

THE TREPONEMATOSES AS A WORLD PROBLEM*

BY

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Some 15 years ago the incidence of treponematoses was at its post-war peak in most parts of the world. It was estimated at the time that there were some 50 million cases of yaws, 20 million cases of venereal syphilis, possibly a million cases of endemic non-venereal syphilis, and a lesser number of pinta cases. The geographical distribution is shown in Fig. 1.

These infections constituted a vast public health problem and important economic losses in terms of manpower resulted from invalidism and reduced

working capacity, particularly in industrial countries from syphilis and in agricultural tropical countries from the endemic treponematoses, especially yaws. For example, 10 per cent. of those infected with yaws become invalids through hand or foot lesions and often, if untreated, with bony ankylosis, so imposing a social burden on the community. In Haiti it was estimated that the production increase in agriculture resulting from the yaws eradication programme amounts to approximately 5,000,000 U.S.A. dollars a year.

Much work against the treponematoses has been carried out by health administrations in many

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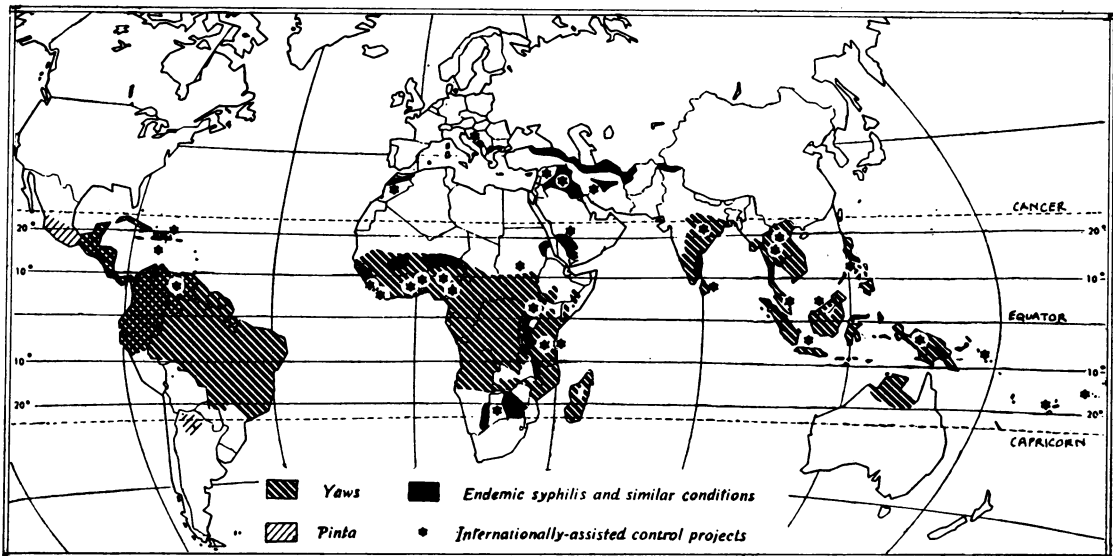


FIG. 1.—Geographical distribution of the non-venereal treponematoses and internationally assisted control projects.

countries over the last 15 years, but, before reviewing some of the changes which have occurred, brief mention may be made of some common features of these infections and their epidemiology.

Whether or not one subscribes to the so-called "Unitarian Theory" of the treponematoses—originally introduced by Butler and Peterson (1927) and subsequently developed by Hudson (1946) and others—these infections should be considered as a group in view of the many similarities of the causal organisms, epidemiology, pathology, clinical, therapeutic, and prevention aspects. These similarities between the four treponemal diseases are shown in Table I.

The natural course of the treponematoses, the factors which favour their spread, and the significance of environmental conditions and host features are interesting epidemiological aspects which are beyond the scope of this paper. The influence of extrinsic and intrinsic factors on the adaptation and possible transmutation of treponemes in what may be an evolutionary cycle is a wide field for future research.

In regard to differences, the relatively high frequency of infectious relapses from latency which occur in yaws as compared with venereal and

TABLE I
MAJOR COMMON FEATURES OF THE TREPONEMATOSSES

Common Characteristics			Venereal Syphilis	Endemic Syphilis	Yaws	Pinta
(1) Organism	<i>T. pallidum</i>	<i>T. pallidum</i>	<i>T. pertenue</i>	<i>T. carateum</i>
(2) Pathology	(a) Clinical	Initial lesions ..	+	+	+	+
		Latent period ..	+	+	+	+
		Late stage ..	+	+	+	+
		Systemic Involvement: Neurological Cardiovascular	+	±	Not proved	No
	(b) Serological	Complement-fixing, precipitating, immobilizing antibodies, etc., with lipoidal and treponemal antigens	+	±	Not proved	No
(3) Treatment	Antibiotics (penicillin, erythromycin, etc.)		← Same for all—differences lie in amounts required for cure and duration of therapy →			
	Metals, trivalent arsenicals, bismuth		← Same for all—differences lie in amounts required for cure and duration of therapy →			
4) Epidemiology	(a) Transmission		Common Rare	Rare Usual, child to child, child to parent	Exceptional Usual, child to child, child to parent	Not described Usual
	Direct: Person to Person (i) Venereal (ii) Non-venereal					
	Indirect: Communal utensils Prenatal		Unusual Occasional	Drinking vessels, Rare	Possible No	Not described No
(b) Reservoir of Infection ..		Adults: prostitutes, amateur and professional; promiscuous males; seafarers; armed forces; latent cases	Childhood: 2–10 years; household contacts; latent cases (relatively frequent)	Childhood: 4–15; contacts in home, school; latent cases	10–30. Infectious cases; latent cases (?)	
(c) Distribution		World-wide; all climates; all socio-economic groups; urban; seaports	Focal; rural; familial; endemic; underdeveloped communities	Tropics; focal; rural; endemic; primitive hygiene conditions	Tropical America; rural; endemic	

