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## Management of Syphilis in the European and African

BY

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### MANAGEMENT OF SYPHILIS IN THE EUROPEAN

As in gonorrhoea, the diagnosis of syphilis should always be confirmed pathologically.

#### *Diagnosis*

*Primary Syphilis.*—All genital sores, whatever their nature, should be examined for *T. pallidum*, no antiseptics being placed on the sore or antibiotics administered until the tests have been taken.

Chancroid is common in Africa and may confuse the picture. Persons suffering from chancroid, if handled properly, can be finally discharged from observation after a period of only three months if syphilis is excluded instead of the years required if syphilis is diagnosed. If penicillin is given for genital sores without diagnostic tests, cases of genital sore have to be observed for the full time as for syphilis.

The correct regime is to perform a dark-field examination of matter from the sore daily for three days and serum tests monthly for three months. If these all prove negative, syphilis can then be excluded. During the time that the dark-field examinations are being made the sores should be bathed only with normal saline, but sulphonamides (e.g., sulphadiazine in doses of 4.5 g. daily for 4-5 days) may be given by mouth. Sulphonamides have no effect upon *T. pallidum* and will heal most other non-syphilitic sores, including chancroid.

*Secondary Syphilis.*—Patients with secondary syphilis can have their diagnosis confirmed both by dark-field and serum test.

*Latent Syphilis.*—In cases of suspected latent syphilis, in whom the only sign is a positive serum test, caution is required. Apart from a greater likelihood of technical difficulties in the performance of serum tests in the tropics, false positive results may be encountered during or following malaria, glandular fever, relapsing fever, leprosy, the collagen diseases and small-pox vaccination.

When false-positive results are suspected, as many tests, quantitated if possible, as are available should be performed on each specimen and the tests should be repeated a number of times.

Truly positive sera usually give a constant pattern with increasing positivity, while false-positive results tend to be weaker in titre giving inconstant results varying not only with each test, but also with successive specimens.

To-day, new tests, depending not on the reagin antibody of the Wassermann test, but on other antibodies more specific, are coming into use in many parts of the world. These include the *Treponemal pallidum* immobilisation (TPI) test and various agglutination tests which are under trial. These new tests, or their future successors, depend on specific antibodies and will one day be most useful in the exclusion of false-positive results in Africa.

### TREATMENT OF SYPHILIS IN THE EUROPEAN

#### *Early Syphilis (Primary, Secondary and Early Latent Syphilis)*

Penicillin is now the drug of choice for the treatment of syphilis and for early syphilis, at any rate, no adjuvant measures are required. Neoarsphenamine and bismuth may be entirely discarded. In-patient treatment is not necessary, the patient being virtually non-infectious after 24 hours.

When penicillin was first introduced, British clinics were loth to abandon completely the old proved long-term arsenic and bismuth schedules and for some time gave, following the intensive course of penicillin, one ten-week course of neoarsphenamine and bismuth in an attempt at "consolidation." As the toxic effects of arsenic, sometimes serious, occasionally fatal, were still encountered, the arsenical course was gradually dropped, although the bismuth course was retained. This too was not without its side-effects, and, with cases of stomatitis still occurring, it also came to be omitted. In the belief that there was nothing that bismuth could do that penicillin could not do better, many British clinics then employed a method of consolidation with ten bi-weekly injections of procaine penicillin with aluminium monostearate in lieu of bismuth. A recent WHO survey, however, indicates that this practice is mainly confined to Europe, largely in the British Isles, and that over 65 per cent. of 277 world clinics now use an intensive course of penicillin alone without other measures (Willcox, 1954).

Experimentally it has been shown that a continuous penicillin serum level for at least 96 hours is the minimum required for the eradication of syphilis, but, for such a serious disease, we must allow for a considerable margin of safety.

The earlier penicillin courses, consisting of eight daily intramuscular injections of 600,000 units of penicillin in oil-beeswax, gave satisfactory results and a similar dosage has since been employed using oily injection of procaine benzylpenicillin, viz., procaine penicillin with aluminium monostearate (PAM), although, with this preparation, the interval between injections can be longer without loss of the continuous serum level.

It is usual now to recommend an initial loading dose of 2.4 mega units of PAM (4 ml. in each buttock)—a so-called "epidemiological dose"—so that should the patient then default he already has enough penicillin to give a detectable serum level for a week, with a good possibility of a cure even if nothing else is given. This may be followed by 6-8 injections of 600,000 units daily or of 600,000-900,000 units every 2-3 days. It is considered by the WHO Expert Committee on Venereal Infections and Treponematoses (1954) that at least 2.4 mega units of PAM should be given for primary syphilis and 4.8 mega units for secondary syphilis.

