International Work in Endemic Treponematoses and Venereal Infections

1948-1963

WORLD HEALTH ORGANIZATION
GENEVA
1965

The World Health Organization (WHO) is one of the specialized agencies of the United Nations. Through this organization, which came into being in 1948, the public health and medical professions of more than 100 countries exchange their knowledge and experience, and collaborate in an effort to achieve the highest possible level of health throughout the world. WHO is not concerned with problems which individual countries or territories can solve with their own resources. It deals, rather, with problems which can only be satisfactorily solved through the co-operation of all, or certain groups of, countries—the eradication of diseases such as malaria, the control of diseases that affect or are a potential danger to many, for example, most of the infectious and parasitic diseases, some cardiovascular diseases, and cancer. Progress towards better health throughout the world also demands international co-operation in many other activities : for example, setting up standards for biological substances, for insecticides and insecticide spraying equipment ; compiling an international pharmacopoeia ; drawing up and administering international sanitary regulations ; revising the international lists of diseases and causes of death ; assembling and disseminating epidemiological information ; recommending non-proprietary names for drugs ; and promoting the exchange of scientific knowledge. In many parts of the world, there is need for improvement in maternal and child health, nutrition, nursing, mental health, dental health, social and occupational health, environmental health, public health administration, professional education and training, and health education of the public. Thus a large share of the Organization's resources is devoted to giving assistance and advice in these fields and to making available—often through publications—the latest information on these subjects. Since 1958 an extensive international programme of collaborative research and research co-ordination has added substantially to the knowledge in many fields of medicine and public health. This programme is constantly developing and its many facets are reflected in WHO publications.

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Introduction

At the thirty-first session of the WHO Executive Board (January 1963), it was suggested that it would be of value if a regular and comprehensive review of one of the Organization's activities were to be undertaken at each future session of the Board. In May 1964, in accordance with this suggestion, the Director-General of WHO submitted the following report on the Organization's programme in endemic treponematoses and venereal infections.

The report was very favourably received by the Board, though concern was expressed about the rising incidence of venereal diseases reported in many parts of the world. The widespread improvement in tropical health as a result of the mass penicillin campaigns undertaken by the Organization in 45 countries, particularly against yaws, was noted, and the need for continued surveillance by strengthened rural health services was emphasized. The necessity for continued and augmented research and further WHO assistance in this respect was stressed by the Board, in view of the very small number of laboratories in the world concerned with these diseases. The Board urged Member States " to exert a determined effort to maintain adequate and effective measures to reduce the incidence of the endemic treponematoses, particularly those of childhood, and the venereal diseases, and, where indicated, to increase their efforts to combat, at the national level, the recrudescence of these infections ".

Endemic treponematoses of childhood*

In the programme against venereal infections proposed by the Interim Commission of WHO and adopted by the first World Health Assembly in 1948, priority was given to the control of early syphilis. This programme was subsequently extended to include the non-venereal endemic treponematoses of childhood (tropical yaws, endemic syphilis, and pinta), in view of their microbiological, immunological, and other relationships, and their uniform response to penicillin. It was decided to give attention to gonococcal infections and "minor" venereal diseases only when special problems arose.

The WHO programme on the endemic treponematoses of childhood and the venereal diseases is guided by the views of the relevant expert committees, sub-committees, and special groups, which make recommendations on technical policies and procedures to the Director-General, the Organization, and health administrations, and by the views of symposia, international or inter-country meetings, etc. convened by WHO to facilitate the coordination and exchange of information and the application of these policies and procedures.

The approximate world distribution of the endemic treponematoses of childhood some 15-20 years ago is shown in Fig. 1. It has been estimated [1] that some 200 million people were then living in rural areas where treponematoses were endemic and that about 50 million actually suffered from these infections.

Yaws was endemic throughout large parts of the tropics and was by far the most important endemic treponematosis; active clinical prevalences ranged from 5.6% (Cameroon) to 30% (Liberia) in Africa, from 2.5% (Brazil) to 50% (Haiti) in the Americas, from 3.1% (Thailand) to 17.2% (Indonesia) in South-East Asia, and from 3.6% (Laos) to 40% (New Hebrides) in the Western Pacific Region. In many areas there were more than three times as many latent cases as active cases, and seroreactivity to lipoidal antigens was encountered in up to 60%-70% of rural populations.

The proliferating, disseminated, relapsing crops of long-lasting, infectious framboesides, the multiple periods of latency, and the plantar, palmar, and bony lesions of yaws cause extensive suffering in children, adolescents, and adults, with permanent, destructive, and disabling sequelae in some 10% of those infected. The economic loss due to this infection is well illustrated by the case of Haiti where, following the mass penicillin campaign, the return to work of previously incapacitated labourers represented an estimated increase of $5 million in annual national productivity.[2]

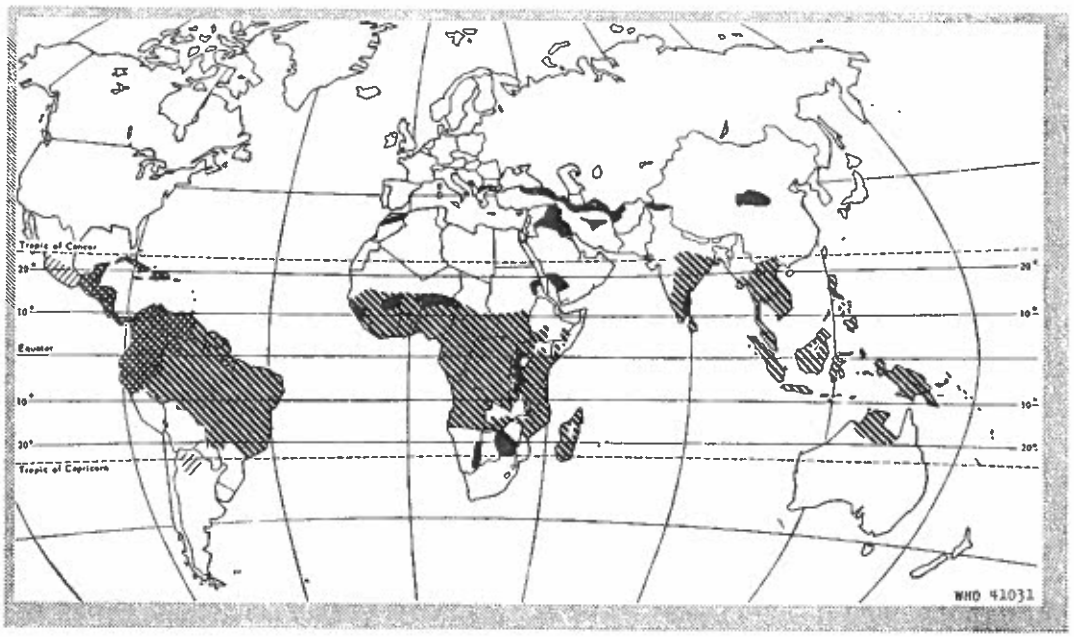
Endemic syphilis occurred not only in the tropics, but in scattered communities outside them, with rates of 3%-5% for early infectious lesions and seroreactivity rates of up to 50%, e.g., in Yugoslavia and Bechuanaland. Oral lesions, secondary syphilides, tertiary and other late incapacitating lesions have serious human, social, and economic consequences, and so do the psoriasiform plaques, secondary multiple pintides, and keratotic lesions of limbs and body provoked by pinta. The last-mentioned treponematosis is confined to parts of tropical America, with prevalence rates of

* A detailed report on international work in the treponematoses from 1948 to 1953, by Dr T. Guthe, Chief, Venereal Disease and Treponematoses Section, WHO, and Dr R. R. Willcox, WHO Treponematoses Consultant, appeared in the February-March 1954 issue of the *Chronicle of the World Health Organization*. This report was reprinted in booklet form under the title *Treponematoses : a world problem*.

[1] *J. trop. Med. Hyg.*, 1957, 60, 27, 62.

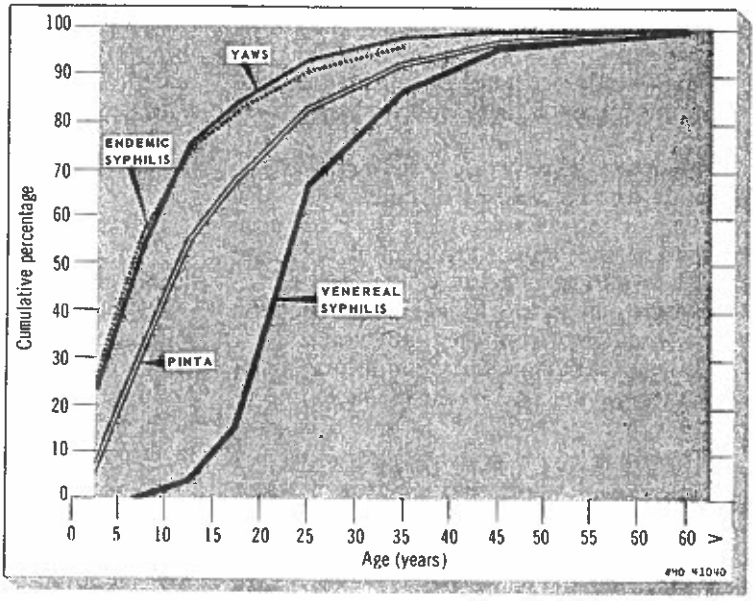
[2] United States Department of State (1950) *Point four: cooperative program for aid in the development of economically underdeveloped areas*, Washington, D.C. (*Economic Cooperation Series*, No. 24).

FIG. 1. GEOGRAPHICAL DISTRIBUTION OF THE NON-VENEREAL TREPONEMATOSES BEFORE WHO-ASSISTED CAMPAIGNS



Yaws Pinta Endemic syphilis and similar conditions

FIG. 2.
ONSET OF EARLIEST CLINICAL MANIFESTATIONS IN TREPONEMATOSES BY AGE *



* Based on 1547 cases of early pinta (Mexico), 1556 cases of early yaws (Haiti, Malaya, Jamaica, Thailand), 1087 cases of early endemic syphilis (Bosnia, Syria, Bechuanaland), 4145 cases of early venereal syphilis (USA).

2%-5% for primary cases and seroreactivity rates of 50%-60% in rural populations, e.g., in Mexico and Venezuela.

The patchy distribution of the endemic treponematoses in some countries reflects such factors as isolation and low socio-economic and hygienic standards. Seasonal and other variations in prevalence are possibly due to physiographical and nutritional factors. Yaws, endemic syphilis, and pinta have the pattern of herd infections, and transmission is characteristically by direct person-to-person contact (though sometimes by indirect contact), the main reservoir of infection being in children, as has been confirmed in WHO-assisted projects (Fig. 2).

Rapid regression of prevalence by mass treatment

The introduction of long-acting penicillins, which remain at treponemicidal levels in the blood and tissues for many weeks following a single injection, profoundly changed the public health approach to the endemic treponematoses of childhood. By contrast with the earlier toxic metal therapy, often used only in individual clinical cases seen at rural dispensaries and hospitals and having at best a palliative effect from the public health standpoint, the long-acting penicillins permitted systematic large-scale treatment surveys covering entire populations and carried out by mobile teams in the course of selective, multi-purpose, or integrated projects.

The use of mass treatment techniques for yaws eradication was first attempted in Haiti, with assistance from WHO and the Pan American Health Organization (which acts as the regional organization for WHO in the Americas). This trial, which was preceded by evaluation studies of the efficacy of long-acting penicillin in yaws, was undertaken following proposals by the United Nations Technical Assistance Mission in Haiti [3] and on the recommendation of a WHO Expert Committee on Venereal Infections. [4] A methodology was gradually developed by WHO on the basis of experience not only in Haiti but in other countries with different yaws prevalence rates (Indonesia, the Philippines, Thailand).

At the same time the successful early campaign against endemic syphilis in Yugoslavia had shown to what extent the treatment of contacts is necessary to ensure effective results, and the technical policies for mass penicillin campaigns formulated by subsequent expert committees owed much to its findings. These committees kept the developing endemic treponematoses programme under continuous review, while many national health administrations in developing countries joined the proposed co-ordinated programme aimed at eliminating these infections as a health problem. This programme was one of the first to lend itself particularly to international aid by WHO and UNICEF. That it had a considerable impact on health in developing countries is illustrated by the following specific results and by the reduction of prevalence obtained in selected areas with different initial prevalences and with small, medium-sized, or large populations:

(1) In Western Samoa the prevalence of active yaws in a population of 108 000 was 11.3% in 1955, with 3.3% infectious cases. Following a systematic treatment survey and resurvey campaign, covering 96%-100% of the population, less than 0.001% total yaws was found in 1958. Only isolated infectious cases have been found since in the rural health programme that developed from the campaign.

(2) In Bosnia, Yugoslavia, mass serological campaigns were held between 1948 and 1953 to detect the prevalence of endemic syphilis in the rural populations affected. They covered about one million people and revealed rates varying from 2.5% to 60.1%, with up to 13.7% active cases and 2.5% infectious lesions. No new case of infectious epidemic syphilis has been reported in Bosnia for several years, although continuous follow-up surveys have been undertaken throughout the area as part of multi-purpose screening (*inter alia* for mycosis of the scalp) carried out in connexion

[3] United Nations (1949) *Mission to Haiti. Report of the United Nations Mission of Technical Assistance to the Republic of Haiti*, New York (Publication II.B.2).

[4] *Wld Hlth Org. techn. Rep. Ser.*, 1950, 13, 16.

Age (years)	Seroreactors diagnosed at beginning of attack phase[a]	Seroreactors during last examination at end of attack phase[a]	Total Population	Prevalence at beginning of attack phase[a] (%)	Prevalence at end of attack phase[a] (%)
0	24	3	950	2.5	0.3
1-4	166	8	2 636	6.3	0.3
5-9	427	43	3 122	13.7	1.4
10-14	528	46	3 457	15.3	1.3
15-19	466	84	2 933	15.4	2.9
20-29	779	152	4 377	17.8	3.5
30-39	574	122	2 314	24.8	5.3
40-49	660	123	2 470	26.7	5.0
50-59	360	89	1 516	23.7	5.9
60-69	177	56	745	23.8	7.5
70-79	50	11	216	23.1	5.1
80+	16	2	70	22.9	2.9
	4 227	739	24 806	17.0	2.98

TABLE 1. ENDEMIC SYPHILIS CAMPAIGN AMONG MOSLEM POPULATION OF ZVORNIK, YUGOSLAVIA: PREVALENCE AT BEGINNING AND END OF ATTACK PHASE *

* Guthe, T. (1964) *Measure of treponematoses problems in the world.* In: United States Department of Health, Education, and Welfare, *Proceedings of the World Forum on Syphilis and Other Treponematoses*, Washington, D.C., p. 11.

[a] The interval between first and last surveys in the attack phase of the campaign was approximately three years. At the beginning of the attack phase, 389 cases (1.6%) with infectious lesions were found. None was found at the end of the attack phase, on the basis of several systematic follow-up surveys.

with the expansion of the rural health service and plans for rural development. Table 1 gives details on prevalence at the beginning and end of the attack phase of the programme in the Moslem population of the small community of Zvornik.

