
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)
It is assumed herein that all treponemal infections of man are caused by one parasite, T. pallidum; that treponematosis appeared first as yaws in tropical Africa in Paleolithic times; that the evolution of endemic syphilis ran parallel with the evolution of human society, culminating in venereal syphilis in the urban communities of the later Neolithic period; that the treponemal syndromes are so fluid that, with a change of climate, or human habits, or both, yaws changes into endemic syphilis and vice versa, and non-venereal syphilis and vice versa; that the millions of Negro slaves exported from sub-Saharan Africa in the course of several millennia carried treponemal infection wherever they went; and that the Middle East, for geographical and sociological reasons, has been a focus of treponematosis second only to tropical Africa.
This paper describes the role that pilgrimage to the Holy Land has played during the past 18 centuries in the transportation of treponemes from the Middle East to Europe, particularly during those centuries when millions of pilgrims were involved in the social and military turmoil of the Crusades.
Also discussed is the influence that the pilgrimage to Mecca has probably had on the distribution, dissemination, and exchange of different strains of treponemes, as millions of people in more than 1,300 celebrations of the annual hajj have converged on the Holy City, shortly to be scattered again to their homes in Africa, Asia, and elsewhere.

This is an analysis of 278 out of 15,628 patients who were found to have positive serological tests for syphilis. Many of these patients had ocular diseases unconnected with their syphilis. The authors enumerate the syphilitic ocular diseases, the eye manifestations of neuro-syphilis, and also the ocular diseases unconnected with syphilis that they found in these patients.

Barrie Jay

This paper from the Dermatological Clinic of the University of Zürich reports the findings in 48 patients with erythema nodosum seen during the period 1958–62, when 28,512 new patients attended the clinic. The commonest causes of the condition were tuberculosis and staphylococcal infection, which each accounted for twelve cases. Drug reactions were considered to be the cause in seven cases, two were attributed to syphilis, and only two cases [an unusually small proportion] were found to be related to sarcoidosis. In ten cases the aetiology of the erythema nodosum was unknown.
In the first of the two cases associated with syphilis, the erythema nodosum appeared on the second day of a prolonged Herxheimer-like reaction which followed the penicillin treatment of sero-positive primary syphilis. In the second case the eruption developed on the legs in a patient with secondary syphilis before treatment was given and disappeared rapidly when penicillin was administered. The histological findings in biopsy specimens of the lesions in these two cases are described and there is a detailed discussion of the literature on the subject.
R. D. Catterall


SYPHILIS (Therapy)

The number of patients with primary or secondary syphilis treated at the First Skin Clinic of the University of Vienna fell from 408 in 1948 to 141 in 1949, fifty in 1950, and sixteen in 1951. This fall cannot be attributed entirely to penicillin treatment, which was introduced at this clinic only in 1950. Moreover, since 1955 there has been a small but persistent rise in the incidence of early infectious syphilis. During the period 1951–60, 141 patients with primary or secondary syphilis were treated with penicillin alone. The total dosage of penicillin ranged from 6–9 to 12 mega units, given in two courses with an interval of 6 to 8 weeks between them. In the early days procaine penicillin in oil was used. Later this was changed to procaine penicillin in water and eventually to a combined preparation of penicillin with antithiamine. Standard serological tests for syphilis were performed every 3 months during the first year of follow-up, every 6 months in the second and third years, and every year thereafter. In the early months of 1963 the treponemal immobilization (TPI) test was performed on the serum of all the patients remaining under observation. Standard tests were also performed on the cerebrospinal fluid (CSF) in most cases.

Of the eighty patients who were fully investigated, none gave positive reactions to the standard serological tests in 1963, and previous tests on the cerebrospinal fluid had given normal results in all cases. However, the TPI test gave a positive result with serum in 31 cases and with CSF in one. These results are compared with those obtained in 35 patients with primary or secondary syphilis who received combined arsenic and bismuth therapy between 1948 and 1950; in eleven of these cases the serum gave a positive TPI reaction in 1963.

