

EVOLUTIONARY CYCLE OF THE TREPONEMATOSES*

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The term "treponematoses" includes yaws, pinta, and endemic and venereal syphilis under their many different local names throughout the world.

Yaws, a non-venereal contagious disease particularly of childhood, is estimated to affect many millions of persons living between the tropics of Cancer and Capricorn. The incidence of infectious yaws has been markedly reduced in recent years by the W.H.O.-assisted and national campaigns based on the mass use of penicillin. In the W.H.O.-assisted campaigns against the endemic treponematoses, some 100 million persons have been examined and 25 million patients or contacts treated. Before these campaigns were in operation it was believed that there were approximately 50 million cases of yaws in the world, 25 million of them in Africa.

Pinta probably affects a million or more people in Central and South America and syphilis itself is world-wide. In many parts of the world syphilis also is not venereal but is a non-venereal contagious complaint of children, particularly in the Middle East (Kail, 1955) and in Africa (Guthe and Willcox, 1954). Such so-called endemic syphilis can be found in Iraq (Akrawi, 1949; Csonka, 1952), Iran (Grem-liza 1956; Ansari, Faghih, Hajian, and Bijam, 1957), Syria (Hudson, 1928, 1937, 1946; Luger, 1958), Saudi Arabia (Chaglassian, Bustani, and Anderson, 1952; El Ghoroury, 1954), Transjordan (Hasselm-ann, 1938), and Turkey (Berke, 1950; Marchionini, 1952; Christiansen, 1954). It was formerly more prevalent in Palestine (McQueen, 1934; Katzenellen-bogen, 1956), Anatolia, and Mesopotamia (Düring-Pascha, 1902; 1918). In this region it has been known under a number of local names, including *bejel* (Hudson, 1928), *Firjal* (McQueen, 1934), *loath*, *latta*, *laghout*, *abo-laghif*, *jifar* (Hasselmann, 1938), and *balash* (Chaglassian and others, 1952).

In Africa, as in the Middle East, endemic syphilis is found amongst primitive tribes in arid areas bordering on the Sahara desert in the north and around the Kalahari desert in the south, particularly in Morocco (Lévy-Bing and Gerbay, 1917), Mauretania, Senegal (Hackett, 1959), Gambia (McFadzean and McCourt, 1954), Sudan (Hewer, 1938), French Equatorial Africa, including the High Volta (Baylet, 1954) and Niger territory (Mathurin, 1953), and Northern Nigeria (*Lancet*, 1956), and also in the south as the *njovera* of Southern Rhodesia (Willcox, 1951; 1955) and the *dichuchwa* of adjacent Bechuanaland (Murray, Merriweather, Keen, and Sachs, 1952). It has also been reported in Asia in Lower Mongolia and in Tibet (Guthe and Willcox, 1954). There are doubtless other foci still to be recorded.

In Europe endemic syphilis was widespread in the 18th and early 19th centuries as the *sibbens* of Scot-land (Gilchrist, 1771; Carmichael, 1814; Cullen, 1844; *Arch. Surg.*, 1896), the *button scurvy* of Ireland (Carmichael, 1814; Faye, 1842; *Arch. Surg.*, 1896), the *radesyge* of Norway (Böcker, 1809; Hünefeld, 1828; Borge, 1905; Grön, 1937), the *saltfluss* of Sweden (Böcker, 1809), the *syphiloid* of Jutland and Schleswig-Holstein (*Dithmarsch Evil*: Hübener, 1835), the *pian de Nérac* of France (Cavaillon, 1958), and the *spirocolon* of Greece (Lancereaux, 1868), with like conditions in Russia and elsewhere. A similar complaint was noted during the early settle-ment of Canada (Carmichael, 1814; Wright, 1855) around St. Paul's Bay and Lake Huron (Lancereaux, 1868). All these have now been identified with endemic syphilis, although a few similar conditions such as *ivkintja* (Australian "boomerang leg") are considered to be due to yaws (Hackett, 1936).

Endemic syphilis died out from most parts of Europe as socio-economic conditions improved during the first half of the 19th century. It persisted

* Paper read at the I.U.V.D.T. meeting in London on October 15, 1959.

longest in South-East Europe, particularly in the provinces of Bosnia and Serbia of present-day Yugoslavia and in the remote mountainous areas of adjoining territories (Glück, 1888; McDonagh, 1915). In Bosnia under the local name of *skerljevo*, it was still found until recent years (Grin, 1935, 1952, 1953; Ostertag, 1950), but has at last been practically eradicated by energetic mass campaigns.

Fuller details concerning the nature and extent of the treponematoses and the steps taken towards their eradication are described (Guthe, 1960). In the present paper the various treponematoses are considered in relation to each other, and also in relation to the intrinsic environment within the host, and the extrinsic environment of the host (Ildsoe). In particular, the cycle of evolution from endemic to venereal syphilis and (environmental conditions permitting) back to endemic syphilis again, is described. The chains of argument are perhaps less strong in respect of yaws and pinta, but these conditions are equally affected by the circumstances which influence the endemic/venereal syphilis cycle.

Transmission of Endemic Treponematoses

The possible methods of transmission of the endemic treponematoses are summarized in the Table.

TABLE
POSSIBLE METHODS OF TRANSMISSION OF ENDEMIC
TREPONEMATOSES
(after Hackett, 1957)

A.	Direct Contact	With Skin Papilloma	Yaws
		With Mucous Patch or Condyloma	Endemic syphilis
B.	Indirect Contact	Animate Objects	Fingers—to skin (Yaws) —to mouth (Endemic syphilis)
			Insects—blood suckers —surface feeders
			Animals
			Congenital transmission
			Inanimate Objects
C.	Ingestion		
D.	Inhalation		

It is unlikely that inhalation and ingestion play a significant role (apart from treponemes conveyed to the mouth itself by fingers and by inanimate objects).

A common method of spread is undoubtedly from an infective lesion to a susceptible patient by direct contact: in yaws, from a skin papilloma to the skin of a susceptible patient, perhaps conditioned by trauma; and in endemic syphilis, from an oral mucous patch to the mouth of another by kissing—again possibly conditioned by traumatic, dietary, or climatic factors. Mucous patch to skin contact may occur by wound sucking—a point noted in the days of sibiens (Gilchrist, 1771). That yaws lesions undoubtedly do result from direct contact has been well illustrated by Hackett (1953), who furnished interesting examples of yaws transmission amongst South African gold miners. But if contact is the essential factor, more lesions would be expected on the body and upper limbs, as children hold and lift each other (Hackett, 1957).

In both diseases the fingers of an infected or other person may convey the infection by *indirect contact* from a skin papilloma of yaws (Hackett, 1957), or from a mucous patch in endemic syphilis (Guthe and Luger, 1957), or from condylomata lata in both conditions, from one patient to another to the skin, nose (by nose-picking), or mouth. The fingers of children have been incriminated as the most important factor in the spread both of yaws (Hackett, 1957) and of endemic syphilis (Guthe and Luger, 1957).

