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)


The author, writing from the Faculty of Medical Sciences, Buenos Aires, presents a critical review of published work on re-infection with syphilis. He states that the statistical concept of treatment “failures” (without distinguishing cases of re-infection) has proved misleading; syphilologists are now accepting less rigid diagnostic criteria in determining the occurrence of re-infection in syphilis; but the mistakes of previous years cannot be corrected and, therefore, statistics for much of the work on the treatment of syphilitic patients are almost valueless.

The author then gives some statistical details of 147 cases of re-infection with syphilis occurring among 6,006 patients with treated early syphilis, an incidence of 2.2 per cent. He has never seen relapse lesions, either primary or secondary in type, in well-treated cases of early syphilis; this he attributes to the use of bismuth. In his view the increase in the number of re-infections in the last 10 years is to be attributed to the general increase of infectious syphilis during the war and post-war years rather than to new methods of treatment. In patients treated with penicillin and bismuth in intensive short courses of therapy there have been fewer re-infections than in those treated with long courses of arsenic and bismuth or with bismuth alone.

Eric Dunlop

See also Laurell, Acta path. microbiol. scand., 1955, Suppl. 103, p. 1.


The course of treated syphilitic primary optic atrophy has been studied in 233 cases at Johns Hopkins Hospital, Baltimore. Because of the relatively small number of patients and the varying treatment previously given it was impossible to consider each form of therapy separately. For the purposes of this study the patients were divided into five groups according to the regimen followed after they were first seen at the hospital:

1. no treatment;
2. metallotherapy;
3. malaria therapy, with or without metallotherapy;
4. penicillin and malaria therapy;
5. penicillin without malaria therapy.

Only patients with initial visual acuity greater than 10/200 were included, “thus eliminating the fallacy of considering non-progression of an industrially blind patient as a treatment success”.

It was found that in patients with initial visual efficiency of more than 40 per cent, the rate of progression was significantly slower than in those with initial visual efficiency of 40 per cent or less, and the authors [justifiably] attribute this largely to the treatment given. Of 141 patients followed up after receiving various forms of antisyphilitic treatment, one-third showed progression of the disease during the first year, one-half at 2 to 3 years, and two-thirds at 4 to 5 years. The rate of progression after treatment did not appear to be significantly influenced by the spinal-fluid cell count before treatment started. The authors state that the results in these cases may have been influenced to a variable degree by previous treatment given elsewhere, which also precluded accurate comparison of the treatment regimens used.

Further, to estimate the efficacy of treatment in any disease the prognosis in the absence of such treatment should be known; this is not known in the case of syphilitic optic atrophy. They emphasize the difficulty of attempting evaluation of treatment in a chronic, variable disease in the absence of untreated controls.

A. J. Gill


The author describes two cases of unilateral Argyll-Robertson pupil in a man (aged 50) and a woman, both negative for neurosyphilis. The man had a history of halusmism.

J. Charlamis


SYphilis (Therapy)


The authors have studied the blood penicillin levels in 22 cases of early syphilis treated with a single dose of 2.4 mega units benzathine penicillin. The drug was dissolved in 6 ml. double distilled water and 3 ml. injected into each buttoc. The method used for assessing the penicillin content of the serum is outlined. In all cases therapeutically effective levels of the antibiotic were maintained for at least 15 days after injection, the values at that time ranging from 0-06 to 0-43 (average 0-045) Oxford units per ml. of serum. Eric Dunlop


The author first used bismuth in 1936 as the sole method of treatment of syphilis; with the advent of penicillin he agrees it is no longer justified to use bismuth alone, but nevertheless he considers it useful to record the excellent results that were obtained by this method, quoting in support the work of many authors of various nationalities. Details of the methods of treatment and the results obtained are given at length [but are mainly now of historical interest]. The author concludes that until penicillin has stood the test of time bismuth is the surest medicament for the treatment of syphilis, resulting, in the author's experience, in clinical and serological cure in close on 100 per cent, of cases. Eric Dunlop


The author records the good results obtained at the University Dermatological Clinic, Buenos Aires, in the treatment of early syphilis with arsenic and bismuth given in intensive courses. Of 439 patients treated intensively for 3 weeks in hospital with arsenoxide and liposoluble bismuth, treatment had to be suspended in eleven. Of 136 of these patients subsequently followed up, only in one was a relapsed chancre seen (in a patient who had received arsenic only); there were three cases of re-infection. Intensive treatment was followed by consolidation courses of liposoluble bismuth when the patient attended for follow-up examination.

Serological tests showed that 53 (79 per cent.) of the 67 cases of sero-positive primary syphilis were sero-negative after the initial course of intensive therapy, 66 (98.5 per cent.) after the first consolidation course of bismuth, and 67 (100 per cent.) after thesecond. Similarly, of the 66 patients with secondary syphilis, 39 (59 per cent.) were sero-negative after the initial intensive treatment and all became so after the second course of bismuth. The six cases of primary syphilis which were sero-negative before treatment remained so. The cerebrospinal fluid (CSF) was examined in 99 cases between 1 and 5 years after the start of treatment and was found to be normal in every case. Of the patients who defaulted after receiving only the initial intensive treatment, eleven were re-examined clinically, serologically, and by lumbar puncture 2 to 5 years later; in all eleven the serological reaction was negative and the CSF normal. The author considers that the intensive use of bismuth was the main factor in producing these good results. Eric Dunlop


The authors report, from the Faculty of Medicine, Buenos Aires, the results in ten patients with early syphilis who were treated with 600,000 units of penicillin in the form of rectal suppositories, two of which were inserted daily for 10 days. In nine cases the disease was a primary infection, five of the patients being sero-negative and four sero-positive; four patients were given in addition 20 intramuscular injections of liposoluble bismuth.

