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 study here reported was undertaken to determine trends in incidence, diagnosis, treatment, and prognosis in cardiovascular syphilis. In the 10 years 1945-54 at the Los Angeles County Hospital, 1,002 patients were admitted with a diagnosis of cardiovascular syphilis, the records of 954 of them being sufficiently detailed for analysis. During the period the incidence of cardiovascular syphilis decreased by 47 per cent.

Approximately 27 per cent. of the 954 patients were found to have syphilitic aortitis, 49-5 per cent. syphilitic aortic insufficiency, 9-3 per cent. aortic insufficiency associated with syphilitic aneurysm, and 14 per cent. syphilitic aortic aneurysm. Complications in order of frequency were congestive heart failure, hypertension and angina pectoris. Serum tests for syphilis gave positive results in 82 per cent. of the patients; radiological findings were normal in only 8-8 per cent. of 633 patients examined.

The authors consider that penicillin is the drug of choice for the treatment of cardiovascular syphilis, and it is noteworthy that no typical cases of therapeutic shock or Jarisch-Herxheimer reaction were observed after treatment with penicillin. In many instances radiological examination evidenced the halting of progressive lesions, and this was confirmed in many cases by microscopical findings at necropsy. Necropsy, performed on 275 of the 521 patients who died, showed a decrease in lymphocytic and plasma-cell infiltration of the aortic wall in those cases of aortitis where penicillin treatment had been given at least 10 weeks before death. Coronary ostial stenosis occurred in 83 per cent. of the male and in only 17 per cent. of the female patients, and it was noted that coloured patients—especially women—have less tendency to develop coronary stenosis.

As expected, prognosis as to long-term survival was best in the younger age groups, but it was noted that the presence of hypertension decreased the period of survival after diagnosis to 2-4 months under the average for the group. True diastolic hypertension in aortic aneurysm was a particularly unfavourable sign.

G. L. M. McElligott

Correlation of Anatomic and Roentgen Changes in Arteriosclerosis and Syphilis of the Ascending Aorta. Lodwick, G. S. and Gladstone, W. S. (1957). Radiology, 69, 70. 10 figs, 10 refs.

The radiological changes in syphilitic aortitis and arteriosclerosis were studied in 72 aortas obtained at necropsy at the Veterans Administration Hospital, Iowa City. The commonly held view that intimal calcification in the ascending aorta is usually due to syphilis was substantiated. Calcification does occur in the ascending aorta in atheroma, principally round the ostia of the coronary arteries and great vessels and on the postero-medial wall. In syphilis the ascending aorta is more uniformly affected, and the pattern is one of numerous small flaky plaques, quite different from the large, dense, isolated plaques of atheroma.

A method of measuring the length and width of the aortic shadow on the postero-anterior chest radiograph is described, the two measurements added together being termed the aortic index. Use of this index takes into account the dilatation and elongation which occurs in syphilis. It was found that, taking both sexes together, 85 per cent. of patients with an aortic index over 20 cm. and 100 per cent. of those with an index of over 24-2 cm. showed serological evidence of syphilis.

D. E. Fletcher


SYPHILIS (Therapy)


The authors report from the Hôpital Saint Louis, Paris, the results of treatment with penicillin since 1957 of 306 patients with early syphilis. The patients were first given 0-1 g. mercuric cyanide intravenously on 3 successive days, this being followed by a total of 15 mega units aqueous penicillin given over 17 days. On the first 3 days 200,000, 300,000, and 500,000 units respectively were injected daily (divided into five to eight doses throughout the day), and then 500,000 units twice a day for 14 days. Clinical and serological follow-up studies were carried out at progressively lengthening intervals. Thanks to the subdivision of the initial doses and to the preceding treatment with mercury, the incidence of Herxheimer reactions was slight or absent. During the last fortnight treatment in many instances was given in the out-patient department.

