Changing patterns of treponemal disease

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It has been postulated that *T. pallidum* of syphilis arose originally from free-living treponemes in mud, of which *T. zuelzerae* still remains representative (Veldkamp, 1960). These organisms then came to be carried commensally by man, as are the dental treponemes today. Disease syndromes then developed as natural selection ensured the optimal survival of mutants most likely to produce the lesions best suited for onward transmission from host to host in the prevailing environment (Willcox, 1972).

The three treponemes which are pathogenic to man are *T. pallidum*, the cause of venereal and non-venereal syphilis, *T. pertenue* of yaws, and *T. carateum* of pinta, all of which have a similar morphology and evoke so-far indistinguishable antibodies in infected persons. In animals, *T. cuniculi* has evolved separately in the rabbit in which it is responsible for a naturally occurring venereal disease (cuniculosis), while a more recently discovered member of the group, *T. Fribourg-Blanc*, has been isolated from monkeys in yaws areas (Fribourg-Blanc, Niel, and Mollaret, 1963).

Of the treponematoses affecting man, venereal syphilis is ubiquitous, yaws is a disease of the tropical belt, endemic syphilis is encountered in adjacent dry areas, while pinta is confined to the Central and South Americas.

Evolution of pinta

It has been postulated (Cockburn, 1961; Hackett, 1963) that pinta was the first treponematosis to evolve within the Afro-Asian land mass, from which it gained world-wide distribution, finally persisting amongst underprivileged peoples in the remoter areas of the Central Americas and the Northern part of the South American continent—being most prevalent today in Mexico, Colombia, Peru, Ecuador, and Venezuela. Some 3 million cases of pinta were believed to exist 20 years ago (Guthe and Willcox, 1954).

The understanding of this disease owes much to the pioneering work of Herrejon (1938) and later of Varela and others in Mexico (Rein, Kitchen, Marquez, and Varela, 1952); Guimaraes, Rodriguez, Costa, Silva, and Padilha Gonçalves in Brazil; Leon Blanco in Cuba; and Sainz in Ecuador.

In Venezuela it has been studied by Iriate, Rossi, and others but particularly by Dr. Martin Vegas, Honorary President of this Congress, and its Coordinating Secretary, Dr. Rafael Medina. Dr. Medina has been described (Smith and others, 1971) as 'the world authority on the non-venereal treponematoses having had more experience with clinical yaws and pinta than virtually any other living physician'. He has contributed much to our knowledge of cross-immunity between the treponematoses (Medina, 1967), and with Dr. Kuhn and colleagues in Atlanta has successfully established the disease in the chimpanzee (Kuhn, Medina, Cohen, and Vegas, 1970).

The lesions of pinta virtually only affect the skin (apart from the odd juxta-articular node) although a case with co-existing interstitial keratitis has been described (Smith and others, 1971). It starts with an initial lesion, and subsequently satellite or more remote skin lesions (pintides) of various hues develop, which may be pink, brown, blue, and black, finally becoming white or achronic. It is spread by direct skin contact amongst poor peoples, particularly in the lower age groups. Half of the series of Rein and others (1952) comprised persons below 15 years of age.

Evolution of yaws

It has been considered that yaws evolved from pinta as a humid warm environment developed in Afro-Asia. The new climate, resulting in much local moisture from sweating, favoured the production of exuberant skin lesions containing vast numbers of treponemes such as are found in the papilloma and other infective manifestations characteristic of framboesia or yaws (Hackett, 1957). The surface lesions of
yaws, like those of pinta, may remain infective for long periods of time. The absence of clothes with resultant liability to trauma, which facilitates the entry of the organism, and person-to-person contact of sweaty skins in a tropical environment, facilitated its rapid spread amongst primitive communities and its very contagiousness ensured that it was mainly a disease of childhood.