Dark-ground examination carried out before treatment and at 3, 8, and 24 hrs after it in each case showed no treponemes by 24 hrs. The Wassermann and Kahn serological tests for syphilis were performed at the beginning of treatment and at 3, 10, and 20 days, and thereafter monthly for 6 months. The sero-negative
patients remained so, while reversal of the serological reaction occurred in the remainder, as occurs when penicillin is given intramuscularly, clinical resolution of the initial lesions being equally satisfactory. The tenth patient had florid secondary syphilis, but this had entirely subsided by the 10th day of treatment. (Rectal suppositories of penicillin were also employed with good result in the treatment of twelve children with pyoderma gigan- tosum, impetigo, and impetiginized eczema.)

This paper reminds us that penicillin can be given per rectum (as well as by mouth) in those cases where intramuscular injections are not possible.

Eric Dunlop


The authors consider that published reports of the results achieved with antibiotics (mainly penicillin) in neurosyphilis are too optimistic, and that the older type of chemotherapy still has considerable value. They agree that penicillin is invaluable in the earlier lesions but consider that in the treatment of established neurosyphilis its value is doubtful. They strongly advocate the use of “stovarsol” (acetarsol) in courses to a total of 30 g., particularly in the treatment of general paralysis of the insane. At the Neurological Clinic, University of Toulouse, they have employed this treatment as a supplement to penicillin therapy, the drug being administered by mouth and by intramuscular injection in doses up to 3 g. per day, in some cases with courses of bismuth in addition.

Most of these cases had initially derived little benefit from penicillin in large doses, but clinical improvement and return of the cerebrospinal fluid towards normal followed swiftly after what the authors describe as “classic chemotherapy”.

[Acetarsol is little used in Britain to-day, and even tryparsamide, which at one time had a considerable vogue, has been largely abandoned. The value of bismuth after penicillin therapy is doubted by many, but the drug is still employed and its use seems rational. Treatment with these older remedies will probably be restricted to cases that respond inadequately or too slowly to penicillin.] Robert Lees


Cortisone and Syphilis. Observations on the Results of Adrenocortical Treatment in 90 Cases of Syphilis.

The authors report, from the National Institute of Hygiene, Paris, the results of the administration of cortisone in ninety cases of syphilis observed over a period of 4 years. The cases included all types of syphilis—early, late, and congenital—and very adequate serological studies were carried out. The dose of cortisone was 100 mg. per day for periods ranging from 5 to 30 days according to the type of case.

The main findings were as follows:

(1) Cortisone given before specific treatment of syphilis prevents or reduces the intensity of the Herxheimer reaction. This is particularly valuable in cases of cardiac and neurosyphilis.

(2) Cortisone produces a regression of the clinical signs of syphilis; this was more obvious in cases of early syphilis, but was also seen in gummata and was deduced in cardiovascular and neurological lesions. Interstitial keratitis responds to the topical application of cortisone. Treponemata disappear from primary lesions in 2 to 5 days.

(3) The serological reactions for syphilis showed a fall in titre in many cases, but in others no significant change was recorded.

(4) The pain in resistant cases of tabes dorsalis was lessened. Some improvement in Charcot’s arthropathy was achieved by intra-articular injection of cortisone.

[This article is a valuable study of the effect of cortisone in syphilis, but in practice the use of the hormone will probably be restricted to the abolition of the Herxheimer reaction in cases in which this might be dangerous, to the treatment of syphilitic disease of the eye, and possibly as an adjuvant in selected cases of syphilis of the nervous and cardiovascular systems. The paper contains a considerable mass of interesting detail which is worthy of detailed study by syphilologists.] Robert Lees


From the Stanford University Syphilis Clinic, San Francisco, comes a report of 44 cases in which aneurysm or aortic disease developed from 1 to 20 years after adequate antisypilitic treatment. All except one of the patients received arsenicals and bismuth, two of these being given penicillin as well; the remaining patient was treated with penicillin only. The series included eighteen cases of neurosyphilis, sixteen of latent syphilis, two of benign tertiary and neurosyphilis, and seven of benign tertiary syphilis. Only one patient was treated in the primary stage (and this was a second infection).

The author states that serological tests are generally considered to be important in judging the effect of treatment; in nineteen cases in the series the results of such tests were negative or doubtful and no correlation could therefore be detected between the serological response and the clinical outcome. He does not consider that any reasonable amount of chemotherapy will guarantee protection from the subsequent development of cardiovascular syphilis. Finally, he deprecates the “widespread tendency to give penicillin on any suspicion of syphilis and then to dismiss the patient as being safe from any complications”.

V. E. Lloyd

Hypersensitivity to Penicillin and the Prophylaxis with Iodine ("Mirion") and Bismuth. (Penicillinüberempfindlichkeit bei vaskulärer Lues und deren Vorbehandlung mit Jod (Mirion) und Wismut.)


Treatment of Early Syphilis with Two Injections of Penicillin. (Tratamento da sífilis recente com duas injeções de penicilina.)


SYPHILIS (Serology)


The treponemal immobilization (TPI) test has proved very valuable in the confirmation of positive reactions in the standard tests for syphilis (STS) in pregnancy. It gives positive results more often when the STS reactions are in agreement than when they differ among themselves, and brief details of the results obtained with 24 STS-positive sera are given to illustrate this point. It is emphasized, however, that when a pregnant woman has been treated for syphilis in the past and shows no clinical evidence of infection, the adequacy of past treatment should govern the decision whether further treatment is needed rather than the result of the TPI test.

