

Treponematosi in Perspective

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Prefatory note

Since I have been the heretic and dissenter of my generation, and since by the nature of life's span this must be a sort of "summing up" of my opinions, I have presumed in this exposition of my views on treponematosi to depart from protocol, to use the personal pronoun and to introduce the material informally. It is my hope that the reader will find the story more interesting if it is told episodically and in chronological sequence.

My contribution has been, if anything, to bring sociological considerations to bear on this medical problem, to emphasize their importance in the evolution of treponematosi and to show how—in its different forms—this disease, although caused by only one species of parasite, has adapted itself to the manner in which human beings have lived, in all periods and climes. This is a new way of thinking, but it is possible to hope that time will eventually bring the requisite adjustments so that "our strivings will be forgotten and our conclusions accepted as obvious".

I have mentioned the names and referred to the contributions of many people. Any omissions have been entirely inadvertent. The references, with a few exceptions, have been limited to recent years because the literature is familiar and available and because many are given in the monographs and papers cited.

Bejel

Soon after the new clinic in Deir-ez-Zor on the Euphrates was opened, a Bedouin child with a muco-cutaneous eruption was admitted and I was told the "native" diagnosis. It was then, exactly 40 years ago, that the Arab word *bejel* was first transliterated, a word that has stood ever since for a type of endemic syphilis. Arab and French doctors in the area were confusing bejel with congenital syphilis, as doctors had mistaken endemic syphilis elsewhere (e.g., in Uganda and Bechuanaland). It was impossible, however, to miss the fact that bejel was *contagious*, transmitted from child to child and sometimes from child to parent. That this non-venereal disease was caused by *Treponema pallidum* I had no doubt. The character of early and late lesions, the positive serology, the identification in the

darkfield, and the quick response to Salvarsan and mercury were all diagnostic. Yet bejel did not conform to the conventionally held picture of syphilis; in many respects it more resembled yaws.

C. S. Butler, 1928

No one whose "medical memory" spans less than three decades can imagine the confusion in this field in the 'twenties. Take as an example C. S. Butler's presidential address before the American Society of Tropical Medicine in May 1928. Butler, who, with Peterson, had coined the word "treponematosi" in Haiti the year before to meet the need for a non-committal word between yaws and syphilis, made three points, all of them in opposition to the bulk of current opinion. He contended (a) that mercury was effective in curing yaws, (b) that *pertenue* was morphologically identical with *pallidum*, and (c) that gangosa was a late lesion of yaws and not a disease *sui generis*. In the discussion, an eminent man rose to defend the morphological differentiation of *pertenue* and closed with the observation that if yaws was syphilis, then leprosy was tuberculosis.

Endemic syphilis

In the same year, Kristian Grön published his comprehensive study of the syphiloids of Europe, past and present, under the title of "endemic syphilis"; by coincidence, that year E. I. Grin in Bosnia and I in Syria published our first papers. In 1932-33, when the first serological and clinical study of bejel was published, I called it the endemic syphilis of the Euphrates Arab. In 1935, when Grin published a report (his first in English) on the endemic syphilis of Bosnia, he discussed the relationship of yaws, endemic syphilis and sporadic syphilis in terms well ahead of his time.

In 1932 Blacklock, in a significant contribution to the yaws-syphilis discussion, pointed out that the clue lay in syphilis as it occurred among primitive people. "The effects of extragenitally acquired syphilis in the native children of rural areas of the tropics are those about which we chiefly require

^a Present address: Cedar Grove, Wisconsin, USA.

information.” Just such information was being accumulated in the Deir-ez-Zor Clinic. In the course of 12 years’ residence I demonstrated that endemic syphilis—like yaws—was a non-venereal childhood disease with manifestations of sabre-shins, plantar hyperkeratoses, depigmentations, juxta-articular nodules and gangosa. Other studies at the Clinic showed that bejel also resembled yaws in failure to produce clinical symptoms in the nervous and cardiovascular systems, was only rarely transmitted congenitally, and did not cause miscarriages or lessen maternal fertility.

Non-venereal ?

Rather strangely, it was difficult to get acceptance for the idea that bejel was non-venereal. A special consultant of the US Public Health Service, who visited Deir-ez-Zor after I left, reported in 1938 that the alleged non-venereal character of bejel was a “myth”, and suggested an unnatural practice to account for the frequency of mucous patches in the mouths of affected children.

It must be remembered that in those days the word syphilis, used in any connexion, inevitably carried a venereal connotation. This is still too often true. A prominent syphilologist wrote to me in 1932 that there must be a venereal link at some point in any syphilitic chain of infection. In 1933 Pusey wrote that well over 90% of syphilis infections were due to sexual contact, and most of the remainder were acquired orally. When in 1936 I published *Bejel: Nonvenereal Syphilis*, the paradoxical title elicited editorial comment in both the *Journal of the American Medical Association* and the *British Medical Journal*. Some progress has been made since then. Recently, a venereologist indignantly rejected the possibility that any syphilologist could have made the above remark about a “venereal link”. Yet the same limited view led a speaker at the 1962 World Forum on Syphilis and Other Treponematoses^b to say “every syphilis case is the result of intimate sexual contact with another syphilis case”. He was, of course, speaking about venereal syphilis, but he did not say so. A colleague showed irritation when he read Hutchinson’s words, “The first step, in order that we should understand syphilis, is to recognize that it is by no means necessarily a venereal disease”. As recently as

1956, some British doctors, while agreeing with me in general, found the term “endemic syphilis” unfortunate on two grounds: (a) because syphilis means a venereal disease, and prefacing it with endemic cannot alter this fact; and (b) because endemic syphilis, by its very name, suggests its origin from a venereal disease, whereas it probably evolved from a non-venereal disease such as yaws.

One gets the impression that many people today in the fields of public health and venereal disease control, while granting intellectual assent to the existence of a non-venereal endemic form of syphilis, shrink from taking it into account, just as the authors of medical textbooks have thus far ignored it.

Since endemic syphilis was even more burdened with this handicap in the 'thirties and we were therefore compelled to seek a neutral word for the innocent syphilis of Bedouin children, I retained “bejel” for several years as a convenient label. In 1938 I suggested that “bejel” had served a useful purpose but should be dropped in favour of a more comprehensive term. One still finds it used, however, as a type or in a geographical sense.

Intermediate

“Bejel”, however, acquired another significance; as the picture of endemic syphilis became sharper, it clearly presented diagnostic confusion with yaws. Wedad of Basra, Iraq, who had treated many of the marsh Arabs, published his illustrated monograph in 1936 and expressed his belief that bejel was yaws. Thoms reported from Arabia that the children with endemic syphilis whom he treated in the humid date-palm oases had lesions that could easily be ascribed to yaws. In the years before the Second World War, as I discussed bejel both in the USA and abroad with medical audiences comprising both syphilis and yaws experts, opinion as to its position was divided, because our reports had demonstrated that bejel was in so many respects intermediate.

