

SEROLOGICAL STUDIES OF YAWS IN THAILAND

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Manuscript received in March 1955

SYNOPSIS

The serological aspects of anti-yaws campaigns are discussed. Serological reactions in untreated yaws are considered according to each type of lesion and by age-groups; the serological pattern in types I and II show much similarity in that the majority of cases fall in the high titre levels while with types IV and V there appears to be a more even distribution of cases at all titre levels. A uniform serological response is seen in the early lesions for all age-groups and this is also true of hyperkeratosis cases. There are more type IV cases among the younger age-groups showing high titres, while in the older groups there is an upward trend towards the negative side. Type V also shows a regressive serology.

The serological response to treatment with penicillin in three different schedules (4 ml \times 2, 2 ml \times 2, and a single injection of 4 ml) is then compared. There was no marked difference between the response at the end of one year with all three schedules; with a larger amount of material, however, it is likely that the 2 ml \times 2 dosage would be seen to be less effective than the other two schedules. Serological response to treatment with any schedule would be governed by the number of cases having a high initial titre among the group under consideration. The decrease in titre, after being comparatively rapid in the first six months after treatment, is slow, and reversal to seronegativity at the end of a year occurs only in a small number of cases.

The role of mass serological examinations in large-scale campaigns is considered. While the serological approach is shown to be the only scientific one, the impracticability of mass serological investigation is brought out. It is stressed, however, that in a mass campaign a serological service is essential for pilot studies, orientation of incidence of latent yaws, check on diagnosis, and assessment of dosage and of the necessity for re-treatment.

The possible reasons for prozone phenomena in slide flocculation tests are discussed. The presence of reagin-like substances of extraneous origin to treponemal infection, as well as of reagin, in yaws patients may be responsible for some of these phenomena.

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This paper is a review of the serological aspects of yaws as seen in the Treponematoses Control Programme of Thailand. This project was initiated by the Thai Government in May, 1950; the World Health Organization provided technical assistance, and the United Nations Children's Fund assisted with supplies of drugs and equipment.

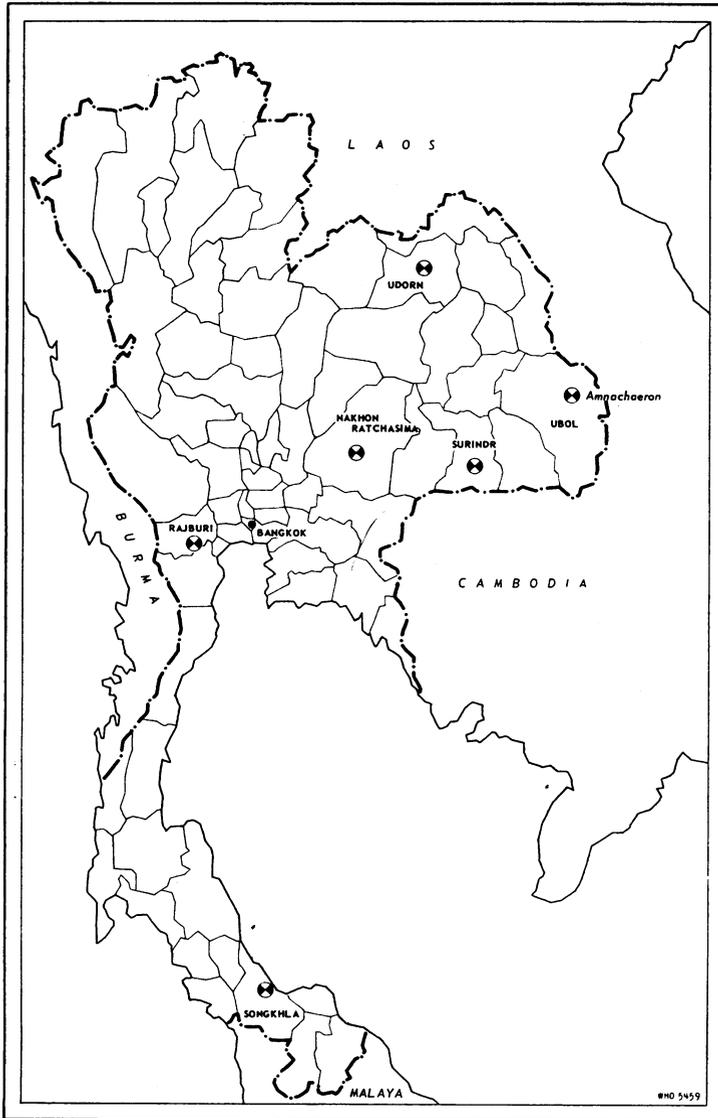
The Kingdom of Thailand lies between the tropic of Cancer and the equator in south-east Asia. There are three seasons—the hot weather, the rainy season, and the cold weather. The hot weather lasts from March to May, the rainy season from June to October, and the cold weather from November to February. The central part of the country is of rich alluvial soil and is criss-crossed by innumerable watercourses. The northern part also has much alluvial country in its valleys, while forested mountain-ranges rise from 5000 to 6000 feet from these basins. The eastern part is flat and has a long hot and dry season. While the other regions are rich in rice cultivation, orchards, and forests, the north-eastern part is an unproductive and impoverished rural area. The whole country is served by few railways and has few good roads; an air service links the larger towns.

