XIV. THE PRESENT-DAY TREATMENT OF THE VENEREAL DISEASES

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It is common knowledge and almost universal experience that, since the introduction of the antibiotics, particularly penicillin, there has been a marked decline in the prevalence of the venereal diseases. In 1947 there were 5,318 new cases registered at the municipal clinics in Cape Town; in 1952 the figure was 3,317. None of these drugs suppress sexual activity, but by cutting short the period of infectivity they *tend* to lessen the incidence rate of venereal disease and prevent the occurrence of those complications for which special procedures and skill were necessary. Moreover, the extensive use of penicillin throughout the world in numerous and varied clinical conditions is no doubt suppressing much incubating venereal disease or curing latent cases.

Though specialization in this field will probably cease with the present generation, the experience and knowledge of the present-day venereologist should not be too lightly discarded.

The invitation to write this article contained the suggestions that the views put forward should be based on personal experience, should be lucid in presentation and, if need be, dogmatic in expression. An attempt will be made to confirm to these desiderata. None the less, the statements advanced here fairly represent the opinions of fellow-specialists in this field. Minor personal preferences of course exist, but the guiding principles conform to the accepted standards of the World Health Organization and to those of specialist workers.

A short summary of the symptomatology of the venereal diseases is given with suggestions about the proper procedure to adopt in each case. While it is easy to give counsels of perfection and difficult to carry them out, they should always remain as a standard to maintain wherever possible, and to modify only to the demands of circumstances which cannot be overcome.

Wherever a postal service exists specimens can be submitted for examination—as they should, since the venereal diseases are the subject of special legislation imposing obligations on the patient as well as on his medical attendant.

CLINICAL FEATURES

The signs and symptoms of the venereal diseases are usually associated with the following:

(*a*) urethral discharged in the male; urethral and vaginal discharge in the female.
(*b*) Lesions ('sores') on the external genitalia.
(*c*) Skin eruptions.
(*d*) Various signs such as enlarged glands, tumours, disease of the cardiovascular and central nervous systems, bone lesions, etc.

These various syndromes will be considered briefly

so that the practitioner will have some guide to the proper procedure to adopt.

(*a*) *The presenting lesion is a urethral discharge with an additional vaginal discharge in the female.*

The male urethra is a popular throughfare for various micro-organisms, and it is a great error to assume that the gonococcus is always the intruder. As a matter of fact, non-gonococcal urethritis is almost as common nowadays as the gonococcal type. Such infections may be due to organisms other than the gonococcus, e.g. *B. coli*, *Pseudomonas*, *Proteus vulgaris*, etc., some of which are insensitive to penicillin. The practitioner must not be surprised therefore at his failure to cure such cases if he does not take the trouble to satisfy himself that the urethritis in question is not due to the gonococcus. Trichomonads cause a urethritis in the male, usually the spouse or sex partner of a female with an undetected or uncured trichomonas vaginitis. Abacterial urethritis may be due to some viral condition, or to a stricture, or to local traumatic or pathological conditions, or to disease of the upper urinary tract. No attempt is made here to give a list of all the possible causes of urethritis; but enough has been said to warn against the bad habit of giving penicillin blindly, and of diagnosing gonorrhoea without justification, at the risk causing much unnecessary unhappiness and domestic strife.

Procedure. In urethritis a smear should always be taken. For this purpose the urethra should be milked forwards, by patient or examiner, starting from the perineum.

In the female, on the gloved finger being placed in the vagina and the urethral orifice pressed gently upwards and backwards, any pus present will show itself at once. A speculum should be passed, and if an abundant frothy discharge is seen at the fundus and, after swabbing, the cervical orifice looks free from any discharge, trichomaniasis can be suspected. In the search for the gonococcus material must be taken from the cervical canal, and if the examiner is not going to stain and examine the smears himself, he can mount both the urethral and cervical specimens at either end of a slide distinguished by the letters C and U. Slides so made are dispatched to the laboratory or—if the practitioner does his own microscopic work—are stained by Gram's method and the diagnosis 'gonorrhoea' only made when large groups of gram-negative, bean-shaped diplococci are seen—preferably within a leucocyte. He need not wait for the diagnosis to be reported from the laboratory before commencing treatment (detailed in a latter portion of this article), but the label of a venereal disease must not be attached to a person without cause. If it is impossible to have a smear examined, the patient and sex contacts should receive appropriate treatment without the diagnosis 'gonorrhoea' being mentioned.

