for a further 30 minutes. After a further washing in buffered saline the slide was mounted in diluted glycerine and examined microscopically by ultra-violet light. Where the serum under test by this method contains antitreponemal antibody this becomes fixed to the organism and, because of its globulin nature, subsequently unites with the fluorescein-labelled antiserum so that the treponemes become fluorescent under ultra-violet light. Mechanical rotation of the slides during treatment with the serum and antiserum improves the results, while the application of acetone to the fixed smears for 15 minutes before the addition of the serum has been found to reduce background fluorescence.

The examination of sera from rabbits at various intervals after infection with syphilis and of a few human sera showed that the fluorescence technique was more sensitive than the treponemal immobilization test, but gave results which agreed well with those of the treponemal complement-fixation test. The ease and speed of the test recommend it as a possible alternative to other treponemal tests if further investigation confirms its specificity and sensitivity.

A. E. Wilkinson


During the 10 weeks between April 18 and June 25, 1955, the New York City Health Department conducted an intensive house-to-house blood-testing programme in two districts of Harlem where there was a known high prevalence of syphilis. Of the 23,675 persons tested, 6,701 were white, 14,872 non-white, and 2,102 were classified as "others." Among 8,739 Puerto Ricans included in the survey there were 5,978 white and 917 non-white subjects and 1,844 "others." The results are tabulated according to age, sex, and colour of skin.

Standard serological tests for syphilis (S.T.S.) gave a total of 3,406 abnormal reactions, an overall S.T.S. reactivity rate of 14.4 per cent. Analysis showed that for all non-whites this rate was 17.6 per cent., for non-white Puerto Ricans 11.3 per cent., for white Puerto Ricans

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9.2 per cent., for "other" Puerto Ricans 12.9 per cent., and for indigenous whites 4 per cent. Subsequent screening of the positive reactors showed syphilis to be present in 1,918 persons (8.1 per cent. of those tested). Of these, 406 were new cases, 911 were cases requiring further treatment, and 601 were considered adequately treated. Syphilis was found to be twice as prevalent in non-whites as in Puerto Ricans, but false positive reactions occurred in 31.7 per cent. of Puerto Ricans, a figure three times that found in non-whites. On the basis of the percentage of cases of syphilis found in the population examined it was estimated that there are 4,572 undiscovered syphilitics in Central Harlem and 10,199 syphilitics requiring further treatment.

Of the 3,406 positive reactors, 2,116 later reported to the Health Department Clinic and underwent additional physical and radiological examinations. Genital smears for detection of gonorrhea were obtained from all the women and smears for Papanicolaou staining were made from the cervical secretions of 1,011 women over 21. The results of this additional multiphasic screening are also tabulated. They revealed eighteen cases of gonorrhea, 23 of previously unknown diabetes, thirteen of squamous carcinoma of the uterine cervix, three of active pulmonary tuberculosis, and twenty with evidence of heart or lung disease. The authors stress the value of such multiphasic screening procedures and point out that if the survey had not been specifically directed to syphilis detection it would no doubt have yielded many more cases of undiscovered diabetes, chest disease, and cancer.

Benjamin Schwartz


In this introductory note to a series of studies of the localization and estimation of serum antibodies in human syphilis and experimental syphilis in rabbits and their quantitative relation to the serum proteins, reported from the Dermatological Clinic of the University of Siena, the author points out the advantages of continuous-flow electrophoresis, which allows the quantitative separation of serum components with different mobilities in an electrical field by virtue of the fact that slower moving components need not travel through material previously in contact with faster moving components and can therefore be collected in a much purer state than with the standard procedure. The strength of current used must be such as to allow effective separation and yet not to cause undue heating of the paper.

The apparatus, which is described, consists of a direct-current generator and the electrophoresis cell proper. Linear electrodes extend the whole length of the paper, which hangs vertically with its upper end in a trough containing buffer; serrations at the lower end of the paper overhang a series of test-tubes in which the fractions are collected. Two small beakers with a feeder wick are placed against the paper; one of which contains the material to be examined, the other bromphenol blue, a substance which has a mobility similar to that of albumin, but is clearly visible and thus allows the progress of the separation to be followed. About 5 ml. serum can be separated in 36 to 48 hrs. For final identification a unidirectional electrophoresis of the same material is performed and the protein content of the various fractions is determined by a rapid ultraviolet differential absorption method at 215 and 225 μμμ in a Beckman spectrophotometer. For this method sodium barbitone buffer is unsuitable, because it interferes with the ultraviolet reading. The serum fractions are freeze-dried and preserved in vacuo until required.