Through the centuries yaws has been one of the world's most prevalent infections, which for practical purposes had been contained between the Tropics of Cancer and Capricorn although with modern travel the occasional case may be encountered in temperate zones (Fig. 1). Before the WHO-assisted mass campaigns were extensively mounted, it was estimated that some 50 million cases existed, half of them in Africa (Guthe and Willcox, 1954). In these campaigns against the endemic treponematoses organized by WHO in 46 countries, the prodigious total of 160 million people has been examined and 50 million treated with penicillin as clinical cases of yaws or endemic syphilis, or as latent cases or contacts (Guthe, Ridet, Vorst, D'Costa, and Grab, 1972). The incidence of the disease has been reduced to extremely low levels in many areas (e.g. from 2.95 to 0.005 per cent. of clinically active cases in Western Samoa), although continued seroreactivity to tests with treponemal antigens has suggested that the disease continues to be transmitted in the community, possibly at a subclinical level. It is stated that early infectious cases are now virtually eliminated from Venezuela.

Yaws, unlike pinta, can have more serious complications remote from the skin, such as early osseous involvement and late gummatous manifestations. Although not thought to have cardiovascular or neurological complications, or to be transmitted to the fetus, in the so-called Caracas project, Smith and others (1971) found ocular abnormalities, raised immunoglobulin levels in the cerebrospinal fluid, and treponemes in the aqueous humour of some patients with late yaws.

Evolution of endemic syphilis

A further development followed in the more arid regions bordering on the yaws areas where the still very warm but now dry climate, frequently cold at night, necessitated the wearing of clothes, thus preventing skin-to-skin transmission. Only organisms producing lesions of the mucous membranes could now survive by means of direct transmission by kissing, or indirectly through the intermediary of common eating or drinking vessels (Grin, 1953) or fingers (Guthe and Luger, 1957), although condylomata lata and skin lesions are encountered, particularly in moist areas. Because infection tended to occur before puberty, sexual spread was seldom noted as by the time the children were old enough for sexual intercourse they had already acquired the disease. In all of the endemic treponematoses, there is the vicious circle of poverty creating disease and disease creating poverty (Fig. 2).

Endemic syphilis acquired prominence when it was described usually in desert or near-desert regions in a number of Middle-Eastern countries under the name bejel (Hudson, 1928; Csonka, 1952) or balash. It is also found today in Africa in countries

FIG. 1 Primary dark-field positive yaw on ankle of West Indian child who had been resident in London for only a few months
bordering on the Sahara desert in the North (Basset and Boiron, 1965), and it has also been found in the South adjacent to the Kalahari desert in present-day Rhodesia—where under the name *njouera* it was observed by the author when making a survey (Willcox, 1951a, b), and in adjacent Botswana (Murray, Merriweather, Friedman, and de Villiers, 1956). It also still exists in the Karoo in the Transvaal (Du Toit, 1969) and in the North-Western Cape areas, and has recently been observed around Bloemfontein (Scott and Lupus, 1973). In these areas gangosa-like lesions and other late complications may be encountered. The 'give-away' sign of its existence is the finding of a nipple chancre in a mother caused by her infected child.

Foci of endemic syphilis were present in Europe, in Bosnia, Yugoslavia, even after the second world war, but have since been successfully eradicated by mass campaigns (Grin and Guthe, 1973). Between the wars it extended over wide areas of the Southern U.S.S.R., Turkey, and the then Palestine. There are also many historical examples, including the sibbens of Scotland, the button scurvy of Ireland and the radesyge of Norway (Lancereux, 1868).

**Emergence of venereal syphilis**

Venereal syphilis develops from endemic syphilis as social advance limits transmission between children; as the children grow up they are then susceptible to its sexual transmission (Willcox, 1960). With this trend some unhygienic habits still persist (e.g. sharing of pipes and toothpicks, widespread mouth-to-mouth kissing, wet nurse practices, etc.), and both venereal and non-venereal syphilis exist together, the former being found in the older age groups in those who have not experienced the childhood infection. It is considered probable that endemic syphilis was once widespread in non-tropical regions including Europe, where it was recognized as a venereal disease only at the end of the 15th century, when Christopher Columbus and parts of the Americas were unfairly incriminated.