In the 'typical' case, i.e. where an abundant thick, creamy discharge appears within a week of an isolated sex exposure, the clinical diagnosis of gonorrhoea is likely to be correct; but even under these conditions it should not be recorded as a venereal disease without proof—especially in married persons. In South Africa proof usually implies diagnosis by smear alone; in other countries culture is insisted upon. Whenever possible and practicable the practitioner should avail himself of skilled laboratory facilities to detect the offending organism and its susceptibility to the various antibiotics.

(*b*) *The presenting lesion is a 'sore' on the genitalia.*

This may be a sore, papule or other sign; whatever it is the patient must be examined thoroughly, the whole skin and mucous membranes inspected, the glands palpated and—in the adult female—a speculum passed.

Syphilis should always be suspected and no penicillin ever given until the decision is reached to treat the patient for this disease. This decision should never be lightly made; the only unequivocal proof is finding the *Treponema pallidum* in the suspected lesion, and this investigation should be carried out wherever possible. Clinical appraisal is a good second best when examination discloses an oval, or round, indurated sore accompanied by local adenopathy. Chancroid, herpes, epithelioma, lichen planus are some of the many conditions which may be located on the external genitalia. The Wassermann test does not always help, for it may be negative in early syphilis, or positive owing to an underlying condition not associated with the lesion under consideration.

Procedure. This will vary with the type of case; as for example between the promiscuous unmarried male and the married person for whom the diagnosis of syphilis if of great domestic and social import. Ideally, dark-ground examination should be done on every case that at all resembles syphilis. A specimen of blood must be taken for a Wassermann and other tests and the patient examined thoroughly so as to exclude other conditions, e.g. scabies, lichen planus, etc. Secondary syphilitic lesions must not be forgotten here, nor herpes, which seems to be on the increase, nor, in the isolated lesion, carcinoma.

During the waiting period, while investigations are being carried out, saline lotions may be used locally and sulphonamides given by mouth; but *no penicillin or other antibiotics, some of which have treponicidal properties, should be given.* Sudden improvement and/or retrogression during sulphonamide therapy points to a chancroidal infection. If it is decided to treat the case as syphilis, then contacts should be sought and the patient warned of his obligations under the Public Health Act. But beware of diagnosing syphilis without taking into account the implications of such a verdict!

(*c*) *The presenting lesion is an eruption on the body.*

Practitioners should remember that *a vesicular or bullous eruption in an adult for all practical purposes, is never syphilis.* Intense itching, too, is against syphilis. Naturally, the patient must be carefully examined all over, the mucosae inspected and the glands palpated. Enquiries should be made about the taking of drugs and the sexual history should be ascertained. Severe constitutional signs and symptoms are not a feature of syphilis. On the other hand, the Wassermann reaction has a high diagnostic value: a positive reaction

makes the diagnosis of a generalized eruption as syphilitic at least a probability; a negative practically excludes it.

Procedure. Take a specimen of blood for a Wassermann and other serological tests for syphilis. Specimens may be sent through the post provided the precautions and suggestions of the laboratory are observed. If special circumstances warrant, a second opinion is desirable, since the diagnosis of secondary syphilis can be of great significance to the patient. The doctor who takes the responsibility of treating such cases before laboratory or expert confirmation is obtained, may find his clinical judgment supported by the immediate and dramatic improvement to penicillin. On the other hand, he may to his chagrin observe no improvement, and he has now introduced an element of confusion into a problem where clarity, if not certainty, should prevail.

(*d*) *The presenting lesion is a chronic ulcer, discharging inguinal glands, tumour, or some symptom showing involvement of the cardiovascular or central nervous system.*

Two of the recognized venereal diseases—lymphogranuloma inguinale (lymphopathia venereum, poradenitis) and granuloma venereum—are relatively rare in South Africa, the latter more so than the former. Even chancroidal infection is not common, and the late skin, bone, cardiovascular and nervous manifestations of syphilis are certainly much rarer today than they were, say, 10 or 15 years ago. Still, they do crop up from time to time. Enlarged, broken-down glands with multiple sinuses, in the groin chiefly, may be a fairly early manifestation of lymphogranuloma inguinale. This is a disease of great chronicity presenting in its later stages many puzzling clinical pictures such as rectal stricture and elephantiasis of the genitalia accompanied by ulceration. There is some evidence that the causal virus may go further afield and produce pathological changes in organs remote from the portal of entry.

Large, foul ulcerations of long standing on the genitalia, in the folds of the groin or stretching backwards into the perineum suggest the possibility of granuloma venereum. The disease is due to a small gram-negative oval body, the so-called Donovan body, which is found by appropriate staining in the cytoplasm of large mononuclear cells. Very few cases have been reported in South Africa—possibly because they have not been recognized.

