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ENDEMIC SYPHILIS AND YAWS

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SYNOPSIS

Endemic syphilis and similar conditions are compared in this paper with yaws. Both are non-venereal and endemic, and they have very similar epidemiological characteristics. There is also considerable similarity in the clinical manifestations at the various stages of yaws and endemic syphilis, the differences that do appear being mainly due to different environmental and living conditions. No antigenic or immunogenic differences between syphilis and yaws have yet been demonstrated, and the sensitivity of both to penicillin is the same. Control measures for both diseases may be based on similar principles.

The author considers the treponematoses to be closely related infections, and stresses the "unitarian" view put forward by various writers.

Recently Guthe & Willcox [12] presented a comprehensive summary of the nature and extent of the treponematoses as a public health problem of world-wide range, giving a sound basis for the international health activities in treponematoses control.

There is today a steadily increasing recognition, continually supported by new developments, that the treponematoses should be regarded as a closely related group of infections which, under different environmental influences, may in different ways develop essentially similar or even identical clinical syndromes.[4, 8, 19]

It seems reasonable, therefore, to consider the treponematoses from the epidemiological point of view as:

(1) non-venereal juvenile treponemal infections occurring in endemic form, and

(2) predominantly venereal adolescent infections occurring in sporadic form.

To the first group belong the following endemic treponematoses:

(*a*) endemic syphilis, comprising similar or identical conditions with different local names, such as "bejel" (Iraq and Syria),[1, 5, 18] "njovera" (Southern Rhodesia),[33] "dichuchwa" (Bechuanaland), [25, 29] and other forms