A group of 57 women who had a history of unexplained abortions or neonatal deaths, or who had given birth to a malformed or macerated foetus, were studied at the University Dermatological Clinic, Marseilles. In the group as a whole there had been a total of 245 pregnancies which resulted in only 93 living children. Although all the women had given negative STS reactions, most had been given antisyphilitic treatment because no cause for the accidents of pregnancy had been found. On retesting, 47 were found to give negative reactions to the STS and the TPI test, whereas nine gave a positive and one a doubtful reaction to the TPI test, with a positive STS reaction in four instances. A comparison of the obstetric histories of the TPI-positive and TPI-negative patients showed no significant differences, and in view of the high sensitivity of the TPI test these results are considered to support the view that syphilis is not an important cause of the accidents of pregnancy.

Of 29 patients with suspected congenital syphilis, seventeen had lesions which might be attributed to such an infection; the TPI reaction was positive in seven of these cases and the STS reactions in six. Six patients who were asymptomatic but whose siblings were congenital syphilitics were all TPI-positive, although in two cases the STS reactions were negative. In two out of three further cases in which there were no signs of infection and the STS reactions were negative, although the parents were syphilitic, the TPI reaction was positive, constituting the only evidence of infection.

Transplacental passage of the immobilizing antibody may occur in infants born of syphilitic mothers and may persist for long periods. In these circumstances the quantitative STS may be more useful than the TPI test in determining whether infection of the child has occurred.

A. E. Wilkinson


The Neurath test, introduced in 1947 by Neurath and others (Amer. J. Syph., 1947, 31, 436; Abstr. Wld Med., 1948, 3, 191), if proved to be of comparable specificity to the treponemal immobilization (TPI) test, would be of great value in distinguishing biological false positive reactions from syphilitic reactions, as it is adaptable for use in any serological laboratory.

In this paper from the Veterans Administration Center, Los Angeles, the results of parallel testing with the TPI, Neurath, and standard serological tests for syphilis (STS) on 144 samples of serum, 85 from syphilitic and 59 from other patients, are reported. The latter group included 39 with positive STS reactions and fourteen others with signs suggestive of syphilis. The Neurath and TPI reactions agreed in 88 instances (61.1 per cent.) and differed in twenty (13.9 per cent.); in the remaining 36 (25 per cent.) the Neurath test gave inconclusive results. These results are similar to those reported by Roy and others (Amer. J. Syph., 1953, 37, 338; Abstr. Wld Med., 1954, 15, 122). Among seventy patients giving positive reactions with the Neurath test, the TPI test was negative in fifteen, including seven who had received treatment for unconfirmed syphilis, while of 83 patients with positive or doubtful TPI test results, five (6 per cent.) gave a non-syphilitic and 23 (29 per cent.) an inconclusive reaction to the Neurath test. In this series, therefore, the Neurath test was not of practical value in distinguishing biological false positive reactions from syphilitic reactions as shown by the STS.

The sera were also subjected to the Kolmer and Kahn
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In this interim report from the U.S. Naval Medical School, Bethesda, Maryland, the authors describe modifications of the treponemal agglutination test technique previously reported by the senior author (Canad. J. publ. Hlth, 1953, 44, 61). The chief modification is that x-irradiation of the rabbits used to prepare the treponeme suspensions has been replaced by treatment with cortisone, 6 or 7 mg. cortisone per kg. body weight being injected subcutaneously each day, starting 3 or 4 days before infection of the animals by intratesticular injection of the Nichols strain of Treponema pallidum. The tests are harvested on the eighth to tenth day after inoculation, veronal buffer being used to elute the treponemes instead of the usual basal medium. The suspension so prepared contains many erythrocytes, but it can be clarified by centrifugation at 2,500 r.p.m. for 20 min. This produces some unavoidable haemolysis which precludes the use of heat to kill the treponemes, but this can be satisfactorily effected by the addition of 1,000 units of penicillin per ml. of suspension.

The test was found to be satisfactory at room temperature if preceded by a period of shaking for 6 hrs on a Kahn shaker. Under these conditions agglutinated treponemes formed loose bundles rather than the tight clumps seen after shaking at 37°C., as was originally suggested. The authors state that suspensions which showed no spontaneous agglutination when shaken with an equal volume of saline or serum negative for syphilis for 8 hrs at room temperature were satisfactory for use as antigens. Comparison of this test with the treponemal immobilization (TPI) test on a small number of serum samples showed very satisfactory correlation, and gave some reason for hope that certain factors detrimental to the TPI test may not affect the agglutination test.

A. E. Wilkinson


Previous reports on the use of Treponema pallidum as antigen in the serological diagnosis of syphilis are reviewed and a relatively simple agglutination reaction, developed in the International Treponematosis Laboratory at the Johns Hopkins University, is described, in which a stable, heat-treated suspension of the organism is used. This suspension was found to be agglutinated by two antibodies. One of these appears to be the Wassermann reagent, being present in syphilitic serum, in the serum in seventeen out of 56 cases with biological false positive reactions, and in the serum of rabbits immunized with VDRL antigen-reagen floccules, and being completely absorbed by VDRL antigen. These observations provide an explanation of the observed specificity of the standard tests for syphilis (STS). The other antibody is a specific treponemal agglutinin, the effect of which is enhanced by ageing or heating the antigen, and by the removal of some divalent cation normally present in serum (probably Ca++) with ethylenediamine tetra-acetate (EDTA). The optimum pH is 7.6 to 8 and optimum temperature 37°C.; the reaction is complete after 15 hrs.