I held firmly to *T. pallidum* as the cause of bejel but others would have preferred *T. pertenuis* or even a third parasite. An illustration of the current thinking is shown by the remark of the then editor of the *Archives of Dermatology and Syphilology* who said bejel could not be yaws because it was too far north of the equator. He assured the audience that if my photographs had been in colour he could have settled the diagnosis by looking for the typical amber crust of yaws. On another occasion the same man expressed his satisfaction that I had called bejel

^b World Forum on Syphilis and Other Treponematoses (1962) *Proceedings* . . ., Washington, D.C., US Department of Health, Education, and Welfare.

syphilis "and not yaws". I replied that "and not yaws" was his phrase and not mine, that I was prepared to call bejel syphilis, but not to rule out the possibility that it was also yaws.

Parsimony

Becoming further involved in the controversy about "yaws and syphilis, the same or different?" (the title of a 1940 paper), I was impressed—as Blacklock had been—by the fact that much of the argument was irrelevant. The mere existence of endemic syphilis had wiped out many of the classical points of clinical differentiation; major arguments were still being based on obviously epidemiological distinctions such as how the disease was acquired or on what continent. I therefore invoked the law of "parsimony", based on two propositions: (a) that one parasite cannot cause more than one disease; and (b) that infections caused by indistinguishable parasites must be the same disease. In the whole gamut of infectious diseases these propositions were being disregarded only in the treponemal field. Why should advocacy of the causal identity of yaws and syphilis be met with indifference or hostility when synthesis in the case of other infections, such as leishmaniasis, the typhus group or borelliasis was hailed as a scientific achievement? It was obvious that many would regret the establishment of unity between yaws and syphilis.

Obviously, one reason was that many minds were closed on the subject, convictions had been fixed too long, especially among those influential men who had spent much of their lives maintaining the plural concept. As for younger men, why be unconventional when opinion was so weighted in one direction? Why go into the wilderness with Butler and Holcomb? Syphilis—meaning venereal, of course—was one of the major concerns of all students of medicine, especially since its divorce from dermatology, but yaws was foreign, limited to the tropics, still regarded as a skin disease. To the average medical student four decades ago, yaws was somewhere towards the bottom of the list, along with Dum-dum fever and Madura foot. Amazingly, this is probably still true to some degree.

Many writers have justified the rigid separation of yaws and syphilis on the ground that it was useful and convenient to distinguish the venereal from the non-venereal, the serious disease of civilized adults from the exanthem of "native" children, "our disease" from the exotic one. If it were once admitted that they were the same disease, the practical

ramifications and the inevitable adjustments would be incalculable. Besides sweeping revisions of medical books, the educational material of social hygiene would need to be radically changed, the programme for eradication of syphilis would acquire a whole new dimension and the history of treponematosis would have to be completely rewritten.

A paradox

In those years preceding the Second World War the orthodox position was complacent acquiescence in the dogma of plural disease; but a disturbing factor was intruding. Just when it seemed to be settled that syphilis was an adult venereal disease caused by *T. pallidum*, and yaws an "innocent eruptive childhood disease" caused by *T. pertenue*, clinical reports from several countries adjacent to the Mediterranean were describing an "innocent eruptive childhood disease" caused by *T. pallidum*. Cutting straight across the conventional categorization, K. Grön reported endemic syphilis in southern Russia, as did Grin in Bosnia, von Dühring in Turkey, Lacapère in North Africa, Hewer in the Sudan, McQueen & Torrance in Palestine, Clawson, Heggs & Corner in Iraq, Mylrea & Thoms in Arabia, Napier in Aden, and Crosley, Rost & Hudson in Syria. Two hundred years ago, this embarrassing dilemma would have been resolved by tossing these examples of non-venereal syphilis into the catch-all of syphiloids, but this would not do in the day of serology and microbiology. Endemic syphilis had to be faced.

In 1941 I reached the conclusion that yaws and syphilis belonged together as one disease and were being held apart by the force of conventional opinion, under the mistaken impression that their separation was more useful and convenient than their union. In 1942 at a session of the American Society of Tropical Medicine I read a paper entitled *A Unitarian View of Treponematosis*. In the title I retrieved the neutral word that Butler had coined in 1927 and then abandoned. In the intervening 15 years the resistance to change from "spirochaete" to "treponeme" had been giving way; even the *Journal of the American Medical Association* began using "treponeme" in 1943.

One disease

This paper proposed that syphilis, yaws, pinta and the many local forms of endemic treponematosis be grouped together—not as the "treponematoses"

—but as one disease, treponematosi, which presumably had its origin at some time in the remote and unknown past. I speculated that the ancestor of *T. pallidum* was a saprophyte (perhaps the suggestion came from Bessemans) and that the parasitization of man took place in Central Africa, whence the disease was carried by migration, commerce and the slave trade to the other continents; thus, treponematosi was probably in the New as well as the Old World before the Age of Discovery. It was my belief that the manifestations of treponematosi were directly related to the climatic and sanitary conditions of human life, changing their character as the disease moved from hot to cooler climates and from primitive to civilized communities.

I submitted that in urban life the environment gradually restricted the transmission of the treponemes to sexual intercourse; as a result treponematosi then became a venereal disease. Since both venereal and non-venereal forms might be present within a narrow geographical compass—such as a city characterized by venereal syphilis surrounded by a rural area characterized by yaws—it seemed reasonable to account for the difference on epidemiological grounds. Although the climate was the same, the hygienic level in the city would be higher than in the village outside, and urban life and customs more conducive to venereal contacts. Endemic treponematosi would thus change into sporadic; but if the fluctuation in hygiene and *mores* was in the other direction, venereal syphilis would revert to some form of endemic treponematosi, yaws if the climate was hot and humid, endemic syphilis otherwise. It was surmised that such changes might occur in a few years, a few generations, or in the course of centuries, depending upon the speed with which environmental conditions changed. However, in any and every case, I believed the parasite was and remained *T. pallidum*. The distinction between the different forms was not based on etiology but on epidemiology. There was no objection to the common names yaws and syphilis, but I hoped that clinicians and pathologists might think in terms of the whole disease, keeping in mind the key word treponematosi.

First monograph

When Dr Henry Christian, editor of *The Oxford Medicine*, asked me to contribute a chapter introducing the treponemal infections, it seemed appropriate to expand the above ideas in a monograph

entitled *Treponematosi*.^c This was completed in 1945 while I was on duty at Pearl Harbor.^d

I followed Manson and others in associating the origin of yaws with Central Africa. Hamlin influenced my thinking about the Paleolithic origin of treponematosi in Africa, and its subsequent diffusion by human migration to all regions of the Old World, then across the Aleutian bridge to the New. Since treponematosi was globally distributed in prehistoric times, it was idle to speak of Columbus' sailors bringing syphilis to a syphilis-free Europe in 1493.