endemic non-venereal syphilis should be mentioned, because this aspect is very important in the control and possible eradication of the disease. The fact that the endemic rural treponematoses are usually *acquired* in childhood should also be emphasized, as approximately 50 per cent. of a population with a normal structure is made up of children and adolescents.

With the increasing availability of penicillin in the post-war period, many countries turned to the organization of programmes aimed at controlling the treponematoses: syphilis control on the one hand and mass campaigns against the endemic treponematoses on the other. International assistance has been rendered in many such programmes since 1948, when the World Health Organization was established and it was officially decided to give a high priority to this work, as well as to campaigns against malaria, tuberculosis, and other conditions of universal concern which retard social and economic development. In fact, W.H.O. has assisted 61 countries and territories by providing more than 150 V.D.T. advisers, consultants, and experts, by awarding more than 300 fellowships in the V.D.T. field, and—together with U.N.I.C.E.F.—in procuring supplies and equipment at a cost well in excess of \$9,000,000.

Such programmes were made possible by the advent of practical, inexpensive, long-acting penicillin preparations, particularly P.A.M., which had a great effect on the reservoir of infection when wisely used with epidemiological and other control techniques. To-day we know that penicillin has contributed greatly to the recession of the treponematoses wherever it has been widely used. Its effect on syphilis has been evident for some time; the results on yaws and the other endemic treponematoses are less well known.

Penicillin has become "the queen of drugs" in the developing, as well as the highly-developed, parts of the world, and is generally accepted as a potent health weapon. The astonishing amount of 600 tons of penicillin is now produced yearly, and it has been misused both by the public and by the medical profession, not only in the treatment of the treponematoses but also in most other fields of medicine. Penicillin reactions caused by the sensitization to the drug of large sections of the population present a world-wide therapeutic problem at the present time.

(a) *Syphilis*.—The limitations of statistics on venereal diseases are well known, and it is certain that data based on reported cases are *minimal* data. Over a period of years they are nevertheless of value

in showing trends in the extent of the problem and its variation. Figs 2, 3, 4, and 5 show numbers of cases of syphilis (and gonorrhoea) in some countries of Europe, the Americas, Africa, and Asia.

Syphilis has receded in all areas except in Africa, but the downward trend of gonorrhoea is almost everywhere very slight, while in Africa its incidence is increasing. It is a unique situation in communicable disease control that the same drug, applied in two different diseases with identical modes of transmission and similar epidemiological features, shows success in the one and failure in the other.

The obvious fall in the incidence of syphilis in most areas brought it down in some countries to only 15 to 20 per cent of its peak a few years ago. There has been a recrudescence in the U.S.A., Belgium, Denmark, Italy, and some other countries over the last few years, while in Africa practically no recession in this treponematoses is discernible. The most useful index of the prevalence of syphilis in a population is—for obvious reasons—the sero-reactor rate in pregnant women. Thus, in W.H.O.-sponsored surveys of pregnant women, 1.2 per cent. of sero-reactors was found in Pakistan, 1.9 per cent. in Afghanistan, 3.5 per cent. in Hong Kong, 2 per cent. in the Philippines, 5 per cent. in Burma, 7 per cent. in Taiwan, 5 to 10 per cent. in Korea, 2 to 15 per cent. in India, 8 to 10 per cent. in Iran, and 14 to 30 per cent. in Morocco. In Ecuador 15 per cent. of sero-reactors was found in males and females in the age group 15 to 60, in Turkey 5 to 10 per cent., in Egypt 7 to 15 per cent., in Saudi Arabia 18 per cent., and in Ethiopia 30 to 60 per cent. In many of these areas a decline in prevalence has resulted from the control programmes which have been carried out, but the findings suggest that the problem of venereal syphilis continues to exist.

There is also evidence that syphilis is prevalent in ports in some countries, with a resultant influence on the incidence in seafarers. It is therefore logical that steps should be taken to strengthen the Brussels Agreement of 1924 through a stricter definition of its articles and the establishment of minimal criteria of V.D. control practices in ports. These problems were considered by a special study group of health administrators and by an Expert Committee on Venereal Diseases convened by W.H.O. in 1955 and 1959 respectively.