(3) In Haiti, with a population of approximately three million, yaws was highly prevalent. Since 1950 more than 1.3 million clinical cases, latent cases, and contacts have been treated in surveys and resurveys. Concomitant prevalence studies at sampling levels of 2.5%-5.6% have shown steady progress towards the epidemiological eradication of yaws:

Year	*Infectious yaws in population (%)*
1950-1954	35.7
1955	1.085
1956	0.412
1957	0.208
1958	0.095
1959	0.017
1960	0.019
1961	0.001
1962	0.0006

(4) In Indonesia the average prevalence of yaws in the islands of Java and Sumatra, with an estimated population of some 63 million people, was 8.7% at the start of the campaign in 1950. In other islands it was 18.2%, the range being from 2% to 60%. From mid-1950 to the end of 1962 initial surveys were carried out covering 94.7% of the populations of Java and Sumatra and 49.8% of the populations of five other islands. This yaws campaign, the world's largest, was integrated into the rural health services from the beginning, and has yielded excellent data. Table 2 shows the findings for some 18 million people in 58 regencies in east and central Java.

A rapid regression of prevalence to a fraction of 1% of the rural population has been recorded in most countries or areas where mass campaigns against the endemic treponematoses of childhood have been carried out with international assistance—or without it, as in Brazil (yaws) and Mexico (pinta). Many of the yaws endemic areas where the initial prevalence was high have been covered, and considerable progress in reducing the reservoir of infection appears to have been made.

TABLE 2. RESULTS OF YAWS SURVEYS IN EAST AND CENTRAL JAVA, AS AT 30 JUNE 1963

	Initial treatment survey	Last resurvey before consolidation [a]	First completed survey in consolidation
East Java (29 regencies):			
Estimated population	9 030 858	9 279 304	9 703 256
Population examined	7 732 036 (85.62 %)	7 926 257 (85.42 %)	8 003 765 (82.49 %)
Total yaws found	921 451 (11.92 %)	122 449 (1.54 %)	77 107 (0.96 %)
Infectious yaws found	—	—	4 400 (0.05 %)
Central Java (29 regencies):			
Estimated population	9 343 279	9 889 645	10 406 584
Population examined	7 682 408 (82.22 %)	8 297 250 (83.90 %)	8 670 753 (83.32 %)
Total yaws found	593 155 (7.72 %)	73 159 (0.88 %)	28 166 (0.32 %)
Infectious yaws found	—	—	2 216 (0.03 %)

[a] There were several resurveys between the initial treatment survey and the last resurvey before consolidation.

The approximate numbers of persons treated and examinations undertaken by health administrations in surveys and resurveys up to 1963 are shown in Table 3.

An estimated 50-60 million persons continue to live in areas of medium or low prevalence of endemic treponematoses where no intensive effort has been made to control these diseases. The number of infected persons in these areas is estimated to be 10-15 million.

Mass campaigns and rural health

The suffering of children arouses general concern, the incapacitation of young adults results in loss of manpower, and external lesions make the public more aware of the treponematoses in their midst. When people with little previous experience of medical services see how penicillin makes surface lesions disappear within a matter of days in children,

TABLE 3. ENDEMIC TREPONEMATOSES SURVEYS BY WHO REGION UP TO 1963

Region	Persons examined at initial surveys	Examinations at all surveys and resurveys	Persons treated
Africa	26 154 900	77 185 800	18 700 100
Americas	7 269 200	9 458 000	5 210 200
Eastern Mediterranean	758 000	1 860 100	324 500
Europe	145 000	883 500	52 500
South-East Asia \ Western Pacific /	100 525 700	260 474 600	17 957 700
Total	134 852 800	349 862 000	42 245 000

the desire for better health in general and for wider community health services is stimulated. Some health administrations have taken advantage of this situation to promote the improvement of rural health services and to enlist the help of the community in installing or improving health centres (e.g., in the Pacific Islands and in Nigeria).

In some countries, pending the eventual establishment of rural health centres, the functions of mobile teams in endemic treponematoses surveys and resurveys have become much wider during the expansion and consolidation phases of the programme. Thus, with the rapid decline in the prevalence of yaws, field teams have turned their attention to smallpox vaccination as well (e.g., in Cambodia, Thailand, Nigeria, and Haiti), so that the campaign against yaws has made it increasingly possible to extend the WHO smallpox eradication programme: in the course of yaws campaigns by health administrations, some 30 million smallpox vaccinations were administered between 1958 and 1963. Leprosy case-finding has also been carried out during yaws campaigns (e.g., in the British Solomon Islands, Malaya, Togo, Indonesia, and Nigeria). During consolidation and surveillance activities in the yaws project in Thailand [5] between 1959 and 1963, 1 679 656 primary and 11 251 456 secondary smallpox vaccinations, 244 400 combined cholera and typhoid immunizations, and 162 700 treatments for conjunctivitis were given, and some 2000 cases of leprosy diagnosed.

In no case has the complete eradication of the endemic treponematoses, according to the criteria given in the fifth report of the WHO Expert Committee on Venereal Diseases and Treponematoses, [6] been achieved in any large area. On the other hand, the transmission of endemic syphilis has ceased in Bosnia, Yugoslavia, and the transmission of yaws in certain Western Pacific islands, Haiti, and some areas of Thailand and Indonesia. Practical difficulties have arisen when infection has been reduced to a level at which it is manageable by surveillance organizations (usually based by preference on the local rural health centres).

As early as 1952 the first International Yaws Conference [7] took up the question of the relationship between the two complementary approaches: (*a*) a long-term programme to provide developing rural communities with organized permanent preventive and curative health services, and (*b*) immediate steps to make available the benefits of modern medicine in the form of mass campaigns. It emphasized the opportunity provided by yaws campaigns for promoting health services in both contexts during the attack, expansion, and consolidation phases of mass campaigns.

In some areas mass campaigns against the endemic treponematoses have undoubtedly helped pave the way for a more rapid establishment of rural health services. In others there has been an integrated approach from the outset of the campaign. Thus, in Java, public health staff have been participating in surveillance campaigns in rural areas for more than ten years. In 1962, surveillance was being carried out by rural dispensaries in the 1989 subdistricts of the country where yaws control was in progress; at the time, these dispensaries covered 72% of the country's population. In the Philippines, the mass campaign against yaws was part of the public health structure and was integrated from 1954 onwards into the developing network of some 1300 health units.

In other countries, studies in experimental areas preceded systematic integration work based on: planning of requirements; training, re-training, and supervision of personnel for multi-purpose activities; co-ordination of preventive and curative services, etc. Thus, by 1963, epidemiological surveillance in all 45 " yaws provinces " in Thailand had been integrated into the expanding rural health services.

In some other areas, for example, in the Americas and Africa, it has not been possible to take full advantage of the " spearhead " opportunities of endemic treponematoses work. Resurveys and sampling surveillance either continue to be undertaken by mobile

[5] Ministry of Public Health of Thailand (1963) *Public health in Thailand*, Bangkok.

[6] *Wld Hlth Org. techn. Rep. Ser.*, 1960, 190, 29.

[7] *Bull. Wld Hlth Org.*, 1953, 8, 355, 371.

units, or are gradually lapsing. Small outbreaks of yaws and the formation of new foci of infection have occurred, and will continue to occur, where there are no rural health services to stamp them out or resurveys have been discontinued for other reasons.

Endemic treponematoses are infections of the more isolated areas of the world. Social and economic progress and improvements in hygiene and education gradually tend to repress them, as has been shown in Ceylon, where yaws—hyperendemic at the beginning of this century—had almost entirely disappeared even before the advent of penicillin. The use of long-acting penicillin, mass techniques, and increased epidemiological knowledge have made it possible to speed up this process considerably, thus alleviating much human suffering within a short time, even if the ultimate eradication of endemic treponematoses in large areas will probably require the presence of local health services to carry out continued epidemiological surveillance.

Experience in the early campaigns against the endemic treponematoses focused attention on certain general problems relating to mass campaigns and communicable disease eradication and to the improvement of health in developing rural areas. While in 1948 WHO's first overall programme stressed the importance of a direct attack on diseases causing " wastage of human life and effort ", this approach was viewed as a " spearhead " for the promotion of general health services in the Organization's " General programme of work for the first period " (1952-57).[8] That campaigns should be considered as a stage in the achievement of overall integrated health programmes was stressed, with particular reference to rural health services, in the " General programme of work for the second period " (1957-61).[9] The " General programme of work for the third period " (starting in 1961) [10] included research on methods for the progressive assimilation into the general health services of communicable disease programmes as these approached their objectives. From the start the endemic treponematoses programme of WHO has developed in accordance with the policies just outlined. Similar problems of integration have arisen in connexion with campaigns against malaria, tuberculosis, trachoma, leprosy, etc. A special study group convened by WHO in 1964 studied the relationships between mass campaigns and the general health services, drawing widely on the experience gained in the course of the campaigns against yaws.

[8] *Off. Rec. Wld Hlth Org.*, 1951, 32, 55; 1952, 42, 24; 1954, 55, 20.

[9] *Off. Rec. Wld Hlth Org.*, 1955, 63, 416.

[10] *Off. Rec. Wld Hlth Org.*, 1960, 102, 54.

WHO assistance

The objectives of WHO-assisted projects in the endemic treponematoses have been: (*a*) to eliminate sources of infection and halt the transmission of the disease with the aim of achieving epidemiological, and eventually complete, eradication (see page 10); and (*b*) to transfer responsibility for continued epidemiological surveillance to the developing rural health services when the prevalence has been reduced to a low level. If, for one reason or another (e.g., in transitional situations), the local health services are inadequate, continued periodic surveillance may be effectively carried out in the form of simplified surveys by mobile multi-purpose units (smallpox vaccination, leprosy case-finding, etc.).

Between 1949 and 1963, campaigns were undertaken in 49 countries and areas, with emphasis on the epidemiological aspects, population coverage, treatment of cases and contacts, training, and health education. The methodology gradually developed by WHO for the conduct of these campaigns was adjusted to different levels of prevalence and different environments. Technical advisers—usually medical officers, laboratory technicians, and public health nurses, often forming a team—were made available. They normally stayed in a country for several years to promote the project from its pilot stage until a planned national programme had been achieved, training schedules for all types of personnel consolidated, and adherence to the principles of yaws eradication ensured. A list of major WHO-assisted projects against the endemic treponematoses is given in Annex 1.

In some regions (Africa, the Americas, the Western Pacific), intercountry teams are beginning to assist governments in assessing the yaws problem. In addition, an interregional evaluation team has begun special combined epidemiological and serological evaluations of the long-term outcome of mass campaigns, using random sample surveys and specific immunofluorescent (FTA) and immobilizing antibody (TPI) tests.

The decline in the prevalence of infection following yaws projects in endemic areas and the reluctance of health administrations to undertake extensive activities in areas where yaws already has a low endemicity are reflected in requests for international assistance. As compared with the 31 WHO-assisted projects against the endemic treponematoses in operation in 1958-59, only 14 are provided for in the budget for 1964-65. Tables 4, 5, and 6 show the estimated international expenditures on endemic treponematoses and venereal disease projects in these periods by region, source of funds, etc.

In view of the characteristic epidemiology of endemic treponematoses, an attenuation of the imm[illegible] problem is possible. There has, howev[illegible]n a tendency to regard the rapid regress[illegible] of lesions as constituting an attenuation of the problem as a whole. This is not altogether so, since it makes it more difficul[illegible]in an adequate appreciation [illegible] sustained effort to reach set [illegible] similar situation may be observed in all communicable disease programmes, both national and international. Thus, in 1955 the Second International Conference on the Control of Yaws [11] drew up a pl[illegible] eradication in Africa, and m[illegible]n 1956 and 1957 provided for t[illegible]on of activities in West Africa, [illegible]th spec[illegible]eference to border problems, but in the countries and areas of East Africa where prevalence is relatively low, no intensive yaws campaigns have gone forward with international assistance.

In other regions, intensified activities have been more extensively co-ordinated, e.g., in South-East Asia and the Western Pacific Region, by means of the First International Symposium on Yaws Control (1952),[12] an inter-country yaws co-ordination meeting (1959), and an Asian Yaws Conference (1961). This applies to some extent also to the Americas, where co-ordination—particularly in the Caribbean area—has been helped by a seminar on treponematoses eradication (1957),[13] an International Symposium on Venereal Diseases and Treponematoses held in Washington, D.C. (1956),[14] and a World Forum on Syphilis and Other Treponematoses also held in Washington, D.C. (1962).[15]

Training

Between 1948 and 1963, 252 individual fellowships were awarded by WHO for the study of clinical, epidemiological, and laboratory aspects of endemic treponematoses or venereal diseases at institutions abroad or with field projects undertaken by health administrations. In the same period, a further 106 short-term fellowships were granted for group training or for participation in regional or international meetings on endemic treponematoses organized by WHO.

In view of the importance of endemic treponematoses campaigns in the promotion of rural health, special attention was given almost from the outset to the training of local staff at all levels. Several thousand sanitarians, rural auxiliaries, and other health workers were trained in organized courses forming part of endemic treponematoses projects in developing countries. They were brought into close contact with the rural populations, came to know their problems and needs, and learnt to co-ordinate their work with that of other health staff. They also gained an idea of the other diseases prevalent in the countries where they worked. This was a valuable preparation for their duties in multi-purpose and integrated health services.

[11] *J. trop. Med. Hyg.*, 1957, 60, 27, 62.

[12] World Health Organization (1953) *First International Symposium on Yaws Control*, Geneva (*World Health Organization: Monograph Series*, No. 15).

[13] *Bol. Ofic. sanit. Panamer.*, 1957, 42, 252.

[14] United States Department of Health, Education, and Welfare (1956) *Curr. Lit. vener. Dis.*, Washington, D.C. (special issue).

[15] United States Department of Health, Education, and Welfare (1964) *Proceedings of the World Forum on Syphilis and Other Treponematoses*, Washington, D.C.

TABLE 4. ESTIMATED EXPENDITURES ON ENDEMIC TREPONEMATOSES PROJECTS BY WHO REGION AND BY SOURCE OF FUNDS DURING THE TWO-YEAR PERIODS 1951-52, 1958-59, AND 1964-65

	Reg.[a] US$	TA[b] US$	OEBF[c] US$	Total US$	Reg.[a] US$	TA[b] US$	OEBF[c] US$	Total US$
	Africa				Americas			
1951	—	—	—	—	32 359	—	128 000	160 359
1952	—	—	—	—	25 849	—	—	25 849
Total	—	—	—	—	58 208	—	128 000	186 208
1958	12 805	106 893	223 000	342 698	22 690	40 786	109 500	172 976
1959	2 600	134 428	516 000	653 028	23 506	24 836	112 400	160 742
Total	15 405	241 321	739 000	995 726	46 196	65 622	221 900	333 718
1964	27 273	123 941	145 000	296 214	33 997	—	46 840	80 837
1965	30 113	140 633	119 000	289 746	42 304	—	41 310	83 614
Total	57 386	264 574	264 000	585 960	76 301	—	88 150	164 451
	South-East Asia				Europe			
1951	8 400	—	59 577	67 977	—	—	144 000	144 000
1952	—	23 862	23 600	47 462	2 100	—	—	2 100
Total	8 400	23 862	83 177	115 439	2 100	—	144 000	146 100
1958	—	21 826	429 000	450 826	—	—	—	—
1959	—	16 976	424 000	440 976	—	—	—	—
Total	—	38 802	853 000	891 802	—	—	—	—
1964	—	36 860	133 500	170 360	—	—	—	—
1965	—	40 090	230 000	270 090	—	—	—	—
Total	—	76 950	363 500	440 450	—	—	—	—
	Eastern Mediterranean				Western Pacific			
1951	16 800	—	145 000	161 800	—	—	35 400	35 400
1952	—	25 076	100 000	125 076	—	—	35 400	35 400
Total	16 800	25 076	245 000	286 876	—	—	70 800	70 800
1958	—	—	—	—	88 023	34 126	33 250	155 399
1959	—	—	—	—	77 782	36 179	34 000	147 961
Total	—	—	—	—	165 805	70 305	67 250	303 360
1964	—	—	—	—	35 647	—	4 000	39 647
1965	—	—	—	—	38 635	—	10 000	48 635
Total	—	—	—	—	74 282	—	14 000	88 282

[a] Regular budget.
[b] Technical Assistance funds.
[c] Other extra-budgetary funds, including Voluntary Fund for Health Promotion.