Epidemiology

The indigenous yaws of sub-Saharan Africa—my argument ran—had a florid skin eruption because the human skin was sufficiently warm and moist for the surface survival of treponemes, but, as Ramsay observed in Assam and Sellards in the Philippines, yaws lesions at higher altitudes were fewer and dryer and at the same time appeared in the mouth and about the folds of the body. The same phenomena occurred as treponematosi spread out from the humid area into the savannah and desert zones north and south of the equator, changing into endemic syphilis.

The epidemiological conditions of endemic syphilis consisted—like those of yaws—in (a) low levels of personal and community hygiene, and (b) the transfer of treponemes from one child to another in a liquid medium such as saliva, in the course of play or in the close proximities of family life.

As human beings developed urban civilization, the levels of hygiene rose and opportunities for child-to-child transmission gradually decreased. More and more individuals reached maturity without having contact with treponemes; instead, they fell victims as adults to infection carried by moisture in the genital area. This type of contact permitted transfer of treponemes in spite of scrupulous cleanliness. Thus changes in treponematosi matched each change in man's social evolution, from the childhood infections of yaws and endemic syphilis in primitive and unhygienic villages to the adult infection of venereal syphilis in advanced urban cultures. One cannot say when modern syphilis began because it was preceded by an infinite series of transitional

^c Hudson, E. H. (1946) *Treponematosi*, New York, Oxford Loose-Leaf Medicine.

^d Years later I found this note in my Navy service file, dated 1 April 1940: "Dr Hudson . . . has had considerable experience in tropical countries and has perfected a product known as bejel which he has used extensively in Syria."

forms. Thus, looking for a syndrome like modern syphilis in the ancient world is looking for the rationally impossible; the civilization out of which it was to spring had not yet evolved. Modern syphilis is an artificial disease in the same sense that modern civilization is artificial.

Taxonomy

It seemed sound to subordinate disease classification to microbiological taxonomy, and unsound to name a new parasite for each syndrome unless the differentiation of those parasites was clear, definite, constant and of a reasonable order of magnitude. It may be recalled that Hutchinson once remarked that one would not think of putting two sheep in different species merely because one had a black face and the other no horns. There are certain biological rules for the naming of new species, and these have been disregarded by creating a new species of treponeme to match each treponemal syndrome. No taxonomist likes to give different specific names to organisms that he cannot tell apart.

Concluding the monograph, I declared my faith in the orderly processes of nature, preferring the dynamic idea of a continuing metamorphosis of treponematoses integrated with the evolution of human society and rejecting the static concept of three or four treponemal diseases with specific parasites and fixed clinical boundaries. I felt that the world concept of treponematoses would provide social hygiene organizations with a fresh and powerful psychological argument in their campaigns against venereal syphilis. The public should be told that civilized man had eliminated childhood non-venereal treponematoses through personal and community hygiene, but had left the door open for attack during the reproductive age. Venereal syphilis therefore "is an unwelcome by-product of civilization's ascent to higher levels of hygiene".

The bejel type

After the Second World War reports of endemic syphilis began turning up in many countries of the subtropical and temperate regions of the Old World, often in association with savannahs, mountains and deserts. In most cases these reports mentioned bejel as the type of non-venereal treponemal syndrome being described. In the following list^e the names of the reporters are given in parentheses; though the list is admittedly incomplete, it shows

how extensively endemic syphilis is distributed: Gambia (McFadzean, McCourt & Wilkinson); Gold Coast, Nigeria, Rhodesias, Sierra Leone (Willcox); French West Africa and Equatorial Africa, French Cameroons, French Sudan and Upper Volta (Mathurin; Vaucel; Baylet; Ridet); Bechuanaland (Murray et al.); Uganda (Davies); Ethiopia (Guthe; Manson-Bahr); Sudan (Grin); Arabia (Chaglassian, Bustani & Hamilton; Ghouroury; Gasparini); Syria (Rizk et al.; Luger); Iraq (Akrawi; Csonka; Tuomioja; Jones; Hudson); Iran (Csonka); Turkey (Christiansen); Afghanistan (Cutler); "Himalayan foothills from Kashmir to Assam" (Rajam). In addition, *irkinja* in central Australia and yaws in Tahiti have been reassessed and transferred to endemic syphilis. Suggestions have also been made that yaws and pinta in the New World should be reviewed to see if endemic syphilis was being overlooked in the temperate zones and mountainous regions of Central and South America.

Pinta

In May 1948, at the Fourth International Congresses of Tropical Medicine and Malaria, in Washington, I was asked to discuss Blanco's paper on the relation of pinta to syphilis and yaws. I have never felt that pinta was such a "freak of nature" as its regional backers have made it. It is agreed that there is a dyschromic treponematoses in those regions, perhaps more than anywhere else in the world, but that it is a disease *sui generis* with a specific parasite remains doubtful. If an epidemiologist were shown a map in which two diseases (caused by indistinguishable parasites, transmitted from child to child in the same manner and diagnosed and treated in the same way) virtually overlap, as do yaws and pinta in Central and South America in the map that appears in certain WHO publications,^f he would certainly be inclined to call them the same disease.

At the Washington Congresses I submitted that if three treponemes were put into the hands of a scientist—any scientist in the world—and he were told that one was from a case of yaws, one from a case of syphilis and the third from a case of pinta, he would not be able to determine which was which by any known test, visual, chemical or biological. Nothing that has happened in the past 16 years has substantially altered the truth of that statement;

^e The names of countries in this list are those at the time of the reports referred to.

^f See, for instance, Guthe, T. & Willcox, R. R. (1954) *Treponematoses: a world problem*, Geneva, World Health Organization; and *WHO Chronicle*, 1964, 18, 403.

and it was repeated at the World Forum on Syphilis and Other Treponematoses. Continuing, I said one of the organisms would be diagnosed a yaws treponeme because it came from a resident of the Haitian countryside, the second syphilis because the patient lived in a city and his disease started with a genital sore, and the third pinta because it came from an individual living in Colombia (or southern Mexico). This is diagnosis not by etiology but by geography and epidemiology. Such an approach might have been tolerated 100 or even 50 years ago, but it is incompatible with modern modes of thought.

At other times I called attention to the frequent occurrence of pigmentary changes in all forms of treponematoses, leucoderma in venereal syphilis, depigmentation in endemic syphilis (North Africa, Arabia, Australia, Syria⁹) and patchy loss of skin pigment in yaws in various parts of the world (sub-Saharan Africa, Java, Guam, Cuba, to mention only a few). Typical pinta cases have been identified in Chicago and Baltimore. Ancient medical lore is full of references to the white patches of "leprosy", a thing that is never seen in true leprosy but characteristic of treponemal infection. The word *empeines*, equivalent of dermatitis, which is favoured to describe the early lesions of pinta, was used in Spain 500 years ago as a synonym of *bubas* and later, in South America, for *bubas seccas*, dry yaws.