As a whole—and keeping in mind the failure to control gonorrhoea—it is clear that the most important venereal diseases are not yet dying, although great strides have been made in the control of syphilis.

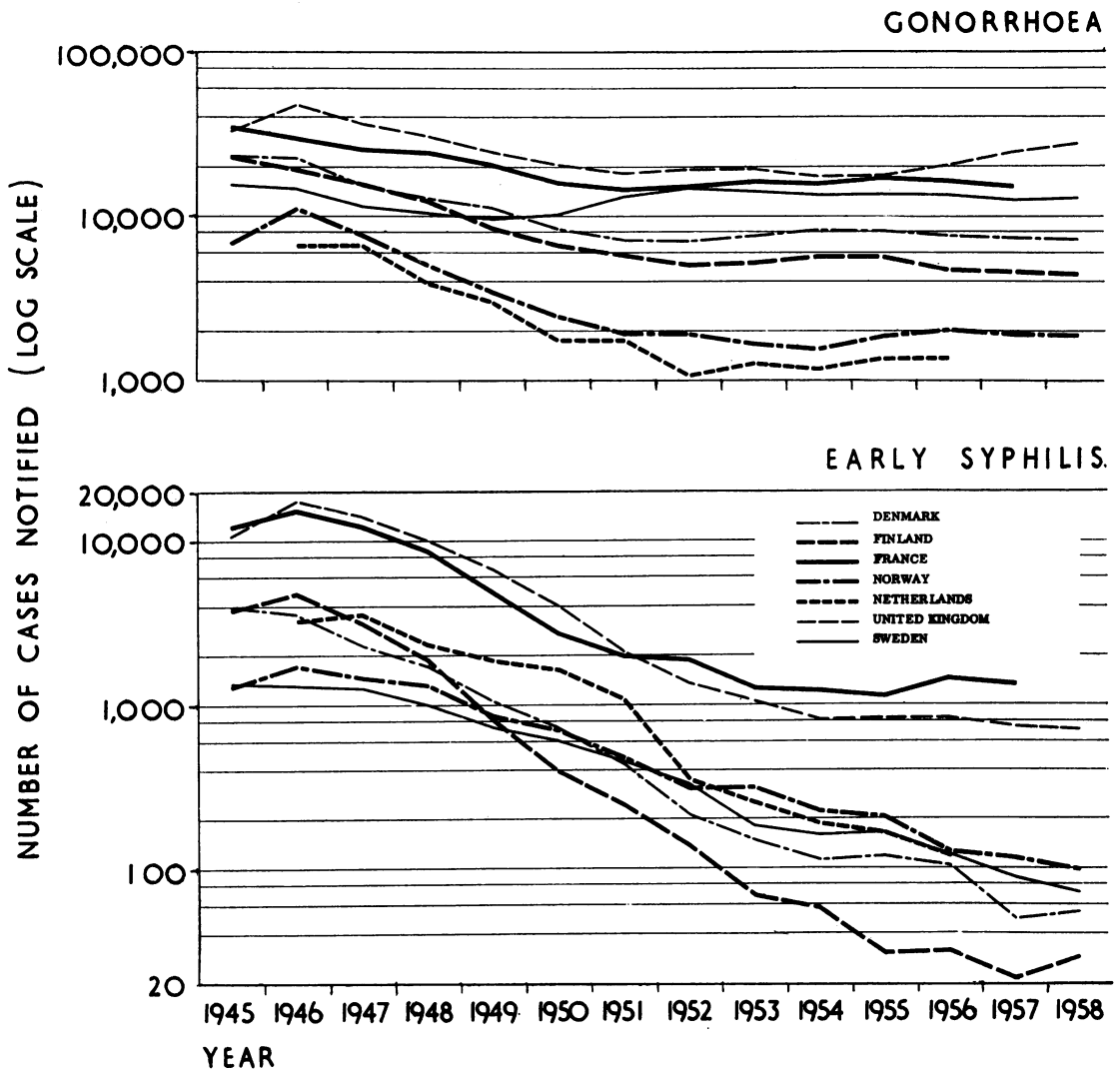


FIG. 2.—Early syphilis and gonorrhoea notifications in Europe, 1945-58.