The antigen is prepared from the tests of rabbits inoculated with Nichols strain T. pallidum and treated with cortisone until a firm orchitis has developed, each pair being minced and gently shaken at 4°C. with two successive 50-ml. amounts of isotonic sodium citrate solution. Gross particles are removed by centrifugation at 1,000 r.p.m. and the treponemes are then sedimented by centrifugation at 35,000 g at 4°C. for 30 min., resuspended (10² per ml.) in saline containing 0.045 M EDTA, and heated to 65°C. for 30 min. Thiomersalate (to 0.01 per cent.) and 1/20 volume of 0.1 M phosphate buffer (pH 7.6) are then added. Maximum agglutinability is obtained by further heating to 83°C. for periods up to 2 hrs. Sera to be examined for the presence of the specific treponemal antigen are first absorbed with an equal volume of VDRL antigen for an hour at 37°C. in order to remove Wassermann antibody if present. After centrifugation the agglutination test is carried out with two-fold dilutions of serum in EDTA saline, the presence or absence of agglutination being determined by the examination of thick wet preparations by dark-ground microscopy. The result is recorded as the highest dilution of serum which gives definite agglutination with an equal volume of antigen suspension.

This test has been carried out on a total of 430 sera. Of 116 sera from normal individuals or patients with diseases other than syphilis, all gave negative results. Of 58 sera giving biological false positive reactions to the STS and negative reactions to the treponemal immobilization (TPI) test, two gave a positive agglutination reaction. (One of these was from a patient whose husband had syphilis.) Of 256 sera from patients with syphilis (about two-thirds of whom had been treated), 241 gave a positive agglutination reaction; these included 89 out of 95 cases diagnosed as latent syphilis on the results of the STS and TPI test, fourteen out of nineteen cases of primary syphilis, fifteen out of sixteen cases of secondary syphilis, 76 out of 78 cases of late symptomatic syphilis, 31 out of 32 cases of asymptomatic neurosyphilis, and all of sixteen cases of congenital syphilis. Among the 302 sera from patients with syphilis or false positive reactions on which both the agglutination test and the TPI test were performed, the results...
were discrepant in only twenty. While further assessment of the test is required, these results suggest that the agglutination test has a sensitivity and specificity comparable to those of the TPI test.  

P. J. L. Sequeira


In performing the treponemal immobilization (TPI) test on 529 samples of serum at the University Dermatological Clinic, Milan, the authors followed on the whole the technique used at the State Serum Institute, Copenhagen, with certain slight modifications which are described. They stress the usefulness of reading the result of the test twice, at 18 and at 42 hrs, since they found that at the later time 5 per cent. of previously negative results became positive. They also stress the importance of obtaining an inoculum in the very early stage of acute orchitis of the rabbit, as delay at this stage may allow sensitization of the treponemes to occur. In order to save time, equilibration of the basal medium in an atmosphere of nitrogen and carbon dioxide and the extraction of the rabbit testes were both reduced to 1 hr. without ill effect. A further saving of time was effected by the simultaneous preparation of two tests in parallel, but keeping the antigens strictly separated. (A photograph shows the lay-out of apparatus facilitating this modification.) All sera for the TPI tests were treated with penicillinase, and for purposes of comparison two flocculation reactions and two complement-fixation tests, in both of which cardiolipin and treponemal (Reiter's) antigen were used, were carried out in parallel.

The results are presented in a table and discussed from the clinical point of view. In sera from fifty non-syphilitic subjects the TPI test was negative in 100 per cent. In sera giving a doubtful result with standard tests the TPI test gave a clear-cut result. The authors point out, however, that a doubtful TPI reaction may occur in cases of primary atypical pneumonia, infectious mononucleosis, leprosy, and malaria, and also if the patient is pregnant. In patients with a primary chancre the TPI reaction is often negative, the "immobilisin" not yet having appeared; in this series in only 16 per cent. of cases with a history not exceeding one year since the cure of a primary sore was the reaction positive. The TPI reaction was positive in 61 per cent. of cases of cured congenital syphilis, and in 71 per cent. of cured secondary syphilis of long standing; in the latter group the classic tests gave an intensely positive result in 15 per cent. and a partially positive result in 18 per cent. Again, while 94-9 per cent. of long-standing cases of accidentally discovered and of "cured" cardiovascular neurosyphilis gave a positive TPI test result, the standard tests gave 45 per cent. strongly positive and 45 per cent. weakly positive results.

The authors conclude that the TPI test is the most specific test for syphilis yet available, although it is often negative in cases of primary syphilis and is unnecessary in those giving a strongly positive reaction in the classic serological tests. The main indication for its use therefore lies in the testing of serum giving a weakly positive result in standard tests, especially in cases in which an accurate clinical history is lacking.  

F. Hillman


It has recently been shown that specific agglutination of killed Treponema pallidum is enhanced by the conglutinating action of fresh steer serum. A preliminary evaluation of this simple test indicated that it might be as sensitive as the treponemal immobilization (TPI) test, but subsequent experiments showed that in its present form it detects more than one antibody and is, in part, a measure of reagin.

The authors, working at the University of North Carolina, carried out a number of experiments designed to determine the effect of the following:

(1) absorption with VDRL antigen on the agglutinating titre of syphilitic serum;  
(2) immunizing rabbits with VDRL antigen-antibody precipitate;  
(3) incubation time on agglutinating titres of syphilitic serum and non-syphilitic reagin serum;  
(4) heat on agglutinability of antigen in syphilitic serum and in non-syphilitic reagin serum;  
(5) heat on agglutinability of antigen in undiluted normal human serum.

The technique of each stage of this investigation is described in detail and the results are clearly tabulated. It was found that there are at least two agglutinating antibodies in syphilitic serum—one agglutinated rapidly and was identified as reagin; the other was not identified. The sensitivity of the antigen increased in proportion to the temperature at which it was inactivated.

The problems presented by these results and the preparation of more efficient antigens are to be the subject of further study.  