Recently the new diamine penicillins (dibenzylethylenediamine dipenicillin G (DBED) and Benethamine penicillin) have been shown dose for dose to give even more prolonged penicillin serum levels than PAM. With these preparations the initial loading dose of 2.4 mega units should still be employed, but the subsequent injections may be fewer and more widely spaced and 0.9-1.2 mega units given weekly for three more weeks may well be amply sufficient. These penicillins are still on trial, however; moreover, they are somewhat more painful than PAM, which is well tolerated. High cure rates, as good as those obtained with PAM, have already been reported in the U.S.A. following only a single injection of 2.3-2.5 mega units (Smith *et al.*, 1954).

*Surveillance.*—Following the treatment of early syphilis, serum tests should be performed monthly for six months, quarterly for one year and six-monthly for a further year, with a cerebrospinal fluid examination at the end of this time.

If possible, a complement fixation (e.g., Wassermann) and a flocculation test (Harris (VDRL) or Kahn) should be made on each specimen, and one of the two tests should be quantitated so that a fall in titre can be observed even if the qualitative tests are still strongly

positive. The cerebrospinal fluid should be examined as to cell count, protein and globulin content, Lange curve and Wassermann reaction.

Even if available, the new treponemal immobilisation and agglutination tests are not indicated at the present time for the routine surveillance of treated syphilis, but rather for the refutation or otherwise of suspected false-positive reactions.

### *Late Syphilis*

Similar courses of penicillin are the standby of treatment in all cases of late and latent syphilis. An X-ray examination of the heart and an examination of the cerebrospinal fluid, in addition to the serum test, should be made on all cases prior to treatment.

An initial intensive PAM course of 600,000-900,000 units daily should be given for 10-14 days and, as no immediate serological response may be expected, there is perhaps something to be said for the British regime of giving a further 900,000 units bi-weekly for five weeks.

There is a possible danger in the penicillin treatment of late syphilis of a Jarisch-Herxheimer reaction, especially in neurosyphilis when epilepsy, mental changes and focal reactions have occasionally been reported. Similarly, in syphilitic aortitis, the possibility that angina pectoris or coronary occlusion might be precipitated by local oedema at the site of the lesions during the first 24-48 hours of therapy cannot be dismissed from the mind, even if the total number of reported cases is few and not all are convincing.

At one time a preliminary course of bismuth and iodides was given prior to the penicillin course in an attempt to minimise this risk. Today it is believed that the Herxheimer reaction is an "all or none" phenomenon and that it may occur even with bismuth and iodides, in which case it is not to be expected later with penicillin; if it does not do so, it may then be provoked by penicillin even after such premedication. Thus it seems that, in fact, there is little that can be done to avoid it, and there therefore is no point in delaying the administration of the penicillin. A harmless if ineffective compromise which is often employed is to commence at once with 250 units of aqueous penicillin G and to increase the dose every 3-4 hours to 500, 1,000, 2,500, 5,000, 10,000, 25,000, 50,000, 100,000 and 250,000 units until 500,000 units has been reached in 30 to 40 hours before switching to the single daily dose of PAM.

Following treatment with penicillin, the cerebrospinal fluid will, if abnormal, become normal or inactive, and gummata will heal. Pathological arrest may be expected in cardiovascular syphilis, but a weakened aorta may continue to stretch even when there is no longer an active syphilitic process. Currently in this field considerable achievements have been reported in surgery, and saccular aortic aneurysms are being successfully excised (Bahnon, 1953) and plastic ball valves have been inserted into the aorta in cases with aortic incompetence. These experimental operations probably represent a signpost to the future.

In treated cases with initially abnormal spinal fluids the fluid should be examined quarterly until normal and again one year after this time. It has been shown that if two normal fluids are obtained at an interval of one year, further neuro-relapse is very unlikely.

Cases of syphilitic aortitis should receive appropriate medical measures depending on the state of compensation and the presence of angina pectoris. Once conditions have become stabilised, serial X-rays of the heart and great vessels should be taken at first six-monthly and then annually.

In all cases of late syphilis, including those with gummatous and late latent syphilis, immediate serum reversal is not usual whatever the treatment given. Post-treatment serum tests should be made quarterly for one year, six-monthly for a second year and afterwards annually. Periodic X-rays of the heart and great vessels should also be taken.

