YAWS IN THE AREA OF THE RIVER HUALLAGA

IN THE FOREST REGION OF PERU.

Thesis submitted for the

M.D. GLASGOW.

by

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MOYOBAMBA, PERU.

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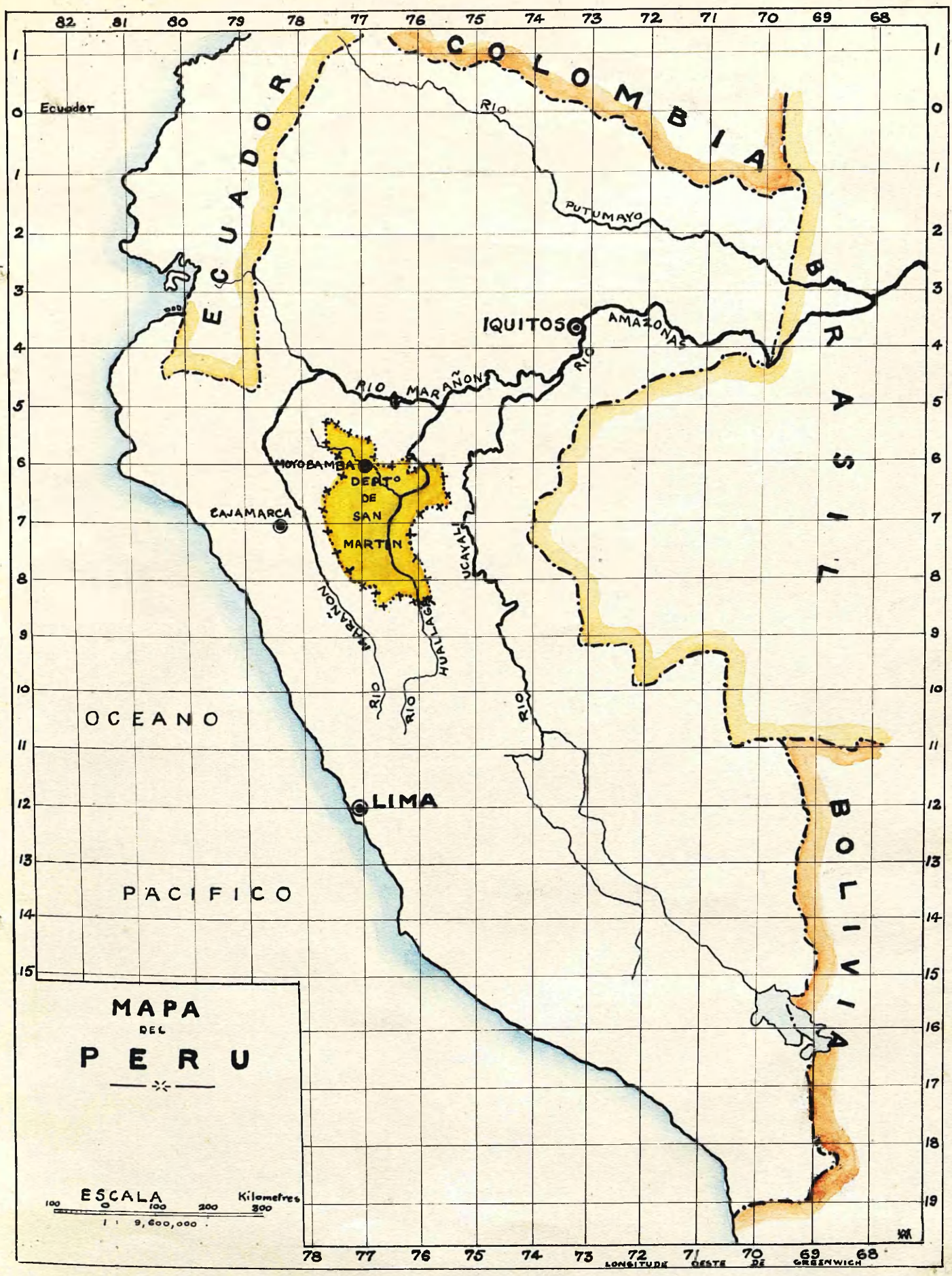
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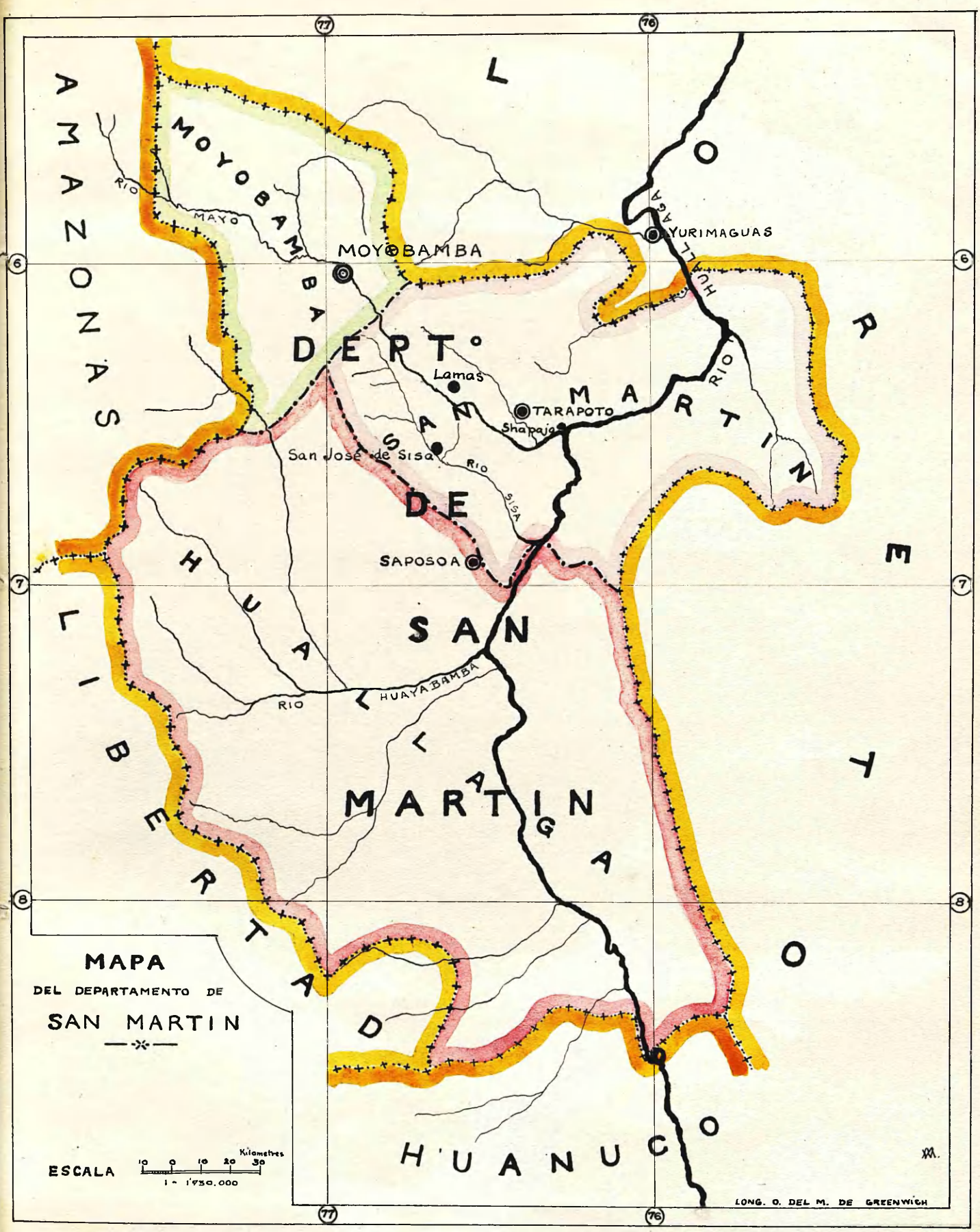
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Introduction.