F. Hillman


This paper from the Friedrich-Schiller University, Jena, is mainly concerned with experiments relating to the problem of the transfer of syphilis by blood transfusion. They showed that rabbits infected by intracardiac injection of an emulsion of Treponema pallidum or of the blood of syphilitic rabbits developed a significant rise in the number of positive reactions to Nelson’s treponemal immobilization (T.P.I.) test 2 months after the inoculation, but that this rise was not so sustained as in the donor animal, which was infected by the usual intratesticular route. It is suggested that this difference in T.P.I. reactions was due to the recipient receiving a smaller amount of infected material, with which it was better able to deal, than the donor animal.

In the performance of human blood transfusions it is generally assumed that syphilitic blood which is kept at 5°C. for 4 days becomes non-infective and may be used for transfusion. In order to test this assumption rabbits were infected with syphilitic human blood by the intracardiac method described. The results were apparently satisfactory, as the animals which received infected blood stored at 5°C. for 5 days did not develop a positive T.P.I. reaction. It seemed possible to the author, however, that the amount of syphilitic human blood employed did not contain a sufficiently high concentration of treponemes to provoke a positive reaction. In the next experiment, therefore, blood from a female patient with secondary syphilis and demonstrable treponemes in genital lesions was injected into mice, part of it immediately and the rest after being stored at 5°C. for 5 days. After 8 weeks all the mice were killed and a suspension of their organs inoculated into the testicles of rabbits. In control animals, which received injections of healthy mouse tissue, the T.P.I. reaction remained negative; all the test animals, however, developed significant positive T.P.I. reactions. The results suggest that the practice of keeping syphilitic blood for 5 days in the refrigerator does not render it safe for transfusion purposes.

G. W. Csonka

The authors, working at the Walter Reed Army Institute of Research, Washington, D.C., have studied the effect of varying the lecithin content of cardiolipin antigens used in the V.D.R.L. slide test and the Kolmer complement-fixation test. It was found that in both these tests reactivity with syphilitic sera was increased by increasing the lecithin content of the antigen, while reactivity with sera which otherwise gave non-specific reactions was decreased or abolished.

A simple test for the differentiation of the antilipid antibodies found in syphilis from those occurring in non-treponemal diseases, based on these observations, is described. Two sets of serial two-fold dilutions of the serum under investigation from 1:1 up to 1:32 are made in triethanolamine buffered saline solution at pH 7-3 and are tested by the V.D.R.L. slide technique:

(a) with V.D.R.L. antigen (which contains 0-15 g. of lecithin per 100 ml.).

(b) with a similar antigen containing 0-27 g. of lecithin per 100 ml., the concentrations of the other components being unchanged.

Values ranging from 4 to 4 are allotted to the degrees of flocculation produced in each series, these values for each antigen being added together and the totals compared. The serological pattern is designated "non-syphilitic" if the V.D.R.L. antigen gives the greater total ("maximal reactivity"), "syphilitic" if the antigen with the increased lecithin content gives the greater total, and "equivocal" if the totals show a difference of no more than 1, based on at least two serum dilutions.

This test was performed on sera from 119 cases in which the diagnosis of syphilis had been confirmed by positive dark-ground findings or positive reactions to specific treponemal tests, such as the treponemal immobilization (T.P.I.) test. The pattern was syphilitic in 113, equivocal in 4, and non-syphilitic in two cases, these last two sera coming from patients with secondary and latent syphilis respectively. The test was also performed on 45 sera which were regarded as having given non-specific reactions in standard serological tests, the specific treponemal reactions being negative; in 38 of these cases the pattern was non-syphilitic, in three equivocal, and in four syphilitic.

A. E. Wilkinson


Biol. méd. (Paris), 47, 181. 7 figs, 45 refs.

The technique used in performing the treponemal immobilization (T.P.I.) test at the Hôpital Saint-Lazare, Paris, where some 20,000 sera have now been tested, is described in considerable detail. The high specificity of the test is emphasized and the technical factors which may influence its sensitivity and also its reproducibility are discussed.

The author states that a qualitative T.P.I. test suffices for diagnostic purposes, but when the test is used to follow the serological response to treatment a quantitative technique becomes essential, the immobilization titre (Tₐₑ) being defined as the greatest dilution of serum which will immobilize 50 per cent. of the treponemes under the test conditions. It is suggested that titres should be classed in three groups: "low" (<1:100), "moderate" (1:100 to 1:1,000) and "high" (>1:1,000). When the titre of a patient's serum passes from one group to another the change is of sufficient magnitude to be significant, but variations within the same titre group are not necessarily so.

Because the results of serial tests on a sufficiently large number of individual patients were not available the effect of treatment on the level of immobilizing antibody was examined by comparing the serum titres obtained in groups of untreated and of treated patients at various stages of the infection. In 24 patients with untreated secondary syphilis the titres usually lay between 1:500 and 1:1,000 and tended to be higher in those in whom the disease was of longer duration. Among 37 patients who had been treated for secondary syphilis several months previously antibody levels were definitely lower than those in the untreated group. Out of twenty patients with untreated symptomatic late syphilis, fifteen had titres of over 1:1,000, but in 32 similar treated cases the levels tended to be lower, and in this group the highest titres were found in patients whose treatment was of recent date. This suggests that even when treatment is given late in the disease it may be followed by a lowering of the level of immobilizing antibody. No preponderance of any titre group was found in 59 patients with untreated latent syphilis, but only nine out of 105 patients with treated latent syphilis showed titres of over 1:1,000 and these nine had been treated less than 2 years before the test was performed. In contrast, the patients who showed the lowest titres (<1:100) had been initially treated 5 to 10 years previously.

