ABSTRACTS

This section of the Journal is published in collaboration with the two abstracting Journals, ABSTRACTS OF WORLD MEDICINE and OPHTHALMIC LITERATURE, published by the British Medical Association. The abstracts are divided into the following sections:

Syphilis (Clinical, Therapy, Serology, Pathology, Experimental),
Gonorrhoea,
Non-Gonococcal Urethritis and Allied Conditions,
Chemotherapy,
Public Health and Social Aspects,
Miscellaneous.

After each subsection of abstracts follows a list of articles that have been noted but not abstracted. All subsections will not necessarily be represented in each issue.

SYPHILIS (Clinical)


On the basis of their experience at the Psychiatric and Neurological Clinic of the Friedrich-Wilhelm University, Bonn, the authors discuss the diagnosis, prognosis, and response to treatment of general paralysis of the insane (G.P.I.) from the serological and clinical and the psychiatric aspects. Clinically, G.P.I. usually becomes manifest first as neurasthenia, and only later as a true psychosis. The psychotic symptoms are not particularly characteristic, although loss of intellect and self-control, psychomotor phenomena, and eventually total psychic degeneration are the usual features. Neither in pure tabes dorsalis nor in meningeovascular syphilis do such changes occur. The findings in the cerebrospinal fluid (C.S.F.) are typical and include a positive Wassermann reaction and Lange curve, an increase in the protein content particularly affecting the globulin fraction, and a high cell count. With treatment there is no parallel improvement in the clinical and serological pictures. The abnormalities in the C.S.F. findings rarely disappear completely, improvement usually proceeding slowly for about 5 years after an initial rapid reduction in the cell count and protein level due to clearing of the meningeal lesions. It is emphasized that the serology of the blood, owing to an entirely different mechanism, does not improve in the same fashion as that of the C.S.F.

Anatomically established brain lesions cannot improve, so that there is rarely any improvement in respect of eye signs, facies, dysarthria, or reflexes. However, lesions which are not fibrosed may improve, and epilepsy, aphasia, and hypotonia are usually ameliorated. The psychosis will also gradually improve, though there is often an immediate aggravation after treatment and relapses frequently occur during the months that follow. The longer the disease process has continued, the slower and the less complete the improvement. Once serological cure has been achieved there is little point in giving further courses of penicillin. Without any treatment at all, however, the patient with G.P.I. proceeds to a vegetative existence and ultimate death, the course of the disease varying in length from a few months to many years.

Allene Scott


Report of a case in a syphilitic woman aged 41 with Marfan’s syndrome. Osseous metaplasia of the uvea followed long-term uveitis which was started by surgery for cataract. The pathogenesis is briefly discussed.

N. Orzalesi


Report of a case of bilateral pupillary changes that started with an intrinsic oculomotor paralysis due to botulism and in the period of recovery progressed into a typical Argyll Robertson syndrome. The different theories are reviewed and the author agrees with that of Spiegel, localizing the lesion in the synapses between the cells of the Edinger Westphal nucleus and the afferent fibres of the reflex arc, after the decussion of Meynert.

Alfredo Arruga


Diagnosis and Treatment of Late Syphilis. BEERMAN, H., and SCHAMBERG, I. L. (1963). Geriatratics, 18, 64. 1 fig, 6 refs.


SYPHILIS (Therapy)


In an attempt to find an alternative to penicillin in the treatment of venereal disease demethylchlortetracycline was tried in nineteen patients with dark-field positive primary or secondary syphilis attending a clinic of the Department of Public Health, Washington, D.C. The average dosage was 300 mg. four times daily for 10 days, and with this regimen Treponema pallidum disappeared from moist lesions within 48 hours. Of twelve patients subsequently followed-up for at least one year, four with primary and three with secondary syphilis became seronegative, and quantitative serological reactions were appreciably weaker in the remaining five with secondary disease. There was also significant improvement in serological reactions in three patients followed-up for only 8 to 10 months. Of the remaining four patients, one was lost from the study, one was rejected because he was emotionally unsuitable, one had a reinfecation, and in one treatment failed. This last case, however, might also have been a reinfecation.