The author concludes that while the late results of combined arsenic and bismuth therapy are in no way better than those of treatment with penicillin alone, they are not significantly inferior. R. D. Catterall

Diagnosis and Treatment of Congenital Syphilis in Children attending the Out-patient Department of the Obstetrical and Gynaecological Clinic of the University of Naples. (Considerazioni sui bambini assistiti nell'ambulatorio della Clinica Ostetrica e Ginecologica dell'Università di Napoli per l'accertamento e la cura della sifilide congenita.) FANUELE, G., and CARBONE, M. (1963). Pediatria (Napoli), 71, 1159. 4 figs, bibl.

SYPHILIS (Serology)

The rapid plasma reagin (RPR) card test for syphilis and other treponematoses employs a modified VDRL slide test antigen containing charcoal and is carried out on plastic-coated cards (Portnoy and others, Publ. Hlth Rep. (Wash.), 1962, 77, 645; Abstr. Wild Med., 1963, 33, 232). It was developed to provide a test which could be carried out in the field or at the bedside without the need for any specialized laboratory equipment. In this paper the author reports a comparison of the results of two modifications of this technique with those of the standard VDRL procedure.

In the first method, which could be used for large-scale testing in the laboratory, 0-05 ml. quantities of unheated serum or plasma are pipetted on to commercially available cards with 18-mm. diameter rings and 1/60 ml. RPR card test antigen is added to each and mixed with the serum; the card is then agitated on a mechanical rotator for 8 minutes at 100 r.p.m. and examined with the naked eye for the presence of aggregates. Tests on 925 sera showed that the card test gave 55·7 per cent. of reactive or weakly reactive results and the standard VDRL slide test 53·4 per cent. Quantitative tests showed agreement within one dilution factor in 83 per cent. of cases; in eighteen out of the 21 cases of disagreement the higher titre was given by the RPR card test.

The second method is designed to be used with the supernatant plasma from microhaematocrit determinations, but the comparative tests were performed on unreactivated serum, 0·025 to 0·03 ml. being mixed with 0·01 ml. card test antigen on cards with 14-mm. diameter circles, the cards shaken for 8 minutes as before, and the results compared with those of tests carried out by the first method. Tests on 209 sera gave very similar results, the first method giving 150 reactive or minimally reactive results and the second 149 with 0·03 ml. serum and 152 with 0·025 ml. serum.

The advantages claimed for the RPR card test are that it permits the use of unheated serum or plasma, saves time and glassware, and uses a stable antigen suspension and standardized, disposable apparatus. It also offers a reproducible and rapidly performed quantitative test procedure. A. E. Wilkinson
Immuno-electrophoretic Studies of Blood Serum and Cerebrospinal Fluid in Early Syphilis. [In English.]

Although the serological reactions characteristic of syphilitic infection are rarely positive in the cerebrospinal fluid (CSF) in cases of early syphilis, there is sometimes an increase in the globulin content of the fluid. However, this change has not hitherto been investigated by qualitative techniques such as immuno-electrophoresis. Serum proteins with molecular weights below 200,000 are found in normal CSF, but the presence of proteins of high molecular weight, such as α₂-lipoprotein and α₂-macroglobulin, is thought to indicate a partial breakdown of the blood–brain barrier. The existence of an active immunological process outside the central nervous system (CNS) is reflected in an increase in the CSF content of the serum immunoglobulins—γ-globulins, β₂-A-globulin, and β₂-M-globulin—while the presence of β₂-macroglobulin and γ-globulins with an α₂ mobility is interpreted as the result of an active intracerebral immunological process.

At Rigshospitalet, Copenhagen, immuno-electrophoresis was carried out on specimens of serum and CSF from fourteen patients with dark-ground-positive early syphilis, four being in the primary and ten in the secondary stage. Two specimens of CSF showed a slight pleocytosis and nine a slight increase in total protein content; all fourteen gave negative results with the Wassermann, Kahn, and treponemal immobilization tests. On immuno-electrophoretic analysis of specimens of CSF which had been concentrated a hundred-fold, no β₂-A or β₂-M-globulins were demonstrated but γ-globulins with α₂ mobility were present in eight cases. These persisted after treatment in two out of five of these patients who were re-examined and were also present in two cases in which they had not been found before treatment was given. Following treatment α₂-lipoprotein or α₂-macroglobulin or both were present in the CSF in thirteen of the fourteen cases, suggesting a partial breakdown of the blood–brain barrier. These patients also showed a diffuse increase in the concentration of all the normal CSF proteins. Subsequently the CSF of three out of nine patients examined still showed signs of a breakdown of the barrier despite adequate treatment. (Of the fourteen patients, twelve were given 6 mega units penicillin over a 10-day period and two received 1 g. terramycin daily for 10 days because of sensitivity to penicillin.)