TABLE 5. ESTIMATED EXPENDITURES ON ENDEMIC TREPONEMATOSES AND VENEREAL DISEASE PROGRAMMES RELATING TO HEADQUARTERS ACTIVITIES, CONTRACTUAL TECHNICAL SERVICES, AND OTHER INTER-REGIONAL ACTIVITIES DURING THE TWO-YEAR PERIODS 1951-52, 1958-59, AND 1964-65

	Headquarters activities, staff, expert committees, etc.				Contractual technical services				Inter-regional: symposia, epidemiological teams, etc.			
	Reg.[a] US $	TA [b] US $	OEBF[c] US $	Total US $	Reg.[a] US $	TA [b] US $	OEBF[c] US $	Total US $	Reg.[a] US $	TA [b] US $	OEBF[c] US $	Total US $
1951	57 947	—	—	57 947	8 000	—	—	8 000	—	—	—	—
1952	56 767	—	—	56 767	8 000	—	—	8 000	59 000	—	—	59 000
Total	114 714	—	—	114 714	16 000	—	—	16 000	59 000	—	—	59 000
1958	50 000	—	—	50 000	11 000	—	—	11 000	—	—	—	—
1959	58 400	—	—	58 400	11 500	—	—	11 500	43 940	—	—	43 940
Total	108 400	—	—	108 400	22 500	—	—	22 500	43 940	—	—	43 940
1964	64 298	—	6 300	70 598	49 000	—	8 000	57 000	62 855	—	—	62 855
1965	75 736	—	7 300	83 036	58 000	—	25 000	83 000	62 049	—	—	62 049
Total	140 034	—	13 600	153 634	107 000	—	33 000	140 000	124 904	—	—	124 904

[a] Regular budget. [b] Technical Assistance funds. [c] Other extra-budgetary funds, including Voluntary Fund for Health Promotion.

TABLE 6. TOTAL ESTIMATED EXPENDITURES ON ENDEMIC TREPONEMATOSES AND VENEREAL DISEASE PROGRAMMES, ALL SOURCES OF FUNDS, REGIONAL, INTER-REGIONAL, AND HEADQUARTERS, FOR THE TWO-YEAR PERIODS 1951-52, 1958-59, AND 1964-65

	1951-52			1958-59			1964-65		
	Endemic trep. US $	Venereal disease US $	Total US $	Endemic trep. US $	Venereal disease US $	Total US $	Endemic trep. US $	Venereal disease US $	Total US $
Africa	—	—	—	995 726	—	995 726	585 960	—	585 960
Americas	186 208	525 397	711 605	333 718	45 437	379 155	164 451	13 200	177 651
South-East Asia	115 439	355 716	471 155	891 802	11 050	902 852	440 450	—	440 450
Europe	146 100	133 735	279 835	—	132 111	132 111	—	—	—
Eastern Mediterranean	286 876	824 581	1 111 457	—	272 872	272 872	—	19 934	19 934
Western Pacific	70 800	66 234	137 034	303 360	82 523	385 883	88 282	52 664	140 946
Sub-total	805 423	1 905 663	2 711 086	2 524 606	543 993	3 068 599	1 279 143	85 798	1 364 941
Inter-regional activities			59 000			43 940			124 904
Contractual technical services			16 000			22 500			140 000
HQ activities (staff, expert committees)			114 714			108 400			153 634
Total			2 900 800			3 243 439			1 783 479

Provision of technical information

Health administrations and medical workers have been provided with technical information on all aspects of the eradication of endemic treponematoses by expert advisory panels, institutes co-operating with WHO, WHO-assisted projects, etc. Original documentation on the technical aspects of the subject has been provided by inter-country co-ordination meetings and regional and international conferences.

An international nomenclature of yaws lesions,[16] and publications on the epidemiology of endemic syphilis,[17] the differential diagnosis of yaws,[18] and the biology of the treponematoses [19] have appeared in the WHO *Monograph Series*, and the Organization has also published a bibliography on yaws.[20] WHO has disseminated technical information on endemic treponematoses through guides, manuals, and technical documents aimed at obtaining uniform methods and techniques based on experience in different countries and at promoting collateral investigations and studies.

WHO research programme

When WHO began to promote public health action against the treponematoses in the developing countries, it soon became apparent that both basic and applied research were necessary if the knowledge acquired in the developed countries was to be applied elsewhere. It also became apparent that research on improved and specific diagnostic techniques was needed, and that epidemiological and operational field research would become increasingly important for the formulation of methods for mass campaigns.

Chemotherapy

WHO was associated with the early trials and studies for the evaluation of long-acting procaine penicillin (PAM) [21] and benzathine penicillin [22] in yaws, and of PAM in endemic syphilis [23] and pinta.[24] These and other studies permitted WHO expert committees to outline treatment schedules for mass campaigns. The long-term evaluation of these schedules is still going on, and WHO is also associated with studies of the effectiveness in endemic treponematoses of alternative drugs to penicillin.[25]

Research showed that PAM from different manufacturers varied significantly in respect of treponemicidal blood-level durations, and that substandard preparations could cause unacceptable relapse rates in yaws (and in syphilis) if treatment consisted of a single dose or a limited number of doses. It thus became essential first to establish international minimum requirements for PAM and then to undertake extensive research, which resulted in the development of a standard serum assay method, a penicillin blood-level duration test in the rabbit (to replace testing in humans), and an international reference preparation for PAM.[26] To ensure that substandard preparations were not used by health administrations or by international organizations—such as WHO and UNICEF—engaged in large-scale programmes, more than 1000 different lots of PAM were tested by two WHO reference centres between 1948 and 1963, with a rejection rate of 20%.

Epidemiology and eradication

The natural course of yaws in closed primitive tribes living in stable environments unaltered by treatment or technical progress has been studied in several areas in West Irian (formerly Netherlands New Guinea).[27] Stu-

[16] Hackett, C. J. (1957) *An international nomenclature of yaws lesions*, Geneva (*World Health Organization: Monograph Series*, No. 36).

[17] Grin, E. I. (1953) *Epidemiology and control of endemic syphilis*, Geneva (*World Health Organization: Monograph Series*, No. 11).

[18] Hackett, C. J. & Loewenthal, L. J. A. (1960) *Differential diagnosis of yaws*, Geneva (*World Health Organization: Monograph Series*, No. 45).

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

[20] World Health Organization (1963) *Bibliography on yaws, 1905-1962*, Geneva.

[21] *J. invest. Derm.*, 1949, 12, 11; *Bull. Wld Hlth Org.*, 1953, 8, 55, 91.

[22] *Amer. J. Syph.*, 1954, 38, 397.

[23] *Bull. Wld Hlth Org.*, 1952, 7, 1; 1956, 15, 975.

[24] *Bol. Ofic. sanit. Panamer.*, 1952, 33, 565.

[25] *Bull. Wld Hlth Org.*, 1953, 8, 107.

[26] *Wld Hlth Org. techn. Rep. Ser.*, 1953, 63, 55.

[27] Kranendonk, O. (1958) *Serological and epidemiological aspects in yaws control. Report on a mass treatment campaign against yaws in Netherlands New Guinea*, Amsterdam, Broos.

dies of the clinical and serological course of the disease, its infection and contact rates, and the depletion of the reservoir of susceptibles have provided quantitative data for epidemiological models, which have proved extremely useful in appraising the possible rate of renewed spread of yaws following mass treatment.

Several WHO-assisted projects have provided important information—based on various endemicity levels, attack rates, and the cycle of the disease—on the rapidity and completeness of population coverage needed in relation to the extent and frequency of follow-up examinations. Evaluation of this information has led to the establishment of decisive criteria on the effectiveness and limitations of the methods used in mass campaigns, and provided a sound basis for the use of total, juvenile, or selective (case and contact) mass treatment (TMT, JMT, or SMT) in areas with different environmental conditions and different prevalence levels of clinical disease and subclinical infection. The epidemiological importance of the technique of community-wide treatment of latent cases in yaws—which can prevent new foci from arising—has been brought out. These findings have also been of great interest for campaigns against other communicable diseases, and have made it possible to formulate time schedules for the completion of epidemiological eradication.

The foundations have thus been laid for continuing studies, based on more exact epidemiological and serological surveys of large populations chosen at random, with the aim of evaluating, 10 to 15 years after mass yaws campaigns, the " stock and flow quantities " of infection and disease in relation to eventual eradication. These studies are based on treponemal as well as lipoidal antigen testing (FTA and TPI tests). In Thailand, the Philippines, and Togo, they have revealed a proportion of between 30% and 35% false seroreactions to lipoidal antigen testing in rural tropical areas (using the TPI test as the arbiter test) and an excess of false low-titre seroreactions in the younger age groups, in which primary attack rates were highest when the disease was endemic several years before.

New epidemiological knowledge based on data of this type, collected with uniform methods and techniques, is beginning to emerge. Apart from their immediate value in assessing the extent and transmission of the disease in endemic areas following campaigns, such data provide a baseline for measuring future developments. Being statistically referable to large rural populations, the sera obtained in such studies can be used for other purposes. Thus lyophilized aliquots, together with identifying information, are kept in the WHO serum reference banks (virus diseases programme) for use in multipurpose immunological studies recommended by the Advisory Committee on Medical Research.

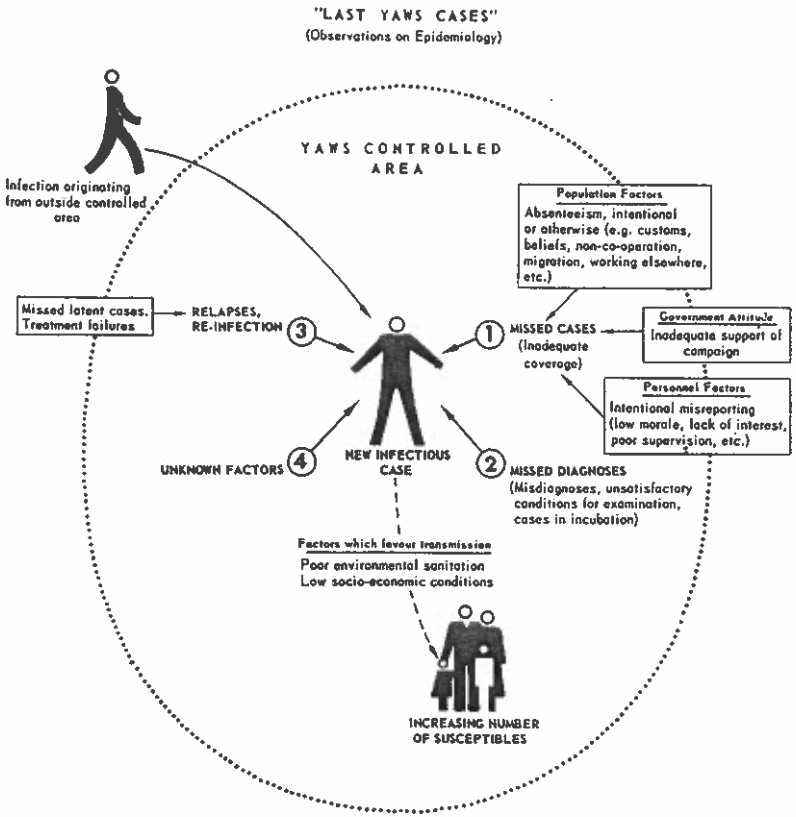
In studies undertaken by health administrations attention has been focused in recent years on the epidemiology of the " last yaws cases " which continue to be found during post-campaign surveillance. The knowledge now emerging of the nature and origin of such cases, which correspond to a descending but asymptotic curve of infection, is essential for further understanding of epidemiological or complete eradication. The factors involved, their relationship, and possible solutions to the problem posed by these cases are illustrated diagrammatically in Fig. 3.

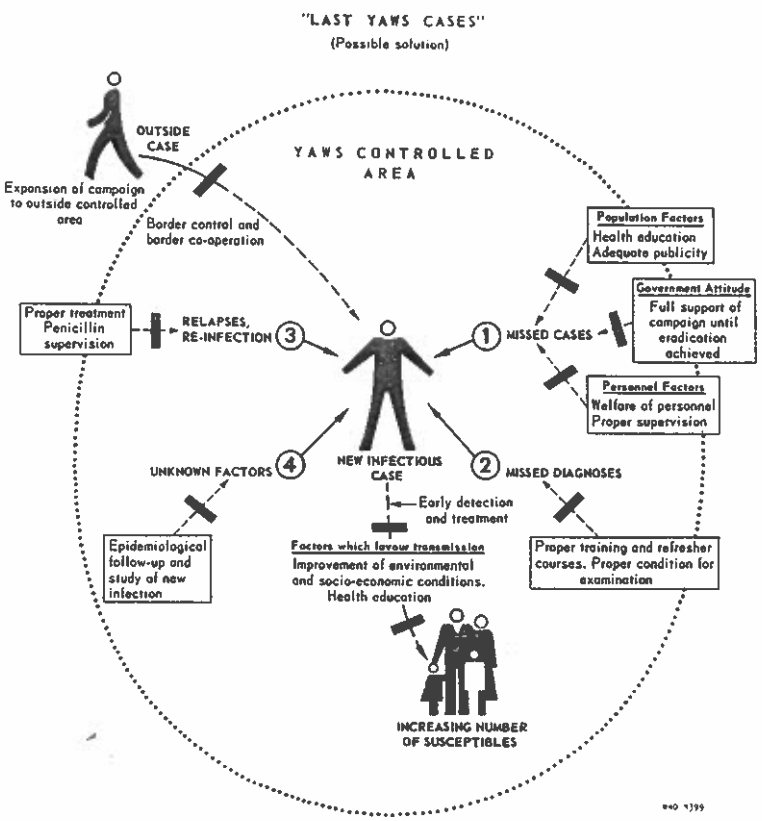
Methodology and standardization

On the basis of the observations, experience, and reports of national workers and WHO advisers and consultants, of material presented at the international yaws conferences, and of technical policies recommended by expert committees, a methodology has been developed for the conduct of mass campaigns against yaws in the attack, expansion, and consolidation phases of the programme.