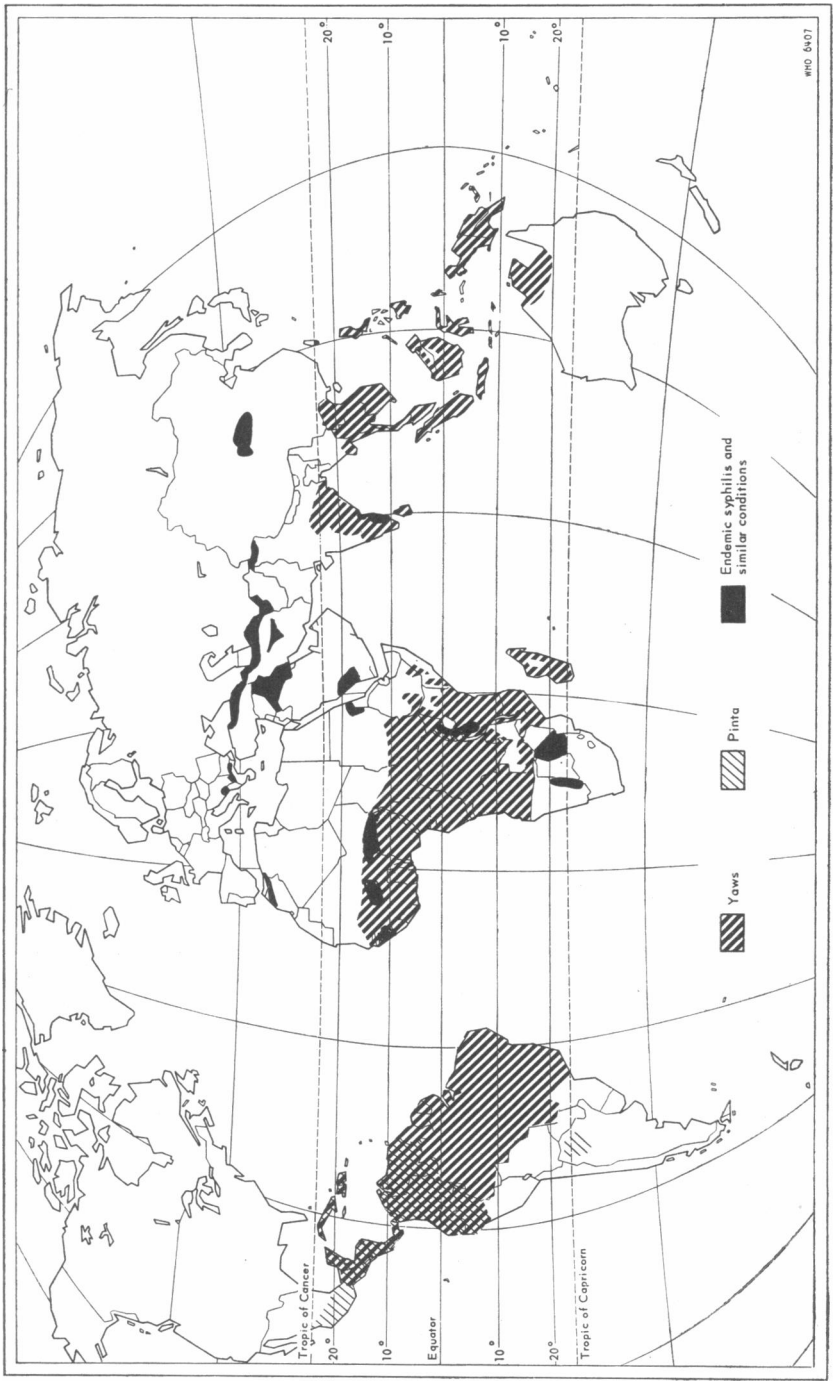


FIG. 1. GEOGRAPHICAL DISTRIBUTION OF THE NON-VENEREAL TREPONEMATOSES

which are no longer found, e.g., the " sibbens " of the British Isles in the seventeenth century, the " radesyge " of Norway in the eighteenth century, and the " skerljevo " of the Croatian Coast in the nineteenth century;

(*b*) yaws, the endemic treponematosis of the tropics;

(*c*) pinta, the endemic treponematosis occurring in Central America.

To the second group belongs venereal sporadic syphilis, which occurs all over the world and which is numerically less frequent than the endemic treponematoses.[11]

This concept of treponemal infections, although it still needs much study is nevertheless justified by the following factors:

(*a*) the morphologically indistinguishable organisms;

(*b*) the close relationship in cross-immunity;

(*c*) the similar antigenic and immunogenic responses of the host, and the similar responses to the same drugs;

(*d*) the great epidemiological resemblance between the treponematoses because of the similar ecological factors; and

(*e*) the similarity of the measures required to control the infections.

Two of the endemic treponematoses are discussed in this paper—endemic syphilis and analogous conditions occurring in countries with temperate climates, and yaws, which is confined to the tropics.

The present geographical distribution of the endemic treponematoses is shown in Fig. 1.

Since endemic syphilis and yaws are both non-venereal treponematoses they have a close similarity in their epidemiological pattern. On the one hand, both are prevalent in under-developed territories among rural populations with low economic and social standards and poor education and sanitation; on the other, with increasing industrialization and urbanization, social development, and education both will progressively decline and eventually disappear as endemic diseases but may linger on as small foci in isolated inaccessible hamlets and villages.

When poor living conditions are present, the family—as the basic social unit in the community—offers the best opportunity, once the infection has entered the family, for that infection to assume an endemic non-venereal character and to spread further within the household so long as the living conditions remain unchanged.

The spread of endemic syphilis and yaws in a family follows certain rules, with some variations, depending upon which member of the family is first infected. The infection is usually transmitted by those having the closest relations in the household, usually the mother and child, or children among themselves. Thus, simultaneous infections will often occur in families with active foci of the disease. Examples of this have been repeatedly observed in endemic syphilis and in yaws (see Fig. 2-5).