Arsenic and bismuth are not indicated in the treatment of late syphilis, and fever therapy has likewise largely fallen into disuse. Fever has a place, in combination with more penicillin, in those few cases of neurosyphilis in which the cerebrospinal fluid response has been unsatisfactory. Some physicians still think that fever is indicated in addition to penicillin in cases of syphilitic optic atrophy, although in recent years doubt has been thrown as to whether its use is justified even for this serious complication (Kenney and Curtis, 1953).

#### *Congenital Syphilis*

The optimal treatment of congenital syphilis is in the prenatal phase, when an intensive course of penicillin as recommended for early syphilis (even a single injection of 2.4 mega units of procaine penicillin with aluminium monostearate

may be sufficient) will cure both mother and foetus. The baby should be observed serologically monthly for three months and then three-monthly until one year old, it being remembered that a syphilitic baby may be born with a negative blood test only to become positive later, and a non-syphilitic baby may be born with a positive test due to the passive transfer of reagin from the mother, which may spontaneously revert to negative. Hence quantitated tests are of great value. In cases in which early congenital syphilis is suspected the long bones should be examined radiologically. Cases of established early congenital syphilis should be treated with an intensive course of PAM, 150,000-300,000 units being given intramuscularly daily for 10-14 days, or 250,000-500,000 units of aqueous penicillin twice daily during this time. Cases of late congenital syphilis should be treated as for late syphilis in the adult. When interstitial keratitis is present the active inflammation of the eyes may be controlled by the instillation of aqueous drops of 1:4 cortisone acetate. These must be continued throughout the natural course of the attack.

#### MANAGEMENT OF SYPHILIS IN THE AFRICAN *Diagnosis*

Syphilis in the African may be venereal or non-venereal.

#### *Diagnosis of Non-Venereal Syphilis in the African*

The subject of non-venereal syphilis and the njevera of Southern Rhodesia has been discussed more fully in another article (Willecox, 1955). Non-venereal syphilis has been reported from many parts of Africa, including Southern Rhodesia, Bechuanaland, South Africa and French Niger Territory (Guthe and Willecox, 1954). Although sporadic outbreaks may occur in crowded urban areas, it is usually an endemic disease of backward rural areas being spread mainly amongst unclothed children by contact, the use of the common feeding bowl and possibly also by flies.

The existence of non-venereal syphilis is indicated by the presence of oral mucous patches and ano-genital condylomata, particularly in children of the 4-10 age group, as these children are too old to have obtained their lesions from congenital syphilis and too young for them to have been acquired in venery. Another important pointer to endemic syphilis is the presence of nipple chancres in mothers of suckling infants who obviously have the disease. Primary sores are unusual in endemic syphilis

in which the inoculum is usually small. When it is massive—as in the case of suckling—or with intercourse—a sore will arise. If the child has congenital syphilis it is unable to infect its mother (Colles' law), as she already has the disease. The occurrence, therefore, of such nipple chancres is indicative of an acquired infection in the infant.

Medical officers in outlying stations in Africa could with advantage be encouraged to report cases of nipple chancre, as they may lead to a more accurate definition of the still hazy map of non-venereal syphilis in Africa.

#### *Diagnosis of Venereal Syphilis in the African*

The diagnosis of venereal syphilis in the African is confused by the presence of soft and other genital sores. Thus, during the Venereal Diseases Survey of the African in Southern Rhodesia undertaken during 1949, it was found of 300 consecutive cases seen at Salisbury that there were 94 cases of soft sore to 140 of syphilis (Willcox, 1949).

It is noted, even now, that in some African territories no allowance is made for this in the Government health returns, cases of venereal disease being loosely classified as either "syphilis" or "gonorrhoea." Much of such "syphilis" is in fact chancroid (and some of the "gonorrhoea" is non-specific urethritis). Mixed infection with chancroid and syphilis is common.

Although many of the cases can be distinguished by the use of dark-field and serum tests, such methods are not infallible when dealing with a group which is unlikely to attend for the necessary follow-up visits. Thus cases of seronegative primary syphilis in which the spirochaete is not found may easily be missed.

Treatment in the African, therefore, has to be geared realistically to a situation in which the dark field is often absent, but, if available, is often not used, both diseases coexist, and default is likely, always remembering that it is better to give the treatment for syphilis to a patient with chancroid than to give the treatment of chancroid to a case of syphilis.

#### *Treatment of Venereal Syphilis in the African*

For the treatment of early venereal syphilis single injection techniques employing a repository penicillin are those of choice. Procaine penicillin with aluminium monstearate (PAM) is a most useful drug, and single injections of 2.4 mega units will give a penicillinaemia for one week. If supplies are plentiful, the dose may be repeated or half of it given a week later.