My remarks in 1948, therefore, concluded with the suggestion that pinta was a useful descriptive term for a syndrome of treponematoses prevalent in Latin America but not confined to that region, whose chief claim for attention was based on its propensity for late achromias.

Two explanations present themselves for such a syndrome; either (a) that a variety—hardly a species—of *T. pallidum* has evolved in pinta areas capable of exaggerating the normal tendency to dyschromia in treponematoses; or (b) that observers of pinta, a syndrome of notoriously imprecise symptomatology, have perhaps subconsciously culled the discoloured cases out of the widely distributed rural matrix of non-venereal treponematoses in those regions, and set them up as a separate disease with a specific parasite. Perhaps there is a mixture of these two factors, but in any case, pinta's right to disease status seems questionable.

⁹ The late Admiral Stitt, former Surgeon-General of the US Navy, used to borrow my slides of depigmentation in bejel to illustrate his lecture on pinta for medical officers, because they were more typical, he said, than any photographs obtainable from Latin America.

It may be that, in those regions of Central and South America, yaws characterizes the hot and humid areas and a treponematoses that should be called endemic syphilis characterizes the more temperate, dryer and elevated areas. Some of the yaws cases and some of the endemic syphilis cases show dyschromias, just as they do elsewhere. It may be justifiable to put these cases together under the head of "pinta", but they could as well be distributed under the categories of yaws and endemic syphilis.

It is said that condylomata, plantar hyperkeratoses and late erosive and gummatous lesions of skin and bones are never seen in pinta cases. Could it be that such lesions do occur, but when observed are attributed to yaws? I am reminded of the period in the history of yaws when it was generally held to be a skin disease without a tertiary stage like syphilis. Consequently, when tertiary lesions were found in yaws cases they were either said to be due to "concomitant syphilitic infection", or—like gangosa—made a separate disease. Later, yaws was acknowledged to have late as well as early lesions. Another fallacy was the early conviction that yaws ought to have the same manifestations in all countries. This led to controversy between the "yaws men" of different regions and continents until it was realized that the disease did in fact exhibit great variation. In regard to endemic treponematoses there are many discrepancies not fully accounted for. Why, for example, should Guam have been notorious for gangosa, and Africa for goundou? Why the disparities in distribution of keratoses and juxta-articular nodules? Why boomerang tibiae in Australia and depigmentation in Latin America? We do not know why, but it would be anachronistic thinking to react by multiplying the disease categories.

Obviously, a great deal of on-the-spot epidemiological work needs to be done on pinta. If this is ever accomplished, I think pinta will be placed not far away from the mainstream of treponematoses. Although it is alleged that outsiders cannot assess pinta, it is probably not the oddity and anomaly it has been pictured.

The World Health Organization

In the post-war years, the most noteworthy event in the treponemal field was the decision of WHO to consolidate efforts against all the forms of treponematoses simultaneously. Because venereal syphilis was already being efficiently handled in the advanced nations, the consolidation in effect gave

WHO a prime opportunity to study and treat endemic treponematoses—endemic syphilis and yaws—as it was occurring in the less advanced nations. And what better time than when mass penicillin therapy first became available! For the first time a large international body devoted to public and private health had the opportunity to study differential diagnosis, epidemiology and many other engrossing problems connected with treponematoses. For many of the countries, because of their rapid strides, the situation at the end of the 'forties offered perhaps the *last* chance to study "pure" "native" diseases, and at the same time the *first* opportunity to study the impact of modern health programmes.

Unquestionably WHO has stimulated the collection of a tremendous amount of information through field and laboratory studies, and WHO and UNICEF have relieved a vast amount of suffering in numerous campaigns in co-operation with local governments. This story is told in full elsewhere. I shall only testify here to my own gratitude to Ohio University for a leave of absence and to WHO for the opportunity to return to the Middle East in 1950-51 with a field team that gathered information about bejel from Euphrates and Tigris villages, from desert nomads and from marsh Arabs. Tuomioja inoculated rabbits and hamsters with treponemes^h from venereal syphilis patients in Baghdad and with treponemes from children with endemic syphilis in the marshes. I found the non-venereal syphilis situation in rural Iraq virtually the same as that which I had described farther up the Euphrates in Syria 20 years before.

Further monographs

In the light of the renewed interest in bejel, I recalled the thousands of clinical records of bejel patients I had left behind in 1936. Perhaps a monograph based on this accumulation of 12 years would add a further dimension to the data on endemic syphilis being gathered by the WHO field teams. In 1952 the National Microbiological Institute of the US Public Health Service approved a grant (E-384) for such a study. The records were shipped from Deir-ez-Zor the same year. Two years later the data had been transferred to IBM cards, sorted, tabulated and analysed, while a third year was devoted to tables, graphs and text. Many original photographs of bejel were available, as well as Rost's skiagraphs. For financial reasons publica-

tion was delayed until 1958. Entitled *Non-Venereal Syphilis*,ⁱ the monograph presented a comprehensive description and discussion of the bejel type of endemic syphilis.

Two other monographs important in the field of treponematoses were published by WHO during those years, Grin's *Epidemiology and Control of Endemic Syphilis* in 1953,^j and Turner & Hollander's *Biology of the Treponematoses* in 1957.^k The authors of the latter kindly permitted me to include in my monograph a discussion of their results and conclusions particularly as they concerned bejel and the parasites of endemic syphilis.

Ses versus sis

At the First International Symposium on Venereal Diseases and the Treponematoses, held in Washington in May 1956, I presented a brief summary of my ideas about the origin of treponematoses: (a) it arose as yaws in Central Africa perhaps several hundred thousand years ago; (b) it was carried out of Africa by Paleolithic migration perhaps 100 000 years ago, becoming endemic syphilis in more temperate climates; (c) endemic treponematoses (yaws and endemic syphilis) was particularly suited for propagation in primitive village life, a milieu in which it still thrives; (d) venereal syphilis evolved from endemic syphilis when urban civilization first appeared in Neolithic times in Mesopotamia five or six thousand years ago. These reactions between man and *T. pallidum* were phases in the evolution of one disease, of which they were clinical variations, syndromes produced under the influence of epidemiological factors.

My title was *Treponematoses—or Treponematoses?* and again I pointed to the advantages offered by the unitary concept, symbolized by the singular ending. Use of the plural, on the other hand, signifies more than one disease and more than one parasite, so that instead of addressing ourselves to the world problem of treponematoses we are actually making *comparative* studies of the treponematoses. The concept of a world view or a world-wide approach is vitiated by use of the plural.

ⁱ Hudson, E. H. (1958) *Non-venereal syphilis*, Edinburgh & London, Livingstone.