The Republic of Peru, a mere strip along the Pacific sea-board of South America, is yet a land of such vast distances that it has three parallel longitudinal divisions into three totally distinct types of country. These three divisions have each its own distinct geographical and climatic characters, its own type of inhabitant and manner of living, and its own medical conditions and problems. They are called the regions of Coast, Sierra and Montaña. The coast region is largely desert made fruitful by artificial irrigation. From it rises the central region of Sierra, the Andean cordillera, varying from three thousand to twenty thousand feet in altitude, extending from north to south of the country, looking westward out to the Pacific Ocean and eastward over the vast extent of Montaña or forest region. This last division is the unknown quantity, or at best the imperfectly known, still largely impenetrable. It is an enormous area, a richly fertile, heavily wooded land, and cut by the numerous rivers, great enough in themselves, that are but the upper reaches of the countless sources of the Amazon. It is with a corner of this third division of Peru, the

sparsely populated forest region or Montaña, that the present work is concerned.

On the accompanying maps of South America and Peru, the line of the River Amazon may be followed, as in fact it is navigated, up from west to east across the selvas or forest region of Brazil to the Peruvian river port of Iquitos. Above Iquitos, entering the Montana of Peru, the main line is seen to be formed by the union of three that come down from the cordillera of the Andes. These three true and very nearly ultimate sources of the Amazon, are the Marañon from the West, the Ucayali from the south, and between them parallel to the latter, the Huallaga. Yaws in the basin of the River Huallaga is the subject of this study.

The basin of the Huallaga corresponds to one of the units or departments into which Peru is divided politically. It is the Department of San Martin, and is subdivided into three provinces, each with its capital town, and its provincial authorities in the different branches of administration, which includes medical and public health service. The smaller northernprovince is Moyobamba, capital

Moyobamba, and this town is also the capital for the whole Department, and its seat of government, for which reason the medical officer of the department is stationed there. The much larger southernpart of the department is divided into the other two provinces called the Province of San Martin, capital Tarapoto, and the Province of the Huallaga, capital Saposoa. In the Province of Moyobamba, where I am stationed, Yaws is a rare disease. In the other two provinces that person is rare who has not had it or is not having it.

The area involved is estimated, probably under-estimated, at fifty thousand square kilometres. The population with allowance for considerable inaccuracy, is in the neighbourhood of sixty thousand, of whom school children number more than nine thousand, and the urban portion of the population is about thirty thousand. It is therefore a relatively thickly populated part of the wide extent of Peruvian forest. Actually the condition is that of towns and villages separated from each other by several days journey through unpopulated country, and in connection with the existence of Yaws, it has to be noted that the sparseness of population per square kilometre has no relation to

the density per room or per bed. The family in the Huallaga is not less inclined to a common bed on the floor than is the family in the over-crowded slum, notwithstanding the lack of excuse in the room for expansion.

Between the three provinces there are differences in altitude and in average temperature that have to be considered in connection with the variation in the prevalence of Yaws. These differences are due to the fact that from the south of the department where Yaws is general to the north where it is less so, one is climbing from the region of great rivers to the higher ground of their tributaries. Continuing from Moyobamba towards the coast, there begins the gradual ascent to the cordillera which is crossed five days foot journey away. Moyobamba then, is supposed, for one cannot claim accuracy for these figures, to be at two thousand five hundred feet above sea-level, with average temperature of 22°C. The Province of San Martin is at one thousand four hundred feet with mean temperature of 25°C. The Province of the Huallaga where Yaws is at its maximum, is at one thousand two hundred feet with mean temperature of

Typical huts of the cuchipe area.

28°C. Conditions throughout are sub-tropical, and there is no definitely marked division between wet and dry seasons.

In all the basin of the River Huallaga or Department of San Martin, the people are for the most part Mestizos, by which is understood the result of descent from original Spanish and original Peruvian Indian. In several villages there are groups of unmixed Indians. The language is Spanish generally, and among these Indians dialects of Quechua. The chief occupation is agriculture, and the manufacture of straw hats as a side-line. Living conditions of the great majority are very poor. Houses in the towns are of pressed earth walls and roof of burnt tiles or of thatch. In the villages, and especially where Yaws is prevalent, the walls are of bamboo cane plastered with mud and the roof thatched, either with grass or with palm leaves. The food is bulky and largely carbohydrate. Yuca, plátano, maize and rice; coffee and chicha (fermented liquor); milk and eggs; fowls, and the flesh of the pig; all these, except milk in abundance. Milk and the flesh of cattle are available but not in daily use. Beans and peanuts

with local fruits and greens complete the diet.

The region is in direct water communication with Europe, sending cotton and tobacco down by raft to Yurimaguas, thence by river steamer to Iquitos, where the trans-atlantic steamers arrive. The natural resources like the medical conditions are a quantity as yet only to be surmised. There is a saying that Peru is a beggar seated on a golden throne, that has reference not to any lost Inca wealth, but to the truly stupendous natural riches not exploitable for lack of ways of transport. Of the throne of gold the area of the Huallaga River is at least a worthy pillar if it be not actually the seat. How great is its wealth in woods and minerals and above all, in agricultural productiveness, nobody yet knows. It is equally true that nobody knows with any exactness quite what may be the natural impediments in the form of disease. It is very possible that for medical investigation there awaits no acquaintance more novel than the hookworm or more exciting than the three Plasmodia of malaria. It is certain that they abound, and in the complete absence of the acute appendix they go accompanied by tuberculosis

and dysentery and gonorrhoea, some cancer and some leprosy. Much routine work and recording of clinical facts must be done to establish tne presence of known diseases under their local names before one can speak even of possibilities. "Poshequismo" from an Indian root meaning "pale" was easy to establish as anquilostomiasis. It is the purpose of the present paper to consider as Yaws the disease that is known universally throughout the Huallaga area by the name of "El Cuchipe". This disease more than all those listed above is the disease of the Huallaga area in general, but especially of the province of the same name. The local name does nothing to enlighten, because its original meaning is not yet ascertainable - it has some connection with the word for a pig - but it is one of many remainders of the Indian Quechua that persist in place names and familiar phrases much as Gaelic does in parts of Scotland where it is no longer spoken.

