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.

SYPHILIS (Clinical)

SYPHILIS (Therapy)

While it is now generally agreed that penicillin is the most efficacious drug for the treatment of syphilis, there remains the problem of how to treat syphilitic patients who have developed an allergy to this antibiotic. Estimates of the proportion of such cases have varied from a few per thousand to as much as 8 per cent., but the average probably lies between 1 and 2 per cent.

From the Municipal Skin Clinic, Dortmund, the author reports the results obtained with "reverin" (pyrrolidinomethyl-tetracycline (PMT)) in the treatment of eight syphilitic patients who were hypersensitive to penicillin. In four cases of primary or secondary syphilis the dosage of PMT was 250 mg. intravenously daily, and in three cases of secondary syphilis an initial injection of 500 mg. was followed by 250 mg. daily for 2 days, and 500 mg. daily thereafter. The average total dose of PMT was about 10 g. Dark-ground examination showed that spirochaetes had disappeared in 17 to 27 hours, the more rapid response being noted in those patients receiving the higher initial doses. Clinically, syphilitic maculae on the palms of the hands and soles of the feet disappeared, ulceration of the labia majora epithelized, and other syphilitic lesions began to heal. Serological reactions, originally strongly positive, became markedly weaker and in one case reverted to negative. A. D. Duff

SYPHILIS (Serology)

The authors of this paper from the University of Marburg sought to compare the specificity of the fluorescent treponemal antibody (FTA) test with that of the Treponema pallidum immobilization (TPI) test. They performed these two tests on 361 sera, the reactions of which to standard serological tests for syphilis (STS) were already known. The method used for the FTA test is described in detail.

It was found that positive FTA tests agreed with positive TPI tests in 83 per cent. of cases, and that negative tests agreed in 98·8 per cent. of cases. These results are further analysed in relation to the stage of syphilis in the patients concerned. Of twenty cases of dark-ground-positive primary syphilis, the FTA was positive in seventeen and the TPI in six. In two out of 38 cases of secondary syphilis, the TPI was negative, but STS and FTA were positive. In 33 cases of tertiary and neurosyphilis and in 26 cases of congenital syphilis, the FTA, TPI, and STS were all positive. In 102 STS-positive cases of latent syphilis, the results agreed except in six in which the FTA was positive and the TPI negative. In respect of this and all other groups of cases where serological findings were not in agreement, the clinical findings and particulars of treatment are described in detail. Of 142 non-syphilitic sera, one sample from a case of herpes zoster gave a positive FTA (the patient was being treated at the time with a number of proprietary medicines). Two sera gave positive TPI tests; one of these was from a patient with porphyria and cirrhosis of the liver, and the other from a patient with non-specific urethritis.

The authors point out that of the twenty cases in which the serological tests did not agree, ten were early cases in which the TPI might be expected to be negative; in the other ten cases (2·8 per cent. of the series) it is probably impossible to decide which was falsely positive, taking into consideration the uncertainty about the previous history and treatment of the cases. The authors consider that the apparently greater sensitivity of the FTA does not imply a reduced specificity. F. Hillman

Quantitative tests for C-reactive protein (CRP), a seroflocculation test utilizing ethyl choladienate, and tests for total serum proteins and total serum glycoproteins were made (at the Harry N. Falk Research Laboratory, University of California, Los Angeles) on 392 sera submitted for the Treponema pallidum immobilization (TPI) test. 285 sera or 72·7 per cent. were non-reactive, and 107 or 27·3 per cent. were reactive.

The quantitative tests for C-reactive protein demonstrated that 66 sera or 23·2 per cent. of the 285 non-reactive TPI sera, and 22 or 20·6 per cent. of 107 TPI reactive sera contained the abnormal serum protein CRP. Thus the sera from patients with biologic false positive (BFP) reactions were not significantly different from those with a reactive TPI test.