Like other sexually-transmitted diseases the incidence of venereal syphilis has been high in times of war, and the period during and immediately after the second war was no exception. The more settled conditions of peace and the introduction of effective treatment with penicillin led to a dramatic fall, but in the past 10 to 15 years numbers have again risen in many countries although in most they remain at less than one-tenth of the wartime peak.

**Continuing evolution of syphilis**

**EFFECTS OF DETERIORATING ENVIRONMENT**

Changes in the distribution, severity, clinical appearances, and other features of syphilis still continue as man's habits and environment alter for the better or worse, particularly since the introduction of penicillin and other antibiotics. The gradually extending process of urbanization has itself contributed to the waning of pinta, yaws, and endemic syphilis in many areas, but a reversal of this process is possible and is reported from time to time when social conditions deteriorate and infections once again occur among children.

Such a reversal from venereal to non-venereal syphilis has been recorded from a number of countries even in the penicillin era (Murrell and Gray, 1947; Fejer, 1948; Eisenberg, Plotke, and Baker, 1949; Rajam and Rangiah, 1952; Rees, 1954; Taylor, 1954). A more recent experience was described by Luger (1972); three children were infected in a crowded ex-barrack building in Vienna, although the room occupied by the family of nine also contained the luxury items of a refrigerator, television set, record-player, and two transistor radios.

With the present population explosion and increasing accommodation difficulties, including the unwelcome growth of shanty towns near to modern cities in many parts of the world, such small-scale reversals of treponemal evolution are to be expected from time to time.

**EFFECTS OF PENICILLIN**

**Action of penicillin**

This antibiotic acts during the growth and division of *T. pallidum* and related treponemes when the cross-linked chains of N. acetyl glucosamine and N. acetyl muramic acid, which form a matrix in the outer cell wall to contain the inner protoplast like
the outer skin of a football (Fig. 3), are breached by
the hydrolytic action of a lysozyme manufactured by
the organism (Fig. 4). The enlarging gap is restored

![Diagram](http://sti.bmj.com/content/50/3/169/fig3)

**FIG. 3** Mureine structure of T. pallidum cell wall after Pelzer (1967), Kern (1972), and Luger (1973)

by means of mureine precursors, which pass through
the cytoplasmic membrane of the protoplast to be
reconstituted through the action of several enzymes
including carboxypeptidases and particularly trans-
peptidase (Fig. 5). These enzymes affect the strengthen-
ing cross-bondings between the adjacent reforming
chains (Pelzer, 1967; Kern, 1972; Luger, 1973)
(Fig. 6).

By the affinity of penicillin for these enzymes,
particularly transpeptidase (Fig. 7), and by inter-
fering with the proper assembly and production of
the mureine precursors, the antibiotic prevents their
effective performance, thereby allowing the un-
affected lysozyme to continue to breach the cell wall
more quickly than it is being renewed. Internal
osmotic pressure will then cause the protoplast to
bulge through the rent in the outer casing and this
may ultimately burst or destroy the organism
(Fig. 8).

**Effectiveness of penicillin**

Penicillin has been shown to be effective in the
treatment of early infections with pinta, yaws, and
syphilis, both endemic and venereal, even in single
injections of the right preparation, notably procaine
penicillin in oil with aluminium monostearate
(PAM) and benzathine penicillin. There are no
signs that *T. pallidum* is becoming resistant to
tenicillin, although the inability to culture the
virulent organism in *vitro* makes precise assessment
of this point impossible (Schamberg, 1963).