The authors suggest that immuno-electrophoretic procedures may be useful in assessing the efficacy of treatment of syphilis.

_A. E. Wilkinson_


From the Sixth U.S. Army Medical Laboratory, Fort Baker, California, the authors describe a modified technique of preparation of treponeme suspensions for use in the fluorescent treponemal antibody (FTA) test and a modified test procedure which is claimed to enhance the specificity of the test. Infected testes from rabbits treated with cortisone are extracted with 50 per cent. inactivated normal rabbit serum in saline. Gross tissue debris is removed by centrifuging for 10 minutes at 600 g and the supernatant fluid added to an equal volume of 0·002 per cent. sodium hypochlorite in saline. This is then centrifuged at 4,000 g for 10 minutes and the deposited organisms washed in hypochlorite-saline, centrifuged, and finally suspended in saline containing 5 per cent. dimethyl sulphoxide and 10 per cent. normal rabbit serum to give a density of 20 to 30 treponemes per high-power field. Aliquots of 0·5 ml. are frozen at −65°C and remain usable for at least 6 months. Once thawed, the suspension is stored at 4°C and can be used for at least 2 weeks. Treponemes so prepared are said to give brilliant fluorescence and not to become detached from the slide during the performance of the test. In carrying out the test 0·01 ml. treponeme suspension is allowed to dry on a slide, fixed for 2 to 3 minutes in an acetone-dry-ice bath at −78°C.; 0·03 ml. of a 1 : 100 (FTA 100) or 1 : 200 (FTA 200) dilution of the patient's serum in buffered saline is then added and allowed to react for 30 minutes at 34°C. After washing, 0·03 ml. conjugate (commercially prepared fluoresceinated goat anti-human globulin) in optimum dilution is added and the slides incubated as before, washed, mounted, and read.

The results of the treponemal immobilization (TPI) and FTA tests on 927 specimens of serum sent to the laboratory for the TPI test were compared. Valid results in the TPI test were obtained with only 765 sera [the remainder presumably being toxic or anticomplementary, an unusually high proportion]. The first 262 sera were examined by the FTA test technique of Fife and others (Amer. J. clin. Path., 1961, 36, 105; Abstr. Wild Med., 1962, 31, 95) using serum dilutions of 1 : 200 and 1 : 100. The TPI test gave reactive results in 55 per cent., the FTA 200 in 52 per cent., and the FTA 100 in 56 per cent. of cases. Difficulties due to loss of treponemes from the slides during the FTA test led the authors to develop the method of preparation of the antigen suspension described above. These suspensions proved satisfactory when a further 503 sera were tested at a single dilution of 1 : 100, giving 56 per cent. of reactive results compared with 57 per cent. with the TPI test. Clinical details regarding the patients whose sera were tested not being available, second specimens were obtained in order to confirm the results.

The authors consider that the TPI and FTA 100 tests are equally sensitive and specific and can be of diagnostic value when paired specimens of serum are tested. The FTA 100 test is also of value in the investigation of sera which give invalid results with the TPI test.

_A. E. Wilkinson_


The value of the Reiter protein complement-fixation (RPCF) test in comparison with other serological tests
for syphilis in cases of treated neurosyphilis was investigated in the Department of Dermatology and Venereology of the University of Helsinki. The 107 patients studied included 45 who were asymptomatic, eighteen with meningovascular disease, twelve with paresis, seventeen with tabs, two with optic atrophy, and thirteen with congenital syphilis. All but four had been given 9 mega units penicillin, combined with malaria in 26 cases; three of the remaining patients had had malaria therapeutically alone and one had received chloramphenical because of sensitivity to penicillin.