Clinical cure of primary sores and regression of lymphadenopathy was rapid. Serological reversal, as judged by the results of complement-fixation and flocculation tests, occurred slightly more quickly in primary cases than in secondary cases of the disease, the complement-fixation reaction becoming negative before those of the flocculation tests. Treated sero-negative cases never became sero-positive. Of the original 306 patients, 243 were satisfactorily followed up, and of these, 230 were considered to be cured, being completely serologically negative. However, seventeen of these patients were reinfected by their previously infected usual partner, in one case twice. Of the thirteen uncured cases, two were considered to be due to failure of the treatment, and four to probable but not certain marital re-infection. In the remaining seven cases, serological reversal was not achieved, possibly owing to penicillin resistance or to unsuspected reinfection. The treponemal immobilization (Nelson) test was performed 254 times on 160 patients; it gave a negative result in all sero-negative primary cases, and a positive result in 5-4 per cent. of sero-positive primary cases and in 14-6 per cent. of secondary cases. The authors stress the length of the observation period in this series (nearly 10 years) and the fact that only complete sero-negativity was accepted as evidence of cure. On this criterion of cure the success rate was thus 94-6 per cent. An analogy is drawn between the Nelson test in syphilis and the Widal test in typhoid fever, it being pointed out that the latter may still give a positive result in cured patients.

F. Hillman


After reviewing some recent published work [no British work is mentioned] on the treatment of neurosyphilis with penicillin, the authors discuss their own results, obtained at the Dermatological Clinic of the Medical Academy, Łódź, Poland, in 76 cases of neurosyphilis. The patients were followed up for 1 to 4 years, with examination of the cerebrospinal fluid (C.S.F.) every 6 to 12 months. Only changes in the C.S.F. were accepted as confirmation of improvement, regardless of changes in the clinical picture. Of the 76 patients, 51 were treated with penicillin only in a dosage of 300,000 units daily to a total of 6, 9, or 12 mega units; all the patients in this group had some organic disorder, such as active tuberculosis or hepatic, renal, or cardiovascular disease, which was regarded as a contra-indication to fever therapy. The remaining 25 patients received the combination of fever therapy and penicillin treatment.

Of the total of 76, the treatment was unsuccessful in 28 cases (36-8 per cent.), six patients showing no improvement, fourteen very slight improvement, and two exacerbation, and six relapsing in respect of C.S.F. changes. The failure rate for the combined treatment was 28 per cent., whereas that for treatment with penicillin alone was 41-2 per cent. The best results were obtained in asymptomatic neurosyphilis, less good results in tabes dorsalis, and the poorest results in cases of cerebrospinal syphilis and of progressive paresis.

H. Makowska


The author recalls attention to the use of potassium iodide as a diagnostic and therapeutic aid in the management of syphilis, pointing out that it is of value in two main diagnostic situations:

1. The late latent stage of syphilis in which weakly positive serological reactions are frequently encountered;

2. In the case of patients presenting mucosal, skin, or bone lesions suggestive of gummatas but in whom serological tests are technically not feasible.

He recommends giving 5 to 10 ml. 10 per cent. potassium iodide three times a day as a therapeutic test of cure, its effect on the existing lesions being observed. [No ill-effects have apparently been observed by the author from this rather large dosage.]

In the elderly untreated syphilitic who appears to be in equilibrium with his disease, the use of combined therapy with potassium iodide and bismuth as advocated

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long ago by Lesser, may be preferable to treatment with penicillin or arsenicals, since it avoids the crises often induced by the latter drugs. Several illustrative case histories are given. Allene Scott


SYPHILIS (Serology)