The role of other animate objects, such as insects, is uncertain, although treponemes have been shewn to persist in wound-feeding diptera (Satchell and Harrison, 1953), and such insects may be found on the open lesions of all of the treponematoses (Akrawi, 1949; Hasselmann, 1938). It has been considered that flies do not play an important part in relation to other factors. Yaws is said to persist after residual spraying with insecticides in malarious areas (Hackett, 1957). Congenital transmission may occur in endemic syphilis depending on the duration of the disease in the mother (Akrawi, 1952b); if the infection is 10 or more years old at the time of conception such transmission is unlikely. Congenital transmission has often been said not to occur in yaws but some possible evidence to the contrary is available (Engelhardt, 1956).

It was shewn many years ago that the treponemes of yaws would not pass through unbroken skin, but entered readily through a scratch (Thomson, 1819; Mason, 1831). A breach in the mucous membrane is required in syphilis, but such breaches need only be microscopic in size. Trauma is thus an important conditioning factor.

Away from the body, treponemes cannot long survive drying, and so the possibility of ground, floors, or floor coverings, clothes or bedding, sticks, bushes, grass, undergrowth, or dust being significant conveyors of yaws is unlikely, although trauma occasioned by bushes, etc. may facilitate the entry of the treponeme from the fingers or mouth through the breach so caused in the skin. Treponemes from endemic syphilis however may remain moist in salivary secretions for longer and the possibility that communal eating and drinking utensils, pipes, etc., may contribute in some measure to transmission is a very real one. This form of transmission, particularly with pipes, would be expected to be more likely in adults than in children. As endemic treponematoses are childhood diseases, some other intermediate factor (*e.g.* fingers) is more likely. These aspects are concerned with the social habits and customs of the affected people.

In the endemic treponematoses, children readily become affected; most infectious yaws lesions, for example, occur in the 6 to 12-year age group (Hackett, 1957). Children may form approximately one half of the population in the undeveloped areas where the expectation of life is low. Once children are affected, the transmission of an infectious disease in a community is vastly facilitated as they are constantly at play with children of other families and engage in closer contact with them than the adults in the same families. Thus still more children acquire the disease and this creates a vicious circle of transmission.

Serum testing in endemic syphilis areas has shewn that 25 to 65 per cent. of persons may be sero-reactive (Guthe and Luger, 1957). In hyper-endemic yaws areas (over 10 per cent. of active cases) over 60 per cent. may be found to be sero-positive (Hackett and Guthe, 1956). Sero-reactors are frequently immune to venereal syphilis, which is therefore seldom seen in the heavily infected areas. The absence of genital chancres is a general feature of the endemic treponematoses; in *sibbens* the privy parts were never involved (Böcker, 1809).

Conditioning Factors which favour the Spread of Endemic Treponematoses

These may be divided into (a) primitive social conditions; (b) social habits and customs; (c) climatic and other environmental circumstances which may accelerate transmission or modify the clinical picture; (d) host factors which may modify the clinical picture and possibly sometimes also encourage transmission. These four factors will be considered

separately although no hard and fast line can be drawn between them.

(a) **Primitive Social Conditions.**—These words are synonymous with poverty. Poverty of accommodation, clothing, eating and drinking utensils, food, education, or enlightenment. Poverty breeds filth and insanitary conditions and results in overcrowding, all of which encourage the spread of disease. Two-thirds of the population of the world live in the undeveloped areas, have an average annual income of 41 U.S. dollars, a daily average food intake of only 2,150 Calories, and a life-expectancy at birth of but 30 years (Winslow, 1951). The endemic treponematoses affect the most primitive members of this low-standard group. Poverty provides another vicious circle by favouring disease, which breeds further poverty through disability and reduced capacity for work. Poverty and the vicious circle created by the extension of the diseases to children are thus self-perpetuating mechanisms in the transmission of the endemic treponematoses (Fig. 1).

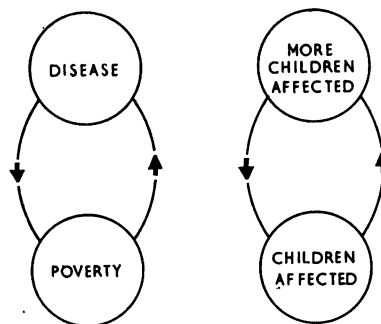


FIG. 1.—Self-perpetuation cycles in endemic treponematoses.

The endemic treponematoses have always been diseases of the poorer classes. *Radesyge* was associated with filthy dwellings (Charlton, 1837), being confined to the "lower order of people" who lived close together (Böcker, 1809), as was *sibbens* in Scotland (Gilchrist, 1771). The same applies to endemic syphilis to-day (Grin, 1953) and also to yaws (Hill, 1953).

A typical mud-walled dwelling in a yaws area of Africa has been described by Zahra (1956):

"The huts are dark, badly ventilated, and difficult to keep clean. There is usually no furniture except a square wooden stool and occasionally a table. The bedstead is usually a mud platform with a small fireplace underneath

it; it is covered with a mattress of palm branches or a raffia mat. During the evening the family sit closely huddled round the fire in the centre of the room.”

Overcrowding and an absence or scantiness of clothing, by increasing the chances of transmission of the treponeme by direct, or indirect contact, are significant transmission factors particularly in respect of yaws (Fraser, 1921).

Endemic syphilis, *e.g.* in the Middle East (Hudson, 1928, Chaglassian and others, 1952) and in West Africa (Hackett, 1959; Murray, Merriweather, Freedman, and de Villiers, 1956) is frequently encountered in nomadic populations. Such people are slaves to their flocks, water supplies, and pastures (Hackett, 1959). In Palestine the disease was commonest in poor refugees (Sansonnens and Bishara, 1952). Nomads usually have temporary dwellings and congestion is more common in temporary than in permanent accommodation (Luger, Mandil, and Trudeau, 1958). Poverty is associated with insufficient clothing, especially for the children (McFadzean and McCourt, 1954). Clothing (and bedding) may be shared (Fraser, 1921; McArthur, 1923; Akrawi, 1949), and scanty clothing means a greater risk of trauma to facilitate entry through the skin, especially of the yaws trepone. Poverty is also associated with inadequate diet, avitaminosis, and cracked fissures around the mouth. The latter may also facilitate the entry of the treponeme of endemic syphilis.

Poverty is often accompanied by poor hygiene and lack of washing. Even if bodies are washed clothes may not be (McFadzean, McCourt, and Wilkinson, 1957). This may encourage skin diseases (*e.g.* scabies) and traumatic breaks of the skin surface through scratching, while poor sanitation encourages the presence of flies. However, poverty and bad sanitary conditions are not the only factors, for yaws is not always present in a poor and insanitary environment (Hill, 1953).