The antibiotic has proved virtually 100 per cent.
successful in the incubation period, when it is widely
used for epidemiological treatment, and in seroneg-
itive primary syphilis; in seropositive primary and in
secondary syphilis the clinical results are excellent,
with re-treatment rates around 3 to 10 per cent., and
even then many such recurrences are probably
re-infections (Idsoe, Guthe, and Willcox, 1972).
Seroreversal of reagin tests is the rule, although the
treponemal immobilization and FTA-ABS tests may
continue to show reactivity which may or may not be
associated with persistence of the organism.

In the late infection gummata quickly heal and
good results are also obtained in neurosyphilis with
meningeal involvement. The outcome is less striking in parenchymatous neurosyphilis, in cardiovascular syphilis, and in complicated late congenital syphilis. In late latent syphilis, and indeed in late syphilis as a whole, seropositivity usually persists, although future complications are largely prevented.

Changes in the clinical pattern

There have been striking changes in the clinical manifestations of syphilis since the introduction of penicillin. Exuberant secondary lesions of skin and mucous membranes are now rare in many areas as are ulcerative skin lesions, and syphilis seems to be becoming a milder disease. This may be partly due to better nutrition and to better standards of hygiene which may well explain the decline in the prevalence of condylomata lata. However, it would not be unreasonable to suppose that the disease would become milder under 'antibiotic bombardment', as those strains of the organism which did not draw attention to themselves by provoking a marked host response would be those more likely to survive.

In the untreated disease approximately one-quarter of the patients used to undergo secondary infectious relapse (Gjestland, 1955) but today this is seldom seen. Likewise the total incidence of late complications are observed to fall wherever figures are compiled (Király and Causse, 1973). Gummata, which were at one time rife—especially when the incidence of early infection was high (Grin, 1953)—have virtually disappeared in many places; at St. Mary’s, where around 10 per cent. of the annual total of cases of early syphilis in England and Wales are encountered, a year or more may pass without a gumma being seen.

Early congenital syphilis has also become very rare, infection in the child having been prevented pre-natally or cured by penicillin while still in utero.

On the other hand, as penicillin is so quickly effective, re-infections with syphilis, at one time seldom encountered, are now common. In 1972, of 165 patients with early infectious syphilis seen at St. Mary’s, 22 (13.3 per cent.) had experienced 26 earlier attacks of the disease, in eighteen instances 3–11 years previously.

Persistence of treponemal forms

After very painstaking examinations Collart, Borel, and Durel (1962), in France, found treponemal forms in the lymph glands and cerebrospinal fluid of both penicillin-treated rabbits and humans who had not been treated early in the disease. They were later found in the cerebrospinal fluid of patients with untreated and treated late syphilis (Rice, Dunlop, Jones, Hare, King, Rodin, Mushin, and Wilkinson, 1970) and also in the aqueous humour (Smith and Israel, 1967) and more recently in Venezuela in patients with yaws (Smith and others, 1971). In only a few instances have these organisms been passaged in rabbits (Turner, Hardy, and Newman, 1969), but animals which have received passaged material may develop positive serological reactions to treponemal antigens and some of these have later been shown to carry treponemes (Yobs, Clark, Mothershed, Bullard, and Artley, 1968). This phenomenon could be related to the occurrence of such reactions amongst apparently normal children in yaws areas where near-eradication of the early clinical disease has apparently been achieved by mass treatment (Guthe and others, 1972).

While some doubt exists as to the significance of these organisms, e.g. whether they are derived from the mouth or other sources, the possibility remains that they are T. pallidum which have not been overcome by the low levels of penicillin commonly encountered in the fluids in which they are found or which may have survived as 'L' forms. These have been observed for some years with cultured treponemes in an unfavourable penicillin environment, and have also been observed in syphilitic tissues.
under the electron microscope (Ovčinnikov and Delektorskij, 1971).