El Cuchipe in my opinion, is Yaws. It is boubas or pian, probably come straight from Brazil up the Amazon, the Maranon and the Huallaga. There it stopped instead of coming on up to Moyobamba,

Mild secondary eruption. Case 7.

Typical primary sore at six weeks.

whose river Mayo joins the Huallaga four days down. Tradition attributes the introduction of boubas to Brazil to the negro slave-trade between that country and the West Indies and Africa. Thirty years ago in the rubber boom that made Iquitos a city (and the Putumayo notorious in the years before the war of 1914-1918 following on Casement's report of the sufferings of the Huitotos,) numerous families went down river from this region in search of riches. It is certain that they brought back a considerable number of Cuchipe cases as they kept returning. But a notably intelligent and educated woman of seventy-five years of age whose memory is clear, not only on events of her own life, but also on the tales of her father who reached the same age, assures me that Cuchipe was an old story "long before there was rubber in Iquitos when Moyobamba was three times its present size". In any case, whether the trading connections of many generations or the rush to the rubber in the beginning of this century provided the opportunity for the disease to get its hold, it is now as thoroughly at home in the villages along the Huallaga as the most congenial conditions can make it. It is not at home, although cases occur, in Moyobamba, over

one thousand feet higher up, and yet cases come up continually for treatment a five to ten days journey. There must be reasons for the failure of the disease to get a footing in Moyobamba. That again is the reason why this study deals mainly with young adults, and that in turn offers an opportunity for comparison with acquired syphilis.

The present paper is a consideration of notes made of 242 cases of Cuchipe as they came along, not because the study is to contribute any new thing to our knowledge of Yaws, but because Cuchipe in the Montana of Peru is possibly a new fragment on the exact Yaws map of the world, and only by the careful recording of it will it be possible to say whether its study will throw light on any of the problems of that disease.

The attempt at the concise definition of Cuchipe results in the restatement of Yaws. I find it to be a chornic contagious disease, characterised by its beginning with a single cutaneous sore and by the appearance within a variable short period of a typical eruption of itching papules which are granulomatous and thickly crusted.

This paper then, in dealing with the facts of 242 cases of Cuchipe, will endeavour to justify

the forming of an opinion on such points as the separate existence of Yaws and syphilis and the exclusive effect of the former on the latter. It will treat of the existence of a very mutilating rhino-pharyngitis as a late result of Yaws, sufficiently terrible to give the impression that it is a serious matter to be content with the disappearance of the eruption after short treatment of children, rather than the elimination of the disease by sufficient treatment. This rhino-pharyngitis in this region has to be distinguished from the similar lesions of uta or espundia, (leishmaniasis), Leprosy, malignant ulceration, syphilis, tuberculosis and blastomycosis.

There is to be noted the great prevalence in the later secondary period and long after, of a crippling lesion on the soles of the feet, economically most important. It is known here as "laja" - "j" like "ch" in "loch" - and corresponds to the condition described as crab-yaws. There is ample confirmation of the accepted truth that cleanliness is next to yawlessness, a note on the difference occasioned in prevalence by differences in altitude and temperature, and some opportunity for

comparison between a few treatments with the suspension of metallic bismuth in glucose "bismostab" and a majority of treatments with Neosalvarsan. It is not without significance that the Cuchipe cases indicate such a comparison by pleading for the injection in the vein in preference to the injection in the buttock, because they want to get away speedily to their distant homes.

It is a matter of regret but inevitable in the circumstances under which this work is being done, that the only laboratory and aid to clinical findings is the use of the microscope to show the causal organism, and that post-mortem findings are not available, partly because it is difficult to get doing post-mortem examinations apart from legal cases, but more reasonably because none of the cases recorded has to my knowledge died.

Historical Section.

Inquiry into the origin and history of Yaws has no happier result than similar inquiry in the case of most subjects of medical interest. It is but small the help medicine gets from the bad habits of historians of old, whose labours in great measure have resulted in the perpetuation of the memories of "battles long ago", and of the lives and doings of kings and queens who might be forgotten and little lost by it. The small beginnings of what are great matters today in citizenship and in science were missed until now they are untraceable. In common with more important diseases Yaws so far has suffered thereby, and the pity is the greater because of the confusion that has existed, since first Yaws was recorded, with a disease whose importance today gives it some claim to the respect even of history, namely syphilis.