Douglas J. Campbell


It has been observed that treponemes immobilized in the Nelson-Mayer test show altered morphology. A study of these alterations through electron microscopy is reported in the present paper. Irregular outline of the treponemal body has been observed as well as breakage of the "crista" with resolution in fibrils, plasmolysis, and fragmentation of the protoplasm and finally, almost regularly, the presence of " pseudocysts " generally located at the ends of the treponemal bodies. These data are in agreement with observations by Doepfner, Gregorczyk, and Greifelt.
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It has been shown that these alterations are to be seen in treponemes already immobilized by the specific antibody plus complement. Only the immobilizing antibody is effective in inducing these morphologic changes, which are to be considered as a pre-lytic immune phenomenon, whereas the group anti-treponemal and antilipidic antibodies (so-called reagin), which, as it is known, do not immobilize the Treponema pallidum, are unable to affect its morphology.

Author's summary


A microflocculation reaction for the diagnosis of syphilis which can be carried out with a dried blood-drop has obvious advantages, especially for the testing of large numbers of persons in a mass case-finding campaign, but so far the accuracy of such methods, except in the most expert hands, has been less than that of the standard tests. The authors, working at the Municipal Hospital, Kassel, have elaborated a technique in which a cardiolipin reaction using VDRL antigen is combined with the MKR II test of Meinicke, as modified by Fischer and Torch. Both tests are carried out on a single slide, on which three drops of blood are allowed to dry, two of which are used for the two dilutions of Meinicke antigen and the third for the cardiolipin. [For details of the technique the original should be consulted.] On prolonged storage of the dried blood an initially positive Meinicke reaction gradually becomes negative, whereas the cardiolipin reaction remains unaltered.

A series of 500 sera, including those of 52 known syphilics, was examined, the results of the slide tests on dried blood being compared with those of the Wassermann reaction using human heart and syphilitic liver as antigens, the citochol reaction, and in many cases also the Kahn and VDRL slide tests. Agreement between the results was good, any positive macro-reaction being accompanied by a positive reaction in at least one, but usually in both the dried-blood micro-tests. The cardiolipin test was slightly superior to MKR II test on dried blood. A number of false positive reactions occurred which were attributable to technical errors, in other cases only one of the two slide tests was involved. Technically, the tests are easy to carry out and are recommended for large-scale investigations.

F. Hillman


The authors of this paper from the Provincial Laboratory for Hygiene and Prophylaxis, Genoa, discuss recent developments in the qualitative differentiation of syphilitic antigens in relation to the serological diagnosis of syphilis and point out that the introduction of cardiolipin in place of the empirical lipid antigen has resulted in greater diagnostic accuracy and better therapeutic and prognostic assessment. Moreover, it makes practicable a simple and rapid test, such as the VDRL micro-flocculation test, which is of utmost value for mass surveys.

To determine the practical value of this test it was carried out on 2,806 sera, including a number from known syphilitic subjects, and the results compared with those of the original Kahn and Meinicke reactions and of the cardiolipin complement-fixation test. The findings, which are presented in a Table and discussed in detail, showed the order of sensitivity of the tests to be: VDRL, standard Kahn, cardiolipin complement-fixation, Meinicke. The incidence of non-specific reactions was 0.25 per cent. with the VDRL and Kahn tests, 0.99 per cent. with the complement-fixation test, and 1.73 per cent. with the Meinicke test. F. Hillman


The distribution of antibodies in sera has been studied at the University of Lund, Sweden, by electrophoresis through eight superimposed filter-paper strips. One strip was treated with a protein dye to show the distribution of the protein fractions and the others were cut transversely into segments from which the migrated protein fractions were recovered by centrifugation. Comparison of the antibody titres of the fractions with that of the parent serum showed that recovery was only partial, owing to adsorption to the paper. Preliminary experiments with known antibodies showed that they appeared as homogeneous components. Agglutinins against the antigens of Salmonella typhosa and Salm. typhimurium, streptococci of Groups A and C, and the heterophil antibody of infectious mononucleosis migrated with the \( \gamma \) globulins, antibodies against the O antigens of Salm. typhosa and Salm. typhimurium were associated with \( \beta_2 \) globulins, while human erythrocyte isoagglutinins were recovered from the region between the \( \gamma \) and the \( \beta_2 \) globulins.

\( \gamma \)-Globulin fractions obtained from normal Wassermann-negative human sera by electrophoresis and by salt-ethanol precipitation were found to give positive Wassermann and Kahn reactions. The Kahn reactions were inhibited by Neurath's eglobulin inhibitor (thought to be a lipoprotein associated with the \( \alpha \) globulins), suggesting that the reactions given by the normally occurring \( \gamma \) globulins were of the biological false positive type. Because both lipid (from the Kahn antigen) and protein (from the \( \gamma \) globulins) could be demonstrated in the floccules, the reactions were thought to be of the antigen-antibody type and not a non-specific flocculation due to lack of protective colloids.

Sera from 31 patients with syphilis at various stages were fractionated. [It is not stated whether any of the patients had been treated.] In primary syphilis (five cases) Wassermann reactivity was associated with the \( \gamma \) globulins, while in secondary syphilis (four cases) it
occurred in both the \( \gamma \) and \( \beta_2 \)-globulin regions, suggesting the presence of two separate reagins. This pattern was also found in fourteen out of 22 sera from patients with late syphilis, but in the other eight cases reactivity was restricted to the \( \beta_2 \) globulins. It is thought that different reagins may occur at different stages of the disease. Similar patterns were found in sera which were thought to have given non-specific reactions in the serological tests for syphilis (STS) owing to the absence of clinical evidence of syphilis and the discordant results given by a battery of STS. Out of eighteen such sera, ten showed reactivity only in those fractions migrating with the \( \gamma \) globulins, four in the \( \beta_2 \)-globulin fraction only, and four in both the \( \gamma \) and the \( \beta_2 \)-globulin fractions. No definite differences were established between the electrophoretic mobility of the reagins in syphilitic sera and in sera thought to give non-specific STS reactions.