With a failure rate of one in thirteen patients (7.7 per cent.) followed up for more than one year or one in sixteen (6.3 per cent.) followed-up for 9 months, the author considers that demethylchlortetracycline shows significant promise as an antisypilic drug.

Benjamin Schwartz


The author, in this paper from the New Jersey State Department of Health, Trenton, notes that the alarming rise in the incidence of infectious syphilis in that State continues. Provisional figures showed that there were 872 cases of primary or secondary syphilis reported during 1961, compared with 670 in 1960. Of 978 contacts of patients with primary or secondary syphilis who were examined during the first half of 1961, 398 (40.7 per cent.) were found to be suffering from early syphilis. To deal with this disturbing increase "administration of epidemiologic treatment to sex contacts of infectious syphilis cases is urgently recommended". The treatment consists in administration of 2-4 mega units benzathine benzylpenicillin by injection or, in patients sensitive to penicillin, 2 to 4 g. daily of "a broad spectrum antibiotic" to a total of 20 to 30 g. in 10 days. The author states that this destroys the treponeme in the incubation period of the disease, eliminates the need for observation for 90 days, and reduces substantially the possibilities of spread. In his experience many patients are "quick to sense a relationship between the treatment and continuation of an active sex life".

[The New Jersey State Department of Health has advocated "epidemiologic" treatment of syphilis for some years. In 1960 a total of 1,425 cases of primary, secondary, and early latent syphilis were reported in New Jersey, compared with 994 cases of primary, secondary, and latent syphilis in all the clinics of England and Wales. (Population of New Jersey in 1960 was about 6,099,000.) Syphilis is undoubtedly a major and increasing problem in New Jersey and there may be special factors, such as movement of population, which must be taken into account. Nevertheless, the maxim of diagnosis before treatment has much to recommend it; it is clearly in the interest of the individual patient and should not be abandoned lightly. To give epidemiological treatment is tantamount to diagnosing syphilis and, if given at all, it should, in the interests of the patient, lead to adequate follow-up of that disease.]
ABSTRACTS

Results of Re-examination after 10 years of 66 Patients with Early Syphilis treated with Penicillin and Bismuth.

SYPHILIS (Serology)


The authors report the results of testing a total of 7,600 specimens of serum and cerebrospinal fluid by the technique of immunofluorescence. The principles and technical details of the test are described. The specimens were also tested by the method in which cardiolipin antigens are used, and 6,200 of them by the treponemal immobilization (T.P.I.) test. In all cases the results of tests which proved positive were expressed quantitatively.

The immunofluorescence test is very sensitive, reasonably specific, and quite reproducible. Fluorescent antibodies appear in the serum early in primary syphilis, reach very high titres during the secondary stage, and persist in a manner similar to immobilizing antibody during the latent stage. In late clinical syphilis the results of the quantitative tests agree closely with those of the T.P.I. test.

The authors conclude that the immunofluorescence test has an important place in the diagnosis of syphilis because of its sensitivity and specificity, and the speed with which it can be carried out. It can also be undertaken by any well-equipped laboratory. They believe that this test and the one-slide flocculation test should be carried out for diagnosis and follow-up. Complement-fixation tests can be abandoned. With these recommended tests, results can be made available on the day the blood is taken or, in urgent cases, within half-an-hour of taking the blood. Positive reactions should be reported quantitatively. The T.P.I. test remains the final arbiter in difficult cases.