Collart, Franceschini, and Durel (1971) believe that, if penicillin treatment is given during the first 3 months of a syphilitic infection, the treponemes disappear and there is no persistent reactivity to the TPI test. In infections of 2 or more years' duration, treponemes are still found after penicillin therapy. Lymph node transfer tests are positive in about 5 per cent. of such cases and cortisone therapy can activate some infections to produce clinical lesions. It is postulated that, in the latent period, the untreated host develops resistance so that the parasites vegetate in a commensal state, but the possibility cannot be excluded that under unknown biological conditions they may recover their virulence.

Venereal syphilis fills treponemal disease vacuum

In areas where near-eradication of yaws has been achieved by mass campaigns or by advancing civilization resulting in urbanization and the wearing of clothes, the herd immunity to syphilis due to past yaws is now removed and venereal syphilis tends to take its place. Such an event has been reported in Tahiti (Van der Sluis, 1969), Western Samoa (Guthe and others, 1972), and in New Guinea (Rhodes and Anderson, 1970; Bell, 1971).

The writer has had the good fortune to witness the situation in New Guinea. Here venereal syphilis has spread through the centre of the country along the new highway, in some parts a rough winding mountainous road, which extends from the port of Lae in the east to Mount Hagen in the Western Highlands.

Syphilis did not exist in this area up to 3 years or so ago, although gonorrhoea was prevalent, as was yaws until a mass campaign was undertaken in 1957. Today syphilis is being carried by the truck-drivers and the so-called ‘passenger-maris’, who prostitute themselves in the villages along the route and with the drivers in their journeys to and from more prolonged prostitutional activities in Lae.

The dissemination of the disease amongst the local population is in proportion to the prevailing sexual freedom, the spread being most extensive amongst the promiscuous Chimbu.

In the male, primary chancres are encountered in half the clinical cases, although many are atypical. Most of the remainder of clinically affected males show condylomata lata, sometimes in the axillae (Fig. 9). In the female, secondary condylomatous lesions are usual but primary lesions are sometimes observed. Secondary rashes are only occasionally encountered but maybe these by themselves do not prompt patients to seek treatment. The same applies to oral mucous patches.

Treponemes resembling T. pallidum can be found in the lesions. Donovoniasis (granuloma inguinale), of which the number of reported cases exceeds 40 per cent. of the reported cases of syphilis in adjacent Papua, need cause no confusion when the lesions are extensive, and can be confirmed by appropriate pathological tests, but may well do so when no darkfield tests for treponemes or smears for Donovan bodies are made.

Thus, even now, towards the end of the 20th century, an opportunity still exists of observing the rapid ‘syphilization’ of a susceptible community.

FIG. 9 Condylomata lata in the axilla (Courtesy of Bell, 1971)

EFFECTS OF MAN’S BEHAVIOUR

Population movement

All the treponematous have been distributed during mass migrations (Hudson, 1965), including religious pilgrimages (Hudson, 1963), and the African slave trade (Hudson, 1964). The role of the seaman and soldier in the spread of syphilis and other sexually-transmitted diseases is traditional. In modern times, of no less importance are migrations in search of work or fleeing from oppression, and latterly the ‘travel explosion’ of tourists (Guthe and Willcox, 1971).

It is estimated that there are now more than six million migrant workers in Europe alone, 20 to 30 per cent. of whom return to their countries each year to be replaced by more recruits. The world figure for tourists in 1971 was around 170 million, approximately three-quarters involving Europe (WHO,
1972). These movements, and the accompanying social circumstances, make possible a far greater international exchange of syphilis and other venereal diseases than ever before and, in the case of the tourist, the diseases may be brought home to the smallest towns and villages.

**Increased promiscuity**

With greater opportunity for the two sexes to meet without supervision and with the removal of previously inhibitory influences, there has been an increase in promiscuity, both heterosexual and homosexual. Quite small increases in promiscuity can have alarming effects in closed groups. In any 'closed' group of any size, it only needs one additional outside sexual link to introduce venereal disease, possibly to all. This can happen in groups in which half or even two-thirds have only one sexual partner (Willcox, 1973) (Fig. 10).