As a possible explanation of the occurrence of non-specific STS reactions it is suggested that in such cases there is a disturbance of the balance between the reagin which is present in the \( \gamma \)-globulin fraction and the inhibitor which is normally present and prevents the flocculation of lipid antigens. A. E. Wilkinson


The authors report, from the Institute of Hygiene and Microbiology, University of Turin, the comparable results obtained with various sero-reactions for syphilis which were carried out on 8,500 samples of serum, the main object being to assess the value of the microfloculation reaction of Pagniez. The very simple technique of this test and the method of preparation of the antigen are briefly outlined. It was found to give results which agreed well with those of the classic Wassermann reaction, especially for reactions graded as 3+ or 4+, but it tended to give a higher number of positive reactions in Grades 1+ and 2+.

In addition to the above tests the Kahn and the citochol reactions were also performed on 2,500 of these sera and the results subjected to statistical analysis. Assessing the qualitative result only, that is, positivity or negativity, and taking the Wassermann reaction as a standard, an index of resemblance ("index Gini") was worked out. By this index the Pagniez reaction was shown to be the most reliable, followed by the Kahn, and lastly by the citochol reaction, but the differences between the three tests were only very small. If only the degree of positivity was taken into account and the index of linear correlation calculated by the method of Bravais, then the order became citochol, Pagniez, and Kahn, again with a very narrow margin between them. The authors conclude that the Pagniez reaction compares well with the other reactions mentioned and that it is easy and quick to perform. F. Hillman


In an attempt to determine whether a relationship exists between the reagins demonstrated by syphilitic serological reactions and the so-called erythrocyte autoantibodies (EAA) the authors examined, at the State Serum Institute, Copenhagen, 292 blood samples giving positive serum reactions for syphilis, 140 samples exhibiting false-positive serum reactions for syphilis, and 159 samples with negative reactions. Patients with positive EAA reactions which were not due to Rh incompatibility (116 in number) were examined at the city Central Register of Syphilitic Patients, as were 102 patients whose blood samples showed negative results for EAA. The examinations for EAA were carried out (1) by the Coombs antiglobulin reaction, in which erythrocytes affected by antibodies agglutinate in rabbit immune serum containing anti-human gamma globulin while normal erythrocytes do not agglutinate; (2) by suspension of the erythrocytes in "macrodex", a very agglutinogenic medium which may sometimes cause erythrocytes affected by antibodies to agglutinate while normal erythrocytes do not.

The results showed that 4-4 per cent. of all samples giving a positive serum reaction for syphilis, regardless of aetiology, also gave a positive reaction for EAA. Of the 116 EAA-positive patients, 11-2 per cent. had a positive serum reaction for syphilis as against only 2-0 per cent. of the EAA-negative patients. The authors conclude that "the simultaneous presence of syphilitic reagins and erythrocyte auto-antibodies is more frequent than can be explained by coincidence". R. R. Wilcox


The author has compared the sensitivity of the cardiolipin microfloculation test (CMT) with that of the Wassermann, Meinicke II, citochol, Sachs-Georgi, and Kolmer cardiolipin complement-fixation tests in the examination of 330 samples of serum, mostly from treated syphilitic patients (but also some non-syphilitic) at the Max Planck Institute, Munich. In 94.2 per cent. the CMT result was positive (including 16.3 per cent. doubtfully positive) and in 5.8 per cent. negative. Positive results with the other tests, in the order given above, were obtained in 38.5 per cent., 82.4 per cent., 85.5 per cent., and 26.4 per cent. respectively. The author concludes, therefore, that the CMT is much more sensitive than any of the other serological tests employed, but that the number of doubtful reactions was also significantly higher. Because of the lack of clinical material a comparison of the test with the classic reactions in early infective syphilis was not possible.

The specificity of the test was studied by examining 41 sera from patients who were clinically non-syphilitic and also 3,000 sera obtained from the immigration authorities, although no clinical details were available for these patients. In the latter group 1-3 per cent. of non-specific reactions were obtained, this being attributed in many cases to recent vaccination or inoculation.
Brief details of the technique of the cardiolipin micro-flocculation test are given [which differ in no significant way from those of the well-known VDRL test].

This paper, like so many published in Europe recently, suffers from an almost complete lack of clinical data. The publication of the results of a large number of serological tests entirely divorced from clinical findings is a relatively worthless endevour and contributes very little that is new to the increasingly complicated subject of serology.

R. D. Catterall

Reproducibility of Results in the Nelson Test. (Beitrag zur Beständigkeit der Ergebnisse vom Nelson-Test.)

In order to determine to what extent the results of the treponemal immobilization test varied when performed on different days, and therefore with different batches of treponemal suspension, one strongly positive serum and one negative serum were tested at the University Institute of Hygiene, Kiel, on twenty separate occasions. The sera were kept at −20°C.

It was found that the positive serum gave similar results in routine complement-fixation and flocculation tests at the beginning of the investigation and again some 9 months later, thus demonstrating that no noteworthy decline had taken place. The degree of immobilization varied little during the 9 months, the mean value for the twenty tests being 95.2 per cent., the lowest reading showing 82.6 per cent. of immobilization. These results compare favourably with those of the best available flocculation tests. As the authors point out, however, small as the variations were, they might be sufficient to change a positive result into a negative one if the serum being tested was initially only weakly positive. It is suggested, therefore, that in testing a weakly positive serum only half the number of treponemes should be used, as in these cases the immobilizing power of the serum may prove insufficient to deal with the larger number of organisms.