It is suggested that the disease which was for religious ceremonial reasons the object of strict control and isolation among the Israelites on their wilderness journey, may have been Yaws. If so, the description in the thirteenth chapter of Leviticus would indicate that the Israelites knew

Yaws as a distinct disease from syphilis as we know it. The description however scarcely fits Yaws, and there are reasons of other than a clinical nature why leprosy should be considered a better translation of the word used "Saraat". Even the passage that most suggests Yaws, is hardly the description one would expect of lesions so very typical as those of that disease, - "The flesh also in which even in the skin thereof is a boil and is healed, and in the place of the boil there be a white rising on a bright spot, white and somewhat reddish,..... and if it be in sight lower than the skin ... the priest shall pronounce him unclean". (1). The primary sore of a Yaws case would not be "in sight lower than the skin", and the doubt is increased when there is laid down,a few verses later, the two points of diagnosis, "a hot burning" with the hair in the bright spot turned white. Further the disease of leprosy in a much more developed stage, impossible to confuse with Yaws, is used throughout the books of the law and of the history of the people of Israel and in the New Testament in a special sense with a spiritual significance which is in perfect accordance with the rules

of ceremonial uncleanness laid down in Leviticus XIII. The disease of leprosy is so dealt with as to the physical symbol of the spiritual state resulting from sin, and this fact makes its selection as the subject of ceremonial exclusion probable in the case of the chapter under consideration. For both reasons, clinical and symbolical, it seems that the case does not fit Yaws very closely.

From Leviticus the history of Yaws as we have its fragments, must jump to an equally doubtful reference at the end of the tenth century. An Arabian physician writes of a disease of Safaat, whose symptoms resemble Yaws, but which might also be syphilis. The name is very like the name Saraat already quoted, but it might be identical and still refer to a different condition. (2)

From the moment Yaws begins to take a real place in medical literature, there is apparent the confusion between it and syphilis. Sydenham writes about it as existing even in the fifteenth century. He says in his treatise on syphilis:- "To me it seems to have taken rise from some nation of the blacks upon the borders of Guinea, for I have been informed by men of great veracity who have lived

in the Caribee Islands that the slaves which are newly brought from Guinea, even before they land, are afflicted with the disease, and as far as I can learn, this disease which so frequently attacks these miserable people, does not differ at all from that which we call the venereal disease with respect to symptoms, but it goes under a different name, for they call it Yaws. It seems to me that this disease was brought to Europe by Spaniards who first contracted it from the negroes they had purchased in Africa". (3)

From the sixteenth century onwards there are records and reports on Yaws, and Garrison attaches to this disease a special interest in the history of medicine, when he notes as the real beginning of modern Tropical Medicine, the first unmistakable description of Yaws. This description consists of a clinical account of the disease in the West Indies by Ovideo g Valdex in the sixteenth century. (4)

From the West Indies come the other earliest reports on Yaws, and the first definite statement that Yaws is syphilis. A French observer named Thevet described the bubas occurring in the West Indies as "no other thing than the poc which rageth

and hath power over all in Europe, especially among Frenchmen". That was in 1558, and the idea is dying hard even today. (5)

In the following century from the West Indies are reports of outbreaks of a disease clinically resembling Yaws by Rochefort in 1656, by Breton in 1665 and by Labal in 1694.

Meantime further confusion had been caused by the occurrence in Eastern America of a widespread epidemic of Yaws a few years after an epidemic of syphilis which ravaged Europe at the end of the sixteenth century. Tradition places the origin of the disease in Africa and blames the slave-ships for its introduction to the West Indies and America, but the evidence is not conclusive. It is the case however, that there were severe outbreaks of Yaws in the slave ships carrying African slaves to America, and that the big West Indian estates provided special hospitals for its treatment.

The seventeenth century has one interesting reference in a report from Scandinavia of a disease called "Radesyge" which may have been Yaws, but which was probably syphilis. (6)

It appears to have been similar to an outbreak in Scotland in 1769 of a disease closely resembling Yaws but which also was probably severe syphilis. It was called "Sibbens" and was apparently contracted from sailors wrecked off the coast of Cumberland in a West Indian ship. Also in the eighteenth century there was described a disease endemic in the rural districts of Ireland under the name of "Button Scurvy". By the description this disease may well have been Yaws. It occurred only among the country folk, and transmission was believed to be by fomites. The lesions developed from an itching spot to the size of a pea and were covered with a dry crust. The palms of the hands, soles of the feet and inner sides of the thighs were the favourite sites.