R. D. Catterall


In view of the recent epidemic recrudescence of syphilis, sometimes in clinically atypical forms, the use of a simple and reliable diagnostic test is desirable. The Nelson-Mayer treponemal immobilization (T.P.I.) test has been widely adopted, but presents certain disadvantages and difficulties. For this reason the more recent fluorescent treponemal antibody (F.T.A.) test is worthy of consideration. The author, writing from the Institute of Clinical Dermatology of the University of Turin, summarizes the reports in the literature concerning the development and value of this test, emphasizing its apparently high specificity and its usefulness particularly in the early stages of the disease. He then reports his own experience in the investigation of serum and cerebrospinal fluid (C.S.F.) from healthy subjects and patients with syphilis with a battery of tests including the F.T.A. test, several standard serological tests, and in some cases also the T.P.I. test. The technique of the F.T.A. test was that of Manucci and Spagnoli (Ann. Sclavo, 1961, 1, 49) except that to increase sensitivity a serum dilution of 1:100 was used instead of 1:200. No loss of specificity was noted. The results were expressed semiquantitatively.

All of 141 sera from healthy control subjects gave a negative F.T.A. reaction, although fourteen gave a positive reaction to standard tests. Of 112 sera from patients with primary chancres, 67 gave positive and fourteen negative results with both the F.T.A. and standard tests and in 31 cases the result of the F.T.A. test was positive and that of the standard tests negative. The results of the standard tests never became positive before those of the F.T.A. test. In all of seventeen cases of secondary syphilis, six cases of tertiary syphilis, and thirteen cases of neurosyphilis, the results of both the F.T.A. and standard tests were positive. The standard tests gave negative results in four of thirteen cases of congenital syphilis and the F.T.A. test in only one. Of seventy cases of neglected syphilis, both tests gave positive results in 63, and the F.T.A. test in three and the standard tests in four of the remainder. In 326 cases of treated or partially treated syphilis the F.T.A. test gave positive results nearly twice as frequently as the standard tests (102 and 57 cases respectively). Whenever the T.P.I. test was carried out, its result agreed with that of the F.T.A. test. Of twenty specimens of C.S.F. from patients with clinical neurosyphilis, thirteen gave a positive response to the F.T.A. test and only eight to the standard tests. In eleven of the thirteen cases the serum also gave a positive F.T.A. reaction, but in the other two cases (of tabs dorsalis) the serum gave a negative reaction. The C.S.F. from twelve non-syphilitic subjects gave negative results with both types of test. In sensitivity and specificity the F.T.A. test is clearly superior to the standard routine serological tests and is comparable to the T.P.I. test. Its main advantages over the latter are that it is relatively easy to perform and that it gives a positive response at an earlier stage in the disease.

F. Hillman


The author has investigated, at Johns Hopkins University Hospital, Baltimore, 192 patients who chronically showed biologically false positive reactions in the standard serological tests for syphilis (S.T.S.). Of this number 97 were detected when undergoing a routine medical examination as healthy subjects, 77 during the investigation of mild localized disease, and a further eighteen while being examined for some generalized disorder. In this last group were found two with frank systemic lupus erythematosus and one patient with Still’s disease. Syphilis was excluded by a negative result in the treponemal immobilization test. Follow-up for at least 2 years excluded the possibility of transient false positive reactions associated with infective hepatitis, and other infectious diseases. It is pointed out that of the 192 patients 143 were women, a female predominance of 3:1.

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Follow-up showed that fourteen patients (all female) had developed systemic lupus erythematosus, 43 had symptoms suggestive of connective-tissue disease, while 81 had raised serum globulin levels or some other abnormality of the serum proteins but no definite clinical evidence of connective-tissue disease. Three female patients developed Hashimoto’s thyroiditis and three other women patients (not in the series) with thyroiditis were observed to show false positive reactions in S.T.S. Of these six patients, three had other diseases, such as Sjögren’s syndrome, glomerulonephritis, haemolytic anaemia, or thrombocytopenia. Several of the patients with false positive reactions had relatives with various connective-tissue diseases. In his discussion the author postulates that the apparently separate disease entities reported above may in fact represent different manifestations in a particular host of a genetically transmitted abnormality of the immune apparatus of “variable penetrance and variable expressivity”, and draws an analogy with the situation in regard to syphilis before the introduction of the Wassermann reactions.  