![Diagram 10](http://sti.bmj.com/

**Male homosexuality**

A noteworthy feature has been the much more frequently recognized association of early syphilis in males with homosexuality, particularly in the larger cities where homosexuals may be responsible for the bulk of infections. Although this would appear fundamentally to be a problem of the more permissive society and greater promiscuity amongst homosexuals, the observed increase is also due at least in part to the fact that such persons now feel freer to discuss their behaviour.

Homosexuality involves about 4 per cent. of adult males and a moderately active homosexual man may have contact with 100 different males each year (Gebhard, 1971).

It is presumed that the numbers of different contacts per unit of time has increased, although there are no firm data to support or refute this. Certainly anal chancre is a more commonly recognized presentation of early syphilis today, although it might be argued that previously they were frequently missed.

Although many individual physicians have presented data concerning the incidence of homosexual infections, there are few nation-wide data. One such study has been recently undertaken in the United Kingdom (British Cooperative Clinical Group, 1973), in which 176 clinics in 153 towns and cities participated and the cases included comprised 90 per cent. of the reported national totals of primary and secondary syphilis treated during the year, and 86·1 per cent. for gonorrhoea.

Of the total of 924 male infections treated, 532 penile infections were believed to have been heterosexually acquired and 172 homosexually; 220 infections were anorectal. Thus homosexuals were responsible for 42·4 per cent. The percentage was highest (45·9 per cent.) in England, those for Scotland and Wales being 13·5 and 9·5 per cent. respectively.

In England, outside London, the percentage of known homosexuals with early syphilis was 25·1, but reached 62·1 in the twenty participating clinics in the capital. In London four out of five of the homosexuals with syphilis were treated in but five clinics in the West End, where they comprised no less than 73·3 per cent. of infections compared with 37·2 per cent. in the other fifteen clinics. (Fig. 11).

![Diagram 11](http://sti.bmj.com/)

**FIG. 10** Diagram to show how a slight extra degree of promiscuity may cause a large increase in venereal disease

**FIG. 11** Percentage of homosexually acquired infections with primary and secondary syphilis in males

A similar pattern was seen in gonococcal infections (Fig. 12); homosexuals represented 9·8 per cent. of the total and 27·6 per cent. in the five clinics in the
West End of London. However, as approximately forty times as much gonorrhoea as primary and secondary syphilis occurred in males, gonorrhoea represents the greater numerical problem (Fig. 13).

It is difficult to explain why syphilis has lurked more commonly in the homosexual male than in the heterosexual female (where the chancre may also be concealed, e.g. on the cervix), unless it is agreed that greater promiscuity in terms of sexual partners over a period of time has occurred in homosexuals now that previously strong taboos have been removed from such behaviour in many countries.

Oral sexual contact
The influence of oral sex in relation to venereal disease has recently been highlighted by Bro-Jørgensen and Jensen (1971), who found gonococci in the throat of 6 per cent. of Danish men and 9 per cent. of Danish women, and by Hellgren (1971) who noted that fifty of 200 Swedish patients with urogenital gonorrhoea admitted to oral sex at their last intercourse.

Oral infections with syphilis remain relatively uncommon. Those which are found today are more likely to be associated with oral intercourse than with kissing, which was regarded as the usual method of contraction 25 years ago.

It has been thought likely that, possibly following the greater dissemination of pornographic and near pornographic films, the practice of oral intercourse is increasing in Western Society. In a recent series of 105 female gonorrhoea contacts seen at St. Mary's, 41·0 per cent. admitted to oral sex with the partner or partners recently involved. (Rectal intercourse had also occurred in 18·1 per cent. of patients—Cornthwaite, Savage, and Willcox, 1974). But here again it must be noted that 20 years ago Kinsey, Pomeroy, Martin, and Gebhard (1953) found that, of younger females who had had some but not extensive coital experience, 16 per cent. had indulged in oral stimulation of the male genitalia as had 43 per cent. of those with more extensive experience. The latter figure (which reached 62 per cent. amongst the more educated) varied little from the 38 per cent. noted in those born before 1900.