FIG. 2. SIMULTANEOUS APPEARANCE OF INFECTIOUS ENDEMIC SYPHILIS, BOSNIA

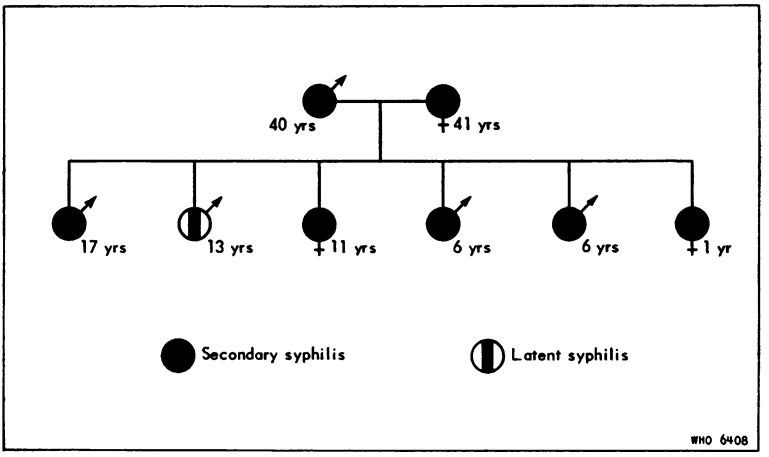
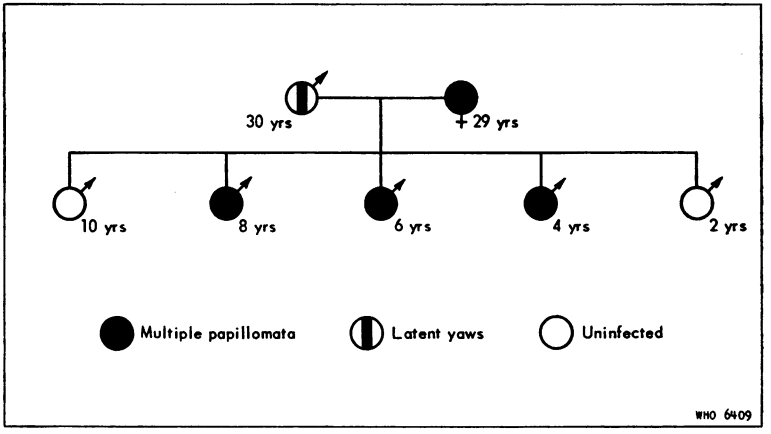


FIG. 3. SIMULTANEOUS APPEARANCE OF INFECTIOUS YAWS IN A FAMILY, THAILAND



It has also been demonstrated that the treponematoses among children are related to a certain extent to the presence of infection in the parents, especially in the mother. Investigations carried out in a highly endemic area of yaws in Thailand (in Surindr Province, where 279 families were investigated) and in one of endemic syphilis in Bosnia (Zvornik county, where 216 families were investigated) illustrate this condition (see Table I).