Cases of latent syphilis in the African may be treated as for early syphilis. Cases of symptomatic late syphilis require more individual attention, but the same treatment may be given initially.

Obviously, if reliance is to be placed on single injection schedules it is essential that the PAM used is up to standard. An investigation was undertaken by WHO a few years ago of PAM manufactured by different countries (Guthe *et al* 1954). It was found that in a number of instances the preparations were faulty as regards the prolongation of serum level (due usually to a poor grinding technique with an insufficiency of penicillin particles of small size).

WHO then formulated a number of specifications for PAM preparations to be used in their mass treatment schemes and to be embodied in the International Pharmacopoeia. The most important of these is that a detectable serum level of penicillin must be obtained in the majority of subjects for 72 hours or more following a single intramuscular injection of 300,000 units. All medical officers treating syphilis in Africa should therefore ensure that the PAM preparation used *does* meet WHO specifications. Currently even more prolonged serum levels are being obtained with DBED and Benethamine penicillins, and these may be used in the future or when PAM of WHO specifications cannot be obtained.

Although the treatment outlined has been that for syphilis, one must budget for the situation in which patients with chancroid and mixed infections may be similarly treated. PAM is fairly suitable for this purpose, and failures to treatment can then be given sulphonamides. Willcox (1950) treated 99 Africans suffering from genital sores, of whom 19 were considered to have chancroid uncomplicated by syphilis, and the remainder syphilis with and without chancroid, with single injections of 2.4 mega units of PAM. Additional sulphonamides were required in 11 cases.

There is considerable administrative advantage in using this treatment for all Africans with genital sores in places where the dark-field and serum-testing facilities are lacking. Those cases, usually of chancroid, which do not respond may then be treated with sulphonamides. Only a few cases, usually due to granuloma venereum, will remain unaffected.

In theory the follow-up of the treated case of syphilis in the African should be as for the

European, and this should be attempted where feasible more in the hope of educating the community than from the immediate practical results expected.

*Contact Tracing.*—Every effort should be made to secure the contacts of cases of infectious syphilis for investigation. It is the author's considered opinion that these persons should be treated with penicillin irrespective of the clinical or serological evidence of the disease. Many such contacts are in fact prostitutes, and some do come to the clinics to-day. For them, especially, a single injection of 2.4 mega units of DBED penicillin, which will provide serum levels usually for two weeks—and in a few cases for as long as a month—is especially valuable.

When, as happens in some areas, a relatively small and defined body of women satisfies the sexual needs of a large community of men, there is much medical and economic justification for repeating these injections every 2-4 weeks.

A very strong case can be made out for the employment of professional social workers whose sole duties are concerned in the bringing in of female contacts to the clinics. They should, to achieve the maximum public health results, concentrate on the consorts of patients with early infectious syphilis. In urban areas of Africa, as in nowhere else, such efforts would be rewarded by rich dividends. African personnel should be trained for this work.

*Treatment of Non-Venereal Syphilis in the African*

The management of non-venereal syphilis is even more a community affair. Much experience of treating the treponematoses (endemic syphilis and yaws) has been obtained in the world-wide campaign of the World Health Organisation, in which already over 13 million persons have been examined and 3½ millions treated with penicillin.

Certain basic principles for mass campaigns have now been evolved. It is useless just to treat established cases from fixed centres, but the whole population must be examined rondavel by rondavel, kraal by kraal. Not only must

established cases be treated, but all household contacts of all ages, and school contacts also—some say all children of school age—must be treated even in the absence of signs of the disease.

Moreover the area must be revisited after 6-12 months and the whole population again examined and similarly dealt with, so that incubating cases, relapses and new cases introduced from outside the area can be prevented from reactivating the focus.

This process must be repeated until the situation is such that the existing medical organisation is capable of dealing with the residue. Such methods have been strikingly successful in eradicating the endemic syphilis from Bosnia (Grin, 1953) and a campaign is currently commencing against the endemic syphilis of Bechuanaland.

Such campaigns, obviously, require special planning, personnel and equipment, and a considerable reorientation of the conventional medical approach to the disease.

SUMMARY AND CONCLUSIONS

1. The modern treatment of gonorrhoea and syphilis in the European has been outlined.
2. In Africa, venereal diseases represent an individual problem in the European and a community problem in the African.
3. The circumstances which dictate a somewhat different approach to the management of these disorders in the two races have been considered, and realistic schedules of treatment to suit these circumstances have been outlined.

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