The tests for CRP on sera from 37 pregnant women, of whom 25 sera (67·5 per cent.) were TPI non-reactive, and twelve (32·4 per cent.) were TPI reactive, demonstrated that CRP was present in the serum of only four (16 per cent.) of the non-reactive sera. Seven (58·3 per cent.) of the reactive sera, however, contained the abnormal serum protein. These data were highly significant at an $\alpha$-level of 1 per cent. Seroflocculations tests utilizing ethyl choladienate as an antigen on the same lots of sera were reactive on 36 sera of 12·6 per cent. of the non-reactive, and 10·3 per cent. of the reactive TPI sera.

Tests for total serum proteins on the non-reactive as well as the reactive TPI sera were not significant. The means for the non-reactive and reactive TPI sera were 7·83 g. per 100 ml. and 7·74 g. per 100 ml., respectively.

Tests for total serum glycoproteins on the non-reactive and reactive TPI sera demonstrated that the serum levels of both types were elevated. The means were 124·47 mg. per 100 ml. and 122·89 mg. per 100 ml., respectively. Although the difference in the means was not significant, the fact that 73·7 per cent. of the non-reactive TPI sera and 72 per cent. of the reactive TPI sera had elevated serum glycoprotein levels may bear some relation to the presence of reagin in the sera.

Correlation of the clinical status of the patient with the results of the four tests for serum abnormalities failed to reveal significant differences between patients with biologic false positive tests for syphilis and those with reactive TPI tests.

Authors’ Summary


In this further report from the Dermatological Clinic of the University of Catania the authors present in detail the results of the intradermal treponemal colour (ITC) test, The fluorescent treponemal antibody (FTA 200) test, and a battery of five classic serological tests (two complement fixation, three flocculation) carried out in parallel in 36 cases of early dark-ground-positive primary syphilis. The ITC test gave a positive response in 33 cases and a negative response in three. In 22 cases (21 positive, two negative) there was complete concordance with the results of the other tests and in twelve (all positive) there was partial concordance; in three of the latter only the FTA reaction was in agreement with the ITC reaction and in two only the FTA and VDRL reactions. In one case the ITC reaction was positive and all the others negative, and in another the ITC was the only positive reaction. The explanation of this last result awaits further experience of the test.

The authors emphasize the simplicity and ease of interpretation of the ITC test and claim that it gives a positive reaction at an earlier stage of the disease than any of the other tests studied.

F. Hillman


Although numerous serological tests are available for the diagnosis of syphilis, a test carried out on the patient’s skin would eliminate various interfering factors and might therefore offer higher specificity and sensitivity. At the Dermatological Clinic of the University of Catania, Sicily, the authors have devised a simple skin test in which an injection of 5 ml. of a 1 per cent. solution of Evans blue in normal saline is given intravenously, followed immediately by the intradermal injection into the flexor aspect of the forearm of 0·1 ml. of a standardized suspension of killed treponemes of the Nichols strain in isotonic saline. As a control 0·1 ml. saline is injected at a distance of 5 cm. from the test site. The relevant technical details of the test are adequately described. In infected subjects a slight coloration begins to appear at the test site within 5 minutes of the injection, and within 20 minutes there is a definite blue, raised swelling, whereas the site of the control injection remains uncoloured. No coloration occurs in non-syphilitic subjects, though in all cases a coloured control reaction can be obtained by the intradermal injection of 0·1 ml. of a 1/10,000 solution of histamine chloride. Colour photographs of positive reactions and controls are reproduced (from which it would appear that the positive reaction is about 15 mm. in diameter).

This intradermal treponemal colour (ITC) test was carried out in parallel with a battery of classic serological tests, the fluorescent treponemal antibody (FTA 200) test, and the treponemal immobilization (TPI) test on four groups of subjects. In a control group of twenty healthy subjects all the tests gave negative results. The ITC test gave positive results in 94 per cent. of 32 cases of dark-ground-positive primary syphilis, the FTA test in 71·8 per cent. and the other tests in smaller proportions. All of sixteen cases of recent secondary syphilis gave positive reactions in the ITC, FTA, and classic serological tests, whereas the TPI reaction was negative in two cases and doubtfully positive in five. Finally, the ITC reaction was
positive in 80·8 per cent. of 68 cases of latent syphilis compared with 74·9 per cent. for the TPI test, 66·1 per cent. for the FTA test, and smaller proportions for the classic tests.