(b) Social Habits and Customs.—Many social habits and customs (*e.g.* methods of eating, drinking, sleeping, etc.) may be conditioned by poverty. Some exist by tradition; others are common to all mankind.

(i) Kissing and Fondling.—The universal habit of kissing and fondling may be particularly important in the transmission of endemic syphilis. McQueen (1934) reported that the Arab “is a lavish kisser”, and kissing has frequently been blamed as a cause of

transmission in this area (Akrawi, 1949). In Africa, too, kissing is frequent between members of the family and servitors (Fraser, 1921; Hackett, 1959). The fondling of children has been cited as a transmission factor for the now defunct sibbens (Gilchrist, 1771) and for the present-day bejel (Akrawi, 1949).

(ii) Eating, Drinking, and Smoking.—In many areas, *e.g.* Africa, it is the custom for the children to feed together (Hackett, 1959), which brings the susceptible members of different families more closely together. Cooking is often undertaken around a communal fire (Guthe and Luger, 1957).

The use of communal dishes and vessels has been repeatedly blamed for the transmission of endemic syphilis (Fraser, 1921; McArthur, 1923; McQueen, 1934; McFadzean and McCourt, 1954; Hackett, 1959). The fingers are frequently used for eating and half-eaten dainty morsels may be passed by hand from one person to another (Fraser, 1921). The fingers may be moistened with infective saliva before making a bolus of farinaceous food and some saliva may be left in the food remaining in the dish. Drinking vessels, however, have been considered more important than eating utensils (Hackett, 1959). The ornate, spouted pot (*ibrik*) as used by the mountain families of Yugoslavia is thought to have been a significant transmission factor in that area (Grin, 1953).

Following the meal, toothpicks are often used and may be exchanged. These may be kept in the mouth for hours (Hackett, 1959). Another possible dietary factor is hard, gross food (Hasselman, 1938), which may cause trauma in the mouth during masticating, eating, and swallowing, and may help to localize mucous patches in the mouth (Lévy-Bing and Gerbay, 1917).

Pipes, which are often exchanged, have been frequently incriminated for the sibbens of Scotland (Gilchrist, 1771) and for endemic syphilis in Africa (Fraser, 1921; McArthur, 1923), and the *argeelar* (or hubble-bubble) has been blamed for endemic syphilis in the Middle East (McQueen, 1934). These inanimate objects are more likely to foster transmission in adults than in children, and would be of more significance in areas where mixed venereal and non-venereal syphilis is found than where syphilis is predominantly a non-venereal disease of children.

(iii) Sexual and Other Practices.—McArthur (1923) noted in Bechuanaland that “the native has many

curious customs about which we know little which may give rise to syphilis insontium, a greater significance than it has in the incidence of European syphilis". Circumcision practices and rites are one such example. Another is an old custom in Egypt, quoted by Madden (1904), whereby babies were never washed for the first year of life for fear of syphilis being attracted to the clean skin.

Most of the curious sexual customs quoted in the literature, perhaps because of their bizarre nature, have often been given greater attention than they deserve as significant spreaders of these infections. These include sodomy (Hasselmann, 1938; Madden, 1904) and bestiality (with donkeys—Hasselmann, 1938), Fraser (1921) described three cases of corporeal chancre arising from the African practice of *Metcha*—what McArthur (1923) later described as "revolting and ribald sex distortions" (manual and corporeal manipulations).

(c) Climatic and Environmental Circumstances.—

Humidity, and various climatic, botanical, geographical, and geological factors which contribute to a raised atmospheric humidity—such as a high annual rainfall or impervious soil—are conducive to the spread of yaws (Hill, 1953). Indeed, yaws is confined to the zone between the tropics of Cancer and Capricorn where such conditions are found. Yaws flourishes in hot climates near the mean annual isotherm of 80°F. where there is comparatively little fluctuation of temperature and where there is an annual rainfall of over 50 in., the number of cases tending to increase in the rainy season (Hill, 1953). The role of sweat, which remains longer on the skin in a humid atmosphere, as a vehicle for the persistence and scattering of viable treponemes on the skin of yaws patients and their transfer to the skin of others conditioned by trauma has not yet been fully evaluated; basic research is still required.

On the other hand endemic syphilis may be found anywhere in the world except where yaws is endemic. Where endemic syphilis and yaws are found near together, as in the Gambia (McFadzean and McCourt, 1954) and in French West Africa (Hackett, 1959), only one or the other is found in any particular place (Hackett, 1959). In these African areas yaws is found near the coast where there is a high annual rainfall, and endemic syphilis in the more arid hinterland where the rainfall is seasonal. Transmission of the latter is greatest in the dry season when mucous plaques are more commonly encountered (Hackett, 1959).

Both in the Middle East and Africa, endemic syphilis has tended to persist in arid, almost desert, areas. While this is probably because civilization has been slow in reaching such localities, so that primitive social conditions have persisted there the longest, the role of the dry atmosphere in causing cracking of the lips, which facilitates the oral introduction of the treponeme (Hasselmann, 1938), may partially explain some of the present-day geographical distribution of this disease.

(d) Host Factors.—Other diseases of the host, *e.g.* skin diseases, may frequently be found in association with endemic treponematoses, and these may be fostered by the same environmental conditions. Scabies was commonly found in patients with radesyge (Charlton, 1837) and a favoid condition of the scalp ("witkop") may be found in endemic syphilis areas of Africa (McArthur and Thornton, 1911; Murray and others, 1956) and in S.E. Europe (Murray and others, 1956). The presence of other diseases in the host might also encourage transmission; these include scabies, tropical ulcer, and any conditions causing a break in dermal continuity (which favours the spread of yaws) and streptococcal fissures and avitaminosis leading to lesions around the mouth which may encourage the entry of the treponeme of endemic syphilis (Hasselmann, 1938).

Endemic syphilis has nearly always been associated with malnutrition. The *radesyge* of Norway was considered to be a degenerative form of syphilis or a combination of syphilis with scurvy (Böcker, 1809). "Button scurvy" was the name of the same disease in Ireland (Carmichael, 1814). The circumoral lesions of vitamin B deficiency are commonly encountered in endemic syphilis areas in Africa and in the Middle East (Willcox, 1951).

Modification of Clinical Picture

Thus far the various factors which may encourage the transmission, and therefore the persistence, of the endemic treponematoses have been considered. Some environmental and host factors, however, may also modify the clinical pattern.

Host Factors.—The significance of racial distribution in certain infections is well known to live-stock breeders (Hasselmann, 1938).