[The significance of the persistence of immobilizing antibody after adequate treatment by current standards is not yet known. Such persistence by itself, however, is not generally regarded as an indication for further treatment.]

A. E. Wilkinson


In this paper the authors discuss the pattern of reversal of serological test results after treatment in 2,820 of 2,954 patients with latent syphilis (see first abstract on p. 261). The technique of the tests and the antigen used have been uniform throughout the past 15 years, the New York State complement fixation test being employed. The range of observation was 5 to 25 years (average 14). Since the clinical observations indicated that there was no progression of syphilis in this group it is claimed that the results of the tests present the pattern of serological reversal in a group of latent syphilitics treated with arsenicals and bismuth and that similar findings may be expected in such a group treated with penicillin. The pattern took the form of a slow gradual achievement of sero-negativity throughout the period of 25 years. Thus by the end of 5 years, 25 per cent. of the patients had reached sero-negativity, but it
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required 11 years for 50 per cent. to do so, while by the end of 25 years 89 per cent. had become sero-negative. To some extent the result was influenced by the duration of the infection before institution of treatment, there being a difference of about 20 per cent. in the time needed for reversal in those in whom the disease had existed for 4 years or longer. The authors emphasize the importance of long-term observation of latent syphilis and urge that repeated courses of treatment are probably futile.

Robert Lees


SYPHILIS (Experimental)


Experimental assessment of the activity of therapeutic agents against Treponema pallidum may be carried out in vivo in man or in animals, but in the former the method is ethically unjustifiable and in the latter the procedure is lengthy and arduous. Alternatively, tests in vitro may be carried out on Reiter's treponeme. It is easy to culture and is antigenically similar to T. pallidum. Such sensitivity tests have been carried out by the authors in Brewer's medium, with added horse serum, containing doubling dilutions of a number of different antibiotics,
large inocula of Reiter’s treponemes and of suitable control organisms being used.

The results in each case are given in detail and may be summarized as follows:

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Control Organism</th>
<th>Minimum Bacteriostatic Dose (per ml. medium)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Reiter’s Treponeme</td>
</tr>
<tr>
<td>I. Penicillin</td>
<td>Staphylococcus</td>
<td>0·3 unit</td>
</tr>
<tr>
<td>Erythromycin</td>
<td></td>
<td>0·37 µg</td>
</tr>
<tr>
<td>Carbomycin</td>
<td></td>
<td>0·37 µg</td>
</tr>
<tr>
<td>Oxycycline</td>
<td></td>
<td>0·6 µg</td>
</tr>
<tr>
<td>Tetracycline</td>
<td></td>
<td>1·5 µg</td>
</tr>
<tr>
<td>Spiramycin</td>
<td></td>
<td>3·1 µg</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Proteus vulgaris</td>
<td>25 µg</td>
</tr>
<tr>
<td>Aureomycin</td>
<td>Escherichia coli</td>
<td>25 µg</td>
</tr>
<tr>
<td>Bacitracin</td>
<td>Staphylococcus</td>
<td>12·5 units</td>
</tr>
<tr>
<td>II. Streptomycin</td>
<td></td>
<td>&gt;1,000 µg</td>
</tr>
<tr>
<td>“Soframycin”</td>
<td>Staphylococcus</td>
<td>&gt;800 µg</td>
</tr>
<tr>
<td>Viomycin</td>
<td>Staphylococcus</td>
<td>&gt;800 µg</td>
</tr>
<tr>
<td>Polymyxin B</td>
<td>Ps. aeruginosa</td>
<td>&gt;1,000 µg</td>
</tr>
<tr>
<td>Neomycin</td>
<td>Staphylococcus</td>
<td>&gt;400 µg</td>
</tr>
<tr>
<td>Tyrothricin</td>
<td>Bacillus subtilis</td>
<td>&gt;400 µg</td>
</tr>
</tbody>
</table>

It was not possible to produce a penicillin-resistant strain of Reiter’s treponeme. No claim has been made in the literature that any of the antibiotics in Group II is effective against T. pallidum in vivo, but references are cited to reports of the efficacy against syphilis of most of those in Group I. One exception is spiramycin, which does not appear to have been used in the treatment of syphilis in man or experimental animals. The authors therefore gave a rabbit, infected by intratracheal injection with the Nichols strain of T. pallidum, three subcutaneous doses of 100 mg. spiramycin per kg. body weight; there was complete disappearance of the treponemes from the fourth day after the completion of treatment, followed by complete resorption of the testicular lesion by the eighth day. Bacitracin also has not been used in human cases and, contrary to the authors’ experience, streptomycin in very large doses has been reported as having some anti-treponemal activity in vitro.

