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, Biological False Positive Phenomenon, Pathology, Experimental).
- Gonorrhea.
- Non-Gonococcal Urethritis and Allied Conditions.
- Reiter's Disease and Allied Conditions.
- Antibiotics and 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)


A rare case of the association of parenchymatous keratitis, diffuse choroiditis, and choroido-retinitis in a case of syphilis is described. The clinical manifestations and therapy are discussed and Jensen's work and Sezary's theory considered. It is concluded that this case can be classified as belonging to the choroido-retinitis of Jensen. M. G. Bucci


SYPHILIS (Therapy)


SYPHILIS (Serology)


In the fluorescent-antibody-absorption (FTA-ABS) test (Hunter et al., *Publ. Hlth Rep. (Wash.*) 49, 410; *Abstr. Wild Med.*, 1964, 36, 325) group antibody, reactive with other treponemes besides Treponema pallidum, is removed from sera by absorption with a standardized...
extract of cultured Reiter treponemes. The sera are then tested at a dilution of 1 in 5 instead of 1 in 200 as in the standard FTA-200 test. This paper from the Communicable Diseases Center of the US Public Health Service, Atlanta, Georgia, reports an evaluation of the test based on the examination of 2,252 sera, including 698 from treated patients, at five laboratories, at all of which the FTA-ABS test was carried out and at four the VDRL test. The control laboratory, which supplied the participants with control sera and reagents, carried out the TPI test in addition. When there was disagreement between the results of the FTA-ABS and TPI tests both were repeated. For evaluation purposes the TPI test was taken as the standard when there was no clinical evidence of syphilis. The overall results are summarized in the Table.

<table>
<thead>
<tr>
<th>Diagnostic Category</th>
<th>Cases (treated)</th>
<th>Percentage of Positive Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>VDRL</td>
</tr>
<tr>
<td>Primary syphilis</td>
<td>191 (88)</td>
<td>77-5</td>
</tr>
<tr>
<td>Secondary syphilis</td>
<td>270 (149)</td>
<td>96-7</td>
</tr>
<tr>
<td>Latent or unspecified</td>
<td>954 (367)</td>
<td>74-0</td>
</tr>
<tr>
<td>Latent syphilis (CV, CNS, or con-</td>
<td>117 (87)</td>
<td>76-9</td>
</tr>
<tr>
<td>certal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BFP or other diseases</td>
<td>334 (6)</td>
<td>55-7</td>
</tr>
<tr>
<td>Presumed normal</td>
<td>384 (1)</td>
<td>0</td>
</tr>
</tbody>
</table>

The FTA-ABS test showed the highest reactivity of any of the three tests at all stages of syphilis and was positive in sixteen out of 25 cases of sero-negative primary syphilis. Three sera from presumed normal individuals gave positive FTA-ABS tests at one laboratory but were found negative when retested at the control laboratory. Sera from 52 untreated patients classed as biological false positive (BFP) reactors on the basis of negative TPI tests gave positive FTA-ABS tests; 89 per cent. of the patients were over 40 years of age and in 72 per cent. no condition was found which might have caused a BFP reaction.

Because of the greater sensitivity of the FTA-ABS test in known syphils and because the Tuskegee study (Rockwell et al., Arch. intern. Med., 1964, 114, 792; Abstr. Wild Med., 1965, 37, 321) has shown that 18 per cent. of patients with known syphilis of more than 30 years' duration may have negative TPI tests, the authors do not think that the positive FTA-ABS results in these 52 cases are necessarily all non-specific. They believe that the TPI and FTA-ABS tests detect the same or very similar treponemal antibodies. They emphasize [very rightly] that the FTA-ABS test is not a substitute for clinical judgement and should not be used as a routine procedure; it should be reserved for problem cases in which, in their opinion, it can usually make recourse to the TPI test unnecessary.

[This is an important paper and should be read by all those interested in the serological diagnosis of syphilis.]

A. E. Wilkinson


In this paper from the University of Tokyo, Japan, the authors report that guinea-pig serum conjugated with fluorescein thiocyanate shows complement activity. They carried out an experiment to see whether fluorescent complement was fixed by the reaction between Treponema pallidum and known syphilitic serum. The reaction was performed on slides, with appropriate controls, a 1:100 dilution of fluorescent serum being used as the source of fluorescent complement; this dilution was chosen as giving reasonably strong reactions but not false positive results. In general this technique and the conventional fluorescent treponemal antibody technique gave results in good mutual agreement, but in one case of syphilis the serum gave positive results with the fluorescent treponemal antibody test but negative results with the treponemal fluorescent complement-fixation test; it is suggested that in this case the antibody did not fix complement. The authors conclude that tests for the fixation of fluorescent complement may be useful in the detection of a number of antigen-antibody reactions.