"There is no doubt that on account of racial peculiarities one meets with a mass of contradictions and variations as compared with textbook standards of the symptomatology of syphilis." (Zimmermann, 1921).

Frazier and Li Hung-Chiung (1948) studied syphilis in White, Negro, and Chinese peoples. Although the disease was essentially the same in all, notable differences in the incidence of the different clinical syndromes in relation to latency were noted in the three races. Atkinson (1882) also noted the greater racial tendency of the Negro to develop annular eruptions, cardiovascular syphilis, and gummata.

Racial tendency was blamed for the early-held opinion that yaws was a disease of the black races (*Arch. Surg.*, 1896), though it was appreciated that Europeans and Creoles were not invulnerable (Mason, 1831; Thomson, 1819). While the better European constitution was thought to account for it, some held the view that Europeans infrequently had yaws because they were less exposed and thus avoided contracting it (Mason, 1831).

Malnutrition or other disease in the host may also influence the clinical syndrome (Hasselman, 1938). The angular stomatitis of vitamin B deficiency may tend to localize the lesions of endemic syphilis in the mouth and so increase the prevalence of these lesions, as in Morocco (Lévy-Bing and Gerbay, 1917).

The clinical picture may also be modified by immunity in the patient. Those with one treponematosis may be partially or completely immune to later infection by the same or another treponematosis—a fact confirmed in animals (Turner, McLeod, and Updike, 1947). Certainly, serological tests for syphilis in tropical areas give conflicting results in different racial groups in different areas (Griffiths, Buckle, and Hill, 1959), and these may result from nutritional causes (with subsequent imbalance of the body proteins) or from differing previous antigenic experiences. How far these factors can modify the subsequent clinical picture of a treponemal infection or prevent its occurrence is not fully known.

The age of the patient at the time of infection may certainly modify the clinical picture. Thus, Hutchinsonian teeth are found in congenital syphilis because the baby had syphilis at a particular time (when the tooth buds were being formed); sabre tibia is found in syphilitics infected before the bones have become set; and cardiovascular syphilis does not usually occur if the patients are infected at birth, or when young. Similarly, congenital transmission of syphilis is unlikely to occur in patients affected early in childhood.

Many diseases tend to run a milder course in children than in adults. In Fiji, at one time, mothers

intentionally inoculated their children with yaws because, like measles, it was considered better to get it over in childhood (*Arch. Surg.*, 1896); this practice was also used in Africa for yaws (Mason, 1831) and endemic syphilis (Davies, 1956).

Persons with treponematosis may become superinfected. Certainly the opportunities of superinfection are countless if judged by the frequency of re-infection in treatment campaigns where only clinical cases, and no contacts, are treated.

When the host already has endemic treponematosis in a latent form the clinical picture may be altered. It has often been postulated that gummata and other tertiary syphilitic lesions may result from allergy following superinfection of a previously sensitized host. This theory was well known to Jonathan Hutchinson and the French master syphilographers. It was cited by McDonald (1934) as a possible explanation for the occurrence of cardiovascular lesions in some patients with congenital syphilis. Grin (1953), struck by the fact that in Yugoslavia the incidence of gummata was high in those areas where the incidence of early lesions of endemic syphilis was also high, considered that superinfection might well be the explanation. Murray and others (1956) showed pictorial examples of gumma of the breast in women with longstanding latent syphilis believed to have been superinfected by their children who had recently contracted the endemic disease. The view that gummata may arise from superinfection of latent cases (and indeed may therefore be an indication of activity of an endemic focus) is now widely held (Grin, 1953; Guthe and Luger, 1957). This theory would certainly explain the many examples of precocious tertiary syphilis encountered in historical times, and also today in countries where syphilis is widespread (Willcox, 1955). It would also explain why, as syphilis has declined in prevalence (and superinfection has become less likely), it has become a somewhat less spectacular disease.

The clinical picture may be modified by the presence of traumatic lesions in the host. The possible localization of mucous patches in the mouth as a result of trauma has already been cited (Lévy-Bing and Gerbay, 1917). That trauma may localize gummata has also been noted (Csonka, 1953). Murray and others (1956) state that gummatous ulceration may occur in African women on the waist where the rough skin skirt is tightly tied, or on the back where the baby's body presses when being carried.

Environmental Factors.—Climatic and other environmental factors may also modify the clinical manifestations (Hasselmann, 1938). Fraser (1921) held that climatic rather than racial factors were responsible for the clinical picture of yaws. Thomson (1819) noted how apparently healthy West Indian Negroes developed the disease when removed from a mountainous area to the more humid climate of a sugar estate.

The condylomata lata of secondary syphilis are found in the moist sweaty areas of the body. Usually encountered in the ano-genital region in dirty persons, they are sometimes found in the axilla or under pendulous breasts. This is a world-wide experience in venereal syphilis. It is logical to consider that a similar mechanism may operate in respect of yaws, exuberant cutaneous lesions being found in persons living in humid climates where body sweat evaporates slowly and bathing habits are restricted. In such circumstances there may be differences in the type and location of lesions in different seasons (Hill, 1953), *i.e.* with variations in humidity.

Bathing and washing habits and the use of clothing may modify the clinical picture by restricting the presence of exuberant cutaneous lesions. The clinical picture may also be modified by the size of the inoculum, and therefore by trauma which may permit the entry of a larger inoculum than might otherwise be the case. In yaws most initial lesions are usually below the knee (Hackett, 1957) being probably due in the first place to trauma (Hill, 1953).

The absence of the primary sore in endemic syphilis has often been noted (McArthur, 1923; McQueen, 1934; Hudson, 1937; Hasselmann, 1938; Akrawi, 1949; Murray and others, 1956). McArthur and Thornton (1911) found only thirty chancres in 1,550 patients in Bechuanaland. Only eight were considered sexual in origin—the rest being commensal. McDonagh (1915) reported that in S.E. Europe the ratio of extragenital to genital chancre was 20:1. In endemic syphilis a primary sore *can* be produced experimentally (Akrawi, 1952a), and nipple chancres are encountered if a child with endemic syphilis infects the previously uninfected mother (Willcox, 1951; Akrawi, 1952a).

If the inoculum is small no primary sore will follow—and this would seem to be usual in endemic syphilis areas. The size of the inoculum again may affect the manifestations of super-infection. If the inoculum is small, the state of allergy low, and

immunity high, superinfection may result only in an increased serological titre (Guthe and Luger, 1957). If the inoculum is large, or often repeated, visible lesions may occur. Basic research is required on this subject, but such a theory would explain the high rate of gummatous lesions within the mouth and nose (gangosa). There appears to be some difference due to climatic, environmental, or other circumstances, between the endemic syphilis of Bosnia and that found in Syria and Bechuanaland. More secondary rashes are said to be observed in Bosnia where congenital and neurovisceral syphilis are apparently more common (Guthe and Luger, 1957). In Bosnia, however, more patients are affected later in life.