In 1718 Bontius reported framboesia as endemic not only in the West Indies but also in Java, Sumatra and other Dutch colonies of the East. In these parts it was known as "Anboyna Pox". (7)

A step forward in the investigation of the etiology of Yaws was made in 1769 when Edward Bancroft noted the transmission of the disease by flies. (8)

For the next advance one has to go forward to the later part of the nineteenth century. In 1881 Yaws was experimentally differentiated from syphilis by Charlouis. His experiments are historic, though Powell casts doubt on their scientific value because they were performed before the days of antiseptics. (9) He inoculated thirty-two chinese prisoners with scrapings or actual pieces cut from the scab of a Yaws patient. Twenty eight of then developed typical lesions of Yaws at the site of inoculation. He also inoculated with syphilis a negro suffering from typical Yaws. A primary syphilitic sore resulted and was followed by the usual secondary eruption. This showed that the Yaws-infected persons are not immune against syphilis. (10)

In 1891 Numa Rat published a monograph on the disease giving a clinical picture of the condition which has since become a classic. (11)

Since the beginning of the century real progress has been made, principally by two discoveries, one in the etiology and the other in the treatment of Yaws. In 1905 Castellani in Ceylon observed a spirochaetal organism present constantly

in Yaws. He named it Treponema pertenue castellani and this is now generally accepted as the causal organism of the disease. (12) The same worker demonstrated the presence of this organism in the spleen, lymph glands and bone marrow of persons suffering from non-ulcerative lesions, and by reproducing the disease in monkeys by inoculation he established the etiology of Yaws on a sure basis.

Schobl who in these days is publishing his results of experimental work of the same nature on the Philippine monkey, asserts that the West Indian natives in early times possessed the knowledge that Yaws could be transmitted by inoculation of the secretion from an ulcerative Yaws lesion, and that they used the knowledge to inoculate their children so as to give them immunity. (13)

The advance in treatment came in 1911 when Nichols first treated Yaws cases with salvarsan. (14). Alston added the observation that the serum of patients so treated showed curative properties when injected into patients with Yaws. (15)

If the origin of Yaws as disease is still lost in the obscurity that surrounds all early medicine, there is some interest in the consideration of its

history in different countries, its introduction to new areas and its disappearance from others.

The latter point is the subject of a study in American countries by Leger. (16) He refers especially to French Guiana, Guadeloupe, and Martinique. In French Guiana the disease was described by Bajon in 1777 as common, having been introduced by African slaves. In 1902 Clarac reported it as rare except among new comers. In the years 1917 to 1919 Leger found only three cases by bacteriological diagnosis, and since then no further cases have been reported in the annual medical reports. In Guadeloupe in 1725 Yaws was reported as common by Pere Labat, who believed the disease to have been well known to the native Carib population before the coming of African slaves. Now Yaws is not seen in Guadeloupe. In Martinique it persists only in certain areas. In most islands of the British West Indies Yaws is widespread, but in Barbadoes it has nearly disappeared.

In India no case of Yaws had been observed till 1881. Hirsch (17) says that the only reference to Yaws in India before 1881 was made by Huillet in his "Hygiene des Blanchs de Pondichery" who did not

see the case he described, but gave his account at second hand from a French observer. From the description it is evident that the lesion was not in fact one of genuine Yaws.

In Burma an epidemic of Yaws occurred in 1894 (18) and sporadic cases were reported in Travancore, Calcutta and Pondicherry. In 1887 a coolie woman came from Ceylon with three daughters, the youngest being infected with Yaws. The other two girls contracted the disease and from these three cases a widespread epidemic occurred in the tea-gardens of Assam, and spread subsequently to the neighbouring states. (19)

On the origin of Yaws in Assam, Ramsay writes that from the intensity of infection and from the history of the infected tribes of Assam it would appear that these tribes brought the disease with them at the time of the invasion of the province. The Manipuris were subsequently infected by the invaders, and only in later years did the disease spread through the medium of bazaar contact to Gengali settlers and tea garden coolies. It is interesting to note that Manipuris distinguish Yaws from syphilis, calling Yaws "chako" and syphilis "gurnee".

"Yaws, according to Castellani, is common in Burma, Malay, Siam, Java, Batavia and Ceylon, and is present in the Philippine Islands, Samoa, New Hebrides and Fiji. It is also endemic in the Nicobar Islands and among the aboriginal tribes of Australia. It is a well known fact that the intervening seas between Australia and Asia are in many places very shallow, and that in bygone days many of the islands appear to have been connected up; Does this point to a common origin of Yaws, at any rate, in the far East, if not for the old world?" (20)

In this connection it may not be out of place to refer to the similarity of the Indian tribes of the montana of Peru to the Asiatic type known as Mongolian. They are a marked contrast to the Indian of the sierra, who is of Inca descent, and their physical features, the broad face and low forehead, high cheek bones, bullet head and coarse scanty hair and beard, give some foundation for the theory of Asiatic origin.