The yaws control programme began with the institution of a headquarters at Rajburi (see Fig. 1), approximately 106 kilometres west of Bangkok, the capital. This served as an administrative office and as a training centre for the personnel posted to the project; in September 1950 a serological laboratory was opened there and became the training laboratory.

The campaign began in the Province of Rajburi and, as more personnel were obtained, was extended to other provinces. The method of operation was the institution of a sub-headquarters in a province under a medical officer, who was in charge of from five to six teams each of five sanitary inspectors; sufficient clerical and other office staff were also provided. These teams, fanning out from the sub-headquarters, carried out a clinical survey of the whole population, and all cases of yaws found were given repository penicillin. From August 1952 onwards, people who had been in contact with infectious yaws were given prophylactic penicillin treatment.

In addition to the Rajburi laboratory, others were opened at Nakhon Ratchasima, Amnachaeron, Udorn, Songkhla, and Surindr (see Fig. 1). The Amnachaeron laboratory was used for control work. Later, the equipment was transferred to Songkhla, while the laboratory in Udorn received a new set of equipment. All these laboratories were under the direct supervision of the headquarters laboratory. From time to time exchange experiments were carried out between the various laboratories, with very satisfactory results. It was also a routine practice in each laboratory to test split specimens on each test day; at least four specimens chosen at random were split into two portions and tested separately, the technician being unaware of the relationship between the portions. In an unselected series of 168 such specimens which were split and tested at the Rajburi laboratory, 139, or 82.7%, were in complete agreement while 29, or 17.3%, gave a difference

FIG. 1. THAILAND, SHOWING SITES OF LABORATORIES



⊗ = laboratory

of only one dilution. The results from testing split samples in Amnachaeron, Nakhon Ratchasima, and Surindr were very similar to those quoted above.

The serological results recorded in this paper are only the VDRL (Venereal Disease Research Laboratory, Chamblee, Ga., USA) test results.

This test was uniformly used in all the laboratories, while other tests such as the Kline, Meinicke (Kvittingen's modification), and standard Kahn test were also used in combination with the VDRL over certain periods. The VDRL antigen used was always well within the manufacturer's expiry date, and was frequently tested at Rajburi with known control sera, both negative and of known quantitative values.

For the quantitative test, the serial dilution method was used, in which results are expressed in logarithms to the base two of the dilution; for example, titre 5 is equivalent to positive up to dilution 1/32, titre 6 is equivalent to dilution 1/64, and titre 5.5 is between the two (1/48). The mean titre is calculated on the basis of seropositive reactors only.

The report on the serological reactions in untreated yaws was compiled from results in the Rajburi laboratory obtained from cases reporting at the clinic, and also from the Nakhon Ratchasima laboratory which carried out the examinations for Surindr Province before the establishment of a portable laboratory in this latter region. Specimens from Surindr were despatched by train on the same day that they were collected and were tested in Nakhon Ratchasima the following day.

The laboratories at Rajburi and Amnachaeron carried out serological examinations for the control areas of Nongratoon and Amnachaeron respectively to study the effect of different schedules of treatment with repository penicillin. The results obtained in the Amnachaeron laboratory were analysed. The uniformity level of sensitivity in the laboratories at Amnachaeron, Nakhon Ratchasima, and Rajburi was checked on several occasions by the testing of the specimens in Rajburi and one of the two other laboratories.

The diagnostic groups used in the campaign were based on the recommendations of the First International Symposium on Yaws Control, held at Bangkok in 1952,⁴ and of the WHO Expert Committee on Venereal Infections and Treponematoses.³

The lesions were grouped under six types:

- type I : (a) initial lesions
(b) multiple papillomata
(c) "wet crab" yaws
(d) other early skin lesions
- type II : Hyperkeratosis, palmar and/or plantar
- type III : Ulcerative lesions
- type IV : (a) bone and joint lesions
(b) bone and joint pains
- type V : Latent yaws
- type VI : Other manifestations such as gangosa, juxta-articular nodes, depigmentation.