Inter-relationship of the Treponematoses

It is not the purpose of this paper to engage in the old controversy whether yaws and syphilis are one or two diseases. Many (*e.g.* Butler, 1936—who coined the term treponematosis; Grin, 1935; Hudson, 1946) consider them to be caused by the same organism which produces a different clinical picture because of environmental and immuno-biological influences within and without the host exerted during countless passages through the centuries. Pinta is excluded from this argument as less is known about this condition.

The spirochaetes of endemic syphilis (bejel) and venereal syphilis have the same morphology (Rizk, Garabedian, Chaglassian, and Pipkin, 1951a) and a similar disease pattern is produced in rabbits (Rizk, Shwayri, and Garabedian, 1951b). It is true that differences have been noted in the disease patterns of rabbits and hamsters infected by treponemes from patients with yaws, endemic, and venereal syphilis (Turner, Hollander, and Schaeffer, 1953; Turner and Hollander, 1957), but the differences are rather of quantity than of quality and it is remarkable that the differences so far found are so slight. Even the demonstration of such differences does not exclude the possibility that these too have resulted from environmental influences and they may disappear in an altered environment. Under laboratory conditions in animal passage a shift towards the venereal type of treponeme is in fact noted. There is no reason why such should not occur in nature (Guthe and Luger, 1957).

The reported differences between yaws and syphilis have in the past been based on the disease pattern of yaws in children in tropical areas and that of venereal syphilis in the towns. Much has been made of the apparent absence of cardiovascular and neurological involvement and of congenital trans-

mission in yaws as compared with venereal syphilis. A better comparison would be that between endemic syphilis and yaws.

In endemic syphilis such complications have frequently been reported as rare or even absent. The fact that endemic syphilis, like yaws, is usually a disease of childhood would explain the relative rarity of congenital transmission, although this *has* been reported (Akrawi, 1952a). Although cardiovascular syphilis is rare, some cases have been recorded (Akrawi and Rahim, 1951). So too cardiovascular involvement is rare in congenital syphilis, and the age of the patient at the time of infection would appear to be an important factor in the incidence of this particular complication. Similarly neurosyphilis has been stated to be uncommon in endemic syphilis (*e.g.* in Palestine—McQueen, 1934; and in Turkey—Marchioni, 1952). However, while the clear-cut picture of paresis or of tabes dorsalis may be rare, there are several reports of meningo-vascular syphilis (Akrawi, 1952b; Hoff and Shaby, 1940; Zec, 1951). It has to be remembered that paresis may not be recognized under primitive conditions (Zec, 1951; Grin, 1956). Moreover, in populations with a life expectancy of 30 years, such complications have relatively little time to become manifest. Also it is possible that repeated exposures to small inocula of treponemes may provoke some immunological protection against neurovisceral and placental lesions (Guthe and Luger, 1957).

The available evidence of cardiovascular and neurological involvement and of congenital transmission is much less striking for yaws than for endemic syphilis although Engelhardt (1956) reported that yaws could be transmitted congenitally. However, as has for a long time been noted, the complications expected of syphilis tend to be labelled as due to syphilis even when they occur in a yaws area (*Arch. Surg.*, 1896). Data relating to the late complications of the endemic treponematoses are still largely confined to individual observations of small numbers of cases. More extensive investigations involving fluoroscopy and examinations of the cerebrospinal fluid are required.

Thus many of the apparent differences between the diseases *can* be partially or wholly explained. Where yaws and syphilis exist closely together, as in French West Africa, only one disease is found in a particular village (Hackett, 1959), which to some extent favours the unitarian view. What is evident, however, is that yaws is conditioned climatically in its distribution and that yaws and syphilis are so

close immunologically that, whether they are the same or two similar diseases, their inter-relationship is not basically altered.

This issue could be finally settled by inoculating human volunteers with treponemes from yaws and endemic syphilis under humid and arid climatic conditions and observing the resultant clinical picture (Murray, 1959). To-day freeze-dried cultures of the different treponemes are available and the volunteers, once infected, could be readily and promptly cured with penicillin: thus some of the major difficulties of such experiments have been removed. Once cured, the volunteers could be switched from the humid area to the arid area and *vice versa*, and the experiment could be repeated. Such experiments would not need to be conducted in remote areas. It should be possible to construct two buildings with the requisite internal climatic conditions of temperature and humidity under strict laboratory control almost anywhere in the world. More complicated experiments than these are frequently being undertaken in the fields of aviation and space medicine. It is realized that there are still many practical and other difficulties in arranging for such experiments but if undertaken they could finally settle this controversial problem.

Regression of Endemic Treponematosis and Emergence of Venereal Syphilis

Thus far it has been shown that, in a primitive social environment, conditioned by local social habits and also by trauma, the endemic treponematoses spread among children. Once a family of children is affected the momentum of transmission increases as the children of different families play together. As a result of environmental factors, within the host and climatically and otherwise outside the host, the clinical picture may be modified. Treponematoses bring their disabilities and debility. The already poor population cannot then work at full capacity. This increases poverty and helps to maintain the conditions essential for non-venereal transmission. Patients with the early disease may remain infectious for many months, or even years. Superinfection may produce a high prevalence of gummatous lesions. The full picture of the endemic treponematoses is thus developed. In these circumstances, most of the children are infected; when they later become exposed to venereal syphilis in the towns, infection is not acquired (McArthur, 1923) as they already have the endemic form, and penile chancres are therefore extremely rare.

With improvement of social conditions the endemic treponematoses begin to disappear. It was noted that siccus waxed and waned (Gilchrist, 1771) and both siccus and button scurvy yielded to improvements in cleanliness and food (*Arch. Surg.*, 1896). The agents of improvement are better communications, access to markets, and new ideas of clothing and housewifery, the introduction of a school or medical clinic bringing the elements of health education, and a perceptible, if small, rise in the general standard of living with all that this entails. Such events will reduce markedly the risks of transmission. Endemic syphilis might die out completely as social conditions improved, but without provision for the treatment of known cases this would take many years (Murray and others, 1956).

The history of venereal syphilis is steeped in the non-venereal links of syphilis insontium. Procedures at public baths, wet-nursing, small-pox vaccination (before the introduction of calf lymph), catheterization, midwifery (before the invention of rubber gloves), blood transfusion, tattooing, and glass-blowing are but some of the mechanisms by which venereal syphilis has been scattered non-venereally, gaining a new lease of life by subsequent venereal transmission, when otherwise it might have died out (Lancereaux, 1868; Bulkley, 1894; Guthe and Willcox, 1954; Willcox, 1953).