F. Hillman


GONORRHOEA


A comparative study of the effects of instillation of silver nitrate solution, penicillin, and bacitracin into the eyes of newborn infants was undertaken at the Pediatric Service of the U.S. Naval Hospital, Corona, California. After instillation of silver nitrate in a 1 per cent. solution, there was swelling of the eyelids with purulent discharge from the eyes in about 50 per cent. of infants so treated. Of 5,394 newborn infants whose eyes were treated with penicillin (either in a solution of 5,000 units per ml. or in an ointment containing 1,000 units per gramme), fifty had mild and nine had moderate reactions; there were no severe reactions to this treatment. Follow-up examinations during the first 2 weeks of life showed that 3·2 per cent. of infants developed eye infections. Bacitracin ointment (500 units per gramme) was applied to the eyes of 2,380 newborn infants; sixteen developed mild and five moderate reactions but none showed severe reactions. Up to the 14th day of life, 1·6 per cent. of the infants in this group had developed eye infections. When the number of children with local reactions was added to the number developing infection, it was found that 4·2 per cent. of the penicillin-treated group and 2·3 per cent. of those given bacitracin were affected, a difference which is not statistically significant. The author concludes that specific chemotherapy should not be employed as a routine to prevent the development of ophthalmia neonatorum, but that infections should be treated when they arise. Bacitracin appears to be a safe, effective, and relatively non-irritant agent if chemoprophylaxis is considered desirable.

R. M. Todd


The author supports the suggestion of using an oily solution of penicillin in place of the normal 2 per cent. solution of silver nitrate. In 15,000 cases, there was only one failure and no side-effects were seen. The non-specific conjunctivitis which frequently occurs in babies was attributed to Staphylococcus aureus carried by nurses. Chloramphenicol or tetracycline proved useful in such cases. Prophylaxis is based on strict hygiene.

M. H. T. Yuille

The methods of prophylaxis used in 34 obstetric clinics in Europe are discussed. Silver nitrate 1 per cent. is still considered to be very effective. No allergies or bacterial resistance have been noted, although 30 per cent. of the cases show conjunctival irritation. The sulphonamides and penicillin are no longer used.

A 0·5 per cent. solution of Desogen (Gelgy) dyed with methylene blue is recommended on the basis of bacterial and clinical investigations. The effect on virus infections, sensitivity, and the problem of resistance remains to be worked out.

I. E. Gaynon


Credé’s method is obsolete. The author has obtained remarkable results in 9,000 new-born infants with Oláh’s method: a drop of 30 per cent. sulphacetamide or 30 per cent. Albucid.

P. Weinsteim


The investigation described in this paper from St. Mary’s Hospital, London, was designed to determine whether gonococci isolated from patients under treatment in the London area showed any evidence of increasing resistance to streptomycin. In 1951 the author reported the results obtained with streptomycin in the treatment of 62 patients suffering from acute gonorrhoea. In 1951 the author reported the results obtained with streptomycin in the treatment of 62 patients suffering from acute gonorrhoea. In 1951 the author reported the results obtained with streptomycin in the treatment of 62 patients suffering from acute gonorrhoea [Brit. J. vener. Dis., 27, 92; Abstr. Wild Med., 10, 413]. In 33 out of the 52 who remained under observation for varying periods treatment was thought to be successful; of the remainder, eight were treated for residual non-gonococcal urethritis, five failed to respond, and six were alleged to have been re-infected. In 1956, a further 109 patients suffering from acute gonorrhoea were treated with streptomycin, a single injection of 0·5 to 1 g. being given. Of 88 patients who remained under observation, 53 responded to treatment, eighteen were treated for residual non-gonococcal infection, and eleven for gonorrhoea which failed to respond, and six were alleged to have been re-infected. The failure rate was not significantly greater in 1956 than in 1951. In the second series, the results with a dosage of 1 g. were much the same in white patients as in Negroes, but with a dosage of 0·5 g. the failure rate in Negroes was significantly higher than that in white patients, for reasons which, the author states, were obscure.

A. J. King


In this report of a joint anti-gonorrhoea campaign carried out by the Dade County Health Department, Florida, and the University of Miami School of Medicine, the authors point out that the problems in controlling gonorrhoea are chiefly related to the frequent absence of symptoms of the disease in infected females and to the difficulty of demonstrating the infection bacteriologically in such cases. In an attempt to decrease the rate of spread of gonorrhoea in Dade County, all female contacts of male patients with gonorrhoea were treated with 2·4 mega units benzathine penicillin (1·2 mega units injected into each buttock). As such a dose has been reported to maintain a therapeutic level of the antibiotic for at least 6 weeks, it was thus hoped to cure the gonorrhoea present in these women and to protect them from re-infection for approximately 6 weeks. Meanwhile the male patients were treated with 600,000 units of 72-hour repository (procaine) penicillin and could therefore be re-infected sooner, so providing the most effective way of locating infected females.