FIG. 4. AN INFECTED FAMILY WITH OLD CASES OF YAWS AND NEW ACTIVE FOCUS, THAILAND

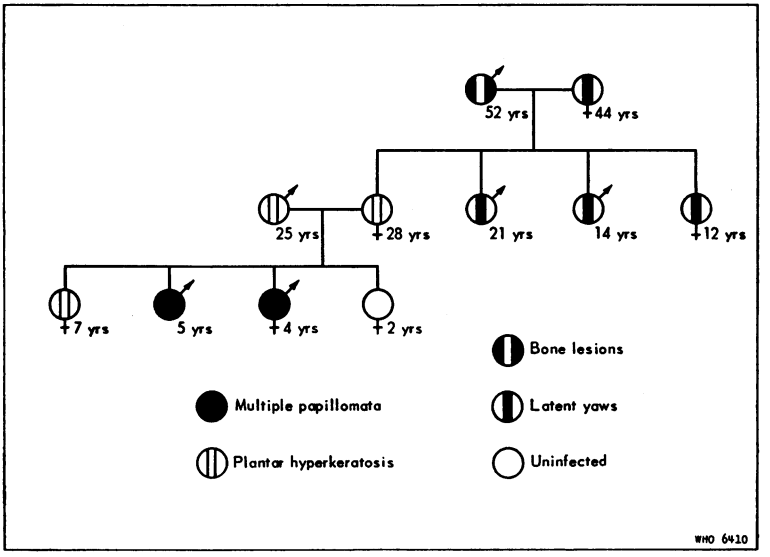


FIG. 5. AN INFECTED FAMILY WITH OLD CASES OF ENDEMIC SYPHILIS AND NEW ACTIVE FOCUS, BOSNIA

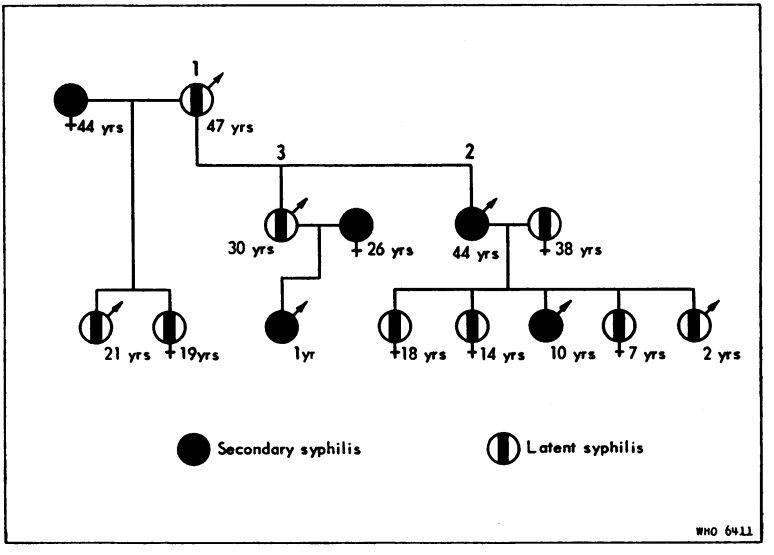


TABLE I. RELATIONSHIP OF SPREAD OF YAWS AND ENDEMIC SYPHILIS IN THE FAMILY IN HIGHLY ENDEMIC AREAS *

Persons infected	Infection among children (%)	
	yaws	endemic syphilis
Both parents	82.8	81.1
Wife only	80.4	60.3
Husband only	32.4	36 3

* Based on investigations made in Thailand and Bosnia, Yugoslavia.

The onset of endemic syphilis and of yaws occurs in most instances before the age of 15 years, regardless of the prevalence of the disease in the area. This is governed by the environmental conditions which produce the treponematosis in an endemic form. In such conditions the children are always the section of the population most exposed to treponemal infection, whether in or outside the household. There is abundant evidence based on observations in areas of endemic syphilis and yaws that this epidemiological peculiarity is caused by environmental factors and is static in its nature. When, owing to altered living conditions, infection ceases to occur in children the treponematosis also gradually ceases to appear as an endemic disease.

The number of the infected persons in any age-group in a given area is affected by two main influences in addition to the time of onset:

(*a*) the prevalence in the previous age-group; and

(*b*) the incidence of new infections occurring in the particular age-group under consideration;

A variety of other factors may, of course, increase or decrease the number of infected cases in the area concerned.

All these factors are variable and may, in the course of time in different age-groups, serve as indices of the present or previously existing epidemiological conditions.

When these factors are stable for some time a characteristic age distribution will result; this distribution will rise rapidly in the second decade of life, more gradually up to the fifth decade, and thereafter usually decrease slightly. If, for instance, the endemicity of the treponematosis is steadily regressive, the prevalence of the disease in the higher age-groups will gradually rise and then finally completely flatten out.

These circumstances are demonstrated in Fig. 6, which shows conditions in expansive and regressive yaws foci in Thailand, and in Fig. 7, which shows those in an active focus of endemic syphilis in Bosnia.