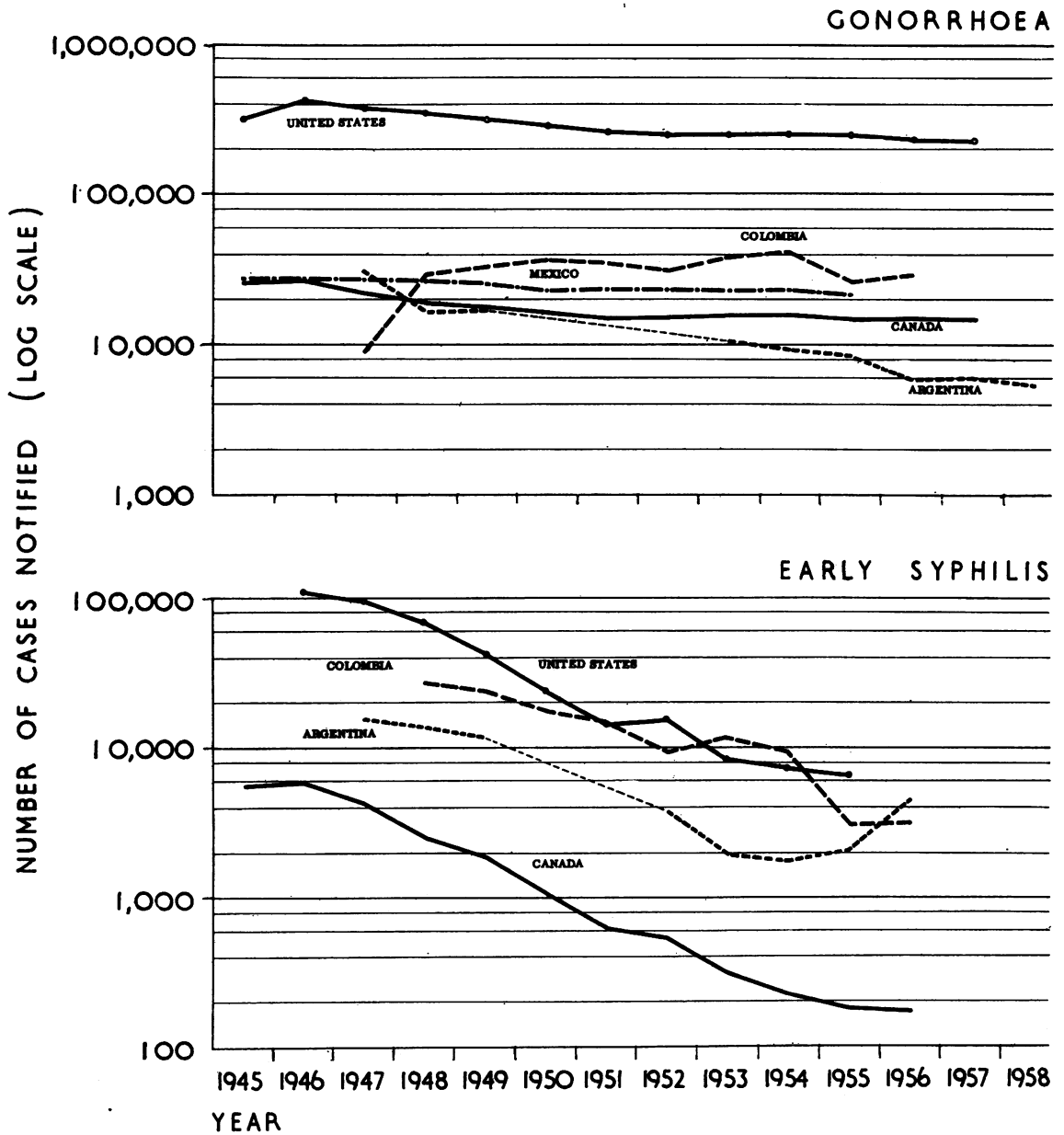


FIG. 3.—Early syphilis and gonorrhoea notifications in the Americas, 1945-58.