This programme of treatment was begun in June, 1954, and there was an apparent immediate decrease in the number of proven cases of gonorrhoea, the average of 180·1 cases per month for the first 6 months of that year falling to 146·8 cases per month for the last 6 months. This decrease has continued, and from a Table given it is seen that the mean monthly average of cases was 136·1 for the year 1955 and 122·0 for 1956. During the years under survey the morbidity rate per 1,000 of the population in the area fell from 3·1 in 1954 to 2·4 in 1955 and to 2·1 in 1956. Over the same period the incidence of gonorrhoea in two neighbouring metropolitan areas in Florida showed a rise in one and no significant change in the other. The massive doses of penicillin used did not produce more allergic reactions in patients than did smaller doses, and pain in the buttocks, when it occurred, usually did not last for more than 24 hours. The authors conclude that the use of long-acting penicillin will not immediately eliminate gonorrhoea from a population; however, it should offer the possibility of a steady, slow decline [unless, of course, the method contributes towards the production of a penicillin-resistant strain of gonococcus].

Benjamin Schwartz


NON-GONOCOCCAL URETHRITIS AND ALLIED CONDITIONS


The author, writing from Monterey, Mexico, describes the results obtained with oxphenarsine hydrochloride ("Mapharsen") in 24 male patients with trichomonal urethritis (proved in fifteen and suspected in nine).

There was no irritation or other form of intolerance of the drug, and permanent cures, it is claimed, were achieved in all 24 patients. The entire urethros-vesical field was washed out once daily for 3 to 5 days with a freshly made solution of oxphenarsine hydrochloride (0-06 g. dissolved in 0-5 litre sterile water at 45°C.). After the first treatment no trichomonads were seen on microscopic examination. In cases in which microscopic examination revealed the presence of associated bacteria, treatment was continued for a few more days, but the oxphenarsine was replaced by 500 mg. chloramphenicol. Observation for 2 weeks is advocated, since relapse will occur during that time if complete cure has not been achieved. Many of the author's patients were followed up for more than a year, and in none did trichomonal reappear.

Douglas J. Campbell


It has been claimed that "Aminitrozole" (2-acetyl-amino-5-nitrothiazole), given by mouth, is an effective remedy for trichomonal infection of the genito-urinary tract, although this claim has not been substantiated in Britain. The present author, at St. Mary's Hospital, London, used this preparation in the treatment of 49 male patients suffering from non-gonococcal urethritis. Of 28 cases in which the urethral secretion was examined for the presence of Trichomonas vaginalis by dark-field microscopy of wet specimens, the organism was found in only one. The dosage of aminitrozole was 100 mg. three times a day for 6 to 10 days. There were no toxic effects. Altogether 45 patients were followed up, although only fifteen remained under observation for more than one month. There were 22 known treatment failures, these being much the same as those obtained in 29 cases in which a placebo was given. It is concluded that aminitrozone is not a useful drug in the treatment of non-gonococcal urethritis. The fact that gonococci were found in the secretion of six of these patients on later microscopic examination suggested re-infection during the period of observation.

A. J. King


The author reports, from St. Mary's Hospital, London, additional observations on the results obtained with urethral suppositories containing 0-2 per cent. nitrofurazone and a local anaesthetic in a water-dispersable base ("Furacin") in the treatment of non-gonococcal urethritis. Of the 23 male patients, nine had acute or subacute (not necessarily severe) urethritis and fourteen had chronic urethritis. The suppositories were inserted twice a day for a period of 1 to 3 weeks. No intolerance was observed.

The case histories are described and the results of treatment summarized. In four cases the treatment failed, and in five of the remaining nineteen there was a relapse within 3 months. In two cases the follow-up was inadequate and in one progress was not observed after treatment. There was immediate improvement in two cases, but in one of these the follow-up period was only 26 days and in the other cystitis developed, for which antibiotics were administered. Of the nine cases in which treatment was considered to be successful, five were of mild urethritis [which, of course, has a tendency to clear without treatment].

The author concludes that "no strong curative claims may yet be advanced for local Furacin therapy". [This is not surprising, since the results of the trial as described are not impressive.]

Leslie Watt

Reiter Syndrome in Females. Three Cases. [In English.] Refvem, O. Acta rheum. scand., 3, 282. 14 refs.