G. W. Csonka

Syphilitic Reagin. A Physico-chemical Investigation.

Evidence suggesting that the reagin principle of syphilitic sera may be complex has been obtained at the Veterans Administration Hospital, Oteen, North Carolina. In order to concentrate the serum, strips of dry gelatin were placed in the sera to be tested, when water and other substances capable of diffusion entered the gelatin until equilibrium was reached. Tests carried out before and after such treatment on 130 sera giving “strong” or “moderately strong” reactions [data on only 26 sera are presented] showed that with the exception of three sera no significant change in titre occurred with the quantitative Kolmer and Eagle complement-fixation tests, despite a two- to six-fold concentration of the serum. In contrast, quantitative Kahn and Kline tests showed a rise in titre proportional to the diminution in volume of the serum. In twenty samples of low-titred sera (less than four Kahn units) no significant change in titre occurred with either type of test. It was therefore suspected that two reagin principles were concerned, one of which was diffusible into gelatin.

A separation of the two reagins was effected by repeated treatment of the sera with gelatin and reconstitution to the original volume with saline solution. After this treatment, the complement-fixation reactions became progressively weaker, while the flocculation-test titres persisted. It was not found possible, however, to elute the reagin from the gelatin.

It is suggested that the reagin detected by the flocculation tests is a large molecule which cannot diffuse into gelatin, whereas that responsible for the complement-fixation tests, for which the name “co-reagin” is suggested, has a smaller molecular size which enables it to diffuse into the gelatin.

A. E. Wilkinson


Review of the Nelson-Mayer Test in 528 Cases. (Considerazioni su 528 test di Nelson-Mayer.)

Cardiolipin Antigen. VIII. Course of and Mutual Relations between Various Seroreactions in Syphilis-Infected Rabbits. [In English].

Comparative Study of Rein-Bossak Test with Kahn, Kolmer, and VDRL Tests.


Prophylactic Vaccination and Biological False Positive Reactions in the Serological Diagnosis of Syphilis. (Vaccinazioni profilattiche e false reazioni biologiche positive nella diagnosi sierologica della lues.)


Experience with Cardiolipin in the Diseases of Children, with Special Reference to Congenital Syphilis. (Ueber die Erfahrungen mit Cardiolipin bei Krankheiten des Kindesalters unter besonderer Berucksichtigung der Lues congenitalis.)
Gonorrhea


**SYPHILIS** (Pathology)

**Histopathological Studies of Pinta, Yaws, and Syphilis.** (Studien über die Histopathologie von Pinta, Framböse und Syphilis.) Hasselmann, C. M. (1955). *Arch. klin. exp. Derm.,* 201, 1. 8 figs, 21 refs.

Comparison of the pathological changes associated with the three treponematoses, pinta, yaws (framboesia), and syphilis, shows important differences between them. Thus in the primary lesion of pinta no proliferation of the intima or media of the small vessels occurs such as is seen in syphilis. In the later stages of pinta and yaws the vessels are still unaffected or show only minimal swelling of the endothelium. Another fundamental difference exists between pinta and yaws on the one hand and syphilis on the other in that the "primary" lesion in the former is both clinically and histologically identical with the subsequent generalized lesions. The lesions of pinta show no superficial erosions, unlike those of yaws and syphilis, and do not become necrotic, as is often the case in syphilis and rather less commonly in yaws.

G. W. Csonka


The authors made angiographic studies of four syphilitic patients with ophthalmoplegia. In three of these vascular lesions were clearly shown, and the authors conclude that haemorrhagic leakage as in intracranial aneurysms may well be the cause of transitory syphilitic ophthalmoplegia.

M. H. T. Yuille

**SYPHILIS** (Experimental)


**GONORRHOEA**


A simple screening procedure for the detection of gonorrhea, suitable for case-finding among patients not attending venereal disease clinics, is described in this paper from the District of Columbia Department of Public Health, Washington. The patients' urine is collected in a bottle, acidified, and examined for macroscopic pus orthreads, the presence of either being considered presumptive evidence of gonorrhea. The specimen is then allowed to stand for at least an hour, decanted, and films of the sediment examined for intra-cellular Gram-negative diplococci.

Among 68 specimens from male patients attending a venereal disease clinic with gonococcal discharges, 55 (80-9 per cent.) were found positive on macroscopical examination, 52 of which were also found positive on microscopical examination. Of 32 specimens from patients attending the clinic without urethral discharges, three were found positive on microscopical examination, of which two had been found positive on macroscopical examination. Among 120 specimens from male and 177 from female out-patients attending the District of Columbia General Hospital for non-venereal diseases, sixteen (13-3 per cent.) of the former and twelve (6-8 per cent.) of the latter were found positive on both macro- and microscopical examination, while two others from male patients were found positive on microscopical examination only. In all these thirty patients the diagnosis of gonorrhea was subsequently confirmed. In addition, sixteen specimens (5-4 per cent. of the total) were found positive on macroscopical examination, but the diagnosis was not confirmed on microscopical examination. The finding of an incidence of gonorrhea of 15 per cent. among males and 6-8 per cent. among females who were not seeking advice at a venereal disease clinic suggests that this method of case-finding may be of some value in areas of high prevalence.