^j Grin, E. I. (1953) *Epidemiology and control of endemic syphilis: report on a mass-treatment campaign in Bosnia*, Geneva (World Health Organization: Monograph Series, No. 11).

^k Turner, T. B. & Hollander, D. H. (1957) *Biology of the treponematoses*, Geneva (World Health Organization: Monograph Series, No. 35).

^h Made available by courtesy of Dr Akrawi.

In 1941 I had compared malaria and treponematoses. Malaria is one disease; we have a world view of it and a programme with a world-wide approach that is leading rapidly toward its eradication. Unlike treponematoses, malaria is caused by three or more species of parasite with differences of a vastly greater order of magnitude than any real or fancied differences among the treponemes. Yet no one on that account insists on talking about the "malarial problem" or "malarial research". People think and talk about malaria as if it were one disease, which it is.

In contrast, treponematoses, a disease of parasites that are almost indistinguishable by any standard, has to be referred to in the plural. Hence such ungraceful expressions as "treponematoses problem" and "treponematoses research", and—of far greater consequence—the contravention of world-wide control and eradication. This situation will continue so long as the people concerned are divided into those involved in the diagnosis, treatment and control of venereal syphilis, and those concerned with the syndromes of non-venereal treponematoses. Perusal of the papers read at the recent World Forum on Syphilis and Other Treponematoses^h shows two bodies moving on parallel tracks; they never join. The test of unity, *thinking* and *acting* as well as *meeting* together, was largely lacking. The plural title blurred the focus, pointed to multiple goals instead of one, and dissipated energies on objectives of secondary importance.

Categories

With regard to biological differentiation of the treponemes, I indicated in 1946 five handicaps inherent in such procedures. (1) Conclusions drawn from animal experiments may not be—and probably are not—directly applicable to man. (2) The experimenter can never be sure what he starts with; there are no "tagged spirochaetes". Consequently, he must identify his spirochaetes from their source, a hazardous and unscientific step akin to circular argument. (3) The yardstick itself is elastic. *T. pallidum* has notorious ability to vary under new conditions. (4) The experimenter always has the nagging question: if I do find differences, will they be *fixed*, or are they related to fluctuating environmental factors? Are they of the order of variations that can reverse themselves? (5) Finally, the differences between species must be *constant* (terms such as "usually", "by and large", "in the vast majority", "fairly stable", "gradual shifting from one to

another", "most but not all", should be barred), *clear* (no gradations, no unexplained overlapping, no "ill-defined but more or less real", no mere quantitative differences, no intermediate forms), and of a reasonable order of *magnitude*.

When Turner & Hollander concluded that treponemes isolated from patients suffering from different syndromes differed in "certain fairly stable biological characteristics", this was taken as strong support for specific differentiation of *pallidum* and *pertenue*, but in the succeeding seven years biological differentiation has been regarded with increasing doubt. Now it can only be made with hamsters.^l If the hamster's reaction is to be relied on to indicate which is which, it must first be ascertained that it is not about to hibernate, since this and other factors upset the response. Even when it shows the "*pertenue* reaction", the possibility of an intermediate form is not certainly eliminated. Turner & Hollander^k had such difficulty in classifying the reactions that they had to postulate an intermediate category (M type) between the syphilis (S) type and the yaws (Y) type. The mere existence of the M type showed that specific differentiation by animal inoculation was in trouble.

Magnitude

There is no question but that the different plasmodia of malaria belong to different species; their differences are of such magnitude that both zoologist and clinician agree. On the other hand, though there are many strains of pneumococcus, neither taxonomist nor clinician proposes to divide up *Diplococcus pneumoniae* into different species, because the differences are *not* of sufficient magnitude. Fortunately for pneumococcal taxonomy there is no clinician committed to the existence of *two* pneumococcal diseases and therefore demanding two pneumococcal species to match them. This comparison is not far-fetched. *Pasteurella pestis* does produce two or more syndromes (cutaneous, bubonic, septicaemic, pulmonary) in man, as well as sylvatic in animals. These are differentiated by the epidemiology; though there may be corresponding variations in the antigenic composition, neither in this case does anyone insist on a separate *Pasteurella* for each syndrome.

Speciation in unicellular organisms is at present so perplexing that one wonders if an antigenic difference between *pallidum* and *pertenue*, even if

^l Guthe, T. (1964) *Acta derm.-venereol.* (Stockh.), 44, 1.

established, would be of sufficient magnitude to confirm them as separate species. Although Turner & Hollander stated that all the strains they studied had some antigenic components in common, search is now being made for those antigenic components that *pallidum* and *pertenue* are presumed *not* to have in common. The choice of this line of research reveals the fact that the classic differential points have failed. Morphology, physiology, pathology, serology, electron microscopy, animal inoculation, cross-immunity, immobilization and fluorescence tests, response to therapy—all have been disappointing. Now to prove the right of *pertenue* to existence, research is reduced to delving into the very biochemical substance of the treponemal cell; and the difficulty here is that little can be done in this field until treponemes can be grown in culture, and cultivation is not yet in sight. In a word, pluralists are now solely dependent on hamsters and hope.

International work in Syria

In 1954-55 the World Health Organization initiated a study of bejel in north-eastern Syria by Luger and his associates. Their base was Deir-ez-Zor, where the original study was begun 30 years before. In 1937 I called bejel "the original and pure form" of endemic syphilis. Luger^m observed that "bejel is the original, pure, unchanged and unmodified endemic syphilis". He confirmed my earlier observations in all essential respects.

In 1957 Guthe & Luger,ⁿ at the XIth International Congress of Dermatology in Stockholm, reviewed the epidemiology of endemic syphilis and agreed with the conclusions of earlier workers that it rested on two factors: (a) village life of low hygienic level, and (b) non-venereal contacts among the children. I recorded the details of this mechanism in 1936. In my observations of village children I had always been impressed by the opportunities for transmission of treponemes from child to child in a liquid medium, which, in the case of oral lesions, meant by the saliva. In spite of the climate, usually dry and much of the year hot, moisture could persist for an appreciable time on common utensils and drinking bowls, and on toys such as whistles and other objects that were passed from mouth to mouth; older children who were caring for babies kissed and fondled them in imitation of their elders; there was the proximity of scantily

clothed and unwashed bodies in the family hut or tent, and the constant accompaniment of flies, fleas and lice. Flies flew from lip to lip or attacked and rasped the skin voraciously; the sucking insects could conceivably carry treponemes as they wandered from host to host.

In 1937 and again in 1946 I contrasted the immunological course of (a) syphilis as it proceeds in an ordinary adult suffering from a venereal infection with (b) endemic syphilis in an ordinary village child. In disease (a) the chancre probably represents the first contact of that individual's body with a treponeme, whereas in disease (b) the child's body almost from birth has been continually subjected to contact with treponemes, small increments of which have been constantly invading. I believe I was following Lacapère in suggesting that many of the characteristic features of endemic syphilis, such as the absence of visceral and neural pathology and the freedom from congenital transmission could be traced back to this multiple exposure to subclinical invasions from early childhood. Luger^m also attributed many of these features of endemic syphilis to such "minute subliminal superinfections".