Criteria have been established for the discontinuation of the mass treatment stage of campaigns, the halting of routine population surveys, and the institution of local surveillance through rural health centres or their equivalents, supplemented by school surveys focusing attention on younger age groups at particular risk of infection. Thus, consolidation normally begins after the completion of the last resurvey in which at least 80% of the

FIG. 3. YAWS CONTROL: SURVEILLANCE PHASE





population was covered, and in which the prevalence of active yaws did not exceed 2% and that of infectious cases 0.5%. The methodology developed employs PAM or benzathine penicillin, generally administered according to uniform dosage schedules. Standard reporting forms relating to initial treatment surveys, resurveys, and penicillin consumption have been evolved. A standard nomenclature and classification of lesions established by a group of experts collaborating with WHO (see page 15), the publication of a yaws atlas,[28] and the provision of manuals in local languages have facilitated diagnosis by field personnel.

Several aspects of research relating to serological methods and to the standardization of techniques and reagents in endemic treponematoses will be described in a subsequent article. It has already been observed that a high proportion of seroreactors to conventional lipoidal antigen-testing are free from treponematoses, and this makes it increasingly necessary to use specific treponemal tests (FTA and TPI) in tropical countries. WHO has recently developed a transport technique for finger-prick blood absorbed and dried on blotting-paper discs, and this may become important in assessing local treponematoses problems in developing countries. A technique for the long-distance shipment of sera deep-frozen at —196° C in liquid nitrogen (to prevent infection and possible decay of antibodies) has also been developed in co-operation with WHO reference centres.

Other research

Developments in microbiological, biochemical, and immunopathological investigations relating to all treponematoses will be outlined in a subsequent article. In certain laboratories participating in the WHO research programme, efforts are continuing to adapt *Treponema pertenue*, the causative organism of yaws, to animals other than the rabbit, and to improve the differential laboratory diagnosis of yaws and syphilis.

WHO also provides various services to research through its reference centres and other laboratories, where collections of strains of pathogenic and non-pathogenic treponemes and of syphilis, yaws, and pinta sera have been built up.

Co-operation with UNICEF and other organizations

From the outset UNICEF has given very important material assistance to the mass campaigns against endemic treponematoses whose implementation on a nation-wide scale has been recommended by WHO, with due regard to the recommendations of the UNICEF/WHO Joint Committee on Health Policy. By 1962 UNICEF's investment in yaws programmes amounted to $7 600 000 for penicillin, equipment, transport, and training of rural health workers. This is said to have been one of the most profitable investments made by UNICEF in terms of the amount of suffering relieved compared with the *per capita* cost. In Indonesia, for example, the *per capita* cost was $0.77 in 1955, rising in 1960 as cases decreased and examinations per case increased.

The International Union against the Venereal Diseases and the Treponematoses (IUVDT) has supported WHO's work on endemic treponematoses in several ways—for example, by disseminating information about WHO-assisted activities and encouraging national voluntary groups to support governmental work.

The Students War Against Yaws (SWAY) is a recent enterprise of Canadian high school students; its aims are to contribute to the WHO Voluntary Fund for Yaws established by the Executive Board of the Organization at its thirty-third session, and to promote an understanding of WHO activities among young people.

The future

In many of the high-prevalence areas in developing countries, low-cost mass penicillin campaigns against the rural endemic treponematoses of childhood (particularly yaws) have significantly reduced the transmission of infection and the prevalence of these diseases—almost to the point of eradication

[28] Hill, K. R., Kodijat, R. & Sardadi, M. (1951) *Atlas of framboesia*, Geneva (*World Health Organization: Monograph Series*, No. 5)

in some instances. Work to this end will continue in these areas for the next few years. In other areas, where prevalence is low, mass campaign techniques have not been applied; selective, multi-purpose, or integrated activities in these areas could accelerate the elimination of the infections.

In environments that are changing as a result of mass campaigns, solutions are needed for several problems of practical importance in rural health. Leprosy case-finding and smallpox vaccination are already being combined with yaws campaigns, but techniques are needed for a wider and more efficient use of the multi-purpose approach. Criteria and techniques are required for a more rational integration of epidemiological surveillance into the work of the developing rural health services, following mass campaigns.

Combined epidemiological and serological evaluation of the results of mass campaigns, based on valid sampling and specific treponemal serum testing, is necessary to determine the nature and extent of low-level transmission and the "come-back potential" of endemic treponematoses in a community, following mass penicillin treatment. Simple measures to counteract recrudescences are needed. In addition, rural health programmes and programmes for the care of adolescents in areas undergoing urbanization, industrialization, and economic development may need to pay special attention to young people from the rural areas of the tropics who have reached puberty without acquiring cross-immunity to venereal syphilis as a result of previous yaws infection.

Intensified field and laboratory research will be needed on these and related problems, and basic microbiological, biochemical, and immuno-pathological research is also essential in order to improve the tools available to the public health services.

Venereal syphilis

The use of long-acting penicillin in single or multiple injections gave excellent results in the treatment of early syphilis, and the dramatic decline in the reported incidence of the disease in many countries between 1948 and 1957-58 is a landmark in the history of public health. The substitution of effective, simple penicillin treatment for toxic, chronic, suppressive metal therapy led, however, to the impression that syphilis was no longer dangerous and had lost many of its complications. In reality, there has been no alteration in the lesion-producing virulence of *Treponema pallidum* in untreated or inadequately treated patients, and it has continued to give rise to prenatal infection of the foetus and to early and late local and systemic lesions, including cardiovascular, locomotor, psychotic, and other complications in adults in developed countries. In addition, reports from developing countries over the past decade mention systemic complications seldom reported previously; this is possibly because longevity in these countries has increased sufficiently to give time for such complications to occur.

Incidence trends

The value of direct comparisons of the incidence in different countries is often limited by differences in methods and completeness of reporting and classification, and in the availability of facilities, staff, etc. For example, a survey in 1962 in which 131245 United States doctors took part showed that twice as much syphilis was treated as was reported.[1] Where data are available over a period of time, however, the reported incidence provides a valuable indicator of long-term trends in early syphilis. WHO studies of such trends from 1945 to 1950 [2] and from 1950 to 1960 [3] showed that in 76 (72.4%) out of 105 countries and areas a persistent rising incidence followed an all-time low about 1955 (see Table 1). This trend has continued since 1960 (see figure), and in some countries the reported incidence has approached or even exceeded the maximum of the years immediately after the Second World War. Between 1950 and 1960, the estimated maximum annual incidence rates were 53.6 per 100000 in the European Region (Yugoslavia, 1950), 250.8 in South-East Asia and the Western Pacific (Polynesia, 1952), 340 in the Americas (Colombia, 1950), 1232 in Africa (Basutoland, 1951), and 3687.5 in the Eastern Mediterranean (Sudan, 1950). In many developing countries reporting systems are deficient or non-existent, and in tropical areas there may be some confusion between yaws and syphilis. On the other hand, following mass penicillin campaigns against yaws, venereal syphilis may be expected to infiltrate into rural tropical regions, where the general population has had relative cross-immunity to syphilis but the new child population is

TABLE 1. EARLY SYPHILIS TRENDS, BY REGION, AS SHOWN IN WHO SURVEY (1950-60)

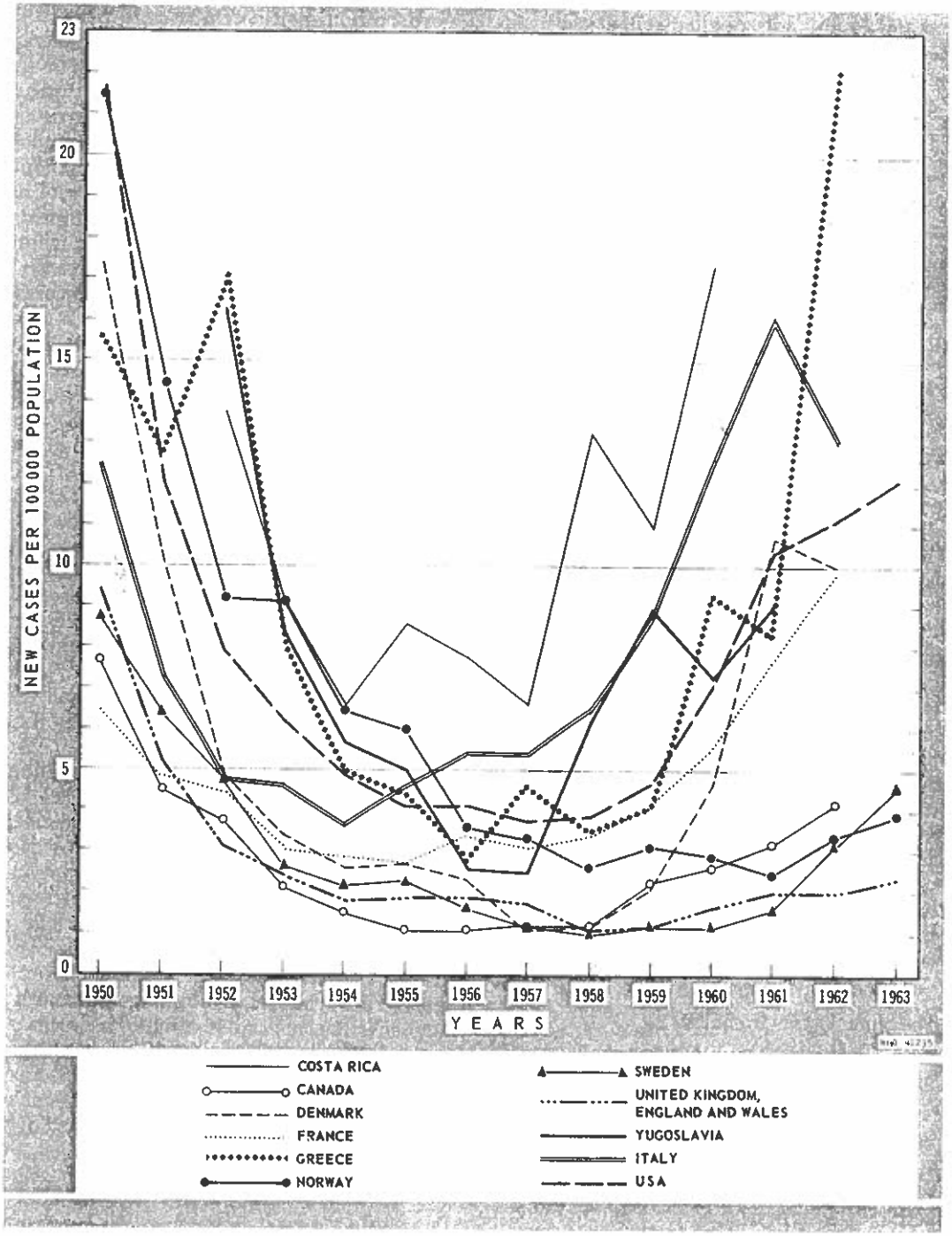
Region	Total number of countries and areas	Number with increased incidence 1957-60	Percentage with increased incidence
Africa	29	23	79.3
America	21	15	71.4
Eastern Mediterranean	12	6	50.0
Europe	20	19	95.0
South-East Asia and Western Pacific	23	13	56.5
	105	76	72.4

[1] *J. Amer. Med. Ass.*, 1963, 186, 46.

[2] *Epidem. vital Statist. Rep.*, 1959, 12, 306.

[3] Twelfth International Congress of Dermatology (1963) *Proceedings of the . . . , Washington, D.C., September 1962.* In: *Excerpta med. (Amst.), Int. Congr. Ser.*, No. 55, vol. 2, p. 833.

INCIDENCE TRENDS OF VENEREAL SYPHILIS IN DIFFERENT COUNTRIES



susceptible when it reaches puberty. The epidemiological importance of this phenomenon in Fiji was pointed out at the fourteenth session of the WHO Regional Committee for the Western Pacific in 1963.

In some countries it has been observed that syphilis (as well as gonorrhea) is becoming more frequent among young people than previously. For example, in Czechoslovakia 4.4% of reported syphilis in 1955 occurred in the age group 15-19 years as against 13.3% in 1959, while age-specific rates for the age group 15-19 years in Canada increased from 5.8 to 8.3 per 100000 between 1959 and 1962. Although there was a marked decline in congenital syphilis following the introduction of penicillin therapy, case rates in children under one year of age per 100000 live births in the USA rose from 4.0 in 1957 to 8.0 in 1962, and age-specific rates in children under one year of age in Canada increased from 0.4 to 1.7 per 100000 between 1960 and 1962.

The upward trend in early infectious syphilis has not been paralleled in early or late latent syphilis or in late complications, for which figures have remained more or less stationary since 1948. However, the " backlog " is considerable in many countries; four to five times more late and late latent cases than fresh infections are reported annually, and the cost of institutional maintenance for patients suffering from syphilitic insanity, disability due to cardiovascular syphilis, locomotor ataxia, and syphilitic blindness has remained high. In the USA it represents an annual loss of some 50000 man-years through disability and more than $50 million in maintenance costs for patients, with another $50 million in loss of income up to the age of 65 (figure based on the 1960 adult income rate).

The changing environment

In recent years, a number of new environmental problems have created obstacles to venereal disease control in both developed and developing countries. The effectiveness of penicillin, together with its low cost and ease of application, in time gave rise to a false sense of security, generated indifference to the risk of infection, and reduced the fear of the consequences of the disease. Furthermore, the breaking-up of old social patterns and the establishment of new ones as a result of technical change, accelerated industrialization, and urbanization have become increasingly important factors in the spread of many communicable diseases, including the venereal diseases. The world-wide rate of population growth in urban areas is currently about two and a half times higher than the rate in rural areas.[4] This marked trend towards urbanization and the absorption of large rural populations by rapidly expanding cities and towns appear to be of increasing importance in the epidemiology of syphilis, which is predominantly an urban disease. Migrant workers and similar groups who have to be integrated temporarily or permanently in new surroundings in their own or a foreign country also contribute to the spread of infection. Furthèrmore, the well-known relationship between the consumption of alcohol and the acquisition of venereal infections is taking on renewed importance because of the growing number of sexually active young wage-earners in technical and other occupations in economically prosperous countries. Finally, as a result of the unprecedented and rapid movement of large numbers of civilian and military travellers by land, sea, and air, as well as the increase in merchant shipping and the consequently greater number of port calls by seafarers, venereal infection is more and more becoming an " international disease ". Certain countries have indicated that as much as 50% of cases diagnosed at home originate abroad, and special sampling studies among overseas merchant ships of one large maritime nation showed that about 20% of the crews became infected during one year.[5] A closely associated sociological problem is brought out by findings in another large maritime nation—that 11.2% of overseas crews were between 15 and 17 years of age.[6]

In many areas, earlier maturity and freer associations between young males and females have led to a revolution of *mores* and to " new standards for a new age ". Efforts in the

[4] United Nations (1961) *Demographic yearbook 1960*, New York.
[5] *Bull. Wld Hlth Org.*, 1963, 29, 773.
[6] *Nor. Dpt Com. Ship.*, 1964, 24, 5.

domains of behavioural science and health education have not succeeded in preventing venereal infections from spreading among young people living in a rapidly changing environment. In recent years there have also been reports suggesting an increased incidence of syphilis (and gonorrhea) among homosexuals in younger as well as older age-groups —if not of homosexuality itself.