FIG. 6. AGE DISTRIBUTION OF YAWS IN A HIGHLY EXPANSIVE AND AN ALREADY REGRESSIVE FOCUS, THAILAND

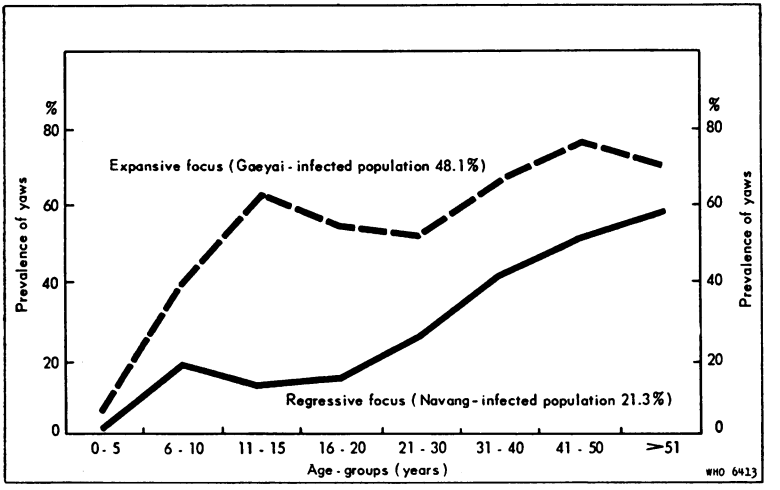
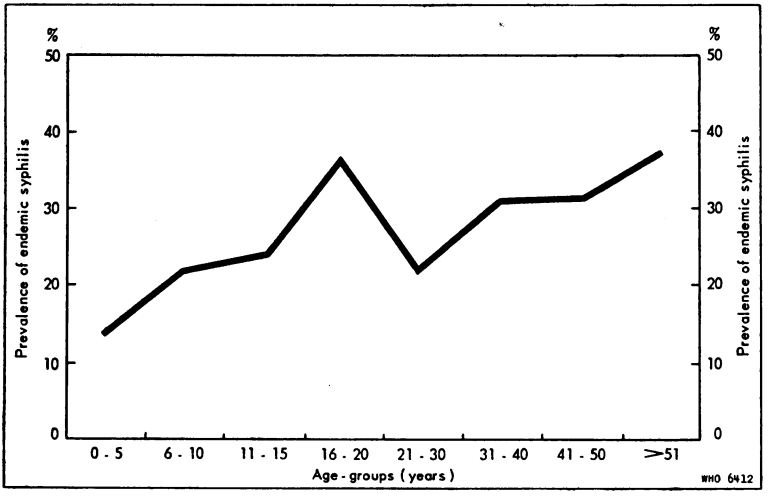


FIG. 7. AGE DISTRIBUTION OF ENDEMIC SYPHILIS IN AN ACTIVE FOCUS, BOSNIA *



* 25.6 % of the population of this administrative unit was infected.

TABLE II. DISTRIBUTION OF YAWS ACCORDING TO SEX AND AGE IN THAILAND *

Age-group (years)	Population examined	Persons infected		Ratio	
		number	%	male	female
0-4	male 554 female 517	26 28	4.7 5.4	100	115
5-9	male 464 female 473	164 122	35.3 25.7	100	73
10-14	male 426 female 409	235 217	55.1 53.0	100	96
15-19	male 350 female 390	169 183	48.2 46.9	100	97
20-29	male 509 female 554	241 252	47.3 45.4	100	96
30-39	male 367 female 380	209 225	56.9 59.2	100	104
40-49	male 254 female 239	163 169	64.1 70.7	100	110
50+	male 246 female 277	139 149	56.5 53.7	100	126
Total	male 3170 female 3239	1346 1345	42.4 41.5	100	98

* Based on clinical and serological findings in Gaeyai village, where the prevalence of yaws was 41.9 %.

Regarding sex distribution in endemic treponematoses, the differences are relatively small, although in yaws usually slightly more males, and in endemic syphilis more females, are infected.[5, 10]

The differences in sex distribution in different age-groups and in different endemic areas, which may sometimes be considerable, can be explained by the different habits of males and females in different age-groups which thus increase or decrease the opportunity of exposure to infection, e.g., trauma, clothing, playground, domestic life, etc.