The overlapping of lesions, so common in yaws, makes it difficult to deal with each type to the complete exclusion of one or more of the remaining types. For the serological studies in this paper, therefore, where more than one type was seen in a case, only the main lesion was considered in making a diagnosis. The most frequent combination of clinical types was type II (especially with plantar hyperkeratosis) and type IV; not infrequently, also, combinations of I with II and of III with IV were noted.

SEROLOGICAL REACTIONS IN UNTREATED YAWS

Two series of cases were analysed—one (examined in 1951-52) from Rajburi clinic, comprising 1254 cases, and the other (examined in 1953) from Surindr, comprising 2278 cases. The cases from Rajburi were those presenting themselves at the clinic, and their distribution in clinical groups did not represent the situation in that part of the country. In the Surindr area (see Tables II, IV, VI, VIII, X, and XII) the cases were found during a survey of the total population^a. The clinical diagnosis of these cases under field conditions would naturally be subject to an element of error, even with experienced workers. This applies in particular to the early lesions of yaws (type I) and to hyperkeratosis (type II). In rural areas with poor hygienic conditions, a considerable number of pyogenic skin lesions is encountered in addition to a large number of infected scabies lesions. In such cases only positive results from darkfield examinations and serological tests can prove the coexistence of yaws. The hyperkeratosis group will also include a number of non-yaws cases when dealing with a population which, as a result of work in the fields, would develop a plantar hypertrophy. This condition may be further confused by the occurrence of traumatic fissures, and fungoid and other bacterial invasion. In the case of chronic ulcerative lesions (type III), a clinical verification is not always possible and cases will be included in this group which, in areas where yaws is not endemic, would not be considered as yaws. With type IV lesions, under which are included (a) bone and joint lesions, and (b) bone and joint pains, clinical labelling will naturally not be accurate, especially with the second sub-group. Type V, latent yaws, includes those with a history of yaws and no clinical manifestations at the time of examination, and those with a positive serology and no clinical manifestations. Type VI, other manifestations, includes cases of gangosa, juxta-articular nodes, and any lesions which could be classed as tertiary yaws or their sequelae. This group permits of a fairly accurate clinical diagnosis.

^a 95% of the population were examined clinically, and 80% of those examined were tested serologically. The persons not tested serologically were almost all very young children. The total incidence of yaws in Surindr was 50%-60%; in some hamlets it was as high as 70%.

Type I: Initial Lesions

In the Rajburi series (see Table I), only those cases showing typical granulomatous lesions were included. All those of doubtful clinical appearance and negative serology (41) were omitted. It will be seen that only 2.5% of the 159 cases analysed gave a weak positive result, whereas the remaining 97.5% gave positive reactions ranging up to a 1/256 dilution. The largest positive group fell in the 1/64 dilution, comprising 28.3% of the total number of cases. While information on the duration of the lesions was not always available, it was noted that one case of only five days' duration gave a titre of 1/64, one of 6 days' gave 1/32, and six cases of from 15 to 25 days' duration gave titres of from 1/16 to 1/128.

TABLE I. SEROLOGICAL FINDINGS IN CASES FROM RAJBURI WITH TYPE I YAWS LESIONS

Age-group (years)	Number and percentage (in parentheses) of cases at titre											Total
	-*	±	+	2	4	8	16	32	64	128	256	
6-10				1 (3.8)	4 (15.4)	1 (3.8)	5 (19.2)	4 (15.4)	7 (27)	4 (15.4)		26
11-20		4 (3.8)	3 (2.9)	3 (2.9)	7 (6.7)	6 (5.7)	17 (16.2)	25 (23.9)	33 (31.1)	5 (4.8)	2 (2)	105
21-30				3 (15)	1 (5)	3 (15)	4 (20)	4 (20)	5 (25)			20
31+					1 (12.5)	2 (25)	1 (12.5)	2 (25)		2 (25)		8
All ages		4 (2.5)	3 (1.9)	7 (4.4)	13 (8.2)	12 (7.5)	27 (17)	35 (22)	45 (28.3)	11 (6.9)	2 (1.3)	159

Average log titre calculated for all reacting sera: 4.48

* 41 seronegative cases with doubtful clinical appearance are not shown.