When syphilis is more prevalent, extra-genital non-venereal infections are more common. Most extra-genital chancres are seen within or around the mouth, and these are often contracted by kissing during, or without, sexual intercourse. The example of a number of participants in a kissing game becoming infected is well known (Schamberg, 1911). As syphilis declines in prevalence such happenings become rare.

As social conditions improve (or treatment facilities are established) more children grow up who have not suffered from, or have been cured of, non-venereal treponematoses. They are now susceptible to venereal syphilis if risks are taken when they visit the towns. Penile sores become more common but, as syphilis is still rife and social conditions are still very much below standard, accidental infection is still frequent. Thus there arises a mixture of endemic syphilis (or yaws) and venereal syphilis. The non-venereal forms tend to be found more frequently in older age groups than when endemic syphilis alone was the rule. Neurovisceral complications are more common. Extra-genital chancres are more frequent and the role of inanimate objects, such as drinking vessels, eating utensils, pipes, etc., becomes important as a factor of transmission.

In time, helped by the establishment of clinics and hospitals by which the period of infectiousness can be dramatically reduced in the treated patients, with a consequent great reduction in accidental syphilis, the disease declines in prevalence and non-venereal spread becomes less and less common. Finally venereal syphilis evolves as in the developed countries to-day. Syphilis has become a venereal disease and the only hope of survival of the treponeme is by the contact of two mucous membranes. But even in modern times venereal syphilis still has an inherent capacity to spread. Olansky and Price (1956) described how seventy cases were traced from one infectious patient.

The events considered in the preceding paragraph can be curtailed dramatically by the use of penicillin. If it is given to the whole population (to include active cases, latent cases, and those incubating the disease), the various transmission factors can no longer operate as there is no infectious material to transmit. But the conditions may still be present should treponematosis be re-introduced.

The question of the introduction of venereal syphilis into areas of yaws and endemic syphilis which have been cleared by mass campaigns is therefore one of current concern for WHO. While the endemic treponematoses are prevalent they provide an immunity against venereal syphilis. Therefore the prevalence of venereal syphilis in the towns in countries in which campaigns against the endemic treponematoses are or have been in operation must also be taken into account in a given area; measures must be taken to deal with the venereal as well as the non-venereal forms of all of the treponematoses.

Reversion of Venereal Syphilis to Endemic Syphilis

It has been stated in respect of yaws that if a low prevalence has been reached under modern social conditions the yaws situation will not deteriorate unless there is a national catastrophe (Hackett, 1959). Should social conditions again markedly worsen, however, or venereal syphilis be introduced into a previously uninfected primitive population, the conditions favourable to non-venereal transmission again pertain and the disease reverts to the endemic form thus completing the cycle which has been described (Fig. 2, opposite). This state of affairs has been noted in small outbreaks in post-war Budapest (Fejér, 1948), in Madras, India (Rajam and Rangiah, 1952), in a coloured community in South Africa (Taylor, 1954), and in slum conditions in Chicago (Eisenberg, Plotke, and Baker, 1949). Incidentally

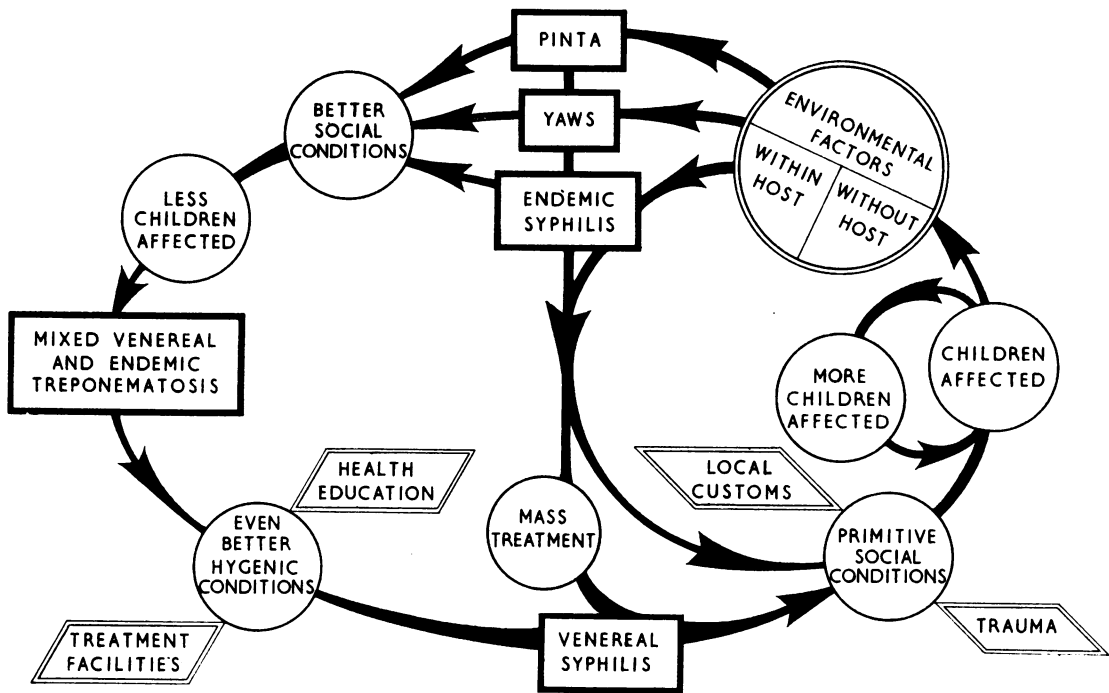


FIG. 2.—Evolutionary cycle of treponematoses.

none of the children in the Chicago series, who came from homes with elementary hygienic conditions, shewed a primary lesion.

Historically there are several reputed examples of venereal syphilis being introduced and perpetuating itself in the non-venereal form. Sibbens was known as *Framboesia Cromwellia*, being originally blamed on the troops of Cromwell's army; the *radesyge* of Norway was blamed on the crew of a Russian schooner which wintered in a coastal port (Lancereaux, 1868), and Norwegian labourers were later blamed for transferring it from Scandinavia to Northern Europe (Hübener, 1835). The introduction of syphilis into the Indian population of Canada is a further example (Lancereaux, 1868). However it is traditional for syphilis to be blamed on outsiders. Even today the disease is nearly always imported—seldom exported!

History of Syphilis

Perhaps an even more controversial subject than the identity or otherwise of the various treponema-

toses is that of the historical origin of syphilis. The Columbian theory still has its adherents (Cavaillon, 1958; Harrison, 1959) in recent years, although many, probably the majority (*e.g.* Butler, 1936; Hudson, 1946) have actively opposed it. Many (*e.g.* Carmichael, 1814) have considered that there was evidence of syphilis in Europe in pre-Columbian times. It is not the purpose of this paper, however, to enter into this controversy except to suggest that the various facts presented must be taken into account.