Tables II and III illustrate these conditions in yaws and in endemic syphilis. The distribution of both diseases is uneven despite similar living conditions.[10, 28]

The clinical manifestations of yaws and syphilis differ in some respects, but these differences can be largely explained by different environmental influences and by the probable subsequent adoption of certain biological

TABLE III. DISTRIBUTION OF ENDEMIC SYPHILIS ACCORDING TO SEX AND AGE IN BOSNIA *

Age-group (years)	Population examined	Persons infected		Ratio	
		number	%	male	female
0-4	male 179 female 178	22 26	12.2 14.6	100	119
5-9	male 266 female 216	46 58	17.2 20.8	100	155
10-14	male 295 female 212	66 52	22.3 24.5	100	110
15-19	male 176 female 162	39 46	22.1 28.3	100	128
20-29	male 210 female 306	44 88	20.9 28.7	100	137
30-39	male 140 female 196	38 46	27.1 32.6	100	120
40-49	male 179 female 168	50 57	27.9 33.0	100	121
50+	male 147 female 181	54 69	36.7 38.1	100	103
Total	male 1592 female 1619	359 460	25.5 28.4	100	112

* Based on serological and clinical findings in the administrative unit of Sapna, where the prevalence of endemic syphilis was 25.6 %.

characteristics by the treponeme, as Hudson has pointed out.[19] There is scarcely a symptom in yaws which cannot be seen with some variations in non-venereal endemic syphilis, and vice versa. The clinical impression that yaws is a distinct disease is perhaps gained when large numbers of patients with predominantly one manifestation or another are seen and not from the observation of individual cases.

In this respect it may be justified to call attention to a similar error concerning endemic syphilis in Bosnia. Since, in endemic syphilis, some manifestations appear more frequently than others, or some manifestations of venereal syphilis do not appear at all, an erroneous clinical concept was formed that endemic syphilis was different from sporadic venereal syphilis. Only thorough clinical and epidemiological investigation established that endemic non-venereal syphilis does not differ from venereally acquired sporadic syphilis and that the apparent variations are mainly due to different

environmental factors.[8, 10, 32] This also appears to apply to the other endemic syphilis conditions, known as bejel, njovera, etc. That this may also apply to yaws is suggested in the realistic unitarian view of treponematoses emphasized by Hudson,[19] Guthe & Reynolds,[11] Guthe & Willcox,[12] and others.

Yaws, like endemic syphilis, may be transmitted by direct or indirect contact. The site of infection depends upon the living habits and environmental conditions in the area.

Insects have been suggested as potential vectors of the infection by several authors,[1, 22, 26] but do not appear epidemiologically important.

In endemic syphilis and similar conditions, primary lesions, although rarely seen, occur mostly in the oral region [1, 5, 7, 32] through the use of common domestic utensils (primarily drinking-vessels), kissing, etc. In yaws, because of different living and environmental conditions, the initial lesions are most frequent on the lower legs and feet, owing to trauma, abrasions by vegetation on uncovered parts of the body, etc.

The rarity of primary lesions in endemic syphilis and their relative frequency in yaws can perhaps be best explained by differences in the size of inoculum.[1, 10] In yaws the inoculum is usually massive, favoured by trauma and abundance of infectious lesions rich in treponemes, while in endemic syphilis the infection usually occurs by the transfer of a small number of organisms under more unfavourable circumstances, producing in general a symptomless infection by absence of primary lesions. Akrawi [1] demonstrated this experimentally in Iraq on volunteers who were exposed to massive infection and who developed primary lesions, while others who were exposed under less favourable conditions developed an asymptomatic infection.