G. L. Asherson


In 1961 Brewer [no reference given] introduced a simplified screening test for syphilis in which the patient’s serum was mixed with V.D.R.L. antigen containing carbon particles coated and dried on plastic-covered cards, but it was subsequently found that V.D.R.L. antigen was not sufficiently stable for this purpose. At the U.S. Public Health Service Venereal Disease Research Laboratory, Atlanta, Georgia, the present authors have developed a similar modification of the rapid plasma reagin (R.P.R.) test as a card test and they describe its use in conjunction with a special plasma collection slide for the rapid separation and collection of plasma from a finger-prick specimen of blood. [For technical details the original paper should be consulted.] The R.P.R. card test and the V.D.R.L. slide test were carried out on blood from 2,402 patients attending venereal disease clinics and selected at random. Of 600 patients with a clinical diagnosis of syphilis, 71.0 per cent. gave a positive reaction to the R.P.R. test and 72.7 per cent. to the V.D.R.L. test. In approximately 8 per cent. of 83 cases of untreated syphilis the results of the two tests were in disagreement, the corresponding figure for 517 cases of treated syphilis being 15 per cent. Of 1,802 patients without a definite diagnosis of syphilis, 6 per cent. gave a positive reaction to the R.P.R. test and only 3 per cent. to the V.D.R.L. test, suggesting that the former might be less specific than the latter. However, of 27 patients with leprosy, none gave a positive reaction with the R.P.R. test, whereas five did with the V.D.R.L. test.

The simplicity of the R.P.R. slide test and the disposability of the equipment used are emphasized, and although sufficient study comparisons have not yet been completed, it is suggested that it “has the elements required for an ideal field test” and may prove more specific than the V.D.R.L. slide test in detecting treponematoses in areas where leprosy is endemic.

Allene Scott


ABSTRACTS


SYphilis (Experimental)


GONORRHOEA


In this paper from the Ospedale Civile dell’Annunziata, Cosenza, Italy, the author first describes the pharmacology and range of activity of triacyctyleolandomycin (TAO) and reviews previously published work on the active blood level and the dosage necessary for the treatment of gonorrhoea. He then reports his own experience in the treatment of cases of gonococcal urethritis. A single dose of 1·5 g. TAO by mouth followed 12 hours later by 1 g. streptomycin by injection failed to cure three out of six cases. However, when an initial dose of 1 g. TAO was given followed by 500 mg. 6-hrly for 2 days and 250 mg. 6-hrly for a further 2 days, sixteen out of twenty patients (80 per cent.) were cured. Side-effects, which occurred in two cases only, included diarrhoea, abdominal distension, and gastritis in spite of the simultaneous administration of vitamin-B complex and the administration of TAO only after food. Ten of the patients became symptom-free within 48 hours and the remaining six by the fourth day. A reactivation test by the administration of beer 3 to 4 weeks later gave negative results in all cases. In the successfully treated cases gigantism and changes in the staining reaction of the gonococci were seen within 24 hours of beginning treatment.

The author points out that although TAO does not provide the ideal single-dose treatment of gonorrhoea, it is less likely than streptomycin to mask concurrent syphilis, it does not give rise to a secondary urethral discharge, and its side-effects are infrequent. F. Hillman