There has been some controversy about the closing of licensed or tolerated houses and the abolition of the regulation of prostitution in countries ratifying or adhering to the United Nations Convention for the Suppression of the Traffic in Persons and the Exploitation of the Prostitution of Others, for it is considered in some quarters that these measures might actually hinder the control of venereal diseases and even help to spread them. It has been noted that the increase in venereal disease in recent years is similar in developed countries where licensed brothels were abolished many decades ago (e.g., the Scandinavian countries) and in those where they were suppressed more recently (e.g., France and Italy), and that in some countries clandestine promiscuity appears to have taken the place of prostitution in spreading venereal infection. Thus the changing environment in certain countries has led to the appearance of " enthusiastic amateurs ", " good-time girls ", " call girls ", " bar girls ", " club girls ", etc., while in others prostitution has remained a means of existence and livelihood, raising epidemiological, social, and economic problems.

World production and consumption of penicillin rose steadily in the first 10 to 15 years after its discovery. The extent of the general " penicillinization " of the public through its use or misuse—often in self-medication—in diagnosed or undiagnosed medical conditions is incalculable, but it is believed that as a result large numbers of people infected with syphilis received curative amounts of penicillin during the long incubation period of the disease.[7] After 1955 or so, penicillin reactions became more frequent, and there was no further increase in the production and use of this antibiotic. However, the production and use of broad-spectrum antibiotics—usually ineffective against *T. pallidum*—more than doubled between 1955 and 1960, and this tendency has continued. Furthermore, the preventive effect on syphilis of penicillin treatment for gonorrhea has become less widespread because of the latter's increasingly frequent treatment with other antibiotics. At the same time the number of people in the younger age groups—the section of the population particularly at risk—has increased. For these and other reasons, fewer and fewer adults are believed to have been exposed to chance prophylaxis after the mid-decade.

Systematic epidemiological investigations —contact tracing, case finding, and the provision of free diagnostic and treatment services—remain basic elements of venereal disease control, but in most countries the possibilities for such investigations have been limited. This is borne out by a world-wide WHO study of the legislative framework within which venereal disease control measures are undertaken in different countries.[8] The lack of uniformity in this field and the need for revision of the legislation in regard to national and international epidemiological requirements were particularly emphasized at a recent WHO Symposium on Venereal Disease Control in Europe, at which the desirability of much greater epidemiological co-operation between the physician and the health authority was underlined. That the situation is similar in the Western Pacific Region is indicated by the conclusions of the first WHO venereal disease control seminar for that region.

WHO assistance

In 1948, when WHO came into being, it was obvious that the best way to tackle the vast problem of syphilis on the international level was to promote the wide use of effective and inexpensive repository penicillin therapy of short duration.

Demonstration projects were undertaken by health administrations with WHO assistance

[7] *Brit. J. vener. Dis.*, 1963, 39, 87.

[8] *Int. Dig. Hlth Legis.*, 1956, 7, 198.

in 35 countries, mostly in developing areas. Emphasis was placed on case finding, epidemiological and laboratory techniques, and health education, as well as on shortened treatment. Training at all levels was an inherent part of these projects, several of which were integrated in or closely associated with the maternal and child health programme, as recommended by WHO expert committees in that field.[9] In certain areas satellite centres, dispensaries, and laboratories were set up as the programme developed. The feasibility of applying control measures was shown in various local demonstration and training areas in developing countries. Only in a few instances, however, was it possible to develop the projects into sustained selective operations that could eventually be integrated in the national public health services. It was emphasized by expert committees and other groups that, to control venereal infections, permanent programmes should be organized and not just emergency campaigns. Experience had shown that there was a likelihood—as in tuberculosis and other infectious diseases—that the infectious reservoir might build up again quickly after a single intensive case-finding and treatment campaign, as a result of the frequent introduction of new infections from other areas and countries, congenital disease, and relapses in inadequately treated persons infected many years before.

Mass campaign techniques were attempted on a limited scale in high-prevalence areas in a few countries. At the same time, following the recommendations of the WHO/UNICEF Joint Committee on Health Policy, UNICEF made long-acting penicillin widely available, particularly in developing countries. A WHO programme for the rehabilitation of antibiotic plants originally set up by the United Nations Relief and Rehabilitation Agency (UNRRA) helped increase national production in certain countries.

Because of the declining incidence of venereal infections and over-confidence in antibiotics, expenditure on control services was reduced in some countries—in a number of instances abruptly—and in others the integration of case-finding into general health examinations, maternal and child health activities, etc., appears to have been undertaken only slowly or inadequately. Again, in yet other countries, the very fact that penicillin was available on the spot and demonstrably effective tended to create a false sense of security and a consequent waning of interest in a problem considered as already solved. There was a parallel decline in the interest of health administrations in international assistance. While 22 WHO-assisted venereal disease control demonstration projects were in operation during the two years 1951-52, there were 11 such projects in 1958-59, and only six have been provided for in the WHO budget for 1964-65. The sharp decline in estimated international expenditure on venereal disease projects for these years is shown by region and source of funds in Table 2.

Training sponsored by WHO is referred to elsewhere in this programme review, in other contexts. Between 1948 and 1963, 252 individual fellowships were provided by WHO for the study abroad of venereal infections as well as endemic treponematoses, and 82 short-term fellowships were awarded for group training or participation in regional or international technical meetings on venereal disease control organized by WHO. The greater number of the individual fellowships were awarded in the early penicillin period before 1955. These were requested by health administrations mostly for clinical and laboratory studies, while relatively few requested fellowships for studies of the epidemiological and public health aspects. Between 1948 and 1963, WHO reference centres—particularly those at the Communicable Disease Center, Atlanta, Ga., and the Statens Seruminstitut, Copenhagen—trained a large number of serologists and technicians, both within and outside the WHO fellowship programme. Local WHO-assisted country demonstration projects also provided training in all aspects of venereal disease control.

Technical information on all aspects of such control has been provided for health administrations by Expert Advisory Panel

[9] *Wld Hlth Org. techn. Rep. Ser.*, 1957, 115, 5.

TABLE 2. ESTIMATED EXPENDITURES ON VENEREAL DISEASE PROJECTS BY WHO REGION AND BY SOURCE OF FUNDS DURING THE TWO-YEAR PERIODS 1951-52, 1958-59, AND 1964-65

	Reg.[a] US$	TA[b] US$	OEBF[c] US$	Total US$	Reg.[a] US$	TA[b] US$	OEBF[c] US$	Total US$
	Africa				Americas			
1951	—	—	—	—	15 538	—	224 000	239 538
1952	—	—	—	—	62 933	47 326	175 600	285 859
Total	—	—	—	—	78 471	47 326	399 600	525 397
1958	—	—	—	—	—	7 467	14 600	22 067
1959	—	—	—	—	—	9 700	13 670	23 370
Total	—	—	—	—	—	17 167	28 270	45 437
1964	—	—	—	—	—	—	—	—
1965	—	—	—	—	—	—	13 200	13 200
Total	—	—	—	—	—	—	13 200	13 200
	South-East Asia				Europe			
1951	48 558	41 264	152 768	242 590	11 252	—	86 000	97 252
1952	33 479	35 535	44 112	113 126	36 483	—	—	36 483
Total	82 037	76 799	196 880	355 716	47 736	—	86 000	133 735
1958	1 875	2 775	2 000	6 650	—	8 557	70 000	78 557
1959	—	2 400	2 000	4 400	—	13 554	40 000	53 554
Total	1 875	5 175	4 000	11 050	—	22 111	110 000	132 111
1964	—	—	—	—	—	—	—	—
1965	—	—	—	—	—	—	—	—
Total	—	—	—	—	—	—	—	—
	Eastern Mediterranean				Western Pacific			
1951	26 154	47 317	75 000	148 471	5 600	60 634	—	66 234
1952	66 023	135 087	475 000	676 110	—	—	—	—
Total	92 177	182 404	550 000	824 581	5 600	60 634	—	66 234
1958	24 172	71 702	43 000	138 874	17 183	—	22 000	39 183
1959	23 956	70 042	40 000	133 998	18 340	—	25 000	43 340
Total	48 128	114 744	83 000	272 872	35 523	—	47 000	82 523
1964	—	8 334	—	8 334	2 000	—	18 800	20 800
1965	—	11 600	—	11 600	31 864	—	—	31 864
Total	—	19 934	—	19 934	33 864	—	18 800	52 664

[a] Regular budget. [b] Technical Assistance funds. [c] Other extra-budgetary funds, including Voluntary Fund for Health Promotion.

members, co-operating institutions, WHO-assisted country projects, etc. As already mentioned, symposia have been organized in the WHO regions to foster the exchange of technical information and experience. WHO has also organized meetings of study groups and of certain sections of international conferences, etc. In many respects, one of WHO's functions in this field has been that of a " clearing house " centralizing and distributing recent technical documentation. Also of importance has been its dissemination of information by means of guides and manuals taking into account experience acquired in different countries and aimed at obtaining more uniform methods and techniques. The reports of the relevant WHO expert committees and sub-committees periodically advise the Director-General on technical policies.

A list of the major WHO-assisted venereal disease projects between 1949 and 1963 is given in Annex 2.

WHO research programme

The WHO research programme on venereal syphilis and that on endemic treponematoses overlap to some extent. In the early WHO efforts to promote the control of treponematoses through public health programmes in developing countries, it was generally found that both basic and applied research were necessary if knowledge originating in developed countries was to be used in new situations. The standardization of methods, reagents, and techniques was required in the laboratory, and epidemiological operational research became important. At that time only a very few research institutions were still active in this field, and one of WHO's early functions was to maintain interest in such research. In retrospect, the WHO Advisory Committee on Medical Research considered WHO's work in this connexion to have been of special importance at that particular moment. WHO research activities took different forms. Some of these activities arose out of WHO-assisted projects in different countries. In a few instances WHO assistance has aimed at establishing permanent research centres, but most studies and investigations encouraged as part of the Organization's intensified research programme after 1958 have been promoted in existing institutions and laboratories. Technical problems have been suggested for investigation within the co-ordinated framework outlined by expert committees and special study groups, and grants have been made to some of the institutions concerned. This research and related operational and other studies have provided the basis for more than a hundred scientific papers, ten monographs or special publications, and some hundred technical documents. The main aspects of the programme are outlined below.

Epidemiology and public health action, including therapy

WHO was associated with the early clinical trials as well as with long-term evaluation studies of repository procaine penicillin in oil with aluminium monostearate (PAM), which was to become the outstanding preparation for the treatment of syphilis until the development of an equally valuable preparation, benzathine penicillin. These evaluation studies provided the basis for the drawing up, by WHO expert committees, of treatment schedules suitable for both individual and mass case and contact treatment in public health programmes, including procedures applicable in maternal and child health activities. While metal therapy was being replaced by penicillin treatment, this changing field was kept under review by WHO, following the evaluation—carried out in 1949 by the WHO Syphilis Study Commission in the USA [10]—of the epidemiological and public health importance of penicillin in venereal disease control. Optimal management procedures were appraised by a group meeting of members of the WHO Expert Advisory Panel on Venereal Infections and Treponematoses in London in 1952,[11] a survey of treatment practices in different countries of the world was carried out in 1954,[12] and a travel-

[10] *Wld Hlth Org. techn. Rep. Ser.*, 1950, 15.
[11] *Wld Hlth Org. techn. Rep. Ser.*, 1953, 63.
[12] *Bull. Wld Hlth Org.*, 1954, 10, 579.

ling seminar studied methods of venereal disease control in the USSR in 1961.[13]

The early PAM trials were undertaken in several countries, first in the USA and later in the United Kingdom, Finland, Norway, Egypt, and India, while the subsequent benzathine penicillin studies were carried out in France, the USA, the United Kingdom, and the USSR. It is now possible to treat patients with early syphilis adequately within a few days, using single- or few-injection techniques that result in a treponemicidal blood-level duration of several weeks. The drug cost per patient is very low. Some reported " failures " are due to reinfection rather than to relapse, and the few true failures encountered appear to be the result of enzymic, metabolic, or renal abnormalities in the patient. The results of treatment in congenital syphilis and also in late stages of syphilis in adults are likewise satisfactory. Studies on the side effects of penicillin have also been promoted by WHO.[14] The incidence of allergic manifestations increased from 5.9 to 9.7 per 1000 cases treated between 1954 and 1959,[15] with fatalities from anaphylactic shock occurring at a rate approximating one per million injections. The side effect rates appear to have increased only slowly since 1959. Members of the WHO Expert Advisory Panel on Venereal Infections and Treponematoses are engaged in clinical trials and long-term evaluations of the effectiveness in syphilis of alternative antibiotics, for use in penicillin-sensitive individuals, in particular propionyl erythromicin, which has given satisfactory early results.

Operational research in pilot projects[16] has shown that, in areas with a high prevalence of infectious syphilis, mass treatment is effective and economical when adequate treatment can be given to cases and contacts at the same time. This view was upheld in the technical discussions at the Sixth World Health Assembly,[17] and the value of such treatment in endemic situations has been stressed by various expert committees.[18] As well as effecting an immediate reduction in the active reservoir of infection, the use of large-scale " contact " treatment—or preventive treatment on epidemiological indication—in high-prevalence syphilis areas has advantages similar to those gained in tuberculosis by indiscriminate BCG vaccination without prior tuberculin testing, from the standpoints of cost, training, integration, and coverage. WHO has also been associated with studies of the usefulness of the " cluster " technique (case-finding within the same social stratum) in ports, with or without voluntary long-term preventive treatment in female groups presenting risks of infection for others or at risk of being infected. These studies have shown that this technique can contribute substantially to a reduction in the incidence of early syphilis.[19] In developing areas, it has been shown that the organization of mass prenatal (or premarital) screening, as well as mass case-finding in certain occupational groups, can be economical and useful when diagnostic and treatment services are limited and more extensive epidemiological work impractical.

There is a dearth of information on epidemiological and serological problems in developing tropical countries, and only recently has it become possible for the WHO research programme to promote studies based on specific *T. pallidum* immobilization (TPI) and fluorescent treponemal antibody (FTA) testing. These techniques are necessary in view of the limitations of conventional lipoidal antigen testing in tropical countries, as demonstrated in the first of a series of WHO investigations (see previous chapter). Survey techniques applicable in longitudinal studies are in the early stages of development, and for the time being are used more in the evaluation of previous rural mass yaws campaigns than in the control of syphilis.

Diagnostic procedures and standardization

WHO-coordinated inter-laboratory assays of the reproducibility, sensitivity, and specificity of serodiagnostic lipoidal antigen tests have taken the place of the International

[13] *WHO Chronicle*, 1964, 18, 48.
[14] *Bull. Wld Hlth Org.*, 1958, 18, 323; 1959, 19, 427.
[15] *Wld Hlth Org. techn. Rep. Ser.*, 1960, 190, 43.
[16] *Bull. Wld Hlth Org.*, 1952, 5, 377.
[17] *Chron. Wld Hlth Org.*, 1953, 7, 206.
[18] *Wld Hlth Org. techn. Rep. Ser.*, 1953, 63, 17; 1960, 190, 33.
[19] *Bull. Wld Hlth Org.*, 1958, 19, 419.