Transmission of treponemes in large numbers under favourable conditions will result in primary lesions in endemic syphilis too. An instance may be seen in a mother with primary sore of the breast who is infected when nursing her child who has early infectious manifestations about the mouth. " Throwback " infection is relatively common in different parts of the world where endemic treponematoses exist.[2, 10, 13, 25, 33]

The generalized early lesions in yaws are multiform but usually differ in size and abundance from those in endemic syphilis. However, there are many instances when it would be hardly possible to differentiate these clinical manifestations in an individual case. This applies particularly to the papillomata in the anogenital region. This is in agreement with the observation that, in colder climates even within the tropics, yaws occurs in a modified form in which the skin lesions are restricted to condylomata in anogenital and axillary regions.[17, 24, 27]

It is generally said that early oral mucous-membrane lesions, such as mucous patches, which are very common in endemic syphilis and which are often the first observed manifestations of the disease,[1, 5, 10, 32, 33] are

absent in yaws although oral lesions do occur in some areas where yaws is endemic.[13, 27]

Bone and joint lesions are relatively frequent in both yaws and endemic syphilis and show no essential differences in appearance.[5, 6, 14, 19]

The greatest clinical similarities between yaws and endemic syphilis are seen in the late gummata and ulcerating lesions which result from the allergic state of the tissues.

The pathogenesis of these manifestations in yaws seems to be analogous to that in endemic syphilis in that the frequency of late lesions is influenced by exposure to superinfection or reinfection of a host already sensitized from previous infection.[10, 15]

This view was also discussed at the First International Symposium on Yaws Control, held in Bangkok in 1952.[34]

In a family observed in Thailand a child of three years had treponeme-positive hypertrophic papillomata on the buttocks and the mother had gummatous ulceration on the left hand which had developed a few weeks after the child's generalized papillomata. The mother had contracted the infection 26 years earlier; her serum was positive to the Kahn and VDRL tests but treponemes could not be demonstrated in the lesion. The pathogenesis of the destructive late lesion in the mother would probably be best interpreted by supposing that superinfection had occurred in the allergic host already sensitized by the previous infection.

Regarding gangosa and goundou, it appears quite obvious that these are only other names for late manifestations in the nasopharyngeal region encountered in both yaws and endemic syphilis.[5, 10, 33]

In any focus of endemic treponematosis, whether one of endemic syphilis [10, 33] or of yaws,[23, 25, 29] the largest part of the infected population is in the latent stage of the disease. There is also, in both, a close correlation between the activity of the focus and the percentage of seropositive latent cases (see Tables IV and V).

TABLE IV. RELATION OF ACTIVE CASES OF ENDEMIC SYPHILIS TO SEROPOSITIVITY *

Active cases (%)	Seropositive population (%)
1-2	12.8
3-5	13.5
6-10	16.2
11-15	27.0
16-20	29.2

* County of Zvornik, Lopare, Bosnia

TABLE V. RELATION OF YAWS PREVALENCE AND THE PERCENTAGE OF SEROPOSITIVITY FINDINGS *

Yaws prevalence (%)	Total seropositive (%)
1-2	8.5
11-15	54.0
16-20	71.0
21-30	77.5

* Taken from Li & Soebekti [33]

In many latent cases there is no history of infection. This occurs more frequently in endemic syphilis [9] than in yaws.[23] Symptomless infection is probably the cause of this, although the ignorance of the population also has to be taken into consideration.

The difference in the frequency of seropositive latent cases with negative history between endemic syphilis and yaws corresponds to the difference in the occurrence of primary lesions discussed above.

Hyperkeratosis of the soles, and to a lesser extent of the palms, is common in yaws; it is rare in endemic syphilis, but does occur, as do juxta-articular nodules and depigmentation.[5] That these lesions occur in both diseases is, however, more significant than the differences in their frequencies, which probably result from various ecological factors, or than their influence upon the natural history of the disease.

Congenital manifestations in endemic syphilis are rare and are generally believed not to occur in yaws.[1, 10] Their absence was previously thought to be one of the main characteristics of endemic syphilis. Nevertheless, there is sufficient epidemiological evidence to justify the assumption that the rarity or absence of congenital manifestations in endemic syphilis and yaws is due to the similar environmental conditions of the areas where these infections are prevalent.

In endemic syphilis, as in yaws, the infection is usually acquired in early childhood, many years before sexual maturity is attained. Since the infectiousness decreases with time, the probability of congenital transmission of the treponemes is considerably reduced. [1, 10, 20, 32] The low standard of living in endemic areas certainly results in a high neonatal mortality rate, particularly among the congenitally infected children, and this further reduces the occurrence of congenital manifestations.