The serological tests carried out in addition to the RPCF test were the Kolmer and Kahn tests and the VDRL slide test with sitolipin antigen. In the group as a whole these four tests gave positive reactions in 100, 88, 65, and 90 cases respectively. The RPCF test gave a positive result in 41 of the 45 cases in the asymptomatic group and in 59 of the 62 cases of other types. Of the three negative sera in the latter group, two were from cases of tabs and one from a case of congenital syphilis. A positive reaction was obtained in 54 (95 per cent.) of 57 cases treated less than 9 years previously and in 46 (92 per cent.) of the remaining fifty cases, in which a longer period had elapsed. The treponemal immobilization (TPI) test was carried out in 62 cases, especially those in which the RPCF had given a negative result. Only one serum was non-reactive to the TPI test, and examination of a further specimen gave a weakly positive reaction.

A. E. Wilkinson


SYPHILIS (Pathology)


The radiological aspects of the skeletal changes which are present in patients with early congenital syphilis are described in this paper from the Ospedale Infantile “Regina Margherita”, Turin, and the Institute of Radiology of the University of Turin. Because the Wassermann reaction of the newborn is often negative and case histories are frequently unreliable and because the clinical picture of congenital syphilis has altered over the last 25 years and the incidence of syphilis is increasing, the radiological evidence of congenital syphilis has become increasingly important.
The bony lesions of syphilis in the newborn appear before the infant is 5 months of age, and the illustrations in this paper are taken from cases in which they were present at birth. The lesions, which are multiple, are situated mainly in the long bones, but occasionally occur also in the short bones. The most common lesion is an osteochondritis at the diaphyseal-metaphyseal junction. In the first grade widening, condensation, and irregularity of the zone of calcification, with a "saw-tooth" appearance facing the cartilage are present. In the second grade a band of radiotranslucency appears below this area, in the diaphysis. In the third grade there is total destruction of the metaphysis, which is no longer sharply defined against the epiphysis. The band of radiotranslucency is widened and epiphysial detachment may occur; this is in reality the result of pathological fractures which manifest themselves clinically as pseudoparalysis of Parrot. The next most common pathological process is a periostitis; this may be present in the newborn, but appears more commonly at 2 to 3 months of age. A primary diaphysial and a secondary gummatorous type are distinguished. Finally, two forms of osteomyelitis may be present at the diaphysio-metaphysial junction; one is centrally situated and the other is marginal. They appear as radiotranslucent areas in the cortex of the bone. More rarely a syphilitic dactylitis may be present, which differs from the tuberculous form in being accompanied by proliferation of subperiosteal new bone. All these lesions regress more rapidly in early congenital syphilis than in the delayed form. Radiographs are reproduced which show complete resolution of these lesions.

The differential radiological diagnosis of these lesions, in particular from those of rickets and scurvy, is discussed in detail.

F. Hillman


SYPHILIS (Experimental)


At the Institute of Hygiene of the University of Palermo the author carried out two experiments on rabbits to compare the efficacy of penicillin treatment in early and late syphilis and to determine the significance of a persistently positive treponemal immobilization (TPI) reaction after treatment.

In the first experiment four rabbits received a massive intratesticular dose of the Nichols strain of Treponema pallidum. Two months later, when the results of the cardiolipin and Reiter protein complement-fixation tests and the TPI test were positive, they were given a 15-day course of a mixture of sodium benzylpenicillin and procaine penicillin to a total dose of 1.5 mega units per kg. body weight. The results of all the tests became negative during the following 4 to 6 months and extracts of popliteal lymph nodes taken from these animals proved non-infective on intratesticular inoculation into others. In the second experiment four rabbits infected with T. pallidum 4 to 9 months previously were treated with a single dose of 50,000 units of procaine penicillin with aluminium stearate and 1 mg. bismuth per kg. In none of these animals did the TPI reaction become negative, and the complement-fixation reactions became negative in two animals only. After 4 to 7 months the animals were given a course of treatment as in the first experiment. During the next year the titres of all the serological reactions declined, but none became negative. Inoculation with extracts of their popliteal lymph nodes produced infection in fresh animals which could be transmitted to a further set of animals.