In view of the success of a recent film in the U.S.A., the report is awaited of the first case of a chancre at the lower end of the oesophagus!

Other behavioural factors
Other changes in the presentation of syphilis have been brought about by new industrial and other practices. No longer do oral chancre occur in glassblowers, although these were once not so uncommon (Royal Commission on Venereal Diseases, 1916). An interesting recent presentation is that of double chancre arising in the vasectomy scars of a patient who had cooperated in the Indian sterilization programme and who had had a night 'on the town' shortly afterwards (Bai, 1973) (Fig. 14).

Summary and conclusions
(1) The evolutionary patterns of the treponematoses, occasioned by environmental circumstances, from pinta and yaws through endemic to venereal syphilis are outlined. A reversal from venereal to endemic syphilis may occur should social conditions deteriorate.

(2) Changes are still occurring today in the patterns of venereal syphilis, particularly as a result of the introduction of penicillin and of human behaviour.

(3) The mode of action of penicillin and its effects in the various stages of syphilis are outlined. The significance of the treponemal forms found in cases of treated late disease is considered, but notwithstanding these the practical results obtained by penicillin treatment remain excellent.
(4) In developed countries today, syphilis is apparently becoming a milder disease with fewer exuberant lesions, a low incidence of previously common secondary relapses and gummata, and a much reduced incidence of other late manifestations. On the other hand, re-infections and ano-rectal infections have become more common. For this a number of factors are responsible, including better nutrition, better hygiene, and above all the discovery of penicillin, treatment with which would be expected to tend towards the removal of the more virulent strains leaving the more insidious.

(5) Behavioural patterns have also contributed, especially in relation to ano-rectal infections. Data concerning homosexual infections and oral intercourse are presented.

(6) Doubtless, as long as human behaviour changes and the environment evolves, these alterations will be reflected also in the patterns of treponemal disease.

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Modifications des aspects des treponematoses

SUMMARY

(1) On décrit l'évolution des aspects des treponematoses dues aux circonstances de l'environnement, menant de la pinta et du pian à la syphilis vénérienne en passant par la syphilis endémique. De vénérienne, la syphilis peut prendre le type endémique si les conditions sociales se détériorent.

(2) Les aspects se modifient aujourd'hui encore pour la syphilis vénérienne, ceci résultant particulièrement de l'introduction de la pénicilline et du comportement humain.

(3) On examine le mode d'action de la pénicilline et ses effets aux divers stades de la syphilis. On examine la signification des formes treponémiques trouvées dans des cas traités tardivement mais, quoi qu'en soit, les résultats pratiques obtenus par le traitement par la pénicilline restent excellents.

(4) De nos jours, dans les pays développés, la syphilis paraît devenir plus bénigne, avec moins de lésions exubérantes, une faible incidence des reprises secondaires et des gommes, faits communs antérieurement, et une forte diminution de l'incidence des autres manifestations tardives. Par contre, les réinfections et les atteintes anorectales sont devenues plus fréquentes. Un certain nombre de facteurs en sont responsables, dont une meilleure nutrition, une meilleure hygiène et, par dessus tout, la découverte de la pénicilline, traitement dont on peut penser qu'il tend à supprimer les souches les plus virulentes, laissant subsister les souches les plus insidieuses.

(5) Les types de comportement ont aussi joué un rôle, spécialement en ce qui concerne les infections anorectales. On présente des informations sur les infections homosexuelles et celles dues aux rapports oraux.

(6) Il n'est pas douteux qu'aujourd'hui l'état humain changera et que l'environnement évoluera, ceci influencera les aspects de la maladie thponémique.