[It should be noted that this test gave a negative result in 19 per cent. of cases of gonorrhoea with urethral discharge. Routine examination of the urine of the out-patients should have resulted in the detection of pus, if present, and should therefore ultimately have led to the diagnosis of gonorrhoea in any event in the cases discovered.] P. J. L. Sequeira


In 405 patients of both sexes, of whom 252 had acute or chronic gonorrhoea (in some cases with complications) and 153 had non-specific infections of the genital tract, liver function tests were performed before the beginning of treatment; in the patients with gonorrhoea the tests were repeated after completion of treatment, but not in the other cases. The eight liver function tests employed were all flocculation reactions; in addition the serum bilirubin content and the erythrocyte sedimentation rate were determined and the urine examined for bile pigments.

In 77 out of the 252 patients with gonococcal infections no evidence of liver dysfunction was found. In the
remaining 175 (69·4 per cent.) an abnormal result was obtained in one or more of the battery of tests. After treatment, which was usually with penicillin alone, 172 of the patients (68·2 per cent.) still showed some abnormal liver function in one or more of the tests; the tests were performed in most cases 8 to 10 days after treatment. In 7·6 per cent. of the patients the results of more than four tests were abnormal before treatment, and after treatment the proportion was 8·7 per cent.

In the group of patients with non-specific genital infections the results of one or more tests were abnormal in 75·8 per cent., and those of more than four tests in 12·4 per cent., all the tests being performed before treatment was given. In a small number of patients the electrophoretic pattern of the plasma proteins was investigated (but unfortunately no details of the technique used are given). The author states that this is only a preliminary communication.

[The generally acknowledged difficulty in interpreting liver function tests, especially in the absence of definite clinical indications, and the non-specific nature of serum flocculation tests, together with the lack of detail as to the techniques used in this work, make it very difficult to evaluate this paper.]  
R. D. Catterall


The author used penicillin prophylaxis in 2,150 newborn babies and found no specific gonorrhoea although gonorrhoea was present in the histories of 29 cases and acute gonorrhoea in one case. Non-specific irritations were found in 7 to 11 per cent. of the children. Penicillin is therefore recommended for prophylaxis.

W. Leydhecker


More recent literature on the subject is summarized, and the author again holds that prophylaxis with penicillin is superior to Credé's silver nitrate. Cases of late conjunctivitis are rarer after penicillin.

W. Leydhecker


Gonococcal antigen for use in complement-fixation tests is prepared at Ulve Hospital, Oslo, by growing three strains of gonococci on 30 per cent. ascitic-fluidagar with 1 per cent. glucose and 0-1 per cent. cystine (or cystine hydrochloride). The growth is harvested after 24 hrs. incubation, washed, and dried in vacuo over calcium chloride in volumes of 0·1 to 0·3 ml. Samples are titrated for their anticomplementary and antigenic activity and for non-specific complement fixation with negative sera. If an antigen so prepared is strongly anticomplementary it can be made suitable for use by treatment with alcohol. The contents of one ampoule of the dried preparation are re-suspended in 0·1 ml. distilled water, 3 ml of 96 per cent. ethanol added, and the mixture incubated at 37° C. for 48 hrs, being shaken daily. After adding 6 ml. distilled water the mixture is heated at 56° C. for 30 min. and centrifuged at 2,000 r.p.m. for 30 min. The deposit is discarded and the supernatant used as antigen. It can be stored at 4° C. and is sufficiently sensitive to be used at a dilution of 1 : 3 or 1 : 4 in saline.

Of 10,540 sera which were tested with an antigen prepared in this way from one which was originally strongly anticomplementary, 166 gave positive reactions. In seventy of these cases the patient had clinical evidence of gonorrhoea and in 86 gonorrhoea was suspected. In the remaining ten cases the results were thought to be non-specific, there being no history or clinical evidence of gonococcal infection.

A. E. Wilkinson

Paper Chromatographic Investigations of Two Gonococcal Antigen Preparations, the One Alcohol-containing, the Other Aqueous. [In English]. CLAUSEN, O. G. (1955). *Acta path. microbiol. scand.*, 37, 18. 2 refs.

This article from the University Pharmaceutical Institute, Oslo, is published as an addendum to the previous paper (37, 14) and describes the results of examination of the anticomplementary suspension of dried gonococci and of the alcoholic extract of the suspension by paper chromatography.

No polysaccharides, simple sugars, or phosphatides could be detected in either antigen, but three nitrogenous substances, which might be lower proteins or amino-acids, were present in both of the extracts. Two of these, of which one was probably cystine hydrochloride (a constituent of the medium on which the gonococci were grown), were present in considerably greater concentration in the aqueous (anticomplementary) suspension than in the alcoholic extract. The concentration of the other substance appeared to be greater in the alcoholic antigen.

A. E. Wilkinson


An historical review of the efforts to control gonococcal eye infections in infants is given, and both medical and public health measures are discussed. The position of ophthalmia neonatorum in the United States is summarized.

J. R. Hudson


Prophylaxis with silver nitrate is recommended for the newborn infants instead of penicillin which had been proposed by other authors, since antibiotics should be reserved for serious cases when they are really needed. A more general use would increase the number of resistant strains.

W. Leydhecker

Comparative Study of the Effect of Penicillin-Sulphonamide Mixtures given by Mouth in Gonorrhoea. (Vergleichende Untersuchungen über die Wirkung peroral verabrechter Penicillin-Sulphonamid-Gemische...

The clinical features of an illustrative case are described, and the aetiology, differential diagnosis, and treatment are discussed.

Three cardinal points stand out in the diagnosis:
(1) the abrupt onset of urethritis, arthritis, and conjunctivitis;
(2) the repeatedly negative smears and cultures for gonococci and other pathogenic organisms;
(3) the usually self-limiting course.

Treatment, in the absence of any definite aetiology, is empirical, and includes antibiotics, ACTH, and cortisone.

J. R. Hudson


CHEMOTHERAPY


PUBLIC HEALTH AND SOCIAL ASPECTS


MISCELLANEOUS