Any chronic ulceration or skin lesion may be due to syphilis. At times even the experts are confused. In a case recently seen there was a very extensive, untreated tertiary syphilide of 11 years standing! Such lesions, however, are rare in Europeans, who are usually prompt in seeking medical advice.

Procedure. The Frei intradermal test for lymphogranuloma will suggest itself in cases of discharging inguinal glands, elephantiasis or pachydermatous conditions of the genitalia and anal margins. Note that the large cauliflower mass of warts frequently seen in these sites are in quite a different category. The test, though undoubtedly useful, has the disadvantage of all such intradermal tests, viz. doubtful reactions and the persistence of positive reactions long after the disease has ceased.

Finding the so-called Donovan bodies in large monocytes is diagnostic of granuloma venereum (granuloma inguinale). The technique advised is to excise a piece of the suspected lesion and to smear a microscopic slide with the freshly-cut under-surface of the tissue wedge. Special stains, such as Leishman's, Giemsa's or Wright's, have to be used, and the practitioner is hardly likely to undertake the task. Specimens can, however, always be sent through the post to a laboratory.

With chronic skin lesions and unexplained subcutaneous or visceral tumours, the Wassermann test is of limited assistance, because conflicting serological findings are unfortunately all too common. A positive reaction may be only coincidental. Nevertheless immediate treatment with penicillin is justifiable, particularly in the face of some threatened catastrophe such as perforation of the palate. Its dramatic healing effect on bizarre skin conditions or visceral tumours suggests syphilis as a likely cause, but the wise practitioner will always carry out a series of Wassermann tests and will never neglect to send a specimen for histological examination where a malignant growth is possibly at fault.

In cases of cardiovascular and nervous-system disease it is advisable to have expert opinion. The attendant doctor is reminded of the absolute importance, in suspected cases of nervous syphilis, of an examination of the cerebrospinal fluid, which will distinguish between the progressive, active case and the patient who has characteristic, but merely residual, signs of a burnt-out process. Similarly, a leaking aortic valve may persist though the disease which caused it may be cured. It is precisely in such cases that the specialist should be called to give expert guidance.

TREATMENT

The treatment of the venereal diseases—assuming that either a definite diagnosis has been made or that the circumstances warrant no delay in instituting treatment—can be carried out in accordance with the schedules outlined in the following text.

A. *Gonorrhoea.*

Penicillin by injection is the drug of choice. A dosage of 300,000 units will cure over 90% of cases, provided the therapeutic level in the blood is maintained for 8-12 hours; this means employing one of the long-acting preparations. Certainly 600,000 units will cure all uncomplicated gonorrhoea in both sexes. So far no strain of naturally-occurring gonococci has been found resistant to penicillin. This, however, is not true of streptomycin; strains resistant to that drug have been reported.

Penicillin is suitably given as PAM, the oily suspension of the procaine salt with aluminium monostearate. Streptomycin (or di-hydrostreptomycin) can be given in 1 g. doses by intramuscular injection, alone or in combination with penicillin. For simple, un-

complicated gonorrhoea, then, either of the following suffice:

(i) PAM: 300,000-600,000 units by single intramuscular injection.
(ii) Streptomycin: 1 g. by intramuscular injection.
(iii) Penicillin and streptomycin: usually 400,000 units of the former and 0·5-1 g. of the latter, as one combined injection.

If there are any lesions suggestive of syphilis present it is advisible *not* to give penicillin until this disease is diagnosed or excluded. In such cases streptomycin plus sulphonamides by mouth, and saline locally on the suspected syphilitic lesion, is sound interim therapy. On the other hand, if the two diseases, gonorrhoea and syphilis, are present, or the practitioner is satisfied that they are, then a curative dose of penicillin for the latter automatically cures the former.

Gonorrhoea with complications such as epididymitis, arthritis (rare nowadays), iritis etc. requires large doses of penicillin, e.g. 2-5 million units, perhaps more, given in daily doses of 300,000-600,000 units in the form of some slowly-acting preparation. Vulvovaginitis in children due to gonorrhoea responds well to the doses used in adult cases.

The danger of masking an underlying syphilis with such doses as 300,000-600,000 units of penicillin has been exaggerated; but, in any case, *it is sound, commendable practice in treating acute gonorrhoea to give such a large dose of a long-acting penicillin*—1·2 *m. PAM—that any syphilitic infection acquired at the same time may thereby be eliminated.* A specimen of blood for the Wassermann test should always be taken at the first visit.