In Melanesia and Polynesia the history of Yaws shows that the condition existed before the coming of the white man. It is possible that the remote islands were free of it till the advent of the white

man, of European shipping traders and missionaries. Lambert quotes tradition to the effect that labourers returning from other archipelagoes brought Yaws to the Gilbert group about 1860, and that the disease was introduced into the Ellice group by a Samoan preacher in 1867. (21)

The general confusion between Yaws and syphilis resulted in disputes between early voyagers in the Pacific. Several of them tried to blame some previous expedition for the introduction of the "loathesome disease" which they believed had been brought from Europe. The dispute became international when Wallis and Bouganville each tried to blame the other for the supposed introduction of syphilis in Tahiti. It was Marriner Martin, a layman, who first detected that the disease under discussion was not syphilis at all, and that it had been already prevalent in the island before the arrival of the traders. (22) He describes the disease fully and calls it Yaws. Buxton states definitely that syphilis does not occur in the Gilbert and Ellice Islands and that Yaws is very prevalent. (23)

One may deduce from the preceding evidence on the origin and history of Yaws, that its place of origin is a matter of speculation, and the history of its origin in different countries becomes a matter of doubtful tradition even when its introduction appears to have been comparatively recent. Before the fifteenth century there is no information either as to its source or the method of transmission. From the fifteenth century onwards almost every reference to the disease and all the recorded observations are rendered obscure by the confusion between Yaws and syphilis. Consequently the real and definite history of Yaws may be considered to date only from the work of Castellani, by which the exact diagnosis of the disease has been established on a firm basis, and with a special regard to the differentiation from syphilis. Since then it has been possible to study the disease with greater accuracy, and the confusion which existed in the past need no longer impede the workers of the future.

Etiology and Pathology.

The geographical distribution of Yaws is from every point of view irregular, an irregular irregularity that makes it as yet impossible to explain its distribution by any few common salient features of the sites of prevalence. It is definitely tropical, confined to the area 22°N. to 22°S. of the Equator, but within this area great variations occur. Ceylon has it in abundance, while in India it is rare. In Africa and especially of recent years in Kenya and Uganda it is not only common but increasing. In parts of the West Indies it is nearly universal among the native population, and in the East Indies it is very prevalent. One does not hear of it in Australia except as having existed among the aboriginal tribes. In Brazil, Araujo (24) makes his analyses of the disease on tens of thousands of cases, and it has worked up the Amazon from there into the forest region of Peru. It is noticeable that the smaller islands and island groups are favourite sites while the great inland areas that suffer from it are those that, like the area here considered, have access to the world's great waterways. To

some extent it appears to be a disease carried by the commercial intercourse of shipping to communities confined by their geographical circumstances, as the islanders by the sea and the Peruvians of this region by the forest, and once implanted, able to stay and to spread in certain conditions of climate and of dirt.

The necessary conditions of climate are so irregular that one has to admit that the forces governing the continuance of Yaws in some regions and its inability to establish itself or its tendency to disappear in other regions are not known. Araujo has pointed out its irregular distribution in Brazil. (24) Leger, as has been already mentioned, has written of its disappearance from some of the American countries where over a century ago it was very prevalent, but the examination of the facts has not provided their explanation. (16) The cuchipe of this region, comparatively a modern disease, probably not more than a century or two established, is definitely at home in the lower and hotter and drier province Huallaga, is less propagated in the Province of San Martin some two hundred feet higher up, and has so far been

unable to gain a permanent footing in the Province of Moyobamba about a thousand feet higher up. I have yet to hear of a case occurring or coming down to us from the other side of the cordillera from the region of the sierra. It would have to pass over an altitude of thirteen thousand feet from the sierra towns which are at an average height of eight thousand feet, and which are the site of uta, or Leishmaniasis Americana. Pena Chavarria in Colombia finds Yaws most heavily distributed along the rivers and on the coast, and describes it at an altitude of five thousand feet. (25)

On the other hand, the conditions of dirt show no such variations. I think this is the only factor that can make it possible to say that Yaws in any region is proportionately rare in white residents compared with natives. I have not seen a case of cuchipe in a white man, but I have no doubt that if a white man lived right among it and neglected his body he would contract it, because both Indians and mestizos have it, and the latter in greater proportion. The variation in the closeness of the mestizo to one or other of the two original races makes no difference to his

liability to contract the disease. Araujo reports that in Brazil all races are attacked, his exact figures being:- whites 18.4 per cent, negroes 15.2 per cent, half-castes 56.2 per cent, and Indian natives 10 per cent. Taking the different populations into account, he estimates that these figures mean equality among the races in liability to infection. (24)

Age does not appear to influence liability to Yaws, and consequently does influence the actual prevalence in that a majority contract it as children and get over it, so reducing the incidence in adults. A man of 46 years of age recently contracted cuchipe in a village three hundred feet lower down and went with it to another on a plateau one thousand feet above Moyobamba.