That the outbreak of syphilis in Europe at the end of the 15th and early in the 16th century was both widespread and severe is not in dispute. But the reported severity of the outbreak and of the clinical manifestations is not unique. Ignoring possible examples from biblical times (Willcox, 1949), there are others more modern including the outbreak amongst the Indians of Canada (previously quoted), and the spread of the disease in South Africa which has been considered quite comparable with that of the European epidemic of the 15th and 16th centuries (Sax, 1952). Butler (1936), commenting on the high

incidence of gangosa in Guam, where it affected 1 in 35 of the population, believed that the effects of the treponematoses in that area must have been quite as bad, or worse, than those experienced in Europe in historical times. Hibbert (1926) stated that, in the late 17th century and early 18th century, the sibbens of Scotland had excited a terror "which afforded a correct epitome of the general panic which two centuries before had been universal throughout Europe".

That social conditions in Europe in the 18th and early 19th centuries, especially in rural areas, were well suited to the spread of endemic syphilis, and that it did so spread, is also generally agreed. It is logical to believe that social conditions in the rural areas during the preceding centuries were no better.

In South Africa the generalized spread of syphilis is frequently blamed on the opening up of the Kimberley diamond mines in 1866 (Sax, 1952; Murray, 1957). Doubtless in these circumstances penile lesions made their appearance to authenticate the fact that this new industrial activity, which was attracting a huge labour force from hundreds of miles around, was responsible. And yet Livingstone (1857) stated that syphilis was unable to maintain itself in any permanent form in persons of pure African blood in the centre of the continent. This could have been because the indigenous population already had an endemic treponematosis, and the absence of penile chancres suggested that venereal syphilis was not established. In Egypt, where this time the troops of Napoleon were blamed as the introducers of venereal syphilis, it was noted that further down the Nile in the uncivilized interior the ravages of the disease were much worse and "resistance had quite broken down" (Madden, 1904). Perhaps endemic syphilis was already present with a high incidence of gangosa and gummata resulting from superinfection (as in Guam).

The truth of these matters may never be known, but there is a certain pattern in the historical development of syphilis. Usually venereal syphilis tends to be associated with an important historical event—an invasion, occupation, or new discovery which has shaken contemporary thought. Within a few years syphilis is found to be a problem in the towns and this is naturally associated with the colonists, invaders, etc. At this period, medical activities are largely confined to troops and Government employees, and the indigenous population is largely ignored (Davies, 1956), certainly in the interior. Later, explorers, traders, missionaries, and doctors penetrate the hinterland when disease of all

kinds is then usually found to be widespread especially in the remoter rural areas. Syphilis is often apparently more severe in its effects (again possibly due to the high incidence of gummata from superinfection), and for this the poor constitution of the people and their miserable standards of living are incriminated. It is natural to consider that the natives had acquired the disease in the towns where its presence is already known.

After a while, when clinics or hospitals are established by missionaries and others, it is possible to study the disease in the rural areas in more detail. The general absence of the primary sore and the numbers of children affected then give rise to comment. The suggestion may then be made (as in South Africa by McArthur, 1922) that the population is so heavily infected with venereal syphilis that the children are nearly all suffering from congenital syphilis. Or the exuberance of some of the cutaneous lesions in the dirty primitive population suggests that the disease is really yaws (*e.g.* sibbens or the Scottish yaws; *le pian de Nérac* of France and the early controversy concerning the nature of the disease in South Africa—Hugo, 1911; Murray, 1957). Indeed the *radesyge* of Norway was not always considered syphilitic, although it was thought to be so in adjacent Sweden (Charlton, 1837).

Later comes the thought that maybe the disease has been present for centuries in the endemic form. The absence of penile lesions indicates that it is non-venereal. The condition may have been called "leprosy" or by some local name without any sexual association. The possibility must be borne in mind that the invaders, colonists, occupiers, etc., who have caused the political or social upheaval blamed for the introduction of syphilis, may (by attracting a labour force, by providing accommodation for these workers and a better standard of living for the original inhabitants, and by introducing rudimentary medical facilities and the elements of education) have been responsible for the occurrence of venereal syphilis in quite another way, *i.e.* by evolution and not by introduction. By the events described the importance of many of the transmission factors of the endemic disease would be reduced and an increasing number of persons susceptible to the venereal form would be at large. Penile syphilitic sores would then appear in the towns following sexual intercourse. Not surprisingly, this would be blamed on the occupying powers, as no penile chancres had been encountered before they came!

Such a theory has already been considered concerning syphilis in Uganda (Davies, 1956). Here,

instead of there being an extensive outbreak, as reported by Lambkin (1908) and blamed on advancing civilization and the discarding of tribal discipline and taboos, it has been suggested that syphilis was in fact an age-old established disease in an endemic form. As a country is opened-up endemicity disappears and venereal syphilis appears as part of the evolutionary cycle of the disease. Further historical research on such a theory in relation to the outbreak of syphilis at the end of the 15th century in Europe would be well worthwhile.

Summary and Conclusions

(1) By treponematoses is meant yaws, pinta, and endemic and venereal syphilis. Their extent is indicated.

(2) The various means of transmission of the endemic treponematoses are considered. Direct contact with skin papillomata favours the spread of yaws, and direct contact with mucous membranes (mouth to mouth) favours the spread of endemic syphilis.

(3) Indirect contact with animate objects (fingers) is believed to be a significant factor in the transmission of both yaws and endemic syphilis. Inanimate objects, such as drinking and eating utensils, may favour the transmission of non-venereal syphilis. Other animate and inanimate objects possibly concerned with transmission are considered in both conditions. Pinta is excluded from consideration as less is known about this disease.

(4) Conditioning factors which may favour the spread of the endemic treponematoses are described in detail. These include primitive living conditions, social habits and customs, trauma, climatic and other environmental circumstances, and conditions in the host such as malnutrition, etc.

(5) These factors result in the infection of the children (who may form half of the population). Thence, mainly by the fingers of children at play, more children are affected and the rate of transmission is greatly accelerated. As the children grow up, however, they are not susceptible to venereal syphilis, and genital chancres are very seldom encountered.

(6) The type of lesion which results may be conditioned by intrinsic environmental factors

within the host and by extrinsic environmental and climatic factors (*e.g.* humidity). Some consider yaws and syphilis to be due to the same organism, the effects of which are modified in this way. Others consider that the two diseases are due to two closely-related organisms which thrive in the particular intrinsic and extrinsic environments described.

(7) The inter-relationship of yaws and syphilis is briefly considered. The age-old controversy whether they are forms of the same disease modified by environment or whether they are due to two similar but different organisms adapted to the environment could be finally settled by experiments whereby cultured treponemes from lesions of yaws and endemic syphilis were inoculated into human volunteers under humid and arid environmental conditions and the subsequent clinical picture observed. It should be possible to conduct such experiments in an adjustable artificial environment as well as in a natural environment.