A study made in an endemic yaws area in Thailand (Gaeyai village) of the mortality among infants under one year of age of infected and non-infected mothers showed that, in the infected group, the mortality was not very much higher than in the uninfected group.

Five hundred and twenty-three mothers, with 2637 pregnancies, were investigated; the infected mothers (all ages up to 45) had an average of 4.5 pregnancies and the healthy mothers an average of 3.7. This difference was balanced by higher survival rates in uninfected mothers' children. The mortality rate under one year among infants of infected mothers was 16.5% and among those of healthy mothers 14.5%. Analogous conditions were found in endemic syphilis in Bosnia.[10]

So far there has been no definite evidence of the development of cardio-vascular and cerebral affections in yaws. In some endemic syphilis areas these have been described,[1, 3, 10, 32] but the parenchymatous cerebral affections are usually absent or rare, and even when present are mostly found in rudimentary, stationary form.[32, 35]

However, in many areas of endemic treponematosis, the people live under primitive conditions and are usually reluctant to seek medical care. In such conditions many disorders, particularly mental disorders, appear to cause less incapacity than they do in highly civilized populations and therefore may easily remain undiscovered. More adequate observations are needed to elucidate this problem.

There are no differences in serological reactions in endemic syphilis and yaws. In both the amount of reagin decreases with time and is lower in the latent stage in older persons than in younger people, corresponding to the onset of the infection in the childhood.[10, 23, a]

Turner and co-workers [31] suggest that strains of treponemes isolated in different parts of the world from patients with various clinical syndromes produce certain biological differences in inoculated rabbits and hamsters. On the other hand, these strains produce close immunological relationships in animals and have the same sensitivity to penicillin.[30]

The *Treponema pallidum* immobilization (TPI) test has so far revealed no essential immunogenic differences between syphilis and yaws treponemes.[21]

From the above observations it may be stated that endemic syphilis and yaws are very similar and that any differences between them are not necessarily qualitative, but may result mainly from environmental factors which over the course of years have been predominant in the different areas in which these infections are found.

Because of these similarities the measures for controlling endemic syphilis and analogous conditions such as yaws can follow the same or similar principles.

RÉSUMÉ

Les tréponématoses sont considérées comme des infections étroitement apparentées qui peuvent se manifester par l'apparition de syndromes cliniques divers, mais cependant essentiellement similaires, les différences étant surtout dues à des influences écologiques.

L'auteur fait une étude comparée de la syphilis endémique (et autres affections du même ordre telles que le béjel, la njovera, etc.) et du pian. Il s'agit, dans les deux cas, de tréponématoses endémiques non vénériennes présentant des caractères épidémiologiques très semblables quant au début de la maladie qui a lieu au cours de l'enfance, à la propagation de l'infection dans la famille et à sa répartition selon l'âge et le sexe.

Les différences observées dans les manifestations cliniques sont dues principalement à des différences de milieu et de vie et sont plutôt quantitatives que qualitatives.

L'auteur estime que la rareté des lésions primaires dans la syphilis endémique, la pathogénie et la fréquence des lésions tertiaires, et la rareté des manifestations congénitales, tant pour le pian que pour la syphilis endémique, sont dues à des facteurs épidémiologiques.

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[a] D' Mello, J.M.F. (1953) *Serological reactions in yaws* (unpublished working document WHO/VD/SERO/29).

Les manifestations cliniques des divers stades du pian et de la syphilis endémique présentent une très grande similitude.

Dans tout foyer de tréponématose endémique, la majeure partie de la population infectée est au stade latent de la maladie.

On n'a pu démontrer jusqu'ici aucune différence antigénique ou immunogénique entre la syphilis et le pian, et ces deux affections offrent la même sensibilité à la pénicilline.

On peut baser les mesures de lutte contre le pian et la syphilis endémique sur des principes semblables.

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