

PUBLIC-HEALTH ASPECTS OF YAWS

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DISTRIBUTION

Yaws is one of the comparatively few diseases that are limited rather sharply to the Tropics. It encircles the globe in the Torrid Zone, but curiously enough it does not spread when introduced into temperate climates. There are a few records of an occasional isolated case contracted outside of the Tropics, but the disease does not gain a foothold there. Maxwell⁽⁸⁾ states that yaws is imported into China from the Straits Settlements from time to time, but soon dies out. These statements apply to the distribution of yaws as it occurs to-day; it is believed by some authors that certain of the diseases formerly endemic in Ireland may have been yaws.

In several instances the geographical restriction of infectious diseases is readily explained by the corresponding limitation of an essential insect vector. The interest which such sharp limitation arouses is well illustrated by the striking though incompletely studied example of verruga peruviana and oroya fever. These diseases occur in the Andes Mountains and are endemic at altitudes of approximately 1,500 to 7,000 feet (500 to 2,300 meters). Patients when removed to higher or lower altitudes do not serve as foci of infection. Moreover, susceptible individuals may remain in the infected zones during the daytime with impunity, but before nightfall they must proceed to a higher or lower altitude. Hence the inference is drawn that these diseases are transmitted by a night-flying insect limited to this region.

Even within the Tropics it is commonly stated that yaws is restricted to the lower altitudes. Bahr⁽²⁾ noted in Ceylon that people living at altitudes higher than 800 feet (260 meters) rarely contract the disease, even though the surrounding lowlands are thoroughly infected. A striking exception has been reported by Ricono⁽¹⁰⁾ who describes eight cases in

the Mount Fletcher District in South Africa; Mount Fletcher is 5,500 feet (1,800 meters) high.

In Manila, for many years, physicians have frequently spoken of the occurrence of yaws in the Mountain Province of northern Luzon at elevations varying from 2,500 to more than 5,000 feet (800 to 1,700 meters). I recently passed through this province on a brief visit. In exceptional instances, I found that yaws occurring in the people there might readily have been contracted during visits to the adjacent lowlands where the infection is prevalent. This explanation, however, does not apply in the majority of cases. Doctor Pick, of the Philippine Health Service, estimates that he has treated 2,800 cases of yaws in the Mountain Province. He describes the lesions as limited largely to the mouth, the anus, and the vulva, with but few granulomata occurring on other portions of the body.

The limitation of yaws to the Tropics inevitably suggests that it may possibly be transmitted by bloodsucking insects in analogy with other spirochætal diseases such as relapsing fever. This idea has been emphasized by Bahr. In its support it should be mentioned that the mother yaw frequently develops on the lower extremities, which recalls that, in bubonic plague, the causative organism is commonly introduced in the lower extremities, the initial buboes appearing in the groin.

Although the circumstantial evidence, suggesting an intermediate insect host, should not be forgotten, it seems advisable to adhere to the prevailing view that yaws is ordinarily disseminated by contact. The only feasible procedure for attempting the control of yaws in a given community consists in eradicating the foci of infection by treatment of the individual patient.

No plausible suggestion has been advanced concerning the probable explanation of the usual restriction of yaws to the warmer regions of the Tropics. In seeking for a solution, it is perhaps well to keep in mind the possible effect of surface temperature upon the development of the granulomata. Considering first the typical case of the lowlands, it is noteworthy that, of the multiple miliary lesions distributed metastatically from the mother yaw, only a small proportion progress to fully developed granulomata. Although these granulomata may develop on any part of the body, they show a striking predilection for the muco-cutaneous orifices, for the axillæ, and also for the groin and the popliteal spaces. These locations

are either moist or they are protected, to some extent, by the body clothing. However, in the Mountain Province of the Philippine Islands it would seem that the majority of the patients escape the usual general distribution of yaws over the body. These people are very primitive. The men wear only a breechcloth, and the clothing of the women is inadequate to maintain the ordinary surface temperature of the body. The possibility naturally suggests itself that, in the dry skin exposed to the low temperature, the granulomata of yaws might develop only with difficulty.