The authors claim that the advantages of the new test are its simplicity, its early positivity in the course of syphilis, and the fact that it spans all the stages from primary infection to latent disease, in which its diagnostic efficiency matches that of the TPI test. 

F. Hillman


**Behaviour of Neutralizing Antibodies against Herpes in Recent Syphils.** (Comportamento degli anticorpi neutralizzanti erpetici nella sifilide recente.) BUBOLA, D. (1965). *Boll. Ist. sieroter. milan.*, 44, 149. 4 refs.


[The previous work of Collart, Durel, and their collaborators (Ann. Inst. Pasteur, 1962, 102, 596 and 693; Ann. Derm. Syph. (Paris), 1962, 89, 488; *Abstr. Wld Med.*, 1963, 32, 336 and 1963, 34, 15) at the Institut Alfred-Fournier, Paris, on the persistence of *Treponema pallidum* in the lymph nodes of rabbits and human subjects infected with syphilis and treated only after an interval of 2 or more years is one of the most important pieces of experimental investigation in the field of syphology since the introduction of penicillin.]

In this paper the authors report in detail the results of their search for *T. pallidum* in the cerebrospinal fluid (CSF) of infected but untreated rabbits used as controls, infected rabbits treated with penicillin late in the course of the disease, humans with untreated syphilis, and humans with syphilis treated for the first time in the tertiary stage of the disease. They also report the results of the treponemal immobilization (TPI) test on samples of the CSF and the results of inoculation of fluid in which spiral organisms had been found into fresh rabbits.

Each specimen of CSF was allowed to sediment for 8 days at 5°C. without centrifugation, and 20 smears of the deposit stained by the silver impregnation method previously described and examined microscopically, a long and meticulous search being necessary. “Typical” treponemes were found in eleven out of 25 specimens of CSF from control rabbits which were examined at periods ranging from 18 hours to 1,420 days after intratesticular injection with *T. pallidum*, and in two out of six from animals which had been treated approximately 2 years after infection and examined after a further 2 years. In most of the other specimens of rabbit CSF examined spiral organisms of less characteristic appearance were found. Specimens of CSF from 52 human patients with untreated syphilis (mostly primary or secondary) were found to contain typical organisms in twenty cases and less characteristic organisms in 32, while specimens from fifty syphilitic patients who had received delayed treatment (but whose serum still gave a positive TPI reaction) contained typical organisms in 31 cases and less characteristic organisms in nineteen. In each group a number of specimens of CSF in which typical organisms had been found were injected intratesticularly into fresh rabbits, but in only two cases, both in the control group, was there any evidence of transferred infection. In both groups of rabbits the TPI reaction was consistently positive with serum and negative with CSF. A positive TPI reaction was obtained with the CSF of three of the 52 untreated and eleven of the fifty treated syphilitics; in both these groups the serum gave positive results in all cases.

The authors conclude from their findings as follows:

(1) *T. pallidum* establishes itself in the CSF rapidly after infection.

One of the most important research discoveries of the past decade has been that of Collart and others (Ann. Inst. Pasteur, 1962, 103, 596 and 693; Abstr. Wild Med., 1962, 32, 336) who demonstrated the persistence of Treponema pallidum in the lymph nodes of rabbits and human beings after treatment for late syphilis. Their findings suggested that the persistence of certain antibodies in the serum after apparently successful treatment for late syphilis might be due to the continued presence of spiral organisms within the body. (This discovery provided the first logical and intellectually satisfying explanation for the persistence of antibodies in many treated cases of late syphilis.) These workers have more recently reported the results of their search for T. pallidum in cerebrospinal fluid (Ann. Derm. Syph. (Paris), 1964, 91, 485; Abstr. Wild Med., 1965, 38, 180).

Since it was important that the implications of this work should be examined at an independent centre, a study of 46 patients with late syphilis was undertaken at the Venerable Disease Research Laboratory of the Communicable Diseases Center, Atlanta, Georgia. All the patients were inmates of a prison and all except one had had adequate antisypilitic treatment. An inguinal lymph node was removed and was prepared for microscopical examination by silver staining and by fluorescent antibody staining techniques. Details are given of the clinical diagnosis in all the cases and the amount of treatment and the results are fully discussed.