These findings indicate that penicillin therapy is more likely to be effective in early than in late cases of syphilis and that viable treponemata may persist even after massive penicillin treatment in long-standing cases. A positive TPI reaction should therefore be regarded seriously, even in the absence of other signs, in cases of late syphilis.

F. Hillman


GONORRHOEA


At Boston City Hospital, the authors studied 100 cases of acute uncomplicated gonorrhoea in males to ascertain the effect on treatment of penicillinase-producing concomitants. The initial diagnosis was confirmed microscopically, by Gram-stained smear and treatment was given with 600,000 units of procaine penicillin intramuscularly. Patients were considered to be cured if, after 2 weeks, no clinical signs of the disease remained and if gonococci were no longer present in urethral smears. The discharge was cultured at the initial examination and again if symptoms persisted. Two chocolate agar plates were used, one of which contained benzylpenicillin 0.1 unit per ml. After incubation, gonococcal and non-gonococcal colonies were subcultured and identified. The sensitivity of the gonococci to penicillin was estimated and the non-gonococcal colonies were examined for penicillinase production by two methods.

Of the 100 patients ten failed to respond to treatment. A close correlation was found between successful treatment and penicillin sensitivity of the gonococcus. The majority of urethral exudates showed growth of non-gonococcal
colonies on the penicillin-agar culture medium but in only 35 cases were these organisms considered to have been actively multiplying in the urethra. Penicillinase production was shown by 21 of these strains. The treatment failure rate in patients with penicillinase-producing concomitants was four times that in patients without these concomitants, but correlation with the factor of penicillin sensitivity reduced the statistical importance of the concomitants.

The authors conclude that susceptibility of the gonococcus to benzylpenicillin is an important factor in the outcome of treatment. The failure rate is significantly increased when the gonococci are less sensitive to the antibiotic. Concomitant penicillinase-producing organisms cause an increase in the failure rate which is not statistically significant.

Leslie Watt


The authors have analysed the variance of results, obtained at the State Serum Institute, Copenhagen, in repeated sensitivity determinations on identical strains of the gonococcus and in repeated determinations on strains recovered from patients during the same attack of gonorrhoea; sensitivity to sulphathiazole, tetracycline, streptomycin, and penicillin was measured. The estimated variances were almost the same for the two categories of strains and were close to those obtained by other workers in "true" sexual partners. The authors conclude that determination of sensitivity may help in distinguishing between relapse and re-infection and between "true" and "false" sexual partnerships, provided an identical method is used in both tests. It is essential that the variance of the method used should be estimated before any conclusions are drawn.

Eric Dunlop


The authors describe the cutaneous eruption which was the principal manifestation of gonococcal infection in fourteen young adults (2 male and 12 female) seen at the Jefferson Davis Hospital, Houston, Texas, between January, 1957, and April, 1963. The case histories of two of these patients in whom the skin changes followed sexual intercourse with each other are given in detail. Coloured photographs of the skin lesions resulting from the gonococcaemia are reproduced.

The skin manifestations, which usually appeared during the first day of what was apparently a transient bacteremia with fever and arthralgia, tended to be scanty and most commonly affected the distal parts of the limbs. They were discrete, varied from 1 to 2 mm. to 2 cm. in diameter, and started as tiny erythematous macules which evolved rapidly through maculopapular, vesiculo-pustular, haemorrhagic, and sometimes bullous stages. The centre became necrotic with a violaceous border and was surrounded by an erythematous areola. The lesions healed, usually without scarring, in 3 to 4 days, but in untreated cases they could recur with further fever. They were indistinguishable from those seen in meningococcaemia.

Although the precise pathogenesis was not established, the authors consider it likely that the clinical appearance and the presence of pus cells in the lesions represented a bacterial embolization or septic infarct. Gonococcal infection in all patients was undoubted, but a gonococcal bacteriemia could not be demonstrated.