INCIDENCE

In drawing up any detailed plans for the treatment of yaws in an endemic area, one is often embarrassed by the impracticability of securing even an approximate estimate of the total number of cases. On making inquiries, one is frequently told that almost everybody has fresh active yaws. To assume that such is the case would be a fallacy. There is considerable clinical and also some experimental evidence that the majority of patients do not pass through more than one period of typical florid granulomatous eruption. Let us allow the fairly liberal period of two years for the granulomatous stage and assume an average duration of life of fifty years for the community. Considering the disease to be endemic rather than epidemic, the maximum number of cases in the granulomatous stage would average 40 per 1,000 of the population. Obviously such a calculation is merely of theoretical interest. In Parañaque, yaws has been endemic for many generations; recently the Philippine Health Service treated nearly all of the active cases. There were 275 cases in a population of 8,541, or 33 per 1,000 of the population. Unfortunately, in many isolated districts of the Tropics even an approximate census of the population is not available.

The disease is restricted almost entirely to the native people and especially to those of the poorer classes who are inclined to give scant attention to simple personal hygiene. In many localities, yaws might well be classed as one of the diseases of childhood. At the Parañaque clinic 69 per cent of the cases occurred in children under 11 years of age, and the total of those under 16 years was 88 per cent. At Yamasá in the Dominican Republic the parents freely make a practice of exposing children to the disease because they feel that the sequelæ,

especially clavos, are likely to be less severe when the disease develops during infancy.

DIAGNOSIS

For public-health purposes, the diagnosis of the typical granulomatous stage is a simple matter. Secondary pyogenic infection may mask or confuse the diagnosis. Some of the atypical infections may require a little care in differentiating them from cutaneous leishmaniasis, from granuloma inguinale, and from syphilis. Indeed, in obscure cases, it may be impossible, even with the most-refined means of investigation, to differentiate absolutely some of the tertiary lesions of yaws from tertiary syphilis. The X-ray is of assistance in differentiating the bone lesions of the two diseases. Real difficulty arises in the case of ulcers. The history may be wholly unreliable; and the clinical manifestations, the laboratory findings, and the response to treatment are inadequate for differentiating syphilitic and frambœsial ulcerations.

For the purpose of simply checking the spread of yaws in a community it is perhaps sufficient to treat only the primary and secondary stages. We have found no reliable indications in the histories of patients that a mother yaw has been contracted from a tertiary case. On a priori grounds it seems improbable that a tertiary ulcer would afford a serious focus of infection for the spread of the disease.

On humanitarian grounds, and for the sake of relieving the extensive incapacitation caused by the late lesions of yaws, it is imperative to extend the treatment to latent cases. In some regions, the condition known as clavos is especially important. Multiple granulomata develop in the thickened epidermis of the soles of the feet. An attempt at healing takes place and a hard core of tissue forms in the center which eventually falls out leaving deep "nail" holes. Hence, in Spanish-speaking countries, this condition is often called "clavos." Excoriation and fissuring of the epidermis continues, and the pain persists. The results of the serological tests and the therapeutic response indicate strongly that active infection with the causative *treponema* is responsible for the continuance of these lesions.

Finally, a word must be said in regard to the control of field work by the Wassermann reaction. The decision regarding the advisability of including a Wassermann outfit in the

field equipment is probably an individual question and might well be allowed to vary according to local conditions. It is certainly superfluous for the diagnosis and treatment of the ordinary granulomatous stage, being indeed without value as a guide in the immediate effect of treatment. The Wassermann reaction is of distinct value in eliminating some of the nonspecific ulcers which would not be benefited by salvarsan. As a means of diagnosis the more practical procedure could be substituted of the therapeutic test of injecting salvarsan. Unfortunately this procedure is slow, and the results are often masked by the extensive secondary infection. The employment of the Wassermann reaction requires at most only one additional member in the personnel and adds immeasurably to the satisfaction of the work.

TREATMENT

No difficulty whatever exists in deciding upon the remedy which is most suitable for field use. Neosalvarsan at present stands alone in its efficacy, its relative ease of administration, and its availability. Nevertheless, it is a powerful agent and must be employed judiciously by medical men, or under their immediate personal supervision. From the viewpoint of modern hospital practice, intravenous injection is often regarded as the ideal attainment in therapy. Indeed, to many it would seem to be a step backward to suggest oral administration in place of intravenous injection. However, a drug which is efficacious only when injected into the tissues of the body suffers a very real limitation in its general use even in a modern community. For example, the control that exists over malaria to-day in the better-regulated communities would be greatly hampered if quinine could be administered only by injection by trained individuals.