The results of serological tests for syphilis (S.T.S.) carried out at the Central Serological Laboratory, Seville, since 1956 have revealed an incidence of unsuspected syphilis in Spain higher than that in other countries of Europe or of America. The tests employed were the Meinicke, Kahn, Wassermann, and V.D.R.L., the treponemal immobilization test of Nelson and Mayer being performed in addition in doubtful cases. The systematic serological examination of the mothers and children attending the maternal, child welfare and paediatric services in Seville showed that out of a total of 1,353 mothers and children examined, 223 (16 per cent.) gave a positive reaction to S.T.S.; in 174 of these cases there was a history of syphilis, but in 49 (3.6 per cent.) the disease had not been suspected. Of 227 pregnant women tested, 48 (23 per cent.) were sero-positive; in 39 of this group there was a history of syphilis, while in nine (4 per cent.) the disease had not been suspected. Examination of 615 mothers attending the clinics for reasons other than syphilitic infection showed that 112 were sero-positive, this being an unexpected finding in 26 cases (4 per cent.). Lastly, of 531 schoolchildren examined, 63 gave a positive S.T.S. reaction, 49 having a family history of syphilis, while in fourteen (2.6 per cent.) the disease had not been suspected. Eric Dunlop


Since the identification by Pangborn in 1941 of cardiolipin and lecithin as the active constituents of the lipid tissue extracts used as antigens in the serological diagnosis of syphilis numerous investigators have shown that antigens prepared with the purified reagents in optimum proportions give better results than do the original preparations. However, while natural cardiolipin extracted from beef heart is of constant potency, preparations of lecithin from the same source are more variable. In an attempt to overcome this difficulty synthetic lecithin was prepared by the method of Baer and 6,162 comparative slide tests were carried out on routine sera at Mount Sinai Hospital, Cleveland, Ohio, with combinations of cardiolipin with this synthetic product and with natural lecithin.

In reactive tests 97.7 per cent. agreement was obtained between the two combinations, while 99.57 per cent. agreement was observed in non-reactive tests. The authors therefore favour the use of the synthetic lecithin, different lots of which have a constant optimal ratio with cardiolipin, making for greater ease of preparation of the antigen mixture. They point out that it is the general opinion at present that the majority of false positive serological reactions are due to technical defects in the
naturally prepared antigens rather than to biological abnormalities in the patient.


In the climatic conditions of the Russian Far North sheep and guinea-pigs are difficult to breed and feed. The author, in this communication from the Experimental Dermato-Venerological Institute of the R.S.F.S.R. Ministry of Health, therefore describes a modification of the classic Wassermann reaction in which erythrocytes of the Polar deer and haemolytic serum obtained from immunized rabbits are used. However, because the usual methods of preservation of defibrinated sheep blood were found ineffective for the blood of Polar deer, the following formula is suggested by the author for this purpose: glucose 0.8 g., boric acid 0.8 g., and magnesium sulphate 2 g., dissolved in 20 ml. normal saline solution for each 80 ml. blood.

It is stated that this preparation will preserve deer’s blood for 3 months at 4 °C, and for 2 months at room temperature.

Haemolytic serum of high titre (at least 1 in 1,500) was prepared by repeated immunization of rabbits at intervals of 4 months with 50 per cent. suspension of deer erythrocytes. The serum so obtained was prepared for one year by the addition of 4 per cent. boric acid.

A comparison of the results obtained with this modified complement-fixation test on 17,108 samples of serum and cerebrospinal fluid with those of the Wassermann and Kahn reactions as controls showed a divergence between the two methods of only 1 per cent.

\*Use of the Antigens of Reiter’s Treponeme in the Serology of Syphilis and in the Study of the Phenomena of Allergic Sensitization.\*[2] H. Makowska


In continuance of their previous study (Ann. Inst. Pasteur, 1956, 90, 249; Abstracts of World Medicine, 1956, 20, 187) the authors have now investigated, at the Institut Alfred-Fournier, Paris, another Italian product known as soluble treponemal protein antigen (A.T.P.S.) prepared from Reiter’s treponeme by d’Alessandro and Dardanoni. The sensitivity of this antigen in complement-fixation reactions was found to be equal to that of treponemal suspensions, and manipulation was easier.