J. Hamilton-Miller


Fluorescent treponemal antibody (FTA) tests using Treponema pallidum as antigen were performed on sera from twelve patients before and after absorption with five strains of cultivable treponemes (Reiter, Kazan-5, Budapest-4, T. refringens, and T. phagadensis). These sera had FTA titres ranging from 50 to 400 before absorption, and the patients were thought not to have syphilis although two of them had penile sores and reactive lipoidal antigen tests. Absorption with Reiter treponemes abolished reactivity in four sera, and with T. refringens in these and two others. Antiserum to the cultivable treponemes listed above and to Kazan-2 and T. minutum were tested against T. pallidum before and after absorption with Kazan-5, Reiter, T. refringens, and T. minutum. Kazan-5 and Reiter removed reactivity of all the antiserum except that against T. refringens. T. minutum abolished reactivity with the homologous antiserum and with that against T. phagadensis, and reduced the titres of the antiserum against the other treponemes. T. refringens reduced, but did not abolish, the titres of all the antiserum and the homologous antiserum was still positive after absorption with this organism. Sera from fourteen patients with early syphilis showed a decrease in titre against T. pallidum after absorption with Reiter treponemes; after a further absorption with T. refringens, reactivity was abolished in all but three.

These studies are thought to provide evidence for the existence of three antigens shared by T. pallidum and the other species studied, one shared by all the species examined, and others present in T. refringens and the Reiter treponeme respectively. The bulk of the antibody detected by the FTA test in early syphilis appears to be group-specific rather than specific for T. pallidum.

The Reiter, English Reiter, Noguchi, Nichols, and Kazan-2 strains of cultivable treponemes and three strains of *Treponema microdentium* (FM, N-39, and MRB) were grown in NIH thiglycollate broth with 10 per cent. inactivated rabbit serum and adjusted to a density of 15–17 x 10^8 organisms per ml. These suspensions were incubated with normal and human syphilitic sera and guinea-pig serum as a source of complement as in the TPI test. Immobilization was essentially complete after 1 hour and after 5 to 6 hours some strains were lysed. No significant immobilization of any strain was produced by non-syphilitic sera; the Nichols, Noguchi, Kazan-2, and English Reiter strains were immobilized in varying degrees by all the syphilitic sera, while the strains of *T. microdentium* and the Reiter organism were less affected, especially by sera from patients with primary syphilis. The immobilization by serum from a patient with secondary syphilis against any strain could be removed by absorption with the treponemes concerned. Absorption with Noguchi treponemes removed activity of this serum against all reactive strains, including virulent *T. pallidum*. Absorption of an antiserum prepared against the Noguchi strain with *T. pallidum* failed to remove anti-Noguchi activity. Some evidence was found that human syphilitic serum could block the immobilizing activity of the Noguchi antiserum against the homologous organism. A. E. Wilkinson

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The cultivable treponemes studied were: Reiter, English Reiter, Kazan, Kazan-2, 4, 5, and 8, Nichols, Noguchi, three strains of treponemes from the mouth (MRB, FM, and N. 39), a treponeme isolated from mud (*T. zuehlzerae*), and the N-9 strain of *Borrelia vincentii*. Antisera against the individual strains were prepared in rabbits, conjugated with fluorescein isothiocyanate, and used in direct FA tests against the various strains. Marked cross-reactivity was found, confirming the presence of an antigen common to all the strains of treponemes studied, and to *T. pallidum*. Absorption of the conjugates with either Reiter treponemes or *B. vincentii* enabled the strains to be classed in five sero-groups:

1. Reiter, English Reiter, and the six Kazan strains. There appears to be a slight serological difference between the Reiter and Kazan strains.
2. Cultivable Nichols and Noguchi strains.
3. The three oral treponemes, MRB and FM contained an antigen absent from N. 39 and this last has an antigen not found in the other two.
4. *B. vincentii*.
5. *T. zuehlzerae*. A. E. Wilkinson

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The results of tests on 689 sera with the TPI, FTA-200, Reiter protein complement-fixation, cardiolipin WR, and VDRL slide tests are presented. There was overall agreement between the TPI and FTA-200 tests on 607 (88.1 per cent.) of the sera. The FTA-200 was positive but the TPI negative in 54 sera; six of these were from patients with primary syphilis and fourteen from patients with a history suggestive of early syphilis, and five were thought to be non-specific reactions; no information was available about the other 29 patients.