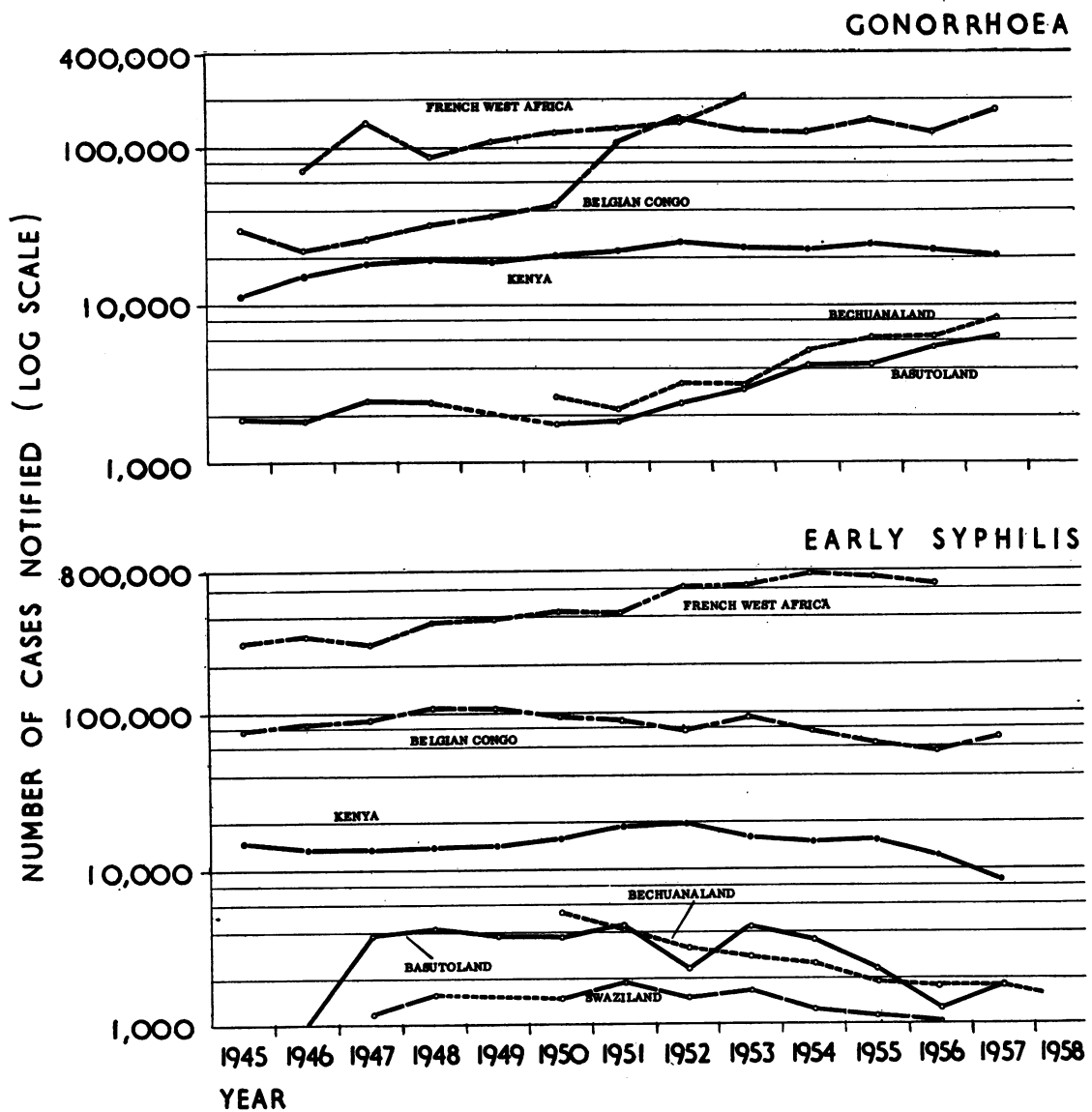


FIG. 4.—Early syphilis and gonorrhoea notifications in Africa, 1945-58.

SYPHILIS, ALL FORMS

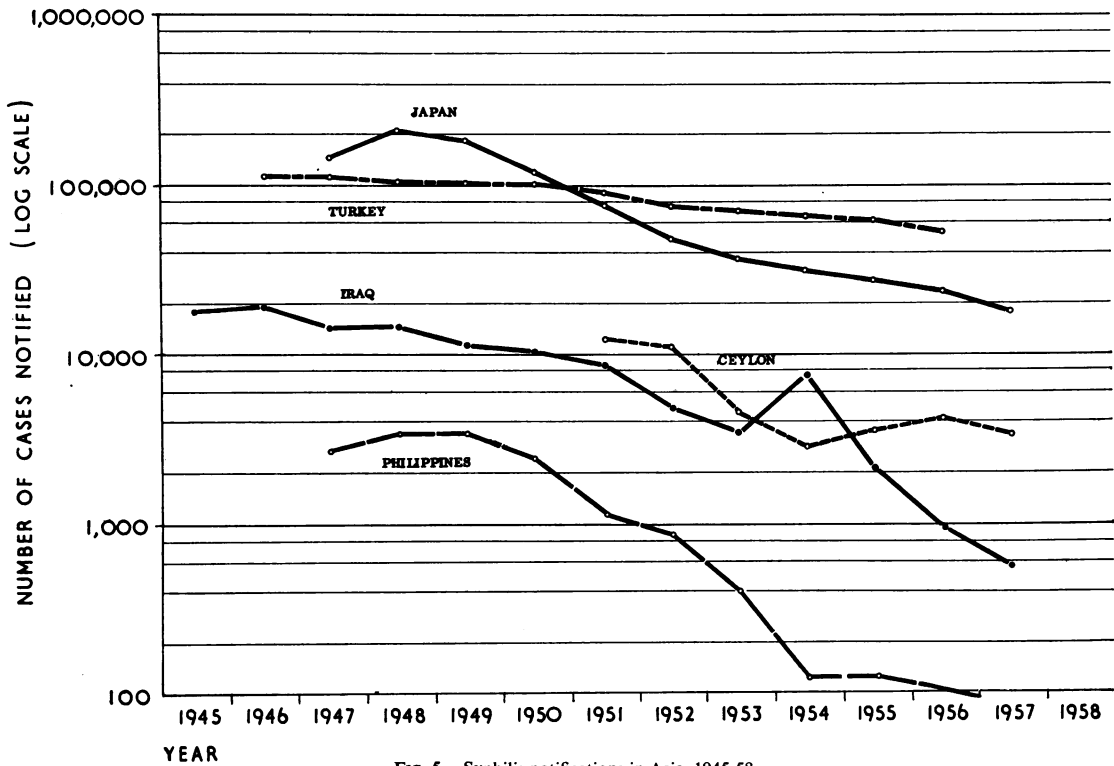


FIG. 5.—Syphilis notifications in Asia, 1945-58.