In a series of trials rabbits sensitized by three intraperitoneal or subcutaneous injections of suspensions of living Reiter’s treponemes were tested 10 days after the final injection by the intradermal administration of a concentrated suspension of living and of heat-killed treponemes and A.T.P.S. A red, infiltrated, allergic reaction appeared in 48 hours and persisted for 3 days. The A.T.P.S. reaction was still positive after 55 days and in a modified form after 198 days, while control reactions were negative. Tests with freeze-dried and ultrasonically killed treponemes and other antigens gave no reaction. In a second series of experiments syphilitic rabbits infected with syphilis 55 to 880 days previously gave a positive reaction with A.T.P.S., even amounting in some cases to some central necrosis, after 724 days. Reiter’s treponemes antigen produced a lesser reaction, heat-killed treponemes giving a negative reaction after 55 days, but living treponemes a strong positive one after 147 days. The German “pallida” antigen gave a smaller reaction, but luetin produced no reaction. Skin tests were then performed with A.T.P.S. and luetin on 15 syphilitic patients in various stages of infection. In no case did A.T.P.S. invoke the slightest positive reaction, whereas luetin revealed allergic sensitization in patients with tertiary syphilis.

In a warning note the authors point out the particular facility with which rabbits are sensitized, and also that sensitization of human subjects is much more specific than that of the rabbit. It is concluded, however, that A.T.P.S. has a place in the serological diagnosis of syphilis, in which it is inferior only to the treponemal immobilization test.

\*Serology of Syphilis with an Antigen consisting of Cultured Treponemes disintegrated by Ultra-sonic Vibration (T.U.S.).\*[3] F. Hillman


In the preparation of the antigen here described from the Faculty of Medicine, Bordeaux, bulk cultures of the Reiter treponemes are grown anaerobically for 9 days in thioglycollate broth with added rabbit serum, the organisms being then separated by centrifuging. After being washed several times in saline the treponemes are suspended in a small volume of 0·3 per cent. phenol-saline and disintegrated by exposure to ultrasonic waves. After further centrifuging at 2,000 r.p.m. for 10 minutes to remove gross particles the supernatant fluid constitutes the antigen, which is stable for up to 2 years when stored at 6°C. It has been used in the Kolmer complement-fixation test, the stock antigen being further diluted to 1 in 10 parts of saline before use. It is said not to be anticomplementary.

Serial tests were carried out on sera from rabbits which had been infected by intratesticular inoculation with the Nichols strain of Treponema pallidum, some animals being left untreated, others given a curative dose of penicillin after 3 to 5 weeks, while a third group were treated 4 to 12 months after infection. The behaviour of the antitreponemal (A-T) antibody was compared with that of reagin, as shown by the Kline and Kolmer tests. The A-T antibody was often found to develop earlier and to rise more rapidly in titre than reagin. When the rabbits were treated early in the infection the A-T antibody titre fell rapidly and indeed disappeared...

Quantitative treponemal immobilization (T.P.I.) test performed samples of the control serum in different laboratories have given considerable variations in titre. Because of this, some doubt has been cast on the reproducibility of the quantitative T.P.I. test. Factors such as the duration of incubation, quality of the complement used, and the state of vitality of the treponemes may influence this variation.

The demonstration of free complement at the end of the test period by the lysis of sensitized sheep's erythrocytes may not necessarily indicate the presence of the component of complement which immobilizes treponemes sensitized by specific antibody. Most human sera, for example, are only weakly haemolytic, but they may immobilize sensitized treponemes more actively than guinea-pig serum with a much higher haemolytic titre. It is suggested that some irregular results may be due to an anticomplementary effect of the serum being tested, which partly destroys the immobilizing fraction of the complement but leaves sufficient haemolytic activity to lyse the test dose of cells, thus giving a falsely low reading. To avoid this the author uses three times the amount of complement originally recommended. Some human sera are said to contain a natural immobilizin for treponemes which requires complement for its action and is thermolabile, so that it does not normally interfere with the T.P.I. test. It is suggested that it may be related to properdin.