Few cases of Reiter's syndrome in females have been reported. In this paper from Rikshospitalet and Diankonhjemmets Hospital, Oslo, three such cases are described. The first patient, aged 41, had acute polyarthritis and bilateral conjunctivitis lasting 2 months. There was gradual improvement with exercise treatment in bed, but 6 months after discharge from hospital there was a relapse, which was associated with a vulvovaginitis. In the second patient, aged 34, the polyarthritis and conjunctivitis developed about 3 weeks after an attack of acute epidemic diarrhoea. Slight vulvitis was present. The third patient, aged 55, had a yellow vaginal discharge, acute polyarthritis, and photophobia without definite conjunctivitis.

In all three cases the erythrocyte sedimentation rate was raised, but the results of other investigations were negative. Urethritis was present in the first case only, and the author suggests that vulvovaginitis should be accepted as a cardinal feature of the syndrome.

K. C. Robinson


Radiographs from 58 male and two female patients with Reiter's syndrome out of a total of 185 seen at St. Mary's Hospital, London, were studied in an attempt to assess the radiological features of the condition. The triad of arthritis, urethritis, and conjunctivitis was present in 35 cases, the last feature being absent in 25. The radiological findings were the same in both groups. Clinically, the arthritis was most common in the distal joints of the lower extremity, the knee and ankle being involved in over 70 per cent. of the whole series of 185 cases, the hand and wrist in over 55 per cent., and the sacro-iliac
joints in 9 per cent. A valuable summary of the differences between Reiter's syndrome and rheumatoid arthritis is given.

Radiologically, in the acute stage the affected joints showed periarticular thickening and localized bony rarefaction. Swelling of tendons, particularly the Achilles tendon and the patellar tendon, could be seen and was regarded as a differentiating feature from rheumatoid arthritis. Periosteal new bone formation was demonstrated in 27 per cent. of cases around the small bones of the feet. Plantar spur formation on the os calcis was sometimes observed after an initial stage of erosion in association with a plantar fasciitis. However, some of the spurs were similar to those seen frequently in routine radiography, and caution is necessary in ascribing them to the disease process. In the chronic stage extensive new bone formation often occurred on the plantar aspect of the os calcis, frequently bilaterally, and foot deformities developed subsequently in some cases. If arthritis was persistent the joint space might become narrowed, serial films showing the development of marginal erosions. In the course of healing such erosions were likely to develop a sclerotic edge, but permanent defects were left. The sacro-iliac joints of 34 patients were investigated; pitting of the articular surfaces and subarticular sclerosis were observed in eleven, but complete ankylosis was not seen. In only one of these cases were spinal changes observed. Other changes included true bony ankylosis, mainly in the small joints of the feet, in eight cases, and the Pellegrini-Stieda type of calcification in the knee in two.

The authors consider that this syndrome is not rare and should be considered in the differential diagnosis of polyarthritis in the male.

R. O. Murray


In this article from the London Hospital the authors report a study of 53 patients suffering from Reiter's syndrome. All had arthritis associated with urethritis, but the conjunctivitis which constitutes the third feature of the syndrome tended to be mild and short-lived, and in 34 cases was absent. Elimination of concurrent gonococcal infection by antibiotics in nineteen patients showed them to be suffering from the classic non-specific urethritis. In each case differentiation from rheumatoid arthritis was made on clinical grounds. In a review of the literature it was noted that the radiological findings had been reported only in isolated instances and this aspect was therefore studied in particular in the present series.

Radiologically, the most commonly affected areas were the feet, the hands, and the sacro-iliac joints. Spinal changes typical of ankylosing spondylitis were found in six cases. The knees, though often clinically affected, rarely showed radiological involvement. The time of appearance of radiological changes was variable. In some cases such changes were evident in the first few weeks or months, being preceded only by periarticular thickening around the small joints of the feet and hands, while in others radiological signs did not develop at all in the course of several years. Erosions of the articular surfaces of the affected joints were common and were invariably accompanied by narrowing of the joint space which might progress to disorganization and subluxation. Periosteal new bone formation of various types was a striking feature in many cases, affecting especially the short bones. Flattening of the arches of the feet, with which dislocation of the metatarsophalangeal joints was usually associated, was seen in several cases. The radiological differentiation of Reiter's syndrome from rheumatoid arthritis may not be radiologically possible, and the authors consider that in atypical cases of the latter condition in males evidence of urogenital infection should be sought.

R. O. Murray


The study herein reported is based on 185 consecutive patients (182 males and 3 females) suffering from Reiter's syndrome seen at St. Mary's Hospital, London, from 1942 to 1956 inclusive. During the same period 22,010 cases of urethritis were treated, so that the incidence of Reiter's syndrome in relation to the total number of urethral infections was 0.8 per cent. Sexual promiscuity was apparent in the majority of patients, and there was usually a history of casual sexual relationship before the onset of the urethritis of Reiter's syndrome. In 87 cases this was associated with arthritis only, and in 98 there were other features, mainly eye and skin lesions. The age at onset ranged from 15 to 59 years, but 82 per cent. of the patients were in the age group 20 to 40 years. The mean duration of the attack in 165 cases was 3.8 months; in the remaining twenty cases no clear-cut remission was noted for 3 or more years. A total of eighty patients defaulted within one year, but of the remainder, some 50 per cent. were known to have had repeated attacks of continued activity over a number of years. In all, thirty patients were observed for 10 years or longer from the onset of the illness.