28 sera gave positive TPI but negative FTA-200 tests; thirteen of these came from patients with a history of syphilis, the other fifteen had all given reactive screening tests and it is assumed that the patients concerned had late syphilis.

Taking the TPI results as a standard, the FTA-200 test was more sensitive than either the Reiter protein complement-fixation test or the tests for reagin antibody, but gave more positive results which were not corroborated by the TPI test than either the Reiter protein or reagin tests. It is concluded that the FTA-200 test does not replace the TPI test for the serological diagnosis of syphilis.

A. E. Wilkinson

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Four cases of ocular or neurosyphilis are described in which the VDRL test was weakly reactive but the TPI test negative, casting doubt on the specificity of the results of the former test. In all four cases the absorbed fluorescent treponemal antibody (FTA-ABS) test was positive:

1. A 54-year-old man with pupillary inequality and ptosis, who gave a history of partly treated primary syphilis as a young man.
2. A woman aged 65 with stigmata of congenital syphilis.
3. A man aged 70 with glaucoma and primary optic atrophy.
4. A woman aged 69 with Argyll Robertson pupils. The FTA-ABS test has been claimed to be as specific and more sensitive than the TPI test which is well known to give negative results in a minority of cases of late syphilis of long standing. The comment that "a careful history and physical examination can be more important
ABSTRACTS

SY philis (Pathology)


Four case reports are presented of patients with clinical signs suggestive of ocular or neurosyphilis and negative serum tests for reagin but in whom treponemes were found by dark-field microscopy or by staining with antibody to Treponema pallidum labelled with fluorescein.

(1) A boy aged 5 with choroido-retinitis. The FTA-ABS test on the serum was weakly positive; the cerebrospinal fluid was normal but treponemes were demonstrated in it by the fluorescence method. The boy’s mother also had a weakly positive FTA-ABS test.

(2) A 23-year-old woman with uveitis and neuroretinitis. The TPI test was negative on her serum but the FTA-ABS test was weakly reactive on one occasion. Treponemes were shown in the aqueous fluid by fluorescent staining.

(3) A woman aged 50 who had been treated for asymptomatic neurosyphilis 26 years previously. She had fundus changes suggestive of retinitis pigmentosa and the FTA-ABS test was positive. Although the cerebrospinal fluid was normal, motile treponemes were found in it and were stained by the fluorescence technique.

(4) A man aged 74 with clinical evidence of tubas with pupillary changes and with an enlarged liver and spleen. TPI, FTA-ABS, and VDRL tests were all negative on the serum. The cerebrospinal fluid gave a negative VDRL test and a normal cell count, but the protein was raised and there was a mid-zone Lange curve. Motile treponemes were found in the aqueous and were also demonstrated by fluorescence staining of cryostat sections of tissue obtained by liver biopsy.

[The excellent photographs illustrating this paper fully document these important findings. It would be of interest to know how many similar patients had been investigated by these methods with negative results. It may also be relevant that the second and fourth patients had been given steroids.] A. E. Wilkinson

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Electron microscopic studies of intact organisms and of ultrathin sections of several strains of cultivable treponemes, and virulent strains of Treponema pallidum including organisms from human syphilitic lesions, are reported. Treponemes have a two-layered outer wall within which lies the cytoplasm bounded by a cytoplasmic membrane. Roudened structures, possibly nucleoid bodies or mesosomes, and ribosomes were seen in the cytoplasm. Bundles of fibrils were observed between the cytoplasmic membrane and the outer wall; they appeared to be inserted into raised basal granules in the cytoplasm of the expanded free end of the treponeme. No flagella were seen; previous reports of these are thought to have been due to misinterpretation of artefacts produced by rupture.

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The classical TPI test is performed by incubating the reagents under strictly anaerobic conditions for 18 hr at 35°C. This period can be shortened by adding lysozyme or by increasing the amount of guinea-pig serum used as a source of complement which itself contains lysozyme. In the method described, the volumes of reagents are increased to: treponeme suspension 2 ml, patient’s serum 2 ml, complement 1 ml. This gives a long column of fluid in the tubes which are incubated at 35°C. for 4 hours. The results of TPI tests by this technique on 524 sera from patients with syphilis or other conditions are compared with those of a battery of tests using lipoidal antigens. The shortened test, using a volume of 5 ml., was also compared with the same method using a total volume of 2 ml. of reagents in the same proportions and with the classical TPI test. There was complete agreement except for one serum which gave positive results with both shortened methods but a negative result with the standard TPI test; syphilis could not be excluded with certainty in this patient.