Under adverse conditions of temperature, inadequacy of the survival medium, incomplete anaerobiosis, or sensitization in vivo in the rabbit, resting forms of treponemes with reduced metabolism are thought to develop. Although they may maintain their shape and motility, these resting forms are relatively resistant to immobilization and may cause irregular results, particularly in quantitative tests, where the curve of immobilization is flattened. These forms are said to be considerably more resistant to penicillin in vitro than healthy treponemes. The importance of sensitization of treponemes in vivo as a cause of unsatisfactory T.P.I. tests is thought to have been exaggerated; by using only rabbits which develop orchitis within 10 days after inoculation it can be avoided.

The part played by specific antibodies in the natural history of syphilis is discussed. The continued presence of immobilizing antibody in late or latent syphilis, even after treatment, is thought to be due to the persistence of foci of resting forms of treponemes which, although they have temporarily lost their powers of multiplication and pathogenicity, continue to act as a stimulus to the production of antibody.

[The experimental data advanced in support of the ideas expressed are very scanty. The technique and interpretation of the results of the T.P.I. test are to be published separately.] A. E. Wilkinson


Significance of the Pallida Reaction in the Diagnosis of Syphilis. (Bedeutung der Pallida-Reaktion in der Diagnostik der Syphilis.) JENEP, E., CSOKA, I., and BIRO, L. (1957). Hautartz, 8, 322. 25 refs.


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Complement-Fixation Reaction with Treponema pallidum (Nichols strain). (La reazione di deviazione del complemento con Treponema pallidum Nichols.) VACCARI, R. (1957). Minerva derm. (Torino), 32, 303. 3 refs.


SYPHILIS (Pathology)


GONORRHOEA


The authors have reviewed the records of some 2,000 female patients treated for gonococcal infection since 1948 at Klosterneuburg Hospital, Vienna. In the year 1948 these patients were treated with combined vaccine—penicillin—sulphonamide therapy, necessary at that time as an economy measure; the total dose of penicillin in such a course was 100,000 units [but the dosage of sulphonamide is not stated]. Out of 408 female patients treated in that year there was only one case of relapse, an incidence of 0·25 per cent. Among 1,071 patients treated between 1948 and 1950 there were fifteen relapses, an incidence of 1·47 per cent. Since 1950 alternate patients have been treated with either 200,000 units of penicillin alone or the vaccine—penicillin—sulphonamide combination previously used. During this period 250 female patients were treated with each schedule and there were eleven relapses in each series, that is 22 relapses out of 500 cases or an incidence of 4·4 per cent. The reasons for the increased number of relapses in the latter series and the possibility of decreasing sensitivity of the gonococcus to penicillin are discussed.

All the patients were followed up in hospital for a minimum period of 3 weeks (in 118 cases for over 6 weeks), thereby excluding the possibility of re-infection. Of the sixteen relapses in the 1948–50 period, all occurred within the first 3 weeks, while of 52 relapses collected up to the present, 49 occurred within 19 days and 41 between the 7th and 17th day after treatment, the maximum incidence of relapse (24 cases, 46·1 per cent.) being between the 8th and 12th days. Only five cases (9·7 per cent.) occurred within the first 5 days, and three after the 19th day. The role of infection of the genital adnexae in relapse is considered; there were 58 patients in the series with adnexal involvement, but none of these relapsed within the period of follow-up.

In a series of twenty female patients with suspected gonorrhoea who were examined daily in hospital the gonococcus was demonstrated in the genital secretions within the first 5 days in four cases, between the 6th and 13th day in thirteen cases, and between the 14th and 22nd day in three cases. The authors stress the necessity for prolonged observation of female patients who have been exposed to the risk of genital infection.

R. D. Catteall


The authors report the treatment at Beth Israel Hospital, Boston, of 53 patients with 56 strictures of the urethra (fifteen anterior, eighteen membrano-prostatic, five posterior, and eighteen mental) by the injection of an aqueous suspension of hydrocortisone (25 mg./ml.). This method was adopted in view of the reported inhibitory effect of hydrocortisone on fibroblastic proliferation in experimental animals and of its possible lytic effect on scar tissue in patients with Peyronie's disease. It is relatively simple and inexpensive, the best results being obtained with simple, circumscribed strictures.