The age-group breakdown of the 159 cases according to titre levels is also shown. No figures are available for the age-group below 5 years, as bloods at that time were not drawn from this group. The first three age-groups follow almost the same pattern of seropositivity. The last age-group, 31 years and above, contains too few cases to show any pattern.

In general it is seen that the serological response to this type of lesion is more or less uniform in all the age-groups. It is also evident that initial lesions give a strong degree of positivity.

The Surindr cases (Table II) included all cases clinically classified. Of 118 cases, 9 were found to be seronegative ; darkfield examination of these was carried out by one of the writers (J. M. F. D'M.) and no treponemes could be demonstrated, while the darkfield examination of 36 of the sero-positive cases did result in the demonstration of treponemes (in 34 cases at the first attempt, and in the remaining 2 cases, who also had scabies, after several attempts). This point illustrates the percentage of error met with in classification on the field. The serological pattern in this series also shows the general high degree of reagin level and the similarity of the various age-groups.

TABLE II. SEROLOGICAL FINDINGS IN CASES FROM SURINDR WITH TYPE I YAWS LESIONS

Age-group (years)	Number and percentage (in parentheses) of cases at titre											Total
	- *	±	+	2	4	8	16	32	64	128	256	
0-5					1 (5.6)		2 (11.1)	1 (5.6)	10 (55.6)	3 (16.7)	1 (5.6)	18
6-10		1 (2)	1 (2)			3 (6.1)	6 (12.2)	10 (20.4)	19 (38.8)	8 (16.3)	1 (2)	49
11-20		1 (3)		1 (3)	3 (9.1)	2 (6.1)	3 (9.1)	7 (21.2)	12 (36.5)	4 (12)		33
21-30							1 (16.7)	3 (50)	2 (33.3)			6
31+						1 (33.3)		1 (33.3)	1 (33.3)			3
All ages	9 (7.6)	2 (1.7)	1 (0.8)	1 (0.8)	4 (3.4)	6 (5.1)	12 (10.2)	22 (18.7)	44 (37.3)	15 (12.7)	2 (1.7)	118

Average log titre calculated for all reacting sera: 5.22

* 9 seronegative cases with doubtful clinical appearance are not shown. In all these cases darkfield examination showed absence of treponemes.

Type II: Hyperkeratosis, Palmar and/or Plantar

544 cases were analysed in the Rajburi series (see Table III), and of these 18% were negative. Of the 82% of reactive cases, the greater number fall into the 1/16 and 1/64 reagin levels. In the lower titre groups there is a marked fall in the number of cases from 1/16 to weak-positive. This would

TABLE III. SEROLOGICAL FINDINGS IN CASES FROM RAJBURI WITH TYPE II YAWS LESIONS

Age-group (years)	Number and percentage (in parentheses) of cases at titre											Total	
	-	±	+	2	4	8	16	32	64	128	256		
6-10	1 (5.3)		1 (5.3)	1 (5.3)	1 (5.3)			4 (21)	4 (21)	4 (21)	3 (15.8)		19
11-20	29 (15.6)	3 (1.6)	7 (3.8)	5 (2.7)	8 (4.3)	11 (5.9)	32 (17.2)	32 (17.2)	48 (25.8)	11 (5.9)			186
21-30	42 (26.6)	5 (3.2)	4 (2.5)	4 (2.5)	6 (3.8)	15 (9.5)	24 (15.2)	26 (16.4)	28 (17.7)	2 (1.3)	2 (1.3)		158
31+	26 (14.4)	13 (7.2)	10 (5.5)	9 (5)	12 (6.6)	15 (8.3)	21 (11.6)	31 (17.1)	40 (22.1)	3 (1.6)	1 (0.6)		181
All ages	98 (18)	21 (3.9)	22 (4.1)	19 (3.5)	27 (4.9)	41 (7.5)	81 (14.9)	93 (17.1)	120 (22)	19 (3.5)	3 (0.6)		544

Average log titre calculated for all reacting sera: 4.16

indicate that type II yaws also has a high degree of seropositivity. It must, however, be considered whether the 18% of seronegative cases represent a group of "burnt-out" yaws with a residual hyperkeratosis (or wrong diagnosis). If this were conceded, it would be expected that a correspondingly high number of cases would be seen in the lower titre levels, especially if the group is not fed by a high incidence of fresh cases (as is the case here) since the difference in number between the active and regressive cases would then not be marked. Hence, it can be assumed that the seronegative group represents a large number of non-yaws cases which were clinically difficult

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