Over a period of 84 months the author treated 500 cases of uncomplicated anterior gonococcal urethritis in males, comparing the efficacy of three preparations of penicillin, two of which were given by mouth and one by injection. Assessment was possible in 245 cases, 255 patients being excluded because they failed to remain under observation or were re-infected. Of the 245 patients 82 received potassium benzylpenicillin by mouth in three doses each of 600,000 units at intervals of 6 hours. This treatment was successful in 59 of the cases. Potassium penicillin was given by mouth to 77 patients in two doses at 12-hourly intervals, each dose being of 600,000 units; this was successful in 51 (66 per cent.). Of a third group of 57 patients given a single intra-muscular injection of 1,200,000 units of procaine benzylpenicillin in oil with
aluminium monostearate (PAM), fifty responded. (The remaining patients were eliminated during the trial because they were unco-operative.) There were no side-effects and five patients who gave a history of reactions to penicillin, other than anaphylaxis, were treated with one or other of the oral preparations without ill-effect. [The author does not state in detail his criteria of cure and mentions only one visit subsequent to treatment, 7 days after the first attendance.] He considers that better results would have been achieved with phenethicillin had the dosage been larger. Orally administered benzylpenicillin was almost as efficacious as PAM given parenterally, a finding which was encouraging, since penicillin by mouth is less likely to produce adverse reactions than intramuscular penicillin. Oral administration was also more comfortable and less expensive for the patients. [He apparently takes no account of the fact that patients cannot always be relied upon to take oral medication when it is prescribed.]


Gonorrhoea is again becoming a major public health problem because of the appearance of penicillin-resistant strains of the gonococcus and the allergenicity of penicillin. While tetracycline is effective against gonorrhoea and is widely used in the treatment of penicillin-sensitive patients, the use of such broad-spectrum antibiotics may permit the overgrowth of non-sensitive organisms, including yeast-like forms such as *Monilia* and *Candida albicans.* It is therefore advisable to administer an antifungal agent such as amphotericin simultaneously when tetracycline is given.

Over a 4-month period at a venereal disease clinic run by the Philadelphia Department of Public Health 212 patients with acute gonococcal urethritis were treated with a single dose of 2 g. of tetracycline phosphate and 400 mg. of amphotericin B given by mouth, while 21 control patients were given a placebo. On return to the clinic at weekly intervals for 3 weeks after treatment cure was assessed from the results of examination and culture of urinary sediment. Of the 191 treated patients who attended at least once for follow-up, 180 (94 per cent.) showed no evidence of infection, whereas infection persisted in all the control subjects, all but one of whom responded quickly to subsequent treatment with tetracycline. Eleven patients, of whom 7 admitted re-exposure, became reinfected during the 3-week observation period. Apart from transient nausea in 4 cases, no serious side-effects were noted and no secondary infection with *Monilia* or other yeast-like organism occurred.


**Failure against Gonorrhoea (Editorial)** *Med. Proc.,* 9, 81.


**NON-GONOCOCCAL URETHRITIS**


A retrospective study of 34 cases of Reiter’s syndrome which had been observed at the University of Michigan Medical Center and Veterans Administration Hospital, Ann Arbor, was attempted. Follow-up contact was established with 26 of the 33 living patients, with seventeen by interview and with nine by questionnaire alone, information concerning the remainder being obtained from the hospital records.

A close association between Reiter’s syndrome and ankylosing spondylitis was confirmed. Acute lumbar or pelvic pain had been noted during the first attack in 27 cases (79 per cent.) and of 27 cases in which the history extended over more than 2 years, with an average of 2·6 attacks of Reiter’s syndrome, pain in the back had been noted in 22. In thirteen of these 27 cases definite radiographic evidence of bilateral sacro-iliac disease had been found. Ankylosing spondylitis had been diagnosed in eight cases, and in several of these the course followed was typical of this condition. No evidence of the development of typical rheumatoid arthritis was found. A history of iritis was obtained in four (31 per cent.) of the patients with radiological evidence of sacro-iliitis but in only one of the other cases. Of the 23 patients followed up whose history exceeded 2 years, 21 were able to work regularly, although only two were free from symptoms of continuing rheumatic activity or from residual effects of previous bone or joint disease.

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ABSTRACTS


Using the method of Tang and his co-workers, the authors confirmed that the elementary-body virus could be isolated by the inoculation of conjunctival scrapings from newborn babies with inclusion conjunctivitis into the yolk sac of embryonated chick eggs. An inoculum obtained from the egg of four passages was inoculated into the everted upper conjunctiva of volunteers, which developed acute conjunctivitis with abundant inclusion bodies. Some of them showed a typical follicular form and a papillary form.