The suspension is injected directly into the tunica propria at the base of the stricture at two sites (at 5 and 7 o'clock or at 3 and 9 o'clock). Strictures of the meatus are injected under direct vision and with no anaesthesia, while those located farther back are approached endoscopically and injected by means of a specially devised needle under local or low spinal analgesia or general anaesthesia. At each treatment the stricture is dilated to its limit without rupture before injection. In cases requiring repeated injections these are given at 2-day intervals up to a total dose of 25 to 150 mg. hydrocortisone. The majority of the authors' cases required three or fewer injections. Prophylactic chemotherapy is advisable except in cases of mental stricture. Of the 56 strictures treated by the authors, 51
responded well, whereas three cases of multiple strictures and two with dense elongated strictures were resistant. The stricture was due to unknown causes in three cases, gonorrhoea in thirteen, other inflammatory diseases in three, and trauma in six, and followed protatetomy in 26 (transurethral 21, suprapubic 3, perineal 2). The majority of the patients were over 60 years old and most had a long history of difficult instrumentation.

The procedure resulted in remarkable relief to the patient, with no need for further instrumentation, in all but the five resistant cases examined, which were eventually cured by internal urethrotomy and injection of the incision site with hydrocortisone. The treatment is also recommended as an adjunct to many surgical procedures involving the urethra from which post-operative stricture might result. Douglas J. Campbell


The author points out that although a review of the public health statistics for seven representative European countries and Canada and the U.S.A. shows that there was a rapid fall (ranging from 50 to 70 per cent.) in the incidence of gonorrhoea between 1946 and 1950 after the introduction of antibiotics, yet there has been no marked change in the number of reported infections in the last 5 years. Attention must therefore be directed to two further aspects of this problem:

1. the detection and treatment of female contacts,
2. the prevention of re-infection.

As is generally known, the male is infectious for only a short time and because of the obvious signs of infection treatment is usually begun fairly early. In contrast, the infectious state of the female continues for a longer period, since signs and symptoms may be minimal, and treatment is often sought simply because of detection of the disease in her partner or as a result of routine health inspection. The author's suggested remedies for this are:

1. greater routine use of adequate existing bacteriological services,
2. routine weekly examination of prostitutes,
3. active tracing of contacts,
4. public education.

These methods will also assist in the prevention of re-infection. He urges that particular precautions should be taken against "ping-pong" infection between partners by treating the asymptomatic partner as well.

In the author's view the most satisfactory therapy for gonorrhoea consists in the administration of a single dose of 2-4 mega units of long-acting benzathine penicillin by intramuscular injection, treatment by mouth being too difficult to control. Sensitivity reactions to penicillin are infrequent, and the fear that such a regimen might obscure an early syphilitic infection is not borne out by any statistical evidence of an increase in the incidence of latent syphilis. The author emphasizes that an efficient social service is indispensable for the control of gonococcal infection. Allene Scott


From a review of the literature and his own experience the author suggests four possible reasons for the failure of silver nitrate prophylaxis to prevent the occurrence of gonococcal ophthalmia neonatorum:

1. The drug is of little or no value;
2. It is not properly administered;
3. Infection occurs from adjacent skin after the drug has been dissipated;
4. There is failure on occasion to implement routine use of the drug.

During the 10 years 1946–56 there were 67,200 live births at the Los Angeles County Hospital, California. Babies were routinely treated before leaving the delivery room with 1 per cent. silver nitrate eye-drops, the eyelids being held apart by a nurse and the drops inserted by a resident, intern, or medical student. Despite this there were forty instances of gonococcal ophthalmia neonatorum. Nearly half the babies involved were prematurely born. In more than half of the cases the diagnosis of gonococcal ophthalmia was made in the third or fourth day of life. Two infants had gonococcal ophthalmia at birth; in these two cases the membranes had been ruptured for 24 and 48 hours respectively before delivery.