(b) *Yaws*. — If we turn to the most widespread of the treponematoses, namely yaws, 10 years ago there were some 50 million cases among the 200 million people at risk in tropical areas. By the end of 1958 some 70 million people had been examined for yaws in the initial surveys of mass campaigns assisted by W.H.O. in Africa, the Americas, South-

east Asia, and the Western Pacific regions, and about 90 million people had been examined in re-surveys.

During these campaigns some 30 million people, either patients with active yaws or latent cases or contacts, received injections of long-acting penicillin. The work done is shown in Table II.

TABLE II
TOTAL WORK DONE IN YAWS CAMPAIGNS, 1950 - 1958

Survey	Region	Population Examined	Persons Treated	Active Yaws	
				Total	Infectious
Initial	African	11,557,320	10,444,986	1,358,956	85,194
	American	4,878,797	4,789,923	—	—
	South-East Asia	45,650,270	7,221,205	4,665,796	—
	Western Pacific	8,459,505	1,104,657	117,798	26,975
	Totals	70,545,892	23,559,971	6,142,550*	112,169*
Re-treatment	African	11,208,556	1,195,710	114,280	39,283
	American	514,092	—	—	—
	South-East Asia	70,129,341	4,504,012	2,866,305	—
	Western Pacific	4,317,889	216,188	16,660	2,944
	Totals	86,169,878	5,915,910*	2,997,245*	42,227*

* Data not complete for all work done.

The proportion of early infectious cases among total active cases, shown in Tables III, IV, and V, where the regression of yaws is indicated in certain pilot areas in Nigeria, Haiti, and Indonesia, is obviously of first importance.

The ultimate stage of the endemic treponematoses campaigns, namely actual eradication, as achieved in Bosnia, Yugoslavia, and Indonesia, between 1949 and 1958, is shown in Table VI, on the basis of findings in a pilot area. No new infectious case of endemic syphilis has occurred in a population of about a million people covered by this programme in the last 5 years.

This fulfils the public health definition of eradication for endemic treponematoses established by the participants at the International Yaws Conference at Enugu in Africa in 1955. If penicillin reactions do not develop into a hazard and if the treponeme does not develop resistance to the antibiotic, it is believed that yaws also could be eradicated within the next 5 to 10 years.

The achievement of eradication, which is the objective of all yaws campaigns, will obviously still encounter many problems. These are connected with the consolidation of initial successes, the ultimate

TABLE III
PERCENTAGE PREVALENCE OF INFECTIOUS YAWS AT INITIAL SURVEY AND LAST RE-SURVEY (NIGERIA)

Area	Number of last Re-survey	Percentage Prevalence	
		Initial	Last Re-survey
Nsukka	VII	3.0	0.05
Udi	III	1.5	0.1
Afeumai	III	7.2	0.15
Ishan	III	6.6	0.4
Owo	IV	3.1	0.02
Igala	III	10.3	0.07
Koton Karifi ..	III	3.5	0.08

TABLE V
RESULTS OF REPEATED RESURVEY WITH THE CONTINUED FINDING OF FEW CASES (WRINGINANOM SUB-DISTRICT, INDONESIA)

Date	Surveys	Coverage (per cent.)	Non-infectious Cases (per cent.)	Infectious Cases (per cent.)
July, 1952	Initial	95	0.7	0.3
March, 1953	RS I	94	1.3	0.32
January, 1954	RS II	96	0.75	0.2
January, 1955	RS III	94	0.2	0.03
June, 1955	RS IV	91	0.2	0.04
January, 1956	RS V	88	0.16	0.04

TABLE IV
SAMPLE SURVEYS IN HAITI, 1958-1959

Department	Population	Population Examined	Active Yaws Cases			
			Total		Infectious	
			Number	Per cent.	Number	Per cent.
North-West	200,673	4,950	20	0.34	2	0.04
North	606,484	14,500	58	0.33	5	0.03
Artibonite	607,188	15,100	26	0.17	2	0.01
West	1,325,150	27,355	96	0.34	17	0.06
South	844,716	21,000	71	0.29	20	0.09
Total	3,584,211	82,905	271	0.32	46	0.05

Comparable data for the earlier spot surveys in 1954 and 1955 were 91,624 persons examined, and 0.65 per cent. of total active yaws and 0.15 per cent. of infectious yaws found. In mid-1957 it was estimated that the total yaws prevalence was 0.5 per cent.