Virulent T. pallidum was demonstrated in nodes from two of the 45 previously treated patients and spiral organisms resembling T. pallidum were demonstrated in three others. Six of the patients were re-treated under supervision, and 3 months after completing this another inguinal node was removed and studied as previously. All the results were negative, as were those of rabbit inoculations.

This work confirms the observations of Collart and his associates that spiral organisms may persist in the lymph nodes of patients treated for late syphilis. The present authors state that the possibility that some of the men in their series may have been re-infected with syphilis as a result of homosexual practices in prison could not be excluded. Inadequate previous treatment, so far as duration is concerned, may also have been another explanation in some of the cases. Further work is required along these lines to clarify many outstanding questions and problems concerning the persistence of T. pallidum after penicillin therapy.

R. D. Catterall


GONORRHOEA


Penicillin by intramuscular injection remains after more than 20 years the treatment of choice in gonorrhoea, being effective, safe, and cheap. This continues to be the view in spite of a profusion of other antibiotics, an increasing number of penicillin reactions, and the emergence of relatively resistant strains of the gonococcus. The problem of assessing any new product, such as the newer penicillins, centres round the variable absorption rates following oral administration, forgetfulness on the part of the patients, premature cessation of therapy by the patient, and the fear of a black market in tablets. Not least to be taken into account is the fact that patterns of sensitivity of gonococci vary with time and place. The routine dosage employed in the months before a clinical trial begins is also relevant. The ever-present problem of differentiation between relapse and re-infection has no satisfactory criteria for its resolution, and this too makes assessment of any new drug difficult.

The present paper from St. Mary's Hospital, London, reviews the results of treating 279 male patients with acute uncomplicated gonorrhoea with aqueous procaine penicillin and 74 others with benzathine penicillin. The results are compared with the response to orally administered newer penicillins—namely, phenoxymethyl penicillin in 85, phenethicillin in 148, cloxacillin in 25, and ampicillin in 356 patients. The best results were obtained with a single injection of 1-2 mega units of aqueous procaine penicillin. Single or double oral dosage with ampicillin was fairly successful, but single or double

The direct immunofluorescent staining technique of Deacon and others (Proc. Soc. exp. Biol. (NY), 1959, 101, 322; Abstr. Wild Med., 1960, 27, 17) for identification of the gonococcus is dependent on obtaining material infected with stainable organisms. However, it is not usually available in cases of acute gonococcal arthritis. Therefore the Rheumatic Diseases Study Group of the University of Texas Southwestern Medical School, Dallas, have studied an indirect immunofluorescent method using formalin-fixed Neisseria gonorrhoeae as antigen for the detection of serum gonococcal antibodies in such patients and compared the results with those in patients with other types of arthritis.

A positive result was obtained in nineteen of 22 patients with definite gonococcal arthritis and in seventeen of 35 with presumptive gonococcal arthritis, but in only seven of 42 patients with Reiter's syndrome and in five of 28 with acute uncomplicated gonorrhoea. Of a total of 105 control subjects tested, a positive result was obtained in only six, the result being negative in all but one of sixteen patients with rheumatoid arthritis and in all of thirty with rheumatic fever of infectious arthritis.

(The pattern of seropositivity with this test would not appear to differ markedly from that previously obtained with the gonococcal complement fixation test.)

R. R. Willeox

Prophylaxis of Ophthalmia Neonnatorum. KAIVONEN, M. (1965). Acta ophthal. (Kbh.), Suppl. 79, 10 figs, 137 refs. All the 599 children born in 1957 and all the 314 children born in 1964 were included in this study. Bacterial samples taken from the conjunctival sac on one of the first days of life were positive in about 35 per cent. Staphylococcus aureus was found in 24-2 per cent. of the 1957 series and in 2-5 per cent. of the 1964 series. Other bacteria, chiefly streptococci and Gram-negative rods were observed in 7-7 and 6-1 per cent. respectively. The bacterial incidence rose fairly rapidly on the first 5 to 6 days and was dependent on the standard of aspepsis as regards Staphylococcus aureus. This bacterium was the only one evidently correlated to the symptoms of inflammation, especially true ophthalmia neonatorum. No case of gonorrhoeal ophthalmia occurred. Half the children were given prophylaxis with 1 per cent. silver nitrate and half with acetylpyridinium-chloride (Biosept) 0-1 or 0-05 per cent. Chemical conjunctivitis was more frequent after silver nitrate and bacterial conjunctivitis after Biosept prophylaxis. A positive bacterial culture was slightly less often obtained after silver nitrate.