The paper that Guthe & Lugerⁿ published on the epidemiology of endemic syphilis was particularly interesting to me because they epitomized so well my long-held views on the close articulation between the sociological setting and the corresponding treponemal syndrome. They said:

"Living habits and practices in under-developed areas have over the centuries established an ecological balance between the environment, the host and the treponeme . . . When this ecological balance is upset through improvement of the environmental conditions, the disease changes its epidemiological, immunological and clinical pattern and may tend to limit itself. But *T. pallidum* may then continue to be propagated by venereal transmission . . . As hygiene improves, the number of childhood cases falls, the number of susceptible adults rises, the number of venereally acquired cases rises, whether from the 'endemic' spirochaetes or imported 'venereal' ones, leading first to transitional and then to pure venereal pattern".

This is just what my colleagues and I observed during the years of our residence in Deir-ez-Zor. Previously, it had been like the other villages along the Euphrates and Khabur rivers, with bejel endemic among the children and late lesions common among the older people. However, when I arrived in 1924, the bejel era in Deir-ez-Zor itself was ending. The town's importance in government and commerce

^m Luger, A. (1958) *Derm. Wschr.*, 137, 25, 57.

ⁿ Guthe, T. & Luger, A. (1957) *Dermatologica (Basel)*, 115, 248.

grew over the years, its population increased, a piped water supply was installed and streets were swept. Parallel to these and other events of improved civic life the early bejel eruptions among children became rarer and late lesions among adults less frequent. At the same time venereal infections became more common. Meanwhile, the outlying villages were not affected by any such modifications in social environment so that Luger 20 years later found them with the same picture of endemic syphilis. The semi-nomad villagers were still living in the manner of their ancestors and they still had the ancestral non-venereal treponematoses.

The cycle

Willcox^o recapitulates the same sequence, from endemic treponematoses through transitional stages to pure venereal treponematoses, following improvements in hygiene and the amelioration of social conditions. He makes a valuable contribution by collecting from medical history and literature all the instances of transition from non-venereal to venereal treponematoses. Then he records those instances in which deterioration in social conditions favoured the other side of the "cycle", from adult venereal to childhood non-venereal syphilis. For many years I have been using those transitions as illustrations of the way the manifestations of treponematoses are linked with social and other epidemiological conditions, expressing this in 1961 in the form of an editorial, *Endemic Syphilis: Heir of the Syphiloids*. If environmental conditions can convert endemic into sporadic syphilis and *vice versa*, there seems no reason to doubt that climatic and social conditions can change the florid yaws pattern into the mucocutaneous bejel pattern, and *vice versa*.

Willcox has provided cogent evidence for the "one-ness" of treponematoses. He says, "Some consider yaws and syphilis to be due to the same organism, the effects of which are modified... Others consider that the two diseases are due to closely related organisms which thrive in the particular intrinsic and extrinsic environments described." But he also says the endemic syphilis "may reappear should social conditions markedly deteriorate", or, if syphilis is introduced venereally "into the favourable environment of a primitive population", it may "spread in endemic form". In other words—and colloquially—epidemiology is all.

Some writers who adopt a tolerant attitude on the separatist issue at the same time feel it would

require centuries for one disease to change into the other. Evidence adduced by Willcox, however, indicates how rapid the change can be. In my view, length of elapsed time is irrelevant; in fact, the change from yaws to endemic syphilis can occur in the same individual if he moves from jungle to desert, or from tropic to temperate zone. (Hutchinson said yaws appeared to be a disease that could not leave its home; for example, an Englishman who acquired yaws in the tropics came home with syphilis.) It seems reasonable to conclude, therefore, that treponemes from a child with endemic syphilis are quite capable of initiating venereal syphilis if introduced among the adults of a sophisticated community. Those who find it hard to accept this view take refuge in such concepts as "venereally acquired endemic syphilis", or "acquired sporadic syphilis contracted non-venereally by children from adults with infectious venereal syphilis".

Those who believe yaws and syphilis to be different diseases become concerned about "the possibility of venereal syphilis invading a population recently treated for endemic treponematoses". It worries them that if WHO programmes cure the inhabitants of a primitive area of their yaws, they may suffer subsequently from what is described as much more serious syphilis. This was the thinking behind the long-held belief that yaws protected against syphilis and therefore had best be left untreated.

No one, however, who believes one syndrome capable of changing into the other would see any problem here. If a primitive population is cleaned of its yaws but allowed to continue its old ways, treponemes—no matter whether of venereal or non-venereal provenance—would soon produce yaws again. On the other hand, as I said in 1937, "If a certain primitive people is taught civilized ways they will lose their yaws anyway, and their infections, if any, will be venereal". Only venereal treponematoses can endure among human beings with the sophisticated habits of civilized life. In present-day Africa the great social changes are causing important shifts in the relative incidence of the non-venereal and venereal syndromes.

Tropisms?

Cockburn^p assumed in his paper, *The Origin of the Treponematoses*, that there are at present three distinct diseases (syphilis, yaws and pinta) of which the first is venereal with a genitotropic parasite

^o Willcox, R. R. (1960) *Brit. J. vener. Dis.*, **36**, 78.

^p Cockburn, T. A. (1961) *Bull. Wld Hlth Org.*, **24**, 221.

which "has little chance of survival if it fails to infect the genitalia". He advanced the theory that *T. pallidum*, being transmitted congenitally, has developed organotropic strains as a result of "passage through a series of foetuses".

Cockburn placed isolation high among the factors responsible for the evolution of the present three diseases. In the case of pinta this was *geographical* isolation and speciation. He assumed that treponemes came with man across the Bering land bridge and that pinta (which he says is not found elsewhere) acquired its unique character subsequently through changes both in the parasite and in the human inhabitants of Central and South America. The other two diseases, he said, with their specific parasites evolved out of *ecological* isolation. He thought it was generally accepted that before the days of Columbus there were treponemal infections both in the Old World and in the New, but he attributed the rise of syphilis in Europe after the Renaissance to the appearance of a "strain that had developed venereal transmission".

Though this author's theories are ingenious, his categories seem too rigid and his numerous premises unsupported. He does not allow the treponeme sufficient flexibility in relation to the human environment. Because he does not mention endemic syphilis he is not obliged to account for it. As to pinta, can it fairly be claimed to exist nowhere else? Do the people of Latin America truly have some unique immunological relationship to it? The most serious objection to Cockburn's ideas, however, lies in the reintroduction of tropism, a concept that was favoured for a while but is now largely abandoned. Though we have stopped hearing about ectodermotropism and neurotropism, here freshly introduced are organo- and genito-tropism.