Serological Conferences held by the Health Organisation of the League of Nations before the Second World War. Twenty-nine laboratories in 16 countries collaborated in studies which led to the establishment of international reference preparations for cardiolipin and lecithin, as well as human syphilitic control sera, in 1951, 1954,[20] 1958,[21] and 1959.[22] In further laboratory investigations lasting four years, 134000 serum samples were tested against various antigens of non-pathogenic treponemes, and in 1958-59 some 6000 samples were tested against various protein antigens from pathogenic treponemes; it was concluded that there were insufficient grounds for proceeding to the international standardization of relevant reagents and methods.

Following the discovery of the immobilisines at the WHO International Treponematosis Laboratory Center, Baltimore, Md., some years ago, WHO organized co-operative studies of the TPI test at leading laboratories in eight countries. The research which followed included clinical correlation of results, exchange of sera, and testing of freeze-dried specimens prepared by WHO reference laboratories, and made it possible for this complex but invaluable tool to be introduced, in a uniform way, into laboratories in other countries. By 1960, 41 participating laboratories were undertaking TPI testing in 23 countries in Africa, the Americas, South-East Asia, and Europe. The qualitative reproducibility of the TPI test has remained variable in all inter-laboratory assays. WHO-assisted research into the quantitative aspects is, however, going forward in respect of both normal techniques (Sweden) and simplified methods (Poland, Spain, and the USSR) which may yet bring this specific treponemal reference test within the reach of a greater number of laboratories. Research in this field continues to be directed mainly towards the establishment of standard reagents and control sera and the simplification of techniques.

Between 1960 and 1962, WHO organized an assay of the FTA test by leading laboratories in six different countries (Denmark, France, Italy, Japan, the United Kingdom, and the USA), and it was shown that the confidence limits of this new technique were about 95% in terms of reactive/non-reactive sera. A second quantitative inter-laboratory study is being undertaken in Denmark, France, India, Japan, the United Kingdom, and the USA with the ultimate aim of standardizing reagents and control sera, if possible. The differences in antibody reactivity to the FTA and TPI tests justify the use of the FTA technique in developing areas, since WHO studies have shown that a large proportion of lipoidal antigen reactions in the rural populations of developing countries are false seroreactions unconnected with the treponematoses. Another WHO-sponsored research project, which was started in 1963 and is scheduled to finish in 1965, aims at simplifying FTA procedures so that finger-prick blood dried on special absorbent paper " rondelles " can be sent by ordinary mail or similar means to a base laboratory in the same or another country for specific immunofluorescent testing. This procedure may become useful for prenatal specific serological testing in maternal and child health programmes, since improved and simplified techniques are needed in this field, particularly in developing areas.

The work leading to the establishment of an international reference preparation for PAM in 1963 was described in the previous chapter.

Microbiology, biochemistry, and immunopathology

Few qualified laboratories have been prepared to undertake basic research work in this complex field, in which progress must be expected to be slow. To co-ordinate and maintain interest in this work, WHO has tried out several approaches, the more important of which are mentioned below.

It has, for example, stimulated basic microbiological and biochemical research aimed at the identification of antigenic protein and sugar fractions of non-pathogenic and pathogenic treponemes which might lead to serological or dermatological tests capable of

[20] *Wld Hlth Org. techn. Rep. Ser.*, 1954, 86, 11.
[21] *Wld Hlth Org. techn. Rep. Ser.*, 1958, 147, 14, 16.
[22] *Wld Hlth Org. techn. Rep. Ser.*, 1959, 172, 14, 15.

differentiating between syphilis and yaws. Some progress has been made in this regard. Preliminary investigations have shown antigenic differences between strains of *T. pallidum*, *T. pertenue*, and *T. cuniculi*, and certain biochemically defined fractions may react with syphilitic serum alone. There is evidence suggesting that by absorption procedures it may be possible to develop a differential diagnostic test between syphilis and yaws, using the immunofluorescent antibody technique in place of the present more cumbersome technique based on the lesion-producing capacity of *T. pertenue* and the "silent" infection capacity of *T. pallidum* in the golden hamster. On the other hand, immunological and immunochemical studies now in progress aim at the identification of protective antibody fractions, and preliminary studies suggest that this may be possible in late latent and late syphilitic infections of man.

Up to the present, however, little advantage has been taken of opportunities for certain much-needed fundamental studies, for example, on auto-sensitization, distortion of immune responses in the natural course of treponematoses, and aberrant immunopathological manifestations in the early stages of infection, although in one project an important contribution has been made to knowledge of experimental immunological immaturity and lesion manifestations in the newborn. The WHO research programme has also given prominence to investigations to elucidate the requirements of pathogenic treponemes in enzymic, gaseous, and other metabolic factors believed to be of importance for their growth and possible cultivation *in vitro*, the eventual development of an immunoprophylactic agent being kept in mind as a desirable objective. As a result of WHO-assisted studies in this field, the fundamental role of lysozyme and other enzymes in the metabolism of *T. pallidum* is becoming known, and some of the conditioning factors for survival *in vitro* are beginning to be better understood. Most recently, a commensal growth factor which enhances the life processes fo *T. pallidum* was isolated.

Finally, tissue culture studies of pathogenic treponemes have been pursued systematically by the various laboratories co-operating in the WHO programme. Cultivation has not been achieved in embryonic tissues of chicks, hamsters, or man, nor in HeLa or other cell lines.

The Brussels Agreement

The Brussels Agreement of 1924 relating to venereal infections in seafarers was the first health instrument providing organized treatment facilities and medical care on an international basis. WHO assumed constitutional responsibility for the administration of this agreement under the protocol concerning the Office International d'Hygiène Publique, adopted by the International Health Conference in New York in 1946. The tremendous expansion since that time of the world's merchant tonnage and the dependence of most nations, directly or indirectly, on international shipping have increased the social and economic importance of the health of seafarers both on board ship and ashore. Between 1948 and 1955 WHO consulted governments, the International Labour Office, and the International Union against the Venereal Diseases and the Treponematoses (IUVDT) regarding the revision of this agreement, in view of the technical progress made since its inception. Following studies by several WHO expert committees, the Joint WHO/ILO Committee on the Hygiene of Seafarers, the First World Health Assembly, and the WHO Executive Board at its fifth and twenty-fifth sessions, the Thirteenth World Health Assembly [23] approved a set of technical definitions and minimal standards as a revised basis for the functioning of the Agreement.

In order to obtain practical information on the impact on seafarers of recent advances in the management of venereal diseases, to utilize this information in the revision of the Brussels Agreement, and to disseminate data on experience gained, an international maritime demonstration and training centre was established by the Netherlands Government and WHO, in agreement with ILO, at the

[23] *Off. Rec. Wld Hlth Org.*, 1960, 102, 23 (Resolution WHA. 13.52).

large international port of Rotterdam (1951-54). Two international training courses on maritime aspects of venereal disease control were organized, with participation from countries in all WHO regions. Substantial technical documentation resulted from this activity.[24] On the recommendation of the IUVDT, an International Rhine River Anti-Venereal Disease Commission was established in 1951, and WHO was entrusted by the governments in the Rhine area with the co-ordination of control measures. By the end of 1953, the incidence of venereal infections among Rhine boatmen had greatly declined, and this activity was terminated by the WHO Regional Committee for Europe. In 1951, 1959, and 1961, WHO published revised issues of the *World Directory of Venereal Disease Treatment Centres at Ports*, as part of its obligations under the Brussels Agreement. Several maritime nations have made it compulsory for this directory to be available to crews on board ship. Various articles and bibliographies on maritime venereal disease control have been published by WHO.[25] Since 1948, as administrator of the Brussels Agreement, WHO has been kept informed by governments, shipowners, and seafarers' organizations about shortages of proper facilities and cases of non-observance of the Agreement in different ports. In some cases WHO has provided consultant and other services for the improvement of venereal disease control in ports, particularly in South-East Asia.

Co-operation with other international bodies

The case-finding and treatment campaign against syphilis which started in Poland in 1948 was the first WHO-recommended project to receive important material assistance from UNICEF. The emphasis laid on maternal and child health by the Joint WHO/UNICEF Committee on Health Policy did not substantially prevent support for comprehensive assistance in some national venereal disease control programmes (for example, in Taiwan). Other aspects of UNICEF's important co-operation were mentioned in the previous article.

The IUVDT has stimulated and supported WHO activities in many ways, e.g., by disseminating information on international venereal disease control work and WHO programmes, and encouraging national voluntary associations to support the efforts of health administrations. The Union has promoted national studies on the behaviour and health education aspects of venereal disease control, with particular reference to the younger age groups and to sociological problems.

The International League of Dermatological Societies (ILDS) was assisted by WHO in the organization of certain sections of the Eleventh and Twelfth International Congresses of Dermatology.

The future

The public health methods available for the control of venereal syphilis are as effective today as they were before the recrudescence of the disease became apparent in many countries a few years ago. Penicillin resistance in *T. pallidum* has not been demonstrated, serious allergic reactions to the antibiotic are relatively few, and effective antibiotics other than penicillin are in reserve. There is, however, an urgent need for more determined application in public health programmes of the knowledge already available, particularly as regards local, national, and international epidemiological surveillance and intensified case and contact finding, so that a greater number of infected persons may more rapidly be brought under adequate treatment. Whether determined public health efforts (including health education) to combat syphilis in developed and developing countries will be capable of counteracting, in rapidly changing environments, the important social, economic, migratory and other factors that now increasingly favour its spread should become discernible within the next few years. Countries showing as yet no apparent upward trend in venereal syphilis may expect

[24] WHO Regional Office for Europe (1956) *Maritime venereal disease control*, Geneva.

[25] See, for example: *Wld Hlth Org. techn. Rep. Ser.*, 1958, 150, 55.

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[20] *Wld Hlth Org. techn. Rep. Ser.*, 1954, 86, 11.
[21] *Wld Hlth Org. techn. Rep. Ser.*, 1958, 147, 14, 16.
[22] *Wld Hlth Org. techn. Rep. Ser.*, 1959, 172, 14, 15.

a recrudescence unless measures are taken in time. Since experience has shown that the wide use of an " ideal " drug cannot treat an infectious disease out of existence, the need for intensified basic and applied research in the future is all the greater. More uniform, specific, and simple methods are required in the laboratory and the field, and particular importance should be attached to biochemical and immunopathological investigations, which may yet lead to the *in vitro* growth of pathogenic treponemes and possibly to the development of an immunoprophylactic agent.

Gonococcal infections

The "minor" venereal diseases—chancroid, lymphogranuloma venereum (Nicolas-Favre disease), granuloma inguinale (Donovanosis),[1] and non-gonococcal genito-urinary infections (non-specific urethritis, trichomoniasis, etc.)—have in general been considered by WHO not to warrant international attention apart from periodic studies and meetings. Gonococcal infections, however, have been a subject of concern in recent years. In 1959, a WHO Expert Committee on Venereal Infections and Treponematoses [2] stressed the special problems connected with these infections, in particular failure to control their spread and "resistance" to treatment. A WHO Expert Committee on Gonococcal Infections [3] was convened in 1962 to review problems of control and current research in this field.

Trends in gonorrhoea

In a number of countries the introduction of easily administered parenteral or peroral drugs with prompt therapeutic effect gave rise to the belief that gonorrhoea was a "mild" disease, cured without difficulty and free from complications. While the incidence of prostatitis and epididymitis declined in many areas from about 30% to 3%, following the replacement of local traumatic therapy by antibiotic therapy, these and other complications continue to occur when treatment is delayed. In the female, Bartholinitis, salpingitis, and sterility have remained frequent: a pilot study, in which venereologists, gynaecologists, surgeons, and medical officers of health took part, showed salpingitis in at least 9% of those infected, resulting in sterility in 2%-3% of cases.[4] In addition, the clinical recurrence of gonorrhoea has apparently risen in both males and females, increasing from 3%-5% in the early antibiotic era to 12%-15% in recent years. The epidemiological, public health, and social implications of these observations should be considered against the background of the increasing frequency of gonococcal infections in young females, and the outbreaks of gonococcal vulvo-vaginitis reported in children living in institutions.[5] There is a dearth of information on the etiology and incidence of ophthalmia neonatorum. However, the abandonment of silver nitrate instillation in the eyes of the newborn (Credé's method) will undoubtedly lead to a number of cases of gonococcal ophthalmia.[6] Other complications—for example, gonococcal meningitis in children—occur in some areas.

In many countries neither gonorrhoea nor syphilis is notifiable. In others it has been shown that the actual incidence of gonorrhoea is several times higher than that indicated by the morbidity statistics. A WHO study of long-term trends covering the period 1950-60 [7] showed that in some countries there was a more or less lasting fall in the reported incidence by the mid-decade; in others the incidence remained stationary; in yet others an upward trend was evident after about 1955. Out of 111 countries and areas surveyed, 53 (47.7%) showed a persistent increase in the reported incidence after 1957 (see table). Rates in Europe ranged from 100 to 500 per 100 000 adult population (persons over 15 years of age). In several countries in the South-East Asia, Eastern Mediterranean, and Western Pacific Regions, they exceeded 1000 per 100 000 adults. Considerably higher rates were recorded in some countries of Africa and the Americas. The WHO Expert Committee on Gonococcal

[1] See: Rajam, R. V. & Rangiah, P. N. (1954) *Donovanosis*, Geneva (*World Health Organization : Monograph Series*, No. 24).

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1960, 190, 23.

[3] *Wld Hlth Org. techn. Rep. Ser.*, 1963, 262.

[4] *Bull. Wld Hlth Org.*, 1961, 24, 367.

[5] *Brit. J. vener. Dis.*, 1961, 37, 142.

[6] *J. Amer. med. Ass.*, 1961, 177, 935.

[7] Twelfth International Congress of Dermatology (1963) *Proceedings of the ..., Washington, D.C., September 1962.* In: *Excerpta med. (Amst.), Int. Congr. Ser.*, No. 55, vol. 2, p. 833.

GONORRHOEA TRENDS, BY REGION, AS SHOWN IN WHO SURVEY (1950-60)

Region	Total number of countries and areas	Number with increased incidence 1957-60	Percentage with increased incidence
Africa	30	10	33.0
Americas	21	11	52.0
Eastern Mediterranean	10	2	20.0
Europe	20	17	80.0
South-East Asia and Western Pacific	30	13	43.3
	111	53	47.7

Infections [8] noted the large reservoir of infection in Africa, in some areas of which the disease appears to be endemic. Many more cases are diagnosed in males than in females: the ratio varies from 2:1 to 4:1 or more, being influenced by the extent of the facilities available, diagnostic standards, reporting methods, criteria, etc., but suggesting a large latent reservoir of infection in females.

The Committee summarized the situation in 1962 as follows: [9]

There was no evidence that the advent and wide use of "ideal" antibiotics over the last 20 years, particularly penicillin and streptomycin, had made any indent on the reservoir of gonococcal infections. The infectiousness of gonorrhoea, its short incubation, the mode of transmission and other factors had not made it possible to evolve epidemiological methods effective against the very rapid spread of the infection. It had nowhere been possible to bring a sufficiently large number of cases and contacts to treatment quickly enough to overtake the rapid spread of the infection in the community. Air travel, furthermore, allowed extremely rapid transfer of infection between countries and continents. There existed also special itinerant groups at particular risk of infection (migrants, seafarers, etc.). Case-finding and contact treatment, rapid epidemiological procedures and cluster-testing techniques, prophylactic treatment, individual and mass treatment of special groups or obligatory hospital isolation of infected persons, legal notification of contacts, etc. had been of limited value: the methods available had been incapable of reversing the epidemiological balance so adverse to the human host in all regions. The failure to interrupt transmission and to control gonococcal infection was world-wide and should be recognized by health administrations, the medical profession, and the public.