TABLE VI
ERADICATION OF ENDEMIC SYPHILIS SHOWN IN FIVE SUCCESSIVE SURVEYS IN MNO* SAPNA, BOSNIA, 1949-1958†

Area †	Early Infectious Lesions (per cent.)					Sero-reactivity (per cent.)				
	Survey 1949	Re-surveys				Survey 1949	Re-surveys			
		I 1950	II 1951	III 1952	IV 1958		I 1950	II 1951	III 1952	IV 1958
1. Kraljevići	7.2	0.2	0.2	0	0	31.1	15.3	1.9	0.7	1.2
2. Ramići	9.3	2.2	1.6	0	0	32.9	18.2	5.4	1.6	0.3
3. Medjedja	6.7	1.1	0.8	0	0	59.6	32.6	27.2	2.2	2.0
4. Godus	4.5	0.3	0.6	0	0	19.8	13.0	4.0	0.8	1.1
5. Sapna	2.0	0	1.4	0	0	17.2	8.3	4.8	2.0	0.6
6. Andjelici	2.6	0	0	0	0	28.6	9.5	1.8	1.1	0.7
7. Mahmutovići ..	3.1	0	0	0	0	19.6	8.0	0.4	0.4	0
8. Kovačevići ..	2.3	1.3	1.3	0	0	17.6	10.1	2.3	0.7	0
9. M. Nezuk	1.2	0	0	0	0	23.3	13.7	3.6	2.9	0.5
10. Jusići	0.5	0	0	0	0	11.8	6.2	15.	0	0

* "MNO" is a small administrative unit.

† 94.5 per cent. of the mean total population was examined.

integration of the mass campaigns into a strengthened local rural health service, and the re-training of auxiliaries for employment in other and preferably broader health activities. While present campaigns have been carried out mostly in high prevalence areas, where the active cases have been reduced from 10 per cent. or more to less than 1 per cent., and where infectious cases in many areas now represent far less than one case per 1,000, future campaigns will go forward in low prevalence areas, with a consequent adjustment of technical policies.

Among the most effective procedures in the past has been the wide use of epidemiological treatment of latent cases and contacts without overt signs of the disease, in addition to clinical cases, on a mass basis. The effectiveness of this procedure is well recognized in several communicable diseases.

The eradication of yaws on a world-wide basis can obviously not go forward without a co-ordinated overall plan to which all countries subscribe. Such a plan is now in existence and it can be expected that eventually this ancient treponematoses can be eliminated as a health problem. The growing educational, economic, and social conscience and the improvements which are obvious in many tropical countries to-day will accelerate the process. There can be no doubt, however, that the road is not easy and that encouragement should be given to health administrations, particularly in newly independent countries, where there is a wide field of work for voluntary national and international organizations, such as the International Union against the Venereal Diseases and the Treponematoses and the International Union for Health Education.

In this connexion it should be realistically considered that, with the eradication of rural yaws, venereal syphilis in cities and towns becomes of greater importance, since the protection against syphilis of cross-immunity from yaws is disappearing as the rural child population grows up. This problem will become urgent within the next 5 to 10 years, and adequate plans should be made in time. Fig. 4 shows that in Africa, for example, there has been no decrease in venereal syphilis in cities and towns during the last few years, and these future problems should therefore be considered now.

A certain role has fallen to W.H.O. in the world-wide campaign against the treponematoses. This role has largely been to catalyse the development of programmes by health administrations. Great assistance has also been rendered by the United Nations Children's Fund (U.N.I.C.E.F.) in the provision of supplies

and equipment for developing countries according to a joint plan based on the decisions of the Joint Health Policy Committee established between W.H.O. and U.N.I.C.E.F.

There are many other fronts where it has been possible to assist in the world-wide struggle against the treponematoses. Mention may be made of the establishment of minimal international requirements for penicillin depot preparations—particularly P.A.M.—to ensure the uniform quality and blood-level duration characteristics of long-acting penicillin preparations of different manufacture. International standards for cardiolipin and lecithin have also been set up, as well as reactive antibody-serum to facilitate comparison of qualitative and quantitative serological tests and their evaluation in different countries. These have been worked out largely through the activities of the W.H.O. Serological Reference Centres at the V.D. Research Laboratory of the United States Public Health Service, under the Communicable Disease Centre in Atlanta, Georgia, and the W.H.O. Serological Reference Centre at the State Serum Institute in Copenhagen. Furthermore, numerous meetings, conferences, symposia, study groups, and other media for the exchange of scientific information have been organized by W.H.O., alone or in co-operation with other interested groups, over the years. The extensive publications programme of W.H.O. in the field of treponematoses has served a similar purpose.

In taking stock of the treponematoses work in the world—the nature and extent of the problem, and the achievements as well as the short-comings over the last decade—it is necessary to realize that, even if the present diagnostic, epidemiological, and other techniques are applied more extensively and intensively, further progress depends also on the acquisition of new knowledge through research in four main fields:

- (1) Fundamental work concerning the biology of the treponeme in relation to the host and the environment is important for the proper understanding of these infections. No-one has yet succeeded in cultivating the treponeme, and new tissue culture methods and knowledge available in the virus field have not so far been tried in the treponemal field. Immunization against yaws and reliable skin-testing methods may depend on this development.