[From the Tables there seem to have been an unusually high proportion of “uncertain” TPI results by all three methods.] A. E. Wilkinson

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in the detection of late ocular and neurosyphilis than any laboratory test is a timely one. A. E. Wilkinson

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https://sti.bmj.com/ Br J Vener Dis: first published as 10.1136/sti.43.3.220 on 1 September 1967. Downloaded from http://sti.bmj.com/ on September 2, 2023 by guest. Protected by
of the fibrillar bundles. In sections T. pallidum does not always appear as a solid cylinder but often as a series of segments separated by narrow regions through which the fibrillar bundles pass. Cysts and cyst-like structures were seen, particularly in older cultures; the possible significance of these as survival forms is discussed.

[The paper is illustrated by some very clear electron micrographs.]
A. E. Wilkinson
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**SYPHILIS** (Experimental)


Rabbits inoculated subcutaneously with the Nichols strain of Treponema pallidum within 48 hours of birth developed a running syndrome, showing slowing of growth at 4 to 6 weeks and the development of lesions containing T. pallidum in the peri-orbital tissue and nose. Most died at 7 to 13 weeks of age with progressive runting. If treated with penicillin at 3 to 4 weeks of age, they grew normally, as did animals infected when more than 2 weeks old.

Ten rabbits infected at birth were treated with 25,000 to 50,000 units of penicillin daily over 3 to 6 days between the 3rd and 8th week of life. Four animals showing more than 27 per cent. growth retardation compared with uninfected controls all died, whereas four of six animals with less than this amount of retardation recovered. Animals developing reagin antibodies appeared to have a worse prognosis than when these were absent at the 63rd day.

The spleen of rabbits dying of runting within 116 days of birth showed atrophy of the Malpighian corpuscles with depletion of lymphocytes and predominance of histiocyte-like cells in the red and white pulp. The thymus showed depletion of cortical lymphocytes and many histiocyte-like cells. Treponemes were not seen in these organs. Possible explanations of the running process are discussed and it is suggested that T. pallidum may interfere with the "peripheralization" of lymphoid development in the rabbit or that an autoimmune process may be involved.

A. E. Wilkinson

**Induction of Anti-Treponema pallidum Antibodies in Normal Rabbits by RNA-immuno-carrier extracted from Serum of Syphilitic Rabbits.** MICHELAZZI et al. (1967). Experientia (Basel), 23, 207.

**GONORRHOEA**


Four media were compared: Difco chocolate medium enriched with Bacto supplement B (a yeast extract) with polymyxin B (25 units/ml) and rifistocetin (10 μg/ml), or with vancomycin (3 units/ml), sodium colistimethate (7.5 μg/ml), and nystatin (12.5 μg/ml), and BBL chocolate agar enriched with a chemically defined supplement (IsoViteX, BBL) alone and with the addition of the vancomycin-Colistimethate-nystatin combination of antibiotics to suppress the growth of contaminants.

Specimens of urethral pus were obtained on swabs from 94 males and of vaginal secretions from 102 females, 47 of whom were contacts of males with gonorrhea. The specimens were suspended in trypticase soya broth and 0·1 ml amounts were plated out on each of the four media. When read after 16 to 24 hours the results were scored both for the density of growth of gonococci and for that of contaminating organisms. The best results were obtained with the BBL chocolate medium with IsoViteX supplement and added antibiotics, both with regard to the numbers of gonococcal colonies and the sparsity of contaminants. Gonococci were isolated on this medium from 91 of the 94 males and from 57 of the 102 females; 75 per cent. of the female contacts of males with gonorrhoea gave positive cultures.