Benjamin Schwartz


The author, writing from St. Mary's Hospital, London, gives an account of the use of actinospectacin ("trobacin"; spectinomycin) administered in single intramuscular injections of 1·4 to 1·6 g., providing 200 mg. actinospectacin sulphate, in the treatment of 151 men suffering from acute uncomplicated gonorrhoea. Of the 134 patients observed after treatment, failure occurred in thirteen (9·7 per cent.) and re-infection in 22 (16·4 per cent.). The antibiotic proved effective in six cases in which penicillin and at least one other therapeutic agent had failed. One of the 151 patients felt dizzy and faint after the injection. There were no other systemic side-effects and no complaint of pain at the site of injection. Two patients were considered to be sensitive to penicillin, and these were treated with actinospectacin without ill effect.

Single injections of the antibiotic were administered in two cases of early syphilis. In one, a case of sero-negative primary syphilis, treponemones could no longer be demonstrated on dark-field examination 38 hours after the injection, while in the other, a case of secondary infection, treponemones were demonstrable 16 hours after the injection.

[Actinospectacin is likely to be particularly useful in the treatment of gonorrhoea in patients who are sensitive to penicillin. Evidence of the treponemical effect of actinospectacin in the experimental animal has been provided by Clark and Yobs (Brit. J. vener. Dis., 1963, 39, 184).]

Eric Dunlop

NON-GONOCOCCAL URINARY TRACT INFECTIONS AND ALLIED CONDITIONS


A fatal case of Reiter's syndrome was extensively studied. The patient had laceration, photophobia, and bilateral conjunctivitis, which progressed to bilateral corneal ulceration. Conjunctival cultures revealed only coagulate-negative staphylococci and achromobacteria. Pathological examination of the cornea revealed hyaline scarring without evidence of inflammation.

This is the second fatal case of Reiter's syndrome to be reported.

P. Henkind

During the acute stage of the disease, treatment is antibiotics, corticosteroids (systemic and intra-articular) massage, and early mobilization. In cases of long duration or in relapse, the authors advise pyretotherapy, and gold and chloroquine salts.

S. VALLON


Two separate viruses were isolated from a typical case of inclusion blennorrhoea and a typical case of trachoma judged by clinical standards. The viruses were cultured by inoculation into the amniotic cavity of 11-day-old chick embryos and demonstrated in the cells of the chick embryo tongue. It is suggested that this method presents some advantages of both speed and ease which merit development. The morphology of the viruses isolated appeared to be identical. Changes noted in the chick embryo eyes are thought to be of significance as the response of a non-human eye to the virus with specific pathological changes.

M. J. GILKES


CHEMOTHERAPY


Since 1956 prophylactic penicillin has been given in one massive dose to all non-allergic recruits on entry at most American military recruit training camps and resulted in a dramatic decline in the incidence of rheumatic fever. Allergic reactions to penicillin have, however, occurred in about 1 per cent. of incoming recruits. Since it is now believed that the haptenes responsible for penicillin hypersensitivity are penicillin derivatives rather than the
penicillin molecule itself, an attempt was made at the Great Lakes Naval Training Center, Illinois, to detect penicillin-sensitive individuals before prophylactic penicillin was given. The recruits received an intradermal injection of penicilloyl coupled to a lysine homopolymer as penicilloyl-polylysine, which has been found to be non-immunogenic but to produce a skin reaction in penicillin-sensitive subjects.

Of 1,022 recruits 868 had a convincing history of previous penicillin treatment and 73 (8.4 per cent.) of these gave a positive reaction to the skin test with penicilloyl-polylysine, compared with four out of 125 (3 per cent.) of those denying previous treatment with penicillin, and three out of 29 whose previous treatment history was "unknown". Of 43 subjects who reported a previous allergic reaction to penicillin, fifteen gave a positive reaction, compared with 58 (6.8 per cent.) of the 825 supposedly non-allergic subjects.

After administration of 1-2 million units of benzathine penicillin intraglutinately to these 825 non-allergic subjects, systemic reactions occurred in ten. Three of these had given a positive reaction to the skin test, the reaction incidence being 7.7 per cent. (2 out of 26) in those giving "strongly positive" responses, 3.1 per cent. (one out of 32) in the "weakly positive" group, and only 0.9 per cent. (7 out of 767) in the negative group. These differences were statistically significant. The reproducibility of the skin test was 90 per cent.

A. Ackroyd


PUBLIC HEALTH AND SOCIAL ASPECTS


MISCELLANEOUS