The trilogy

In the summer of 1962 I completed three papers amplifying ideas on the relation between treponematosis and anthropology (published June 1963),^a pilgrimage (December 1963)^r and African slavery (March 1964).^s Since treponematosis was in my opinion one disease, only one origin had to be accounted for, and that—I suggested in the first of the trilogy—occurred as man did in sub-Saharan Africa in Paleolithic times. Beyond this simple

basic assumption it was only necessary to project historically such events are as consonant with the natural history of the disease. The establishment of endemic treponematosis in the villages of the world when they developed in the Mesolithic and Neolithic times, and the rise of venereal syphilis in the urban civilizations that developed in the Middle East about six thousand years ago were logical steps that ensued naturally. The evolutionary perspective—to use Holcomb's phrase—enables us to reconstruct the past out of present-day materials. In the words of Hutton, the great Edinburgh geologist, "The present is the key to the past. Look at processes going on today, and see how the great changes occurred".

In the pilgrimage paper I reviewed the evidence that the Middle East by the beginning of the Christian era had become a home of treponematosis second only to Africa, and directed attention (a) to the millions of pilgrims and Crusaders who returned to Europe from the Levant in the course of a thousand years; and (b) to the multitudes that more than 1300 pilgrimages have brought to Mecca and scattered again to their homes in Africa and Asia. I suppose no one would gainsay the probability that all these mass movements and demographic upheavals yielded numerous opportunities for the exchange and dissemination of treponemes.

In the discussion of African slavery it was pointed out that from time immemorial Central Africa, the homeland of yaws, has been the source of slaves for the rest of the world, perhaps to the number of 100 million or more. In fact, the currents of Negro dispersion in the history of the world have been of such a geographical sweep and numerical magnitude that the diffusion of treponematosis by Negro slaves has been of global dimensions.

Maps

In the summer of 1962 I was privileged to see a draft of Hackett's important paper, *On the Origin of the Human Treponematoses*.^t It is too impressive and the argument too complex to permit discussion here *in extenso*. I shall therefore have to assume that the reader has digested it in detail.

Hackett seems to have been influenced by Cockburn about pinta, for he regards it as a unique and isolated infection, but he goes a good deal further than Cockburn in his belief that pinta originally covered the earth, was subsequently displaced and

^a Hudson, E. H. (1963) *Ann. intern. Med.*, **58**, 1037.

^r Hudson, E. H. (1963) *Amer. J. med. Sci.*, **246**, 645.

^s Hudson, E. H. (1964) *Brit. J. vener. Dis.*, **40**, 43.

^t Hackett, C. J. (1963) *Bull. Wld Hlth Org.*, **29**, 7.

now remains in the Americas as a refugee disease. His Map 3, giving the "probable extent of pinta" shows it blanketing the world about 15 000 years B.C. Map 4, giving the "probable extent of pinta and yaws about 10 000 B.C.", shows pinta isolated in the New World and yaws dominating both tropical and temperate zones of the Old World. Map 5 introduces endemic syphilis and gives the "probable extent" of the three syndromes in 7000 B.C., pinta in isolation, yaws in its present area, and endemic syphilis in Africa north and south of the tropics, in Australia, and extending through the Middle East into Central Asia. Map 6, dated from about 3000 B.C. to the first century B.C., shows venereal syphilis in a ring around the Mediterranean, while the other three remain as before. Map 7 purports to show (with arrows) (a) the "spread of venereal syphilis throughout Europe" about A.D. 100 and (b) the "spread of venereal syphilis throughout the world and of yaws to the Americas and Ceylon from the 16th century A.D.". In this map pinta has been squeezed between coastal belts of yaws to the east and west, thus differing from the world map which appears in certain WHO publications.^f In that one pinta and yaws in Central and South America cover much the same territory, producing a cross-hatching, but in this map they do not touch.

Hackett's Map 1 shows the "probable geographical distribution of the treponematoses about A.D. 1900". There is no question but that Hackett has worked out his theory of the origin of the "treponematoses" in sufficient detail to cover all contingencies, but it suffers from unsupported premises and pyramided hypotheses. Perhaps his map titles should read "possible" rather than "probable". He is particularly vulnerable to "Ockham's razor", having disregarded the principle that, from alternative hypotheses, one should choose the simpler, the one requiring the least number of assumptions.⁴

Four diseases?

Since the early work on endemic syphilis, particularly in Bosnia and Syria, many people, sensing a dilemma, have explained it away either by saying

⁴ If I may be facetious, let me suggest that the odds in favour of a theory vary inversely as the square of the number of assumptions needed to hold it up. Let us say for the Cockburn and Hackett theories that they have each used four (actually more). Then the odds in favour of their theories are as the square of one over four, or one in 16. On the other hand, a theory that rests on only one assumption has odds of the square of one over one, or about an even chance of being right.

that bejel was yaws due to *T. pertenuis*, or that it was "merely syphilis", differing from venereal syphilis only in minor respects. Both of these evasions have been negated by subsequent events. Hackett meets the dilemma head-on by proposing that endemic syphilis be made a separate disease with a parasite of its own. He says, "At present, endemic syphilis and venereal syphilis are not the same disease and their treponemes, though closely related, do not appear identical". This is in the orthodox tradition, for it is just what happened in each of the other "treponematoses". Yaws looked different, so it was made a separate disease and given a special parasite. When pinta was identified, it got a name and a parasite of its own. Now that endemic syphilis has achieved identity, Hackett proposes that it should have its own name and parasite.

That this creation of a new species by fiat is only tentative is suggested by his relegation of the idea to a footnote, but trial balloon or not, there it is: "treponaridosis" rather than endemic syphilis, and a new parasite, *T. trepenarida*.⁵ He adds, "Were a new name needed for yaws, which it is not, the name 'treponumidosis' might be proposed".

With due respect, the pluralism represented by four diseases and four parasites, though superficially pleasing in its symmetry, constitutes a vulnerable position; questionable also is the proposal to introduce into the nomenclature the dry-moist antithesis, as if this were the only criterion between yaws and endemic syphilis. Rainfall and humidity vary widely; in many regions they are not the crucial core of the epidemiology, since other factors such as vegetation, insects, bathing habits and the use of clothing may be involved.

Two kinds of evolution

Both Hackett and I take an evolutionary view of the origin of treponemal infection in man, but there is this fundamental difference: his is a discontinuous process, a series of discrete steps, envisaging change from one disease to another and from one species of parasite to another by mutation or saltation at a definite time and place; his view finds reversions hard to account for. The opposing view is fluid, picturing changes beginning early and continuing to the present, a succession of strains, forms, transitional stages, metamorphoses and syndromes, often

⁵ Should not the spelling be "*treponaridum*", neuter singular to agree with *Treponema*? "*Trepenarida*", being a hybrid (part Greek and part Latin), is not likely to meet with taxonomic approval.

reversing direction to previous levels when and where environmental conditions change, but always retaining the same etiology, *T. pallidum*.