The various salvarsan preparations fall short of the ideal in this requirement for they are not sufficiently efficacious when administered by mouth for the practical treatment of yaws. Brochard(4) reported fairly successful results in the treatment of nine cases of yaws with old salvarsan administered by mouth. Recently Doctor Albert, in association with Doctor Rosal at the Philippine General Hospital, has tested the oral administration of salvarsan in the treatment of yaws. Neosalvarsan given in dilute solution in daily doses of 60 milligrams was borne without serious nausea by children of 12 years of age. After a week of treatment no noticeable improvement had occurred.

Old salvarsan was then given in gelatine capsules by mouth in daily doses of 150 milligrams. Improvement was noticeable within a week and was very well marked after two and a half weeks. These cases have not yet been reported in full. It is evident, however, that the oral administration does not produce sufficiently rapid improvement to permit its employment in field work. The same objection applies to Castellani's treatment with tartar emetic. With the impatience typical of the average patient, the treatment would not be voluntarily continued until a cure was effected. Indeed, it has not yet been demonstrated serologically that the administration by mouth of either salvarsan or tartar emetic will effect the absolute cure of yaws.

However, there is some ground for encouragement in the fact that salvarsan given by mouth does produce very definite improvement in yaws. It hardly seems to be an unreasonable chemical requirement that effective derivatives should eventually be produced suitable for oral administration in the radical cure of yaws. Indeed, this might afford a preliminary step toward the enlargement of the field for treating and controlling the related disease, syphilis.

A very real question comes up in deciding whether neosalvarsan should, under field conditions, be injected intravenously or intramuscularly. The former is the method of choice, but the number of men available for the Tropics who are adequately trained in the very simple technic of intravenous therapy is surprisingly limited. Moreover, successful injection in a difficult vein, with only untrained assistants to hold the child, perhaps in the uncertain light of the rainy season, requires a greater degree of skill than is necessary in a modern hospital. The procedure is relatively laborious and time-consuming. On account of the contamination with blood, a fresh syringe must be used for each injection. According to the United States Public Health requirements, a minimum of five minutes must be employed for each intravenous injection. Therefore, exclusive of all the time for the preparation of materials, one individual under these restrictions can hardly inject more than ten patients per hour. On the other hand, for intramuscular injection a single syringe, by merely changing the needle, can be used repeatedly without resterilization, and one individual can, without special effort, inject two or three times as many cases as in intravenous work. I have had considerable expe-

rience in Santo Domingo with both methods. After six weeks of intravenous work at Monte Plata, intramuscular injection was adopted at San Cristobal where two hundred cases of yaws in the granulomatous stage were treated. At the outset, it was hoped that the slow absorption from the intramuscular injection would largely obviate the reactions. The results were disappointing in this respect; the reactions were very common, and some of the chills were severe. The therapeutic results however were excellent; the lesions healed promptly, and very few patients required more than two injections. These results are not surprising in view of the accepted teaching regarding the pharmacological action of the salvarsans. According to the consensus of opinion, salvarsan per se is not efficacious against the treponema, but it is readily oxidized in the tissues to a more active product. In the gastrointestinal tract there is no tendency toward oxidation, but in the blood stream oxidation takes place easily, and in the muscles it occurs still more rapidly.

The most serious drawback to the intramuscular procedure consists in the very extensive and at times painful induration at the site of injection. Absorption takes place very slowly. In some communities this method of treatment would seriously injure the confidence of the people, and it would be essential to employ intravenous injection.

To many it may seem very radical to recommend such a toxic agent as neosalvarsan for mass treatment in field operations. However, it was successfully employed in Santo Domingo for more than 1,200 patients. This was accomplished without any trained workers for assisting during the injection or in the immediate after-care of the patients. It was necessary to violate, in minor respects, many of the conditions laid down by the United States Public Health Service for the administration of neosalvarsan. In the first place an excellent grade of distilled water was prepared almost daily in the camp for making up the solutions. However, a sufficient supply of distilled water was not available for boiling syringes; rain water especially collected from a clean canvas tent was employed, although the water remaining in the syringes necessarily contaminated the solution of salvarsan slightly. In the intravenous injection of children, especially a struggling child, it was by no means possible to adhere to the required time of five minutes for the entire injection. For the sake of economy,

the main stock of neosalvarsan was obtained in 3-gram ampules; and, here again, with the various delays incident to injection, it was often impossible to complete the injection of the entire quantity of solution within thirty minutes after its preparation; occasionally as much as forty-five minutes was required. Also, since no ice was available, the solution was always prepared with water at summer temperature. No control could be exercised over the diet or the preliminary catharsis of the patients. In view of these drawbacks, doses slightly smaller than the standard were employed. The scheme of Bergen(3) was modified as shown in Table 1.