(8) In the fully-developed picture of endemic treponematosis, the disease, by the disability and debility it causes, breeds still more poverty, which in turn encourages the further maintenance of the condition in its endemic form.

(9) As social conditions improve a number of transmission factors are reduced in importance. Children then grow up who have not had the endemic disease and who are therefore susceptible to sexually-acquired venereal syphilis when they visit the towns. Genital chancres make their appearance and a mixed venereal and non-venereal treponematosis results. Non-venereal transmission is still not uncommon in adults, and the roles of social customs (*e.g.* kissing), and of inanimate communal objects such as drinking and eating vessels, pipes, etc., are important.

(10) As social conditions are further ameliorated, unhygienic practices gradually cease, and medical care is introduced to shorten the period of infectivity of the cases treated. Non-venereal transmission then becomes a rarity—except occasionally through kissing—and the traditional picture of venereal syphilis has now evolved.

(11) The most striking method of reducing the transmission of the endemic treponematoses has been by the mass use of penicillin. This reduces enormously the period of infectivity of individual patients and (if given not only to active cases but also to latent cases and persons incubating the disease) it

prevents the transmission of the disease as there is no longer any material to transmit. Rapid and spectacular successes have been gained in the many WHO-assisted mass campaigns against yaws and endemic syphilis. As long as the transmission factors remain, however, there is a danger of deterioration should the same or another treponematosis be introduced or re-introduced into the treated area.

(12) That endemic syphilis may reappear should social conditions markedly deteriorate, or may spread in an endemic form if introduced venereally into the favourable environment of a primitive population, has been noted. This completes the cycle which has been described.

(13) Some of the implications of the evolutionary cycle of the treponematoses in different parts of the world are discussed in relation to the spread of syphilis in historical times.

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Cycle d'évolution des tréponématoses.

Résumé

(1) Par tréponématoses on entend le pian, le caraté (pinta) et la syphilis endémique et vénérienne. On indique leur importance.

(2) On considère les différentes manières de transmission des tréponématoses endémiques. Le contact direct avec les papillomes cutanés facilite la dissémination du pian, et le contact direct avec les muqueuses (bouche à bouche) facilite la propagation de la syphilis endémique.

(3) On croit que le contact direct avec des objets animés (doigts) est un facteur important dans la transmission du pian et de la syphilis endémique. Des objets inanimés, tels qu'ustensiles pour manger et boire, peuvent faciliter la transmission de la syphilis non-vénérienne. On considère dans les deux affections, d'autres objets, animés et inanimés, qui pourraient servir d'intermédiaire dans la transmission. De cette considération on exclut le caraté, car on est moins bien renseigné sur cette maladie.

(4) On décrit en détail des facteurs conditionnants, capables de faciliter la propagation des tréponématoses endémiques. Parmi ces facteurs se trouvent les conditions primitives de vie, les coutumes et les usages sociaux, les traumatismes, les conditions climatiques et du milieu ambiant, et l'état de l'hôte, par exemple sous-alimentation.

(5) Ces facteurs résultent en l'infection des enfants (qui peuvent former la moitié de la population). Ainsi, surtout par les doigts des enfants qui jouent, d'autres enfants sont affectés et la fréquence des transmissions est grandement accélérée. Ces enfants, cependant, avec l'âge, ne sont pas susceptibles à la syphilis vénérienne et les chancres génitaux sont rares.

(6) Le type de lésion qui en résulte peut être influencé par des facteurs intrinsèques chez l'hôte et par des facteurs extrinsèques et climatiques (ex. humidité). Certains pensent que le pian et la syphilis sont causés par les mêmes organismes, dont les effets seraient modifiés de cette façon. D'autres pensent que les deux maladies sont causées par deux proches organismes de même famille qui prospèrent dans les conditions particulières de milieu (intrinsèque et extrinsèque) décrites ci-dessus.

(7) On considère brièvement les relations réciproques du pian et de la syphilis. La longue controverse pour savoir s'ils sont des formes de la même maladie modifiée par le milieu, ou s'ils sont dus à deux organismes semblables, mais différents, adaptés au milieu, pourrait être finalement réglée par des expériences au cours desquelles des tréponèmes cultivés à partir de lésions de pian et de syphilis endémique seraient inoculés à des volontaires humains dans des conditions de milieu humides et arides,

et le tableau clinique qui en résulterait serait observé. On pourrait conduire de telles expériences dans un milieu artificiel réglable, aussi bien que dans un milieu naturel.

(8) A son apogée, la tréponématose endémique, par l'incapacité et la faiblesse qu'elle cause, engendre la pauvreté, qui à son tour aide à prolonger l'affection sous sa forme endémique.

(9) L'amélioration des conditions sociales réduit l'importance d'un certain nombre des facteurs de transmission. Des enfants qui n'ont pas eu de maladie endémique grandissent et deviennent susceptibles à la syphilis vénérienne d'origine sexuelle quand ils vont en ville. Des chancres génitaux apparaissent et il en résulte une tréponématose mixte, à la fois vénérienne et non-vénérienne. La transmission non-vénérienne est encore commune chez des adultes, et le rôle des coutumes sociales (ex. baisers) et des objets inanimés communs, tels que les ustensiles pour manger et boire, les pipes, etc., est important.

(10) A mesure que les conditions sociales s'améliorent, les usages peu hygiéniques cessant peu à peu, et des soins médicaux sont introduits pour raccourcir la période d'infectiosité des cas traités. La transmission non-vénérienne devient alors rare — sauf de temps en temps, par voie de baiser — et le tableau traditionnel de la syphilis vénérienne a maintenant évolué.

(11) La méthode la plus impressionnante de réduction de la transmission des tréponématoses endémiques a été l'usage massif de la pénicilline. Celle-ci réduit énormément la période d'infectiosité des malades individuels, et si le remède est donné non seulement aux cas actifs mais aussi aux cas latents, et aux personnes à l'état d'incubation, il empêche la transmission de la maladie, car il n'y a plus rien à transmettre. Des succès rapides et spectaculaires ont été obtenus dans de nombreuses campagnes de masse, assistées par l'O.M.S., contre le pian et la syphilis endémique. Tant que les facteurs de transmission demeurent, cependant, il y a un danger de détérioration dans le cas d'introduction ou de re-introduction dans la zone traitée de la même ou d'une autre tréponématose.

(12) On a remarqué que la syphilis endémique peut réapparaître si les conditions sociales empirent de façon notable, ou peut s'étendre sous forme endémique si elle est introduite par voie vénérienne dans le milieu favorable d'une population primitive. Ceci complète le cycle qu'on vient de décrire.

(13) On discute certaines implications du cycle d'évolution des tréponématoses dans diverses parties du monde en relation avec la propagation de la syphilis dans la suite des temps.