[8] *Wld Hlth Org. techn. Rep. Ser.*, 1963, 262, 5.
[9] *Wld Hlth Org. techn. Rep. Ser.*, 1963, 262, 60.

Research

WHO has recently taken steps to implement certain parts of the research programme recommended by the Expert Committee:

1. Even if all contacts of male urethritis were brought for examination, diagnosis, and treatment within the short incubation period of the disease, gonorrhoea could not be controlled by individual measures because of the persistence of the asymptomatic female reservoir and the difficulty of identifying a large proportion of female "carriers" with present laboratory methods. So far immunofluorescent techniques have not been successful in this respect. A serological test for early diagnosis is required, and research to this end has been undertaken in the USA. Immunological research and investigations into serum diagnosis used to employ avirulent gonococci, since strains grown on the usual media undergo antigenic and metabolic changes, and rapidly lose virulence after a few cultures passages *in vitro*. Only recently has the passage in hens' eggs of stable, virulent, reproducible strains of gonococci been possible, and this should open up the way for the investigation of new antigens to be used in serum diagnosis and perhaps for the development of precipitation tests. WHO is following this work closely so that it may promote inter-laboratory assays, should a breakthrough occur.

2. The WHO Scientific Group on General and Applied Immunological Research and the WHO Expert Committee on Gonococcal Infections considered it unlikely that gonorrhoea control could be achieved except by mass treatment or some type of immunoprophylaxis, if such existed. These groups considered that further research on the immunological aspects of gonococcal infec-

tions was justified and should be pursued. They were in favour of an approach based on the microbiological and serological relationships within the *Neisseriae* group. Biochemical and antigenic studies of *N. intracellularis* have led to the development of trial vaccines against cerebrospinal meningitis; *N. gonorrhoeae* has capsular and somatic antigens similar to those of *N. intracellularis*, and serologically they show cross-reactivity. A joint scientific meeting of microbiologists and immunologists, held in September 1964, considered these aspects of the problem and the lines along which future research on the immunology of gonorrhoea should be conducted.

3. In 1958-59 an increase in clinical failure rates in the treatment of gonorrhoea with penicillin, and subsequently with streptomycin, began to be observed. Gonococcal strains with reduced sensitivity to these antibiotics were later isolated. Not only microbial selection was involved, however—the wide use of repository long-acting penicillin preparations also played a part. These could maintain low concentrations of penicillin in the blood and tissues for several weeks and were effective as long as the circulating strains of gonococci were highly sensitive, but tended, when less sensitive gonococci came into circulation, to increase the rate at which strains developed resistance to penicillin.

In preliminary studies sponsored by WHO after 1962, many hundreds of strains of gonococci were isolated from different countries in Africa, the Americas, South-East Asia, Europe, and the Western Pacific. From these studies it emerged that resistance to one or more current drugs, particularly penicillin and streptomycin, is not a general but a localized phenomenon. A " watch-dog " sampling of circulating gonococcal strains would be useful to health administrators, doctors, and laboratories. It is planned to intensify the sampling of local gonococcal strains in different countries and analyse their degree of resistance, in order to facilitate the selection of the most advantageous antibiotic treatment and dosages suitable for different areas.

4. Preliminary research has shown the diversity of the culture techniques, media, and methods used at present for the determination of changing sensitivity to certain antibiotics. So that the same strains will not be considered " resistant " in one country and " susceptible " in another, according to the procedure used for isolation and examination, uniform media and sensitivity determination techniques should be devised. Preliminary assays of the reproducibility of improved media and methods were organized by WHO from 1961 to 1963 in laboratories in Denmark, the United Kingdom, and the USA.[10] Additional studies now in preparation will be extended to reference centres in France and the USSR; their aim is the further development of a provisional reference method devised in 1962 and based on established international reference strains of gonococci.

Other activities

WHO collects and disseminates technical information on the control of gonococcal infections, and has drawn attention to various aspects of their epidemiology and control in the *Epidemiological and Vital Statistics Report*,[11] a complete issue of the *Bulletin of the World Health Organization*,[12] and some fifty articles and technical documents. Minimal treatment schedules were outlined by an Expert Committee in 1959 [13] and again in 1962 [14] when the changing sensitivity of *N. gonorrhoeae* began to be observed. Minimum requirements for the management of gonococcal infections in seafarers and for relevant equipment on board ships and in ports were included in the revision of the Brussels Agreement by the Thirteenth World Health Assembly in 1960.[15]

The standardization of long-acting penicillin (PAM) as part of the WHO programme against the treponematoses has proved of

[10] *Wld Hlth Org. techn. Rep. Ser.*, 1963, 262, 56.
[11] *Epidem. vital. Statist. Rep.*, 1959, 12, 309.
[12] *Bull. Wld Hlth Org.*, 1961, 24, 293-397.
[13] *Wld Hlth Org. techn. Rep. Ser.*, 1960, 190, 26.
[14] *Wld Hlth Org. techn. Rep. Ser.*, 1963, 262, 30.
[15] World Health Organization (1961) *World directory of venereal disease treatment centres at ports*, 2nd ed., Geneva.

value in gonorrhoea control also, by making it possible to use this antibiotic on a mass scale in early pilot projects in areas of endemic gonorrhoea (for example, in Sudan). A marked decrease in the incidence of gonorrhoea has been observed in certain areas following mass penicillin campaigns against yaws (for example, in Sierra Leone).

Since a high proportion of clinically asymptomatic infections occur in females, the preventive treatment of promiscuous groups helps limit the spread of infection. This approach has been considered in some quarters to be discriminatory and as such contrary to Article 6 [16] of the United Nations Convention of 1950 regarding the Suppression of the Traffic in Persons and the Exploitation of the Prostitution of Others. Opponents of this view consider that, if it were upheld, communicable disease control and the application of public health principles would be prejudiced.

[16] " Each Party to the present Convention agrees to take all the necessary measures to repeal or abolish any existing law, regulation or administrative provision by virtue of which persons who engage in or are suspected of engaging in prostitution are subject either to special registration or to the possession of a special document or to any exceptional requirements for supervision or notification." (United Nations Department of Economic and Social Affairs (1959) *Study on traffic in persons and prostitution*, New York, p. 50).

The future

Better results could be obtained by a more systematic and intensive application of the available public health measures against gonococcal infections, but effective control is unlikely unless further basic and applied research is fostered and co-ordinated. WHO is therefore encouraging biochemical and immunological research on *Neisseriae* as a group, the development of methods for diagnosing asymptomatic infections in females, the improvement of culture media and the standardization of methods for determining the sensitivity of *N. gonorrhoeae* to antibiotics, intensified sampling of the gonococcal strains circulating in different countries so that the changing picture of susceptibility to treatment may be mapped out, and the establishment of epidemiological indications for the large-scale use of chemoprophylaxis and chemotherapy in endemic areas and groups at special risk.

ANNEXES

Annex 1

MAJOR WHO-ASSISTED ENDEMIC TREPONEMATOSES PROJECTS, 1949-1963

Country or territory	*Project and type of assistance*	*Survey method* [1]	*Population at risk, work carried out, results*
AFRICA			
Bechuanaland (Bakwena Reserve)	Endemic syphilis (1953-57): WHO staff; UNICEF supplies; WHO consultant; training; laboratory facilities.	SMT	Population at risk: 40 000, of whom 90% covered by mass surveys and 22 000 treated at initial treatment survey and resurveys. Surveillance completely integrated into health services after 1957.
British Cameroons (whole territory) [2]	Yaws (1954-61): WHO staff, periodic visits from WHO consultants; UNICEF supplies; assistance for participation in international meetings.	SMT	Population at risk: 750 000. Mass campaign by special teams consisting of initial treatment survey and a few resurveys. Important reduction achieved, though not yet sufficient for transfer of surveillance activities to rural health services.
Central African Republic (whole country)	Yaws (1953-63): periodic visits from WHO consultants; UNICEF supplies.	TMT JMT	Population at risk: 1 016 000, partly covered by initial treatment survey carried out by special teams. The project is continuing. In some areas surveillance is integrated into the rural health service.
Chad (whole country)	Yaws (1957-63): WHO consultant; UNICEF supplies.	SMT	Population at risk: 2 500 000. Area of low endemicity. The project is continuing and surveillance is partly integrated into the rural health service.
Congo (Brazzaville) (whole country)	Yaws (1961-63): periodic visits from WHO consultants; UNICEF supplies.	SMT	Population at risk: 800 000. Initial treatment survey and several resurveys by mobile teams of health service. Surveillance, partly integrated into health centre activities, is continuing.
Dahomey (whole country)	Yaws (1958-61): WHO consultant; UNICEF supplies.	SMT	Population at risk: 1 700 000. Initial treatment survey with 85% coverage and resurveys by mobile teams. Control measures are continuing through surveys by teams.
Gabon (whole country)	Yaws (1959-63): WHO consultant; UNICEF supplies.	TMT JMT SMT	Population at risk: 400 000. Initial treatment survey and resurveys. Surveillance is being continued by special mobile teams.

[1] Meaning of abbreviations: SMT = selective mass treatment; TMT = total mass treatment; JMT = juvenile mass treatment.

[2] In 1961, the northern part of this territory joined the Federation of Nigeria, while the southern part amalgamated with the Cameroun Republic to form the Federal Republic of Cameroun.

Country or territory	*Project and type of assistance*	*Survey method*	*Population at risk, work carried out, results*
Ghana (whole country)	Yaws (1956-63): periodic visits from WHO consultants; UNICEF supplies; assistance for participation in international meetings.	SMT	Population at risk: 7 000 000. Initial treatment survey and three resurveys, with 85% coverage by special teams. Long-term surveillance is organized by rural health services into which it is being integrated.
Guinea (whole country)	Yaws (1957-62): periodic visits from WHO consultants; UNICEF supplies.	SMT	Population at risk: 3 000 000. Initial treatment survey and two resurveys with 94.5% coverage. Team activities continue.
Ivory Coast (whole country)	Yaws (1957-63): periodic visits from WHO consultants; UNICEF supplies.	JMT SMT	Population at risk: 3 000 000. Initial treatment survey taken up again in 1961, and followed by one resurvey. Control measures by mobile teams are continuing.
Liberia (whole country, but especially south-east)	Yaws (1953-62): WHO staff, periodic visits from WHO consultants; UNICEF supplies; training; laboratory installation; assistance for participation in international meetings.	SMT	Population at risk: 2 500 000, now reduced by control activities to about 1 000 000. In 1963 renewed operations were undertaken with WHO staff and combined with leprosy case-finding and smallpox vaccination. Surveillance is being continued by multipurpose teams.
Mali (whole country)	Yaws and endemic syphilis (1956-63): WHO consultant; UNICEF supplies.	TMT SMT	Population at risk: 3 700 000. Initial treatment survey with 60% coverage. Endemic syphilis prevalence of 4%-20% indicated in certain areas.
Nigeria (Eastern and Western Regions and southern part of Northern Region)	Yaws (1954-63): WHO staff, periodic visits from WHO consultants; UNICEF supplies; training; laboratory assistance; assistance for participation in international meetings.	TMT at initial treatment survey, SMT in resurveys	Population at risk: more than 15 000 000. Initial treatment survey with 95% coverage by multi-purpose teams, entrusted also with smallpox vaccination and leprosy case-finding. Several resurveys by expanding integrated surveillance services. Assessment of yaws situation by Inter-regional Treponematoses Advisory Team.
Senegal (southern part)	Yaws and endemic syphilis (1957-63): WHO consultant: UNICEF supplies; assistance for participation in international meetings.	TMT JMT	Population at risk in the yaws endemic area: 500 000. Initial treatment survey and resurveys by special teams. Control measures are continuing. In northern part of country, endemic syphilis prevalence of up to 5% reported among seminomads.

Country or territory	*Project and type of assistance*	*Survey method*	*Population at risk, work carried out, results*
Sierra Leone (whole country)	Yaws (1956-63): WHO staff, periodic visits from WHO consultants ; UNICEF supplies; training; laboratory installation; assistance for participation in international meetings.	JMT at initial treatment survey, SMT in resurveys	Population at risk: 2 830 000. Initial treatment survey with 63% coverage, and three resurveys. Surveillance is being continued by special teams entrusted also with smallpox vaccination. Integration of surveillance planned.
Togo (whole country)	Yaws (1956-63): WHO staff, periodic visits from WHO consultants; UNICEF supplies; training; laboratory installation; fellowships; assistance for participation in international meetings.	JMT SMT	Population at risk; 1 500 000. After partial coverage with limited effect, the project was restarted in 1962 with a new initial treatment survey by special multi-purpose teams; 90% coverage, with smallpox vaccination, leprosy case-finding, and trypanosomiasis treatment in north. Resurveys to follow. Training for integration of surveillance into rural health service has been started.
Upper Volta (whole country)	Yaws and endemic syphilis (1952-63): periodic visits from WHO consultants; UNICEF supplies; assistance for participation in international meetings.	TMT	Population at risk: 4 000 000. Initial treatment survey with 70% coverage, and two resurveys by mobile teams. Surveillance is continuing and is partly integrated into rural health service. Incidence of endemic syphilis reported to be 4%-7% in part of the population.
AMERICAS			
Haiti (whole country)	Yaws (1950-63): WHO/PAHO staff; UNICEF supplies; training; laboratory installation; assistance for participation in international meetings.	TMT, later SMT	Population at risk: 3 500 000. Initial treatment survey using TMT with 80% coverage and many resurveys using SMT. Surveillance is being continued in conjunction with smallpox vaccination.
Caribbean area (Dominica, Grenada, Guadeloupe, the Guianas, Montserrat, St Kitts, St Lucia, St Vincent, Trinidad and Tobago)	Yaws (1956-63): WHO staff; UNICEF supplies; training.	TMT	Population at risk: 88 000. Initial treatment survey using TMT. Subsequent resurveys. Surveillance continuing.
SOUTH-EAST ASIA			
Ceylon (15 health districts)	Yaws (1955-59): periodic visits from WHO consultants; UNICEF supplies; assistance for participation in international meetings; training; laboratory installation.	TMT SMT	Population at risk: 140 000, 52% of whom have been treated by teams. All endemic areas covered, and surveillance completely integrated into health service.