Commenting on his findings, the author states his opinion that liability to infection is probably conditioned by the number of gonococci present in the maternal cervix at the time of delivery. The greater risk to prematurely born infants which is apparent is presumed to be due to the poorer resistance to infection of the immature foetus. R. S. Morton


A comparative test using 1 per cent. silver nitrate and 1 per cent. penicillin ointment was made on 2,424 babies born between March, 1955, and February, 1956. Alternate babies received penicillin and a record was kept of any reactions: of the 1,205 receiving silver nitrate, 41 showed conjunctivitis (mild without discharge in 27, and severe with discharge in fourteen. 1,219 received penicillin, and of these 33 showed a reaction (mild in 22 and severe in 11). M. H. T. Yuille


The author reviews the Crede method. It is recommended that with adequate antenatal care and delivery in a modern hospital prophylaxis of ophthalmia neonatorum consists of swabbing the baby's eyes before they are opened. In unsatisfactory surroundings the use of silver nitrate drops is desirable. Ronald Lowe.
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NON-GONOCOCCAL URETHRITIS AND ALLIED CONDITIONS


In an earlier paper (Brit. J. vener. Dis., 1956, 32, 115; Abstr. Wild Med., 1957, 21, 81) a study was reported of the effect of spiramycin on 41 patients suffering from non-gonococcal urethritis, 38 of the patients receiving 1 g. of the drug four times a day for 5 days, and three receiving half this dosage for a similar period. To determine whether the smaller dosage would suffice for satisfactory treatment of this condition, a further 47 patients were given 500 mg. four times a day for 5 days, and in this paper from St. Mary's Hospital, London, the results obtained in the two series are compared. Of the 38 patients in the first series receiving the large dosage, 33 were followed up for 3 months or more: in seven the treatment failed, giving a failure rate of 21.2 per cent. Of the 47 in the second series, 44 were followed up for 3 months or more; there were nine treatment failures, giving a failure rate of 20.5 per cent. Mild toxic effects were noted by fifteen patients.

The author concludes that in non-gonococcal urethritis:

1. the results obtained with spiramycin compare favourably with those achieved with the tetracyclines,
2. the former drug is slightly superior to erythromycin and markedly superior to other antibiotics and the sulphonamides,
3. there is no advantage to be gained by giving spiramycin in a total dose of more than 10 g. over a period of 5 days,
4. this dosage is adequate for most patients suffering from this condition. R. S. Morton


CHEMOTHERAPY


Spiramycin, which forms the subject of this and the two following papers, is produced by a hitherto undescribed actinomycete isolated from soil collected in Dallas, Texas, and named Streptomyces spectabilis, n.sp. It can be resolved by a paper chromatography into five microbiologically active components, Fractions A, B, and C being active against a wide variety of Gram-positive, Gram-negative, acid-fast, and fungal organisms, whereas Fractions D and E have only a low activity. It is unstable in solution at 37° C., losing the greater part of its potency in the first 40 hours. Organisms have been shown to become resistant to it during tests in vitro. It is claimed, however, that streptovaricin does not give rise to resistance to streptomycin or other antimicrobial drugs.

E. G. Rees


Spiramycin is isolated from the culture filtrate by extraction with ethyl acetate and then precipitating it with hexane. It is redissolved in methylene chloride and reprecipitated with hexane. It is a bright yellow-orange material which has a characteristic ultraviolet and visible absorption spectrum. It is labile to alkali. Countercurrent distribution shows it to resolve into four peaks, one of which probably contains two components.

E. G. Rees


Experiments in vivo revealed that spiramycin afforded 100 per cent. protection to mice infected with Mycobacterium tuberculosis var. hominis (H37Rv) at concentrations of 200 mg. per kg. Doses of 40 mg. per kg. administered orally or by the subcutaneous route afforded a significant degree of protection both against H37Rv and bovine tubercle bacilli. Fraction C proved to be the most active component of the spiramycin complex. H37Rv tubercle bacilli failed to develop resistance in an experiment in vivo lasting 84 days, and studies in vitro showed that mycobacteria resistant to streptomycin are attenuated for mice.