It was noted that re-infection with venereal urethritis did not inevitably precipitate a fresh arthritic attack. With repeated attacks recovery became less complete, and some degree of permanent damage was evident in 28 patients. The author states that the various components of the syndrome need not occur simultaneously and that dissociation of symptoms is common.

No precipitating factor other than urethral infection was identified with certainty, but it is suggested that there may be a hereditary predisposition to the syndrome.

Leslie Watt


An association between prostatitis and ankylosing spondylitis is not a new finding, but it is still not clear whether the two conditions are causally related. In this paper from the London Hospital a study is reported of the incidence of prostatitis in 54 male patients with ankylosing spondylitis, 59 with Reiter's disease, and 86 with rheumatoid arthritis.
Reiter's disease was diagnosed on the presence of non-gonococcal urethritis associated with arthritis of acute onset and a variable, often relapsing, course. Conjunctivitis occurred in 24 of the 59 cases, uveitis in six, and keratodermia blennorrhagica in six. From each patient five samples of fluid were obtained by prostatic massage and examined microscopically in a high-power dark field. The criterion for diagnosis of chronic prostatitis was a minimum of ten pus cells per high-power field. By this method chronic prostatitis was demonstrated in 45 (83 per cent.) of the patients with ankylosing spondylitis, 28 (33 per cent.) of those with rheumatoid arthritis, and 56 (95 per cent.) of those with Reiter's disease.

The authors do not consider that the difference between the groups with ankylosing spondylitis and with rheumatoid arthritis in respect of the incidence of prostatitis is due to the different mean age of the patients; there is no evidence that chronic prostatitis is commoner in younger than in older males. The incidence of chronic prostatitis in hospital males is reported to be 20 to 25 per cent.; the incidence in rheumatoid arthritis in this series thus appears to be close to that found in the general population of the same age group.

Radiological examination of the sacro-iliac joints of all the patients revealed unequivocal bilateral sacroiliitis in 49 of the cases of ankylosing spondylitis, seven cases of rheumatoid arthritis, and nineteen of Reiter's disease—findings which might be taken to indicate that there is a causal association between chronic prostatitis and sacroiliitis. However, the authors do not find much support for this in their figures; in all eleven cases of ankylosing spondylitis with a normal prostatic fluid there was unequivocal bilateral sacroiliitis.

The high incidence of chronic prostatitis in ankylosing spondylitis remains unexplained. Kenneth Stone


CHEMOTHERAPY


It is suggested that the inhalation of penicillin from the environment presents a possible explanation of the increasing percentage of penicillin-resistant strains of Staphylococcus aureus found among nasal carriers in hospitals, since the anterior nares are the primary site of colonization in the carrier. The author, working at the University of Edinburgh, has sought evidence for this hypothesis by investigating the penicillin levels in the air of a large general hospital and in a factory where various preparations of penicillin were made up. For the detection of penicillin in the atmosphere, agar plates uniformly sown with susceptible strains of Staph. aureus were exposed either directly to the air (settling plates) or to air taken through an impinger sampler (a modified sieve-plate sampler) at the rate of 25 cu. ft (0.75 cu. m.) per minute. After incubation, zones of inhibition were observed, and that these were due to the presence of penicillin was confirmed by inoculating a sensitive staphylococcal strain on to one part of each zone and the same organism plus penicillinase on to an adjacent part. The method also allowed of quantitative estimation of penicillin levels.

Penicillin was shown to be present in variable amounts in the air and dust of all sites examined in the hospital. The smallest amounts were found in the physicians' side-rooms, and larger amounts in the medical and surgical wards. The air of the hospital dispensary showed considerable antibiotic activity, a proportion of which was due to penicillin (concentration 0.5 to 35 µg. per 100 cu. ft; 0.16 to 11 µg. per cu. m.). The highest concentration of penicillin found was in sections of the out-patient department (1 to 50 µg. per 100 cu. ft; 0.3 to 16 µg. per cu. m.) where penicillin was being administered, for example in the room in which minor surgical treatment was given, and fell off sharply with the distance from these rooms. Similar indicator plates were impressed by the hands and fingers of the staff at work or were inoculated with swabs from the anterior nares of these subjects. Penicillin from both sources was readily detectable. Amounts of penicillin from the fingers sufficient to cause inhibition of growth over the whole plate was often obtained after only a few seconds' handling of articles in the room used for minor surgery. Laboratory experiments showed that air and dust can be readily contaminated with penicillin when preparations of the antibiotics are used and handled.