[The supplement contains Vitamin B-12, 1-glutamine, adenine, guanine, p-aminobenzoic acid, 1-cystine, glucose, diprophosphopyridine nucleotide, co-carboxylase, ferric nitrate, thiamine hydrochloride and cysteine. The concentrations of these are not given.]
A. E. Wilkinson

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Indirect fluorescent antibody (IFA), agglutination tests, and tests for bactericidal activity against Neisseria gonorrhoeae were performed on 19S and 7S globulins isolated from normal human serum by filtration through Sephadex G-200. Fluorescein-labelled antisera specific for human IgG and IgM were used in the IFA test. Purified 19S fractions of human sera showed activity against N. gonorrhoeae by all three methods, but 7S globulins, although active to a high titre in the IFA test using anti-IgG conjugate, had no agglutinating or bactericidal effect. Cord serum, which is deficient in IgM globulins, had no agglutinating or bactericidal action and the IFA test was negative with the anti-IgM conjugate but positive with that against IgG. Using a fluorescent antiserum against human complement (C3), it was shown that C3 was fixed to gonococci by both 7S and 19S fractions of human serum.

Prozones were seen in IFA tests with anti-IgM conjugates, especially when sera had a high IgG reactivity. This was shown to be due to competitive inhibition of the 19S by 7S antibody; this last was found to reduce the bactericidal effect of 19S antibody; no inhibition was found in the agglutination test. The
unequal capacity of different immunoglobulins to produce reactions and possible interactions between antibodies must be taken into account in interpreting the results of immunological tests.  

A. E. Wilkinson

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To see whether the urethral secretions in gonococcal and non-gonococcal urethritis differ from each other cytologically, the authors, at Karolinska Sjukhuset, Stockholm, carried out differential cell counts on stained smears of urethral discharge from 29 consecutive male patients aged 20 to 30 years with urethritis. Subsequent bacteriological examination showed the diagnosis to be gonorrhoea in fifteen cases and non-gonococcal urethritis in fourteen.

Neutrophil leucocytes predominated in the smears from both groups and no clear difference was found between them except for a tendency for lymphocytes to be more abundant in cases of non-gonococcal urethritis; however, the series was too small to permit statistical analysis of this difference. There was no difference in the number of epithelial cells seen. Indeed, in both groups “the exfoliative cytological specimens were found to have an inflammatory, infectious character, that is, preponderantly granulocytic”.  

G. W. Csonka


A review of the literature. It is suggested that 1 per cent. silver nitrate be continued as a prophylactic against gonorrhoeal ophthalmia neonatorum.  

P. Henkind


NON-GONOCOCCAL URETHRITIS AND ALLIED CONDITIONS


REITER’S DISEASE AND ALLIED CONDITIONS


ANTIBIOTICS AND CHEMOTHERAPY


Cephalothin, a semisynthetic derivative of cephalosporanic acid, has been used as an alternative antibiotic in patients allergic to penicillin. Although cephalothin lacks the 6-aminopenicillanic acid structure of penicillin G, it has other structural resemblances to penicillin, and guinea-pig studies have suggested that cross-sensitivity between cephalothin and penicillin may occur. At the Johns Hopkins University School of Medicine, Baltimore, the authors have sought evidence for such cross-sensitization in human beings. Seven out of 54 patients receiving cephalothin were found to be allergic to it, and 51 of the patients (including four of the seven allergic patients) were thereupon studied intensively.

Among the cases of sensitivity, there were two of anaphylaxis, two of urticaria, and three of maculopapular rashes; all appeared within 30 seconds to 7 days of the start of treatment. A history of penicillin allergy was obtained from eleven of the group of 51 patients and five of the seven allergic to cephalothin. Six of the eleven patients allergic to penicillin had positive skin reactions to penicilloyl-polylysine (PPL), compared with five out of forty without a history of such allergy. Three out of six of the patients allergic to cephalothin had positive reactions to the PPL test. Three out of nine Negro women, but only one out of fifteen Negro men, reacted adversely to cephalothin. One out of the seven patients allergic to cephalothin had a history of atopy compared with four of the 47 who were not allergic to it.

The authors acknowledge that their series was small, but they believe the results to indicate that reactions to cephalothin are more likely in patients with a history of penicillin sensitivity, especially if the PPL test gives positive results. It seems probable that these reactions are an expression of cross-sensitivity, since in five of the seven cases the reactions were accelerated, occurring within less than 2 days of the start of treatment and often within minutes. There is evidence that Negro women are particularly susceptible. Atopy may be commoner among subjects reacting to cephalothin. Although recent reports have suggested that cephalothin is a safe alternative in cases of penicillin allergy, the authors conclude that patients with a history of such allergy are particularly liable to adverse reactions to cephalothin.

Joan R. Gomez


PUBLIC HEALTH AND SOCIAL ASPECTS


MISCELLANEOUS