H. Hagisawa


The author considers that "the ideal treatment of non-gonococcal urethritis should be relatively simple, inexpensive, and free from toxicity", and he here reports an investigation carried out at Liverpool Royal Infirmary "with these factors in mind". The 300 patients taking part in the study were treated in three groups: 53 received 5 g. "madribon" (sulphadimethoxine), a long-acting sulphonamide, alone; 32 were treated with 0-5 g. streptomycin followed by 5 g. madribon; 215 received 1 g. streptomycin and 6 g. madribon. In each group the treatment was spread over 5 days. The cure rate of cases followed for a sufficient period was 25·5 per cent. in the group treated with madribon alone against 80 per cent. and 79 per cent. respectively in the groups receiving streptomycin in addition. [It is difficult to evaluate these striking results, as no details on selection of cases, period of observation, or criteria of cure are given.]

G. W. Csonka


CHEMOTHERAPY


A total of twenty patients at the Middlesex Hospital, London, who had shown an immediate general reaction to penicillin were tested intradermally with penicillin and the penicillin nucleus, 6-amino-penicillanic acid, alone and after the addition of γ-globulin. (The mixture was incubated for at least a week before being used.) The penicillin-sensitive subjects, in whom hypersensitivity had been excluded by a prick test, were tested intradermally with successive doses of 1, 10, 100, and 1,000 units benzylpenicillin contained in 0·02 ml. saline at 20-minute intervals until an immediate reaction was obtained. An increase in size of the intradermal weal was recorded as (1) doubtful, (2) positive if it measured from 2 to 3 mm., and (3) strongly positive if there was an increase of 4 to 5 mm.

Addition of γ-globulin gave more positive results, as indicated by larger areas of reaction, but γ-globulin itself tended to increase the size of the weal, so any enhancement of the penicillin tests by γ-globulin should be interpreted with caution. Of the twenty patients six gave positive skin responses to penicillin and four of these were also positive to the penicillin nucleus. This suggests that a cross-sensitivity to various other penicillins must be expected.

A. W. Frankland


PUBLIC HEALTH AND SOCIAL ASPECTS


MISCELLANEOUS


At Holloway Prison, London, 102 women prisoners (serving sentences of at least 14 weeks) with vaginal trichomoniasis (acute in 48, subacute in 51, and asymptomatic in three cases) were treated with metronidazole ("flagyl") given by mouth in doses of 300 mg. twice daily for 7 days without local treatment. Vaginal smears and cultures were negative for Trichomonas vaginalis within one week after the completion of treatment and remained so for the following 12 weeks in 92 cases. In ten cases the results of tests became positive again at some time in the first 6 weeks after treatment, all of these women having long histories of vaginal discharge; in five the infestation was acute and in five subacute. A second course of treatment was given successfully in each case. The clinical response was almost universally satisfactory, only three women having a mucoid discharge (due to some cause other than trichomoniasis) after 12 weeks. Candida albicans was found in 29 of the 102 women, in four of them before treatment with metronidazole. This caused no irritation and was of pathological interest only. The only toxic reaction observed was nausea, of which three women complained. All three completed the course, in two cases with the addition of prochlorperazine.

The results of this study (undertaken under ideal conditions for ensuring proper treatment, observation, and surveillance and with virtually no chance of re-infection from the opposite sex) show that metronidazole can be satisfactorily administered in doses of 300 mg. twice daily instead of the more usual 200 mg. thrice daily in the treatment of vaginal trichomoniasis. R. R. Wilcox


CORRIGENDUM


The abstract of this paper in the March number of Brit. J. vener. Dis. stated that the number of elementary bodies in a known volume of a virus suspension was estimated by counting under the microscope particles stained with Giemsa and viewed by direct illumination. The authors wish it to be made plain that the method depends on examining the stained suspensions under dark ground illumination. Unstained particles seen by dark ground illumination cannot be distinguished from background debris of the same size, but particles stained with Giemsa appear to fluoresce a green-yellow colour and can easily be identified and counted.