Country or territory	*Project and type of assistance*	*Survey method*	*Population at risk, work carried out, results*
India (4 states)	Yaws (1952-61): WHO staff, periodic visits from WHO consultants; UNICEF supplies; assistance for participation in international meetings.	SMT TMT JMT	Population at risk: 3 000 000, of whom 1 000 000 were reached. Of these, 30% were covered by an initial treatment survey carried out by special teams in two states, where the project is continuing. Integration of surveillance in control area planned.
Indonesia (whole country)	Yaws (1950-63): WHO staff, periodic visits from WHO consultants; UNICEF supplies; training; laboratory development; assistance for participation in international meetings.	SMT, TMT in remote areas	Population at risk: 79 000 000. Surveys by strengthened rural health service; central yaws control organization with special teams for problem areas. So far population of 67 000 000 reached with 90% coverage in initial treatment survey; 134 000 000 examinations at resurveys. Population of 22 000 000 remains to be covered by the project, which is still going on.
Thailand (45 provinces out of a total of 71)	Yaws (1950-63): WHO staff; UNICEF supplies; training; laboratory installation; fellowships; assistance for participation in international meetings.	SMT JMT TMT	Population at risk: 17 000 000. Specialized teams carried out initial treatment survey with 80% coverage. Several resurveys, later combined with smallpox vaccination, then surveillance integrated into limited rural health service. Yaws situation assessed by Inter-regional Treponematoses Advisory Team. Integration completed in 1962, combined with smallpox eradication and treatment of minor ailments. Surveillance continued in four provinces. Yaws eradicated.
West Irian [3]	Yaws (1955-60): WHO consultant; UNICEF supplies; laboratory development; fellowships; assistance for participation in international meetings.	TMT at initial treatment survey, SMT in resurveys	Population at risk: 700 000. Initial treatment survey by rural health units, with 97% coverage. Surveillance using this integrated approach is continuing.
EUROPE			
Yugoslavia (Bosnia, Serbia)	Endemic syphilis (1948-63): WHO consultants; UNICEF supplies; training; laboratory installation.	TMT SMT	Population at risk: 1 000 000. Initial treatment survey using TMT with 95%-100% coverage. During four to five resurveys, SMT was applied from 1953 onwards. Whole population at risk serologically screened. Surveillance is being continued by rural health service in conjunction with other activities (favus treatment, screening for skin diseases).

[3] Formerly Netherlands New Guinea.

Country or territory	*Project and type of assistance*	*Survey method*	*Population at risk, work carried out, results*
EASTERN MEDITERRANEAN			
Iran	Endemic syphilis (bejel) (1955-58): WHO medical, laboratory, and nursing advisers; UNICEF supplies; training; fellowships; laboratory installation.	TMT SMT	Population at risk: 300 000. Treatment surveys showed a seroreactor rate of 23‰. Control measures are being continued by national staff.
Iraq	Endemic syphilis (bejel) (1950-56): WHO medical, laboratory, and nursing advisers; UNICEF supplies; training; fellowships; laboratory installation.	TMT SMT	Population at risk: 130 000. In 1951 the prevalence of infectious endemic syphilis was 5.2‰, and in 1955 it was still 4.3‰ despite mass surveys and resurveys. The seroreactor rate varies from 27.6‰ to 56‰. The project is being continued by national staff.
Syria	Endemic syphilis (bejel) (1953-56): WHO medical, laboratory, and nursing advisers; UNICEF supplies; training; laboratory installation.	SMT	Population at risk: 60 000. Preliminary survey by special team with 80% coverage, followed by one resurvey. Control measures are being continued by national staff.
WESTERN PACIFIC			
Cambodia (3 provinces)	Yaws (1959-63): WHO staff; UNICEF supplies; assistance for participation in international meetings.	SMT 1959-60, TMT 1961	Population at risk: 625 000. Initial treatment survey, and resurveys with over 80% coverage, combined with smallpox vaccination, carried out by special teams. Consolidation continued by special yaws project; hyperendemic areas in rest of country (population 400 000) to be covered in two years.
Laos (4 provinces)	Yaws (1953-59): WHO staff; UNICEF supplies; laboratory development; assistance for participation in international meetings.	SMT	Population at risk: 530 000. Coverage of 94% in initial treatment survey and resurveys carried out by teams. Mass campaign completed and evaluation planned.
Malaysia (4 states out of 11 in Malaya)	Yaws (1954-63): periodic visits from WHO consultants; UNICEF supplies; assistance for participation in international meetings; fellowships.	SMT JMT	Population at risk: 1 800 000. Initial treatment survey and resurveys with over 80% coverage, combined with leprosy and filariasis case-finding, carried out by special teams. Continuation of control by spot surveys. Initial treatment surveys in remaining seven states are planned according to returns from medical institutions.

Country or territory	*Project and type of assistance*	*Survey method*	*Population at risk, work carried out, results*
Philippines (4 islands)	Yaws (1951-63): periodic visits from WHO consultants; UNICEF supplies; assistance for participation in international meetings.	SMT	Population at risk: 4 000 000. Surveys by teams from local health service, 85% coverage. Mass surveys completed, surveillance maintained by rural health service. Assessment of yaws situation by Inter-regional Treponematoses Advisory Team.
Tonga (whole area)	Yaws (1962): WHO staff; UNICEF supplies; training; assistance for participation in international meetings.	TMT	Population at risk: 62 000. Initial treatment survey with 90% coverage. One resurvey planned for 1964, then consolidation by health service. Assessment planned by WHO Intercountry Treponematoses Team.
Western Samoa (whole country)	Yaws (1955-57): WHO staff; UNICEF supplies; periodic visits from WHO consultants; assistance for participation in international meetings.	TMT, SMT in resurveys	Population at risk: 108 000. Coverage of 96% in initial treatment survey and two resurveys carried out by special teams. Mass campaign completed and surveillance continued by rural health service.
Western Pacific territories (Cook Islands, Fiji Island group, Gilbert and Ellice Islands, New Hebrides, Solomon Islands)	Yaws (1955-60): WHO staff ; UNICEF supplies ; training; assistance for participation in international meetings.	TMT	Population at risk: 422 000, including 350 000 in Fiji Island group. In this group, 55% coverage, in all other islands 95%, in initial treatment survey and one or more resurveys. Mass campaign completed and surveillance continued by rural health service. Assessment planned by WHO Intercountry Treponematoses Team.

Annex 2

MAJOR WHO-ASSISTED VENEREAL DISEASE PROJECTS, 1949-1963

Country or territory	*Project, type of assistance*
AMERICAS	
Brazil 1953	Cardiolipin production centre.
Ecuador 1950-53	Medical adviser in venereal disease control and laboratory aspects. Training and fellowships. Limited mass campaign in Balua, Portoviejo, and Manula regions.
Guatemala 1951-54	Laboratory adviser. Regional training centre. Fellowships. Supplies and equipment. Centre for inter-laboratory evaluation project carried out in co-operation with other countries of Central America (co-control laboratory at Chamblee, Ga., USA).
Haiti 1950-63	Medical advisers and consultants. Supplies and equipment (UNICEF, PAHO). Clinical, laboratory, epidemiological, and other control activities. Mass campaign against " urban syphilis " in Port-au-Prince and other cities.
Mexico 1952-53	Technical collaboration. Fellowships. Supplies and equipment. Clinical, laboratory, epidemiological, and other control activities. Participation in US/Mexican Border venereal disease programme.
Paraguay 1952-54	Medical adviser. Establishment of training centre and laboratory services. Supplies and equipment. Training and fellowships. Clinical, laboratory, epidemiological, and other control activities.
Peru 1953	Training and fellowships.
Dominica *St Lucia* *Tobago* 1958-59	Medical adviser. Laboratory consultant. Training courses, fellowships. Mass campaigns against venereal syphilis.
Grenada *St Kitts* *St Vincent's* *Virgin Islands* 1956-58	Medical adviser. Laboratory consultant. Training courses, fellowships. Mass campaigns against venereal syphilis.
Guadaloupe *the Guianas* *Montserrat* 1959-63	Medical adviser. Laboratory consultant. Training courses, fellowships. Mass campaigns against venereal syphilis.
SOUTH-EAST ASIA	
Afghanistan 1952-55	Medical, laboratory, and nursing advisers. Establishment of venereal disease centres at Kabul, Kandahar, and Herat. Laboratory services. Supplies and equipment. Local training and outside fellowships. General programme expansion. Development of venereal disease laboratory into public health laboratory programme.
Burma 1949-54	Medical, laboratory, and nursing advisers, and social worker (UNTAA). Survey by consultant. Strengthening of central Rangoon clinic and laboratory. Supplies and equipment (UNICEF). Training, fellowships. Establishment of eight divisional clinics. Field case-finding. Antenatal blood testing, maternal and child health programme co-ordination.

Country or territory	*Project, type of assistance*
Ceylon 1949-53	Medical, laboratory, and nursing advisers. Consultant surveys. Establishment of central Colombo clinic and outlying district and port clinics. Laboratory services, local training, and outside fellowships. Supplies and equipment (UNICEF). Field case-finding. Antenatal blood testing, maternal and child health programme co-ordination.
1954-63	Periodic consultants and fellowships.
India 1949-58	Pilot project in Himachal Pradesh. Establishment of venereal disease centre and laboratory services. Supplies and equipment. Local training and outside fellowships. Small mass campaign, Ghund Valley. Serological sample surveys in different parts of India in pregnant women and other groups. Strengthening of a series of local laboratories with supplies, equipment (UNICEF), and training courses. Improvement of facilities for national postgraduate training, Madras. Advisers, including social worker. Field campaigns and expansion of programme. Establishment of central serological laboratory. Establishment of cardiolipin-lecithin manufacturing unit, Calcutta (UNICEF). Promotion of the creation of a penicillin plant as a basis for a national venereal disease control programme (UNICEF).
Indonesia 1949-55	Consultant. Serological adviser. Supplies and equipment (UNICEF).
Thailand 1950	Consultant. Serological adviser. Supplies and equipment (UNICEF).
EUROPE	
Bulgaria *Czechoslovakia* *Hungary* *Poland* 1947-48	Consultants after cessation of UNRRA activities. Supplies and equipment (UNICEF). Emphasis on prenatal and infantile syphilis.
Finland *Greece* *Italy* 1947-51	Consultants, medical literature, fellowships. Supplies and equipment (UNICEF). Emphasis on prenatal and infantile syphilis.
Morocco 1954-56 1956-63	Consultants. Training and fellowships. Supplies and equipment (UNICEF). Mass serum testing. Field operations. Health education. Periodic visits from consultants.
Spain 1954-63	Periodic visits from consultants. Strengthening of laboratory services in Barcelona, Madrid, and Seville. Population group surveys. Supplies and equipment (UNICEF). Cardiolipin plant. International training courses. Outside fellowships.
Turkey 1952-53	Technical adviser for survey and long-range programme. Ten-year plan. Fellowships.
EASTERN MEDITERRANEAN	
Egypt 1949-52	Medical adviser, laboratory scientist, and health educator. Supplies and equipment. Training. Demonstration and training centre, Cairo. Field surveys and case-finding, Tanta. Field surveys, including oasis cross-points, Upper and Lower Egypt. Broad health education and human relations campaign.

Country or territory	*Project, type of assistance*
Ethiopia 1952-59	Medical, laboratory, and nursing advisers. Establishment of venereal disease centres and laboratory services in Addis Ababa. Establishment of mass campaigns in Dessie and Lekempti. Training sector with health school at Gondar. Field surveys, case-finding, and other control activities. Supplies and equipment.
1959-63	Periodic visits from consultants on epidemiological, laboratory, and training aspects.
Iran 1954-58	Medical, laboratory, and nursing advisers. Establishment and strengthening of central venereal disease clinic in Teheran and clinics in Shiraz, Isfahan, Tabriz, and Meshed. Improvement of provincial centres and laboratory services. Field surveys. Expansion of control programme. Training and fellowships.
Israel 1951	Consultant. Fellowships.
Pakistan 1953-59	Establishment of centres in Karachi and Chittagong. Medical, laboratory, and nursing advisers in both areas. Laboratory services, supplies, and equipment. Training and fellowships. Expansion to rural areas attempted, including field surveys.
Saudi Arabia 1952-56	Medical adviser and laboratory scientist. Establishment of venereal disease centres and laboratories in Mecca, Asir, and Medina. Training and fellowships. Supplies and equipment. Field surveys, programme expansion.
Somalia 1956	Consultant for venereal disease survey.
Sudan 1952-53	Mass campaign against syphilis and gonorrhoea (Murle area).
1957-58	Consultant for venereal disease survey. Supplies. Training.
Tunisia 1961	Consultant for venereal disease survey.

WESTERN PACIFIC

China (Taiwan) 1954-63	Advisers in venereal disease control and laboratory aspects. Supplies and equipment (UNICEF). Demonstration centre in Taipei. Training and outside fellowships. Establishment of nation-wide control service. Field case-finding and mass serological screening. Health education. Periodic visits from consultants for review and evaluation of programme.
Hong Kong 1952-63	Periodic visits from consultants. Technical discussions on control aspects.
Korea 1957	Consultant. Fellowships. Technical discussions on programme orientation.
Laos 1955	Adviser in venereal disease and laboratory aspects. Supplies and equipment (UNICEF). Venereal disease laboratory developed into general public health laboratory.
Philippines 1952-63	Consultant. Supplies and equipment (UNICEF). Training and outside fellowships.

Reviews of International Health Work

Detailed reviews of international health work in specific fields over periods of five to ten years, or more, are published from time to time in the *WHO Chronicle* (usually in instalments) and reprinted afterwards in booklet form. These reviews are intended not only for the specialist, but also for those with a general interest in public health, particularly teachers, students, historians, and librarians. The following studies are available:

TREPONEMATOSES: A World Problem

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Reprint of a special number of the *Chronicle of the World Health Organization*, 1954, Vol. 8, No. 2-3; 79 pages, illustrated. Price: 3/6, $0.50, Sw. fr. 2.—.

A detailed account of campaigns in which WHO and other international organizations have collaborated, in all parts of the world, for the control of venereal syphilis, endemic syphilis, yaws, bejel, and other treponematoses.

DISEASE CONTROL AND INTERNATIONAL TRAVEL
A Review of the International Sanitary Regulations

by H. S. GEAR & Z. DEUTSCHMAN

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INTERNATIONAL WORK IN BILHARZIASIS, 1948-1958

Reprint from the *WHO Chronicle*, 1959, Vol. 13, No. 1; 58 pages, illustrated. Price: 1/9, $0.30, Sw. fr. 1.—.

This booklet sketches the nature and extent of the problem of bilharziasis and outlines the work that has been and is being done by WHO. It discusses the role of molluscicides and engineering in control, and illustrates the variety of special problems that arise by a full account of the WHO bilharziasis project at Leyte in the Philippines.

INTERNATIONAL WORK IN HEALTH STATISTICS, 1948-1958

by H. S. GEAR, Y. BIRAUD & S. SWAROOP

Reprint of a series of articles that appeared in the *WHO Chronicle* between February 1959 and May 1960; 56 pages. Price: 3/6, $0.60, Sw. fr. 2.—.

This booklet describes the work carried out by the World Health Organization between 1948 and 1958 in international health statistics. The Organization not only collects and publishes health data from all over the world ; it also seeks to improve national statistics and statistical services, and to standardize conflicting systems of classification of diseases and deaths to facilitate comparability. This publication contains an historical introduction, a review of the problem of collecting reliable and accurate international statistics, and a sketch of some of the specific statistical studies WHO has undertaken.

WHO AND MENTAL HEALTH, 1949-1961

Reprint of a series of articles that appeared in the *WHO Chronicle* between March and July 1962; 48 pages. Price: 1/9, $0.30, Sw. fr. 1.—.

This booklet surveys those aspects of mental health work with which the World Health Organization has been particularly concerned : the development of psychiatric services ; the mental health tasks of the public health services ; problems of prevention and treatment ; education, training, and research ; and programme development. Laying special emphasis on preventive work, the Organization has assisted the development of psychiatric services in Member States through seminars, conferences, and fellowships and by providing consultants and expert advice. The booklet contains a bibliography of WHO reports and studies on mental health.

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