TABLE 1.—*Dosage of neosalvarsan.*

	Bergen.		Modified scheme.	
	Age.	Dose.	Age.	Dose.
	Yrs.	mg.	Yrs.	mg.
Adults.....		800		600
Subadults.....	18 to 20	750	18 to 20	500
Do.....	16 to 17	600	16 to 17	450
Do.....	10 to 15	450	10 to 15	400
Children.....	7 to 10	300	7 to 9	300
Do.....	5 to 7	225	5 to 6	225
Do.....	3 to 5	150	3 to 4	150
Infants.....	2 or less	75	2 or less	75

This table is intended, of course, only as a general guide for the various ages or, in many instances, for the apparent or the probable age. Obviously, the dosage must occasionally be reduced, or treatment deferred altogether in patients showing marked emaciation, outspoken pulmonary or cardiac disease, and also in febrile conditions other than those due to yaws. The infrequency of arteriosclerosis and renal insufficiency in the Tropics eliminates any necessity for routine examination of the urine.

Other methods of treatment have been recommended, more especially for avoiding the use of injections under unfavorable conditions. Castellani's formula(5) containing potassium iodide and tartar emetic has met with considerable favor; however, this treatment must be continued daily for approximately one month. An adult, or a child over 14 years, must take 300 grams or more of potassium iodide. The cost of this item alone is rather more than 4 pesos as contrasted with 1.8 grams of neosalvarsan at about 0.80 peso.

When one is cut off for weeks from a base of supplies, the essential equipment for the treatment of yaws with neosalvarsan is not complicated, even in regions where the simplest articles of household life are wholly lacking. The exact details will vary with the preference of the individual. The following unit was found practical, and is suggested as a suitable basis for the selection of an outfit:

- 1 small water still with tin condensing coil.
- 2 bottles (0.5 liter) for receiving distilled water.
- A supply of suitable water for washing and boiling syringes.
- 1 khotal or primos stove with complete set of wrenches and pliers and fine wire for cleaning and soft leather for repacking the piston. (New models have a valve for regulating the size of the flame.)
- 10 gallons of kerosene, allowing 1 quart for ordinary use of stove continuously for eight hours. Alcohol for priming stove.
- 1 small box for shielding the stove from drafts. This is essential. The wooden case commonly used for two 5-gallon oil cans is satisfactory.
- 12 syringes, Luer type, 10 and 20 cubic centimeters capacity (for intravenous work), an ample supply of needles, and a stone for daily sharpening of these. If steel needles are used alcohol and ether saturated with vaseline are convenient for drying them when not in use.
- 2 pairs of ordinary forceps.
- 2 wide-mouthed bottles 100 cubic centimeters (with glass stopper or cover) with graduation marks. (A mark at 60 cubic centimeters for dissolving 3-gram ampules of neosalvarsan at the minimum dilution of 0.1 gram per 2 cubic centimeters. Additional graduations can be made with a syringe.)
- 1 container (of tin) for boiling water for dissolving salvarsan.
- 1 container for used syringes.
- 2 copper instrument boilers (25 by 12 by 6 centimeters) with removable tray and with wire tongs for handling tray. Soap, alcohol, and cotton for preparation of patients.
- 2 soft rubber tourniquets.
- 2 triangular files.
- 1 set of cards for records of patients. (Cards are preferable to a bound book for convenience in locating a patient's record on his return visits.)
- Ampules of salvarsan. (3 grams each for the main stock with a few small ampules, 0.6 gram each, for convenience in adjusting the quantity of solution required in closing the day's work.)
- Schedule of dosages for varying ages.
- Stethoscope.
- Clinical thermometers and reagents to test for albumin in the urine.