- (2) We cannot yet distinguish serologically between types and strains of treponemes with present reagin

tests. TPI and other treponemal tests have also failed to differentiate between the S, Y, and M types of treponemes, into which the treponemes of venereal syphilis, yaws, and endemic syphilis can be classified by other complex criteria. Yet such tests begin to be of practical importance with movements of large population groups from yaws areas to temperate zones (*e.g.* the migration of West Indians to the United Kingdom).

(3) Studies of the adaptation and mutation patterns of pathogenic treponemes under the influence of antibiotics and radioactivity are lacking, as are investigations into the differences in the character and amount of mucopolysaccharides in treponemes. The same applies to their metabolic products in relation to the histochemical characteristics in the treponematoses, the collagen diseases and possibly other diseases as well. Yet on such investigations alone could one hope to substantiate a "Unitarian" concept.

(4) The actual mechanism of the transfer of yaws and the mode of infection in endemic syphilis have not yet been clearly defined by epidemiological research. New epidemiological methods in addition to "cluster techniques" and "speed zone epidemiology" are also required to improve syphilis (and gonorrhoea) control in many countries.

These examples of the deficiency in our knowledge point to the need for intensification of both basic and applied research. We can only hope that within the next few years stimulation can be provided by national as well as international funds to foster such research. W.H.O. may have a role to play in this field. A scientific advisory group was in fact assembled by W.H.O. in 1959 to propose a programme and priorities for international research.

The International Union against the Venereal Diseases and the Treponematoses, at its meeting in London, asked the W.H.O. to review this vast and fascinating subject. It has only been possible, however, in this summary to outline broadly some of the problems. It cannot be denied that, as a whole, tremendous progress has been made over the last decade, a progress which could not have been imagined in the era of metal chemotherapy. Ehrlich's dream of a foreshortened intensive therapy for wide use did not come true until the era of Sir Alexander Fleming and Dr. John F. Mahoney. But, in spite of this new treatment, sporadic venereal syphilis remains a health problem in many areas, and yaws has not yet been eradicated. Endemic syphilis has been eliminated in a few areas, but is not of general health significance, and pinta remains a problem only in certain limited areas in the Americas.

The balance between the host and the treponeme may well be extremely fine, and can be illustrated by scales where treponemal factors weigh down one pan and host factors the other. If factors favouring the treponeme predominate at any time, the pointer swings over and visible clinical active manifestations prevail. Effective counterbalancing responses by the host and the environment cause the pointer to swing back in the opposite direction—to sub-clinical activity or to cure with freedom from infection.

Over the last decade the pan has been loaded in favour of the host through the availability and wide use of treponemicidal antibiotics in special and general health programmes and the amelioration of economic and social conditions. In many areas the proportion of clinical cases to sero-reactors is diminishing on a large scale, tending towards complete cure: the pointer is swinging in the right direction, and the fate of the treponemes is now in the balance.

Advantage should be taken of the present momentum of the pointer. Intensified efforts are indeed desirable—nationally and internationally—by voluntary organizations, health administrations, and the medical profession alike.

Summary

The major common features of the treponematoses—syphilis, yaws, and pinta—are briefly reviewed, and the nature and extent of these infections a decade ago and to-day are discussed, with particular reference to syphilis and yaws. The increasing availability and systematic use of long-acting procaine penicillin in oil with monostearate (PAM) in syphilis-control programmes and in mass campaigns against yaws has contributed greatly to the recession of the treponematoses observed in the last decade. There is evidence, however, that the incidence of venereal syphilis has recently begun to increase in several countries, and difficulties are being encountered in the eradication of yaws in developing areas in spite of initial successes. Intensified efforts by voluntary organizations, health administrations, and the medical profession are therefore necessary. A particular role has fallen to the World Health Organization in combating the treponematoses on a world-wide basis. Some details of the programme are described in the present paper, which also underlines the need for further interest in and support of treponematoses research, nationally and internationally.

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Les tréponématoses en tant que problème mondial

Résumé

On passe en revue les principaux caractères communs des tréponématoses—syphilis, pian et caraté—et on discute la nature et l'extension de ces infections il y a dix ans et aujourd'hui, avec référence particulière à la syphilis et au pian. La disponibilité croissante et l'usage systématique de la pénicilline-procaine huileuse avec monostéarate (PAM) au cours des programmes de lutte contre la syphilis et dans les campagnes de masse contre le pian ont grandement contribué au recul des tréponématoses, observé pendant la dernière décade. On a des

preuves, cependant, que le champ de la syphilis vénérienne s'est récemment accru de nouveau dans divers pays, et on a des difficultés à éliminer le pian dans des zones de développement, en dépit de succès initiaux. Des efforts intensifiés par des organisations volontaires, des administrations de la santé et la profession médicale sont donc nécessaires. Un rôle particulièrement important incombe à l'O.M.S. dans le combat des tréponématoses sur une échelle mondiale. On décrit dans cet article quelques uns des détails du programme, et on souligne également le besoin de supporter et de s'intéresser d'avantage à la recherche sur les tréponématoses, sur les plans national et international.