Tests for cure are not necessary in the early, uncomplicated case, but the patient should be kept under observation for at least 3 months, with a further Wassermann test at the end of that time. Patients treated for complications of gonorrhoea should have repeated tests for the presence of the gonococcus in the natural secretions, urine, prostatic fluid, etc. The culture test, so widely used overseas, is not exploited enough in South Africa.

Persistence of discharge does not mean failure to cure, since organisms unresponsive either to penicillin or streptomycin may be the cause. Such cases will have to be treated either with sulphonamides or with the more expensive tetra-cycline preparations.

B. *Chancroid or Soft Sore.*

This disease is usually diagnosed by exclusion. The sulphonamides are very useful; 1 g. 4 times daily for 5-7 days usually suffice. This course may be repeated. Failure to show signs of healing suggests some other condition, e.g. syphilis, malignancy, etc., when appropriate steps must be taken to confirm or exclude these suspicions. Suppurating buboes, if present, will have to be opened in most cases.

Herpes of the genitalia can cause confusion. This condition is not rare. First there is itching and burning, and then a few small vesicles appear, which break down and coalesce. Bland local treatment is usually all that is required. Recurrences are common. Follow-up in these instances should be for at least 3 months, with serological tests to exclude syphilis.

C. *Lymphogranuloma inguinale.*

The sulphonamides are also useful in this disease. (The prefix 'lympho-' distinguishes this virus disease from the granuloma caused by the 'Donovan bodies'). Doses of 1 g. 4 times daily for 10-15 days, continuously or in successive courses with short intervals, is given in early cases. Members of the tetracycline group, e.g. Aureomycin, Chloromycetin, Terramycin, give satisfactory results in doses of 0·5 g. orally 4 times daily for 5-10 days, or longer if healing is delayed.

Serological tests for syphilis should be made at intervals for at least 3 months after cure. Surgical or other intervention will suggest itself in certain cases.

Granuloma Venereum

This rare disease, diagnosed with certainty only by finding the causative organism, the so-called 'Donovan bodies', was formerly very refractory to treatment. Today, fortunately, it responds well to the antibiotics with the exception of penicillin, so that the mutilating effects of this chronic ulcerative malady are prevented.

Streptomycin (or the di-hydro salt) is effective, given in daily 1-2 g. doses by intramuscular injection for 7-10 days, or longer, according to the response obtained. Aureomycin, Terramycin, Chloromycetin have all been used successfully in doses of 0·5 g. 4 times daily. The duration of this therapy will vary with the case. Resistance or relapse require prolongation of treatment, or a changeover to another drug.

TREATMENT OF SYPHILIS

Penicillin is the drug of choice in all types of syphilis. Nothing is gained by using arsenic or bismuth, though in some countries both are still given in addition to penicillin. Some of the other antibiotics have treponemicidal properties in the following order of merit: Carbomycin, Erthryomycin, Aureomycin, Terramycin, Chloromycetin—the last 3 being almost bracketed together. As sensitivity to penicillin is on the increase, we may be faced any day with the necessity of either combating the hypersensitivity or using an alternative drug.

PAM is the penicillin preparation most widely used. It is convenient, efficacious and relatively cheap. There is, however, evidence from the analysis of large numbers of cases that di-benzylethylene-diamine di-penicillin (Bicillin, Wyeth) gives better results.

Penicillin by mouth cannot be recommended, since the most cooperative of patients will find it hard to adhere to the schedule of treatment.

(*a*) *Primary Syphilis. At least* 2·4 M should be given, but there seems to be no need to exceed 4·8 M. Any of the following schedules is suitable: 2·4 M by single injection of Bicillin, or 1·2 M of PAM, or Bicillin, on days 1 and 8; or 1·2 M of PAM or Bicillin on day 1, and thereafter 0·6 M or 0·9 M of PAM at 3-6 day intervals until the total dosage decided on has been given.

The post-treatment period of observation should

be 2 years, with blood tests at intervals of 3-6 months and an examination of the spinal fluid in the 2nd year. Few patients will submit to this, but the doctor should record this as his advice. In a few cases the Wassermann test may remain positive even after the 9th month. Repeat treatment is called for if it is positive at the 12th month or there is a reappearance of syphilitic lesions, which is not necessarily a relapse.

(*b*) *Secondary Syphilis.* A dosage of 4·8 M will give a high percentage of cures. Nothing is gained by giving, say, 2-3 times this dose; doubling the dose does not halve the failure rate.