G. von Bahr


IV. Studies by Immunofluorescence and Double Diffusion-in-Gel Technique on the Antigenic Relationship between N. gonorrhoeae and Other Neisseria Strains. DANIELSSON D. (1965). Acta path. microbiol. scand., 64, 267. 6 figs, 12 refs.

NON-GONOCOCCAL URETHRITIS AND ALLIED CONDITIONS


TRIC agent is a member of the psittacosis/lymphogranuloma-venerereum/TRIC group of organisms and it was first isolated in 1964 from the conjunctiva of a baby with inclusion conjunctivitis and from the urethra of his father who had "non-specific" urethritis. Three of the authors of the present paper also described (Brit. J. vener. Dis., 1964, 40, 25) changes in epithelial cells of the urethra, conjunctiva, and cervix which were considered to be associated with TRIC agent infection.

The present paper from the Institute of Ophthalmology, London, reports investigations of nine men with "non-specific" urethritis and of four of their female sexual partners, in which urethral scrapings were inoculated into yolk-sacs of embryonated eggs. TRIC agent was isolated from two of them and Halberstaedter-Prowazek inclusions were found in three patients with urethritis. The same changes as were seen in epithelial cells and already reported were also observed in eight of ten urethral specimens of the present series and in two of four cervical
scrapings. The agents isolated from the two male patients were further investigated by inoculation into baboons and mice, and the results of electron microscopy and complement fixation and fluorescent antibody tests confirmed the organism to be TRIC agent.

The results of this study suggest that a full investigation for the presence of TRIC agent is indicated in all types of so-called non-specific genital infection. G. W. Csonka

Treatment of Reiter’s Syndrome. WRIGHT, V. (1965). Rheumatism, 21, 30. 4 figs, bibl.


PUBLIC HEALTH AND SOCIAL ASPECTS


MISCELLANEOUS


In addition to the occurrence of iritis and oral and genital ulceration in Behçet’s disease, other manifestations have been described, i.e., thrombophlebitis and arthritis, a type of ulcerative colitis, and pneumonitis. The authors describe the twenty-second case to be reported of central nervous involvement, which took the form of dysarthria, purposeless movements of the eye and face and, later, muscular weakness. No virus could be isolated from the cerebrospinal fluid. The disease is fatal only if there is neurological involvement and 40 to 50 per cent. of cases with central nervous system involvement are fatal. G. Davies


Report on a 45-year-old female with Behçet’s disease. A febrile polyarthritis and intestinal and nasal ulcerations with haemorrhages were the prevailing signs. A preceding attack of iridocyclitis was almost healed. K. Hruby


In fourteen of sixteen patients with Behçet’s disease, a non-specific skin hypersensitivity was found and this was noted also in the buccal and genital mucous membranes. Aphthous ulcers could be reproduced by needle puncture and their histopathological changes were similar to those occurring spontaneously. Corticoids and fever therapy inhibited hypersensitivity and hydrocortisone injected intradermally inhibited the experimental aphthous ulcers. M. H. T. Yuille


This important paper discusses inclusion-positive eye infections seen in London which cannot necessarily be divided into two categories, inclusion conjunctivitis and trachoma. The suggestion that there is a range of ocular pathogenicity, and that some strains in the eye which might cause trachoma may also affect the genital tract is considered, and conclusive evidence has been obtained to associate such genital infection with concurrent cases of trachoma. The suggestion is made that in countries with a low incidence of trachoma this genital infection may form the continuing reservoir of ocular involvement. M. J. Gilkes