E. G. Rees


The toxic effects of streptomycin on the eighth cranial nerve system, particularly the vestibular part, are described in this paper from the National Hospital for Nervous Diseases, London. A patient aged 65 with pylonephritis in the one remaining kidney lost all vestibular function after a total dose of only 3 g. streptomycin sulphate in 3 days. The authors cite fourteen cases in which a dosage of 1 g. daily to a total of less than 20 g. was followed by toxic symptoms. They consider that the incidence of damage from streptomycin is increasing, especially in older people and patients with renal insufficiency, and they attribute this to the wide use of streptomycin as a result of sensitivity tests. Toxic symptoms are unlikely to occur if the daily dose of streptomycin does not exceed 0-5 g., although it is
appreciated that in serious tuberculous infections as much as 1 g. daily may be necessary.  

I. Ansell


The authors, in this paper from the University of Minnesota, Minneapolis, summarize the collected reports of complications attributable to Novobiocin—mainly skin rashes, urticaria, and fever, the overall incidence of which is 12.7 per cent.—and add four cases of their own. Of the four patients, aged 1½ to 15 years, three developed a skin rash after one week on a dosage of Novobiocin of 30 to 40 mg./kg. daily. The fourth patient received 2 g. every 12 hours for 8 days, and on the sixth day jaundice and a purpuric skin rash appeared; the patient died 5 days later. Necropsy revealed generalized lymph-node hyperplasia and acute diffuse hepatic necrosis, which were attributed to the novobiocin.

Norval Taylor


In an investigation carried out under the auspices of the College of General Practitioners, London, members were asked to report any case of an acute immediate reaction to penicillin, such reaction being arbitrarily defined as one occurring within 15 minutes of the injection. In the present paper the author has collected from the reports of several physicians twelve such cases occurring in general practice. The cases, which are described in some detail, are divided into three groups:

(1) those taking the form of an anaphylactic reaction following the intramuscular injection of penicillin into a sensitized subject;

(2) reactions attributed to accidental intravascular injection or "back seepage" in sensitized persons;

(3) those thought to be due to the accidental rapid intravascular injection of procaine penicillin suspensions.

The author recapitulates the usual precautions to be adopted in preventing these reactions, and suggests that the immediate initial reaction should include the injection of 0.5 ml. of 1 in 1,000 adrenaline intramuscularly, the intravenous infusion of an antihistaminic or hydrocortisone, and the administration of positive-pressure oxygen if required. Convulsions thought to be due to procaine are best controlled by intravenous barbiturates. He points out, however, that in many of the present cases the patient recovered without any specific treatment.

I. Ansell


The serum penicillin levels achieved after administration of 60 mg. and 240 mg. respectively of phenoxymethylpenicillin free acid half an hour before breakfast were studied at the Royal Infirmary and the University, Sheffield. The results obtained with the higher dose were also compared with those achieved with corresponding amounts of the potassium and benzathine salts of phenoxymethylpenicillin in twenty healthy volunteers. The potassium salt was most rapidly absorbed and gave the highest concentration. These values were lowest with the benzathine salt. With all three forms of penicillin the mean serum level persisted above 0.6 unit per ml. for as long as 4 hours. In eleven patients with pernicious anaemia the mean serum concentrations of the benzathine salt were higher than in healthy subjects.

I. Ansell

PUBLIC HEALTH AND SOCIAL ASPECTS


MISCELLANEOUS


Benign Oculo-Glandular Lymphoreticulosis (Cat-Scratch Disease). (Sulla oculo-ghiandolare della linfo-reticulosi benigna (cosidetta malattia da graffio di gatto).) RENDE, S. (1956). Riv. ital. Tracoma, 8, 32. 5 figs, 43 refs.