The total dosage can be given by using either PAM or Bicillin (or other respository preparations) in weekly or twice-weekly injections. Since an adequate penicillin level persists for several days after a single injection of these drugs, daily injections are not necessary. A convenient schedule is 1·2 M of PAM weekly for 4 weeks, though a 5-6 day interval would serve. The interval between injections is dependent on the duration of an effective therapeutic level of penicillin in the blood. The post-treatment observation period is the same as in primary syphilis. Serological, spinalfluid and clinical negativity at 2 years, for all practical purposes, indicates cure.

(*c*) *Late and Latent Syphilis,* excluding syphilis of the central nervous and cardiovascular systems. A total dosage of 4·5—6 M is adequate, using either of the long-acting preparations in weekly doses. Not all cases diagnosed by blood tests alone are, in fact, syphilis; many would prove to be 'false positive' reactors if the *Treponema pallidum* immobilization test were available.

Sero-negativity may take a long time to appear; many cases may remain permanently positive to the Wassermann and other tests, though completely cured.

(*d*) *Cardiovascular Syphilis.* Large doses of penicillin are recommended—8-10 M. The long-acting preparations already mentioned are ideal for this purpose, given in weekly doses of 1·2 M, though shorter time-intervals are not prohibited.

Investigations prove that histological retrogression of the syphilitic lesions occurs, and that the dangers of a Herxheimer reaction have been much exaggerated. Medical and surgical measures in cardiac failure or in aneurysm have an important role.

(*e*) *Syphilis of the Central Nervous System,* diagnosed by clinical observation and examination of the cerebro-spinal fluid. The long-acting preparations in doses of 10-12 M give excellent results. The ultimate prognosis depends on the amount of irreversible damage to the nervous system. Herxheimer reactions following treatment may be dangerous. Old-standing optic atrophy will not improve, but many paretics have resumed useful and exacting occupations. Prolonged follow-up studies in these and cardiovascular cases are necessary. Specialist advice, and frequent lumbar puncture and X-ray examination of aortic cases are necessary for a proper assessment of healing. Penicillin alone is efficacious; hyperpyrexia induced by any means, including malaria, seems to give no better results than the drug acting alone.

(*f*) *Syphilis in Pregnancy.* Complete protection of the foetus is achieved by giving 1·2 M of PAM (or other slow-acting penicillin) once weekly for 4 weeks. It should be given as early in pregnancy as circumstances permit. Failures are seen only in mothers with early syphilis who do not complete the schedule. In such cases treatment of the mother and child should be carried on during the puerperium. Further treatment for syphilis for the mother is not necessary in the majority of cases.

(*g*) *Congenital Syphilis.* In the new-born infant, 200,000 units per lb. of body weight as a total dose is curative. It can be given in twice-daily injections of 100,000 units of aqueous penicillin or in daily injections of 200,000 units of procaine penicillin (for convenience sake, all infants can be regarded as weighing 10 lb.). This ensures adequate treatment during the lying-in period. In older infants the oily suspension of penicillin, e.g. PAM, can be used—as in late congenital syphilis—the dosage being adjusted to the age of the patient. In practice adult doses can be given after the age of 5 years. Congenital syphilis must not be diagnosed on the result of one positive Wassermann test.

(*h*) *Prophylaxis* or abortive treatment for syphilis. It has been shown that 1·2 M of a long-acting penicillin, given in a single dose during the incubation period, will protect against syphilis. Not all physicians will agree as to the correctness or advisability of treating a disease whose presence is merely conjectural. The decision to do so or not is a personal problem for each practitioner, though the patient's preference should be sought. Should one 'wait and see' or forestall the event? If treatment is given the patient should be advised to remain under observation for at least 6 months.

Repeat Treatment. In cases where treatment had failed—as shown by progression or a sudden sustained rise in the Wassermann titre—a course of double the dose previously used should be given. Apparent relapse may be a reinfection. The author has seen 3 primary chancres occurring successively in one patient some months after the preceding attack had been cured.

Time and Dosage. The literature abounds with variations of the time and dosage factors, but if the practitioner gives the recommended total in a time period of not less than 10 and not more than 30 days his results will be good. There is nothing magical in the weekly dose; it is largely a matter of convenience. He should not judge his success or failure by the time it takes for the blood test to become 'negative'; this does not happen like the sudden descent of a lift.

In pursuit of clarity individual references have been omitted, but acknowledgment is thankfully made here to all those, who by the publication of their clinical observations and laboratory findings, have built up our knowledge of the present-day successful treatment of the venereal diseases.