In the factory, appreciable amounts of penicillin (10 to 250 µg. per 100 cu. ft; 3 to 80 µg. per cu. m.) were recovered in the penicillin filling room and rather less in the packing room, which appeared to be sufficient to depress the growth of all bacteria in the nares of workers in these rooms. Smaller amounts were recovered from the air of other parts of the factory, a little being found even in the administrative block.

The author considers that destruction of penicillin in dust may be relatively slow and that the amount tends to accumulate. Since environmental penicillin can provide a concentration adequate to inhibit sensitive staphylococci it may well be an important factor in the colonization of hospital carriers with penicillin-resistant strains of the organism. Joyce Wright

PUBLIC HEALTH AND SOCIAL ASPECTS


It is widely believed that the incidence of syphilis has fallen dramatically in the last 20 years and that the disease may soon disappear entirely. But the author of this article, in discussing the epidemiology of syphilis, suggests that the statistics may be misleading and that there
are dangerous factors which have caused a recrudescence of syphilis in the past 3 years and which could result in a considerable increase in morbidity. In France the incidence of primary and secondary syphilis fell between 1946 and 1955 by 92 per cent; in Italy between 1937 and 1951 by 87·6 per cent. and in the U.S.A. between 1947 and 1952 by 88·9 per cent. In regard to these figures the author emphasizes that present-day incidence should be compared with pre-war figures of incidence rather than with those of the immediate post-war epidemic era, and that by such a comparison the present reduced incidence of syphilis is shown to be much less striking. There has always been a tendency to fluctuation in the incidence of venereal diseases throughout the world, with a gradual trend towards a lower level. A periodicity of 8 to 15 years between the upward trends is noted. These movements in incidence were observed long before the discovery of new therapeutic measures, such as antibiotics, and may occur apart from wars or movements of population. Such an era of higher incidence of syphilis appeared to start during the period 1955–7.

Serological tests for syphilis have not shown a fall in positive results comparable with the reported fall in incidence of cases of early syphilis. In France positive serological reactions for syphilis are found in about 1 per cent. of the population, and many of these are believed to be due to recent infection, so that the official returns of the incidence of recent syphilis may be much lower than the reality. Similar statistics are quoted for the U.S.A. and for most of the countries of Europe, in all of which treatment and preventive measures against venereal disease are well organized.

The factors which favour recrudescence of syphilis are partly international and partly national. Among these are the ignorance of the public in regard to sexual matters and the dangers of venereal disease, ignorance or lack of vigilance among the medical profession, and indifference of public health authorities to the tracing of contacts and other epidemiological measures. General factors, such as economic conditions, are also important: for example, it has been noted that syphilis tends to increase during periods of national prosperity, when increased spending power results in flourishing prostitution. Movements of the population, as well as public holidays and celebrations, are further contributory factors; for example, Rabut reported an increase in the number of clients of brothels after the celebrations of Lindbergh's transatlantic flight and also after funerals of nationally important public personages. In the author's opinion the spread of syphilis is predominantly due to certain social categories of persons, such as prisoners, immigrants, prostitutes, and foreign workers, who, as a group, are more heavily infected than other categories. In certain parts of the world there are reservoirs of syphilis which are a danger to all other countries. The efforts of the World Health Organization in collective treatment are likely to be very helpful in this respect, but special measures to prevent the importation of syphilis from these areas of high incidence may have to be adopted by the healthier countries.

Robert Lees
be said that even in the present economically favourable climate the venereal diseases are still a serious problem. 

R. S. Morton


**MISCELLANEOUS**


Lymphogranuloma venereum, a venereal disease usually acquired in tropical or subtropical regions, is caused by a filterable virus related antigenically and morphologically to the virus of psittacosis. Diagnostic criteria are a positive response to the Frei skin test and a complement-fixation titre for lymphogranuloma venereum of 1 in 32 or more. The condition should be distinguished from granuloma inguinale (venereum), which is caused by the Gram-negative pleomorphic organism *Donovania granulomatis*.

The incidence of lymphogranuloma venereum in Britain is low, only 363 cases having been diagnosed in the 5-year period 1951-5. The number of infections acquired in Britain is also low; the reasons for this, it is suggested, are:

(1) The short duration of the incubation period and of the infectious phase, which are usually over by the time the infected male reaches Britain from an endemic area;

(2) The painful buboes, making sexual intercourse difficult.

The infectious phase in the female is believed to be of longer duration.

In this paper the authors report two cases, seen at St. Thomas’s Hospital, London, of lymphogranuloma venereum acquired in Britain. Details are also given of two male patients with the rare pseudo-appendicitis syndrome, a female patient with an ano-rectal syndrome, and a female without symptoms who was probably infectious. The authors state that hyperglobulinaemia, without other evidence of liver disorder, is a well recognized associated disorder of lymphogranuloma venereum. They point out, in conclusion, that the recent influx of West Indians of both sexes into Britain and the rapidity of air travel may make lymphogranuloma venereum a commoner clinical problem in future than it has been hitherto.

Douglas J. Campbell