Hackett starts with a primordial treponeme which mutates successively into *pertenue*, "*trepenarida*" and *pallidum*. The last is "mild" in its effects on man at first, but later it mutates again to produce the "syphilis of the present" about A.D. 1500. This schema is inventive but without factual support, and it ignores the flexibility of *T. pallidum vis-à-vis* its environment. In 1956 I suggested that venereal syphilis had appeared first in the urban civilizations of the Middle East, but postulated no mutation. This event, it seemed to me, occurred there simply because in that area for the first time the human race had created an environment which eradicated the ancient endemic syphilis of children and made possible the venereal disease of adults. Such an event might occur—and probably has—at many times and places, accompanying similar improvements in personal and community hygiene. Throughout its long course as a non-venereal disease, dating back into prehistory, treponematosis, I have no doubt, has been transmitted sexually between adults on many individual occasions. That it did not then become a venereal disease was because the terms of life under which primitive people lived encouraged transmission of treponemes through childhood contacts. When children were so universally infected, sexual contacts were irrelevant in the propagation of treponematosis; but when the epidemiology was right, as in the newly created cities of Mesopotamia, venereal syphilis appeared.

Isolation?

Cockburn thought that the Americas were a refuge area for a lost segment of the human race, an "isolate" so unique that the people who represent the residue of that ancient migration have a unique host-parasite relation to the treponeme of pinta, their inherited monopoly. Both Cockburn and Hackett postulate that—once men had crossed the Bering land bridge—rising sea levels created a barrier behind them and left them and their disease in seclusion from the rest of the world for "some tens of thousands of years" (Cockburn). This makes a tidy theory, but it did not happen that way. Anthropologists are not completely agreed as to when men first entered North America but the present consensus places that event within the past 40 000 years. The earliest radio-carbon dating for men in what is now the United States of America is about 12 000

years ago.¹⁰ The firstcomers were followed by wave after wave of migrants, first by land and subsequently by water or over the ice, right up to historic times. The rise of sea levels did not put a stop to this movement; the coming of man was not a "one-shot" operation but a continuing process. There is little to support the theory that while treponematosis in the rest of the world was passing through the mutations of yaws, "treponaridosis" and venereal syphilis, pinta was whiling away the undisturbed millenia in geographic isolation. Hackett's Map 7 (from the 16th century A.D.) represents yaws only in coastal areas of South America, brought there by African slaves, and leaves pinta in undisputed possession of the remainder; in other words, pinta was the *sole* treponematosis in the Americas before the Age of Discovery. I fear that evidence for this assumption must be regarded as unsubstantial.

In general, it is hazardous to theorize about events of which there are no eye-witnesses or written records; yet cogitation about the origin of a disease clearly has heuristic and analytic value. The theory of origin which in the long run attracts the consensus will be the one that to the greatest degree keeps conjecture to a minimum, accords best with the canons of medicine and microbiology, and harmonizes in all respects with the behaviour of the disease as it is known today.

Medical sociology

Since treponematosis of all diseases seems most closely related to human society and its various modulations, the viewpoint of this essay would not have full expression without reverting in this concluding section to the sociological bearing of the unity advocated herein. A speaker at the World Forum on Syphilis and other Treponematoses^b said that the shifting relationship between the treponeme and the human race, historically and geographically, ought to hold the utmost fascination for the sociologist. "It is unfortunate", he said, "that the topic remains for the most part an unknown chapter among those who teach and practice the behavioral sciences." He might have included the biological sciences as well.

None of the sponsoring and participating agencies of the World Forum, however, has made use of the psychologically effective concept of "one-disease, one-programme". My prefatory note to this essay

¹⁰ Haynes, C. V., Jr (1964) *Science*, 145, 1408.

calls this a new way of thinking. Ernst Mayr ^x said, "The replacement of typological thinking by population thinking is perhaps the greatest conceptual revolution that has taken place in biology".

Similarly, in the field of treponematosi, the

replacement of multiple-disease thinking by single-disease thinking would produce an equally impressive impact in the spheres of medicine, sociology, education and communications. Adoption of the new concept would generate new ideas leading to new policies and in turn to new applications more fruitful in the eradication of treponematosi than any now imaginable.

^x Mayr, E. (1963) *Animal species and evolution*, Cambridge, Mass., Harvard University Press.

Frequency of Oral Submucous Fibrosis in North India

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Oral submucous fibrosis is an insidious chronic disease of unknown etiology, reported mainly in Indians, and affecting the entire oral cavity. The basic change is a fibro-elastotic transformation of the connective tissue in the lamina propria, associated with epithelial atrophy, sometimes preceded by vesicle formation. In later stages the oral mucous membrane becomes stiff and the patients suffer from trismus, with resultant difficulties in eating.

In 1956, Paymaster ^a described the development of a slow-growing squamous cell carcinoma in one-third of his patients with submucous fibrosis at the Tata Memorial Hospital in Bombay. In contrast to this, Sirsat & Khanolkar ^b remarked that this observation was not borne out by their experience.

Because oral cancer is extremely frequent in India, all possibilities of finding oral precancerous conditions should be explored. Therefore, it was decided to look out for submucous fibrosis during surveys of oral mucosal diseases in various parts of India, as no figures are available regarding the frequency of submucous fibrosis in the Indian population.

Material and methods

The surveys were carried out in the cities of Bombay and Lucknow from October 1963 to May 1964. In the two cities all patients coming to the Admission Clinics at the Government Dental

College, Bombay, and at the Dental College Lucknow, were examined until a total of 10 000 had been studied in each place. The patients were examined in electric light and the oral cavity screened by means of two mouth mirrors. The patients were questioned with regard to age, as well as to smoking and chewing habits. In Bombay the religion was also recorded.

The clinical criteria for submucous fibrosis are not well established, because the condition was not described until 10 years ago. The clinical picture is varied. In most patients the earliest clinical change is the appearance of whitish, blanched, depigmented areas, especially in the buccal and labial mucosae (Pindborg et al.^c). Stiffening of the mucosa is a late sign that is not always found, whereas atrophy of the lingual papillae is a rather constant phenomenon. Sometimes the patients complain of blisters and stomatitis. In the majority of patients there is a history of a burning sensation to spicy food, often over many years.

The survey was carried out by the author, assisted by four dentists, specially trained for the purpose in each college.

Findings

The results of the survey are shown in the tabulation opposite:

^a Paymaster, J. C. (1956) *Cancer (Philad.)*, 9, 431-435.

^b Sirsat, S. M. & Khanolkar, V. R. (1962) *Indian J. med. Sci.*, 16, 189-197.

^c Pindborg, J. J., Chawla, T. N., Srivastava, A. N., Gupta, D. & Mehrotra, M. L. (1964) *Acta odont. scand.*, 22, 679.