The main cost of the work is the expense of personnel for the administration of neosalvarsan. Fortunately, in some localities in the Philippines, the Government hospitals with their person-

nel are already available. In these it would be entirely feasible to treat yaws continuously. There are other regions, heavily infected, in which traveling dispensaries could be operated intermittently. The expense of neosalvarsan for Government use is remarkably low; namely, 20 cents United States currency (40 centavos Philippine currency) for 0.9-gram quantities. Therefore, for a series of three injections of 0.6 gram each for an adult, the total cost of the drug would be 80 centavos Philippine currency. The majority of the cases, however, occur in children; for an infant the neosalvarsan for a series of three injections costs 10 centavos.

The total expenditure in money that would be required to bring yaws under control in a given community would necessarily vary widely in different countries. Moreover, if the work were to be pressed rapidly, it would be correspondingly much more expensive. The time required must also vary widely. It would depend in the main upon three factors; namely, (a) the readiness with which patients present themselves for treatment; (b) the consistency with which they return for repeated injections; and (c) the total percentage of cases that report for treatment.

In primitive communities we have found that the people would await with interest the result of the injection of the first few patients. Then they would present themselves even more rapidly than desired. There are always, however, a few stragglers. Moreover, with the striking benefit following one or two injections, there are many who do not bother to return for repeated injections. Furthermore, one cannot expect that 100 per cent of the cases will report voluntarily and with reasonable promptness. The operation of a dispensary for a single period of a few weeks for the treatment of all accessible patients in a given area would certainly be altogether inadequate to bring the disease under permanent control. Repeated visits would be required at intervals of perhaps six or twelve months. Six months after closing the dispensary at Parañaque, an inspection showed the presence of 76 cases of yaws. They were classified as follows: Fifty-six cases were reported to have developed since the closing of the dispensary; 8 were old cases that failed to report for treatment; 12 were only partially cured or were relapses. Too much confidence cannot be placed on this small number of relapses, since two-thirds of the cases received only one injection. In several places a good beginning has been made, only to have the preliminary advantage lost through a

gradual or sudden decline in interest resulting in merely spasmodic activity or even in cessation of the work.

PERMANENCY OF RESULTS

The available data indicate that there is but little tendency to recurrence or reinfection after treatment with salvarsan. In the Windward Islands in 1912-1913, only 5 per cent of relapses occurred after treatment with salvarsan (606).⁽¹⁾ Bergen noted 4.9 per cent of relapses, or possibly reinfections, following the intravenous treatment of 1,626 cases of yaws with salvarsan after a period of thirty-four months; 2.6 per cent of relapses occurred in 655 cases treated intramuscularly. Kurien⁽⁷⁾ records 11 per cent of relapses in the treatment of about 3,000 cases with various preparations of salvarsan, but apparently 90 per cent of the patients received only one injection. Thorough treatment of a community at once reduces to a minimum the foci of infection. It is probable that, having once had the disease, many patients will profit by their lesson.

Fairly extensive treatment of yaws has been practiced of late years, particularly in some of the hospitals of the West Indies. There are doubtless valuable reports from such hospitals to which I have not had access. Indeed, it would be very important to secure information concerning the incidence of yaws in a community in which intensive treatment with salvarsan had been practiced consistently for several years. In Java, in 1913, the treatment of yaws with salvarsan (606) was given thorough consideration. The decision was referred to Kloppers,⁽⁶⁾ who concluded that the plan was not feasible on account of the great expense of salvarsan at that time. McDonald,⁽⁹⁾ in 1915, suggested measures leading to the absolute eradication of yaws in Antigua, a small island of about 108 square miles in the Leeward group in the West Indies.

SUMMARY

Neosalvarsan in the hands of medical men can, with proper precautions, be used safely on an extensive scale under field conditions. The diagnosis of the granulomatous stages of yaws is simple. A Wassermann outfit, though not indispensable, is a valuable adjunct even in field work. The treatment presents no special difficulties. In the Tropics, routine examination of the urine is not a prerequisite before administering neosalvarsan.

Certain details of field operations are still sub judice, or are subject to modification according to varying local conditions.

It has not been accurately determined whether latent or tertiary cases of yaws constitute important sources in the infection of susceptible individuals. Further observations are desirable regarding the feasibility of substituting intramuscular for intravenous injection of neosalvarsan, especially when work is conducted under the disadvantage of limited personnel.

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