There he caused the infection of a younger woman of 20 years of age, who was at the time, six months pregnant. Six weeks after the confinement the dirty old handy-woman of 60 who had attended her came down for treatment, infected through a finger abrasion. Yet the disease has so far seemed to be unable to spread further in that village, where the cold due to the altitude,

is the one notable difference from all the other villages. It is common, when the disease attacks a new family, incomers, for all ages from grandparents to the last baby to be showing some stage of it simultaneously.

What does affect the spread of the disease rather than age is social position, viewed as the wearing of shoes to shop and office in comparison with bare feet in the forest cultivation. The comparison implies the accompanying differences between heavy ankylostome infection and anaemia, with poor though bulky feeding, and no hookworm, good blood condition and varied diet.

Mode of Infection and Transmission.

There is a point that emphasises the synonymity of cuchipe with Yaws in the constant story of the beginning of the disease that is almost a refrain:- "Picadura de mosca - me resulto una llaga": "A fly bit me and made an ulcer". The ulcer in these bare-footed workers is nearly always on the leg or foot. The present series without exception is composed of cases after the development of the primary sore, so that it gives no information about the incubation period, but the general idea of the

patients when they could specify was a month from the insect bite to the development of a papule. Much commoner is the existence of an ulcer for a considerable time and the sudden appearance of the generalised eruption of cuchipe. The people get innumerable insect bites and scratches that heal without further notice, many that get infected and continue as ulcers for prolonged periods without the development of cuchipe, and the proportion of the whole that become the site of origin of an attack of cuchipe is small.

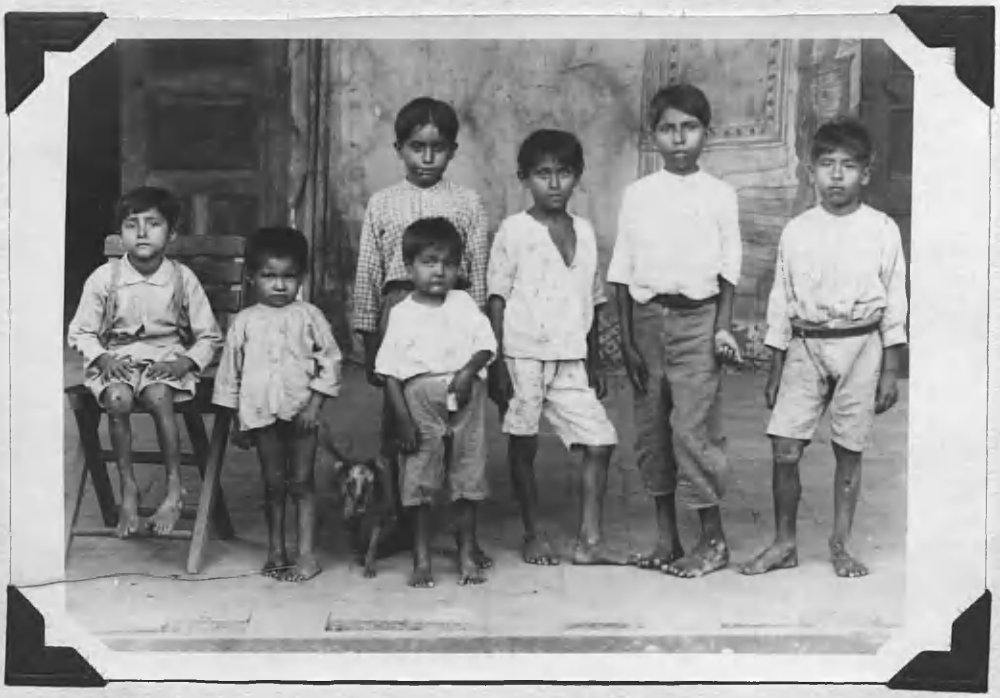
In the majority of cases there is direct infection of an open sore with material from a Yaw. There are ample opportunities for contagion to take place in the bodily contact of hut life, the sharing of bed and blanket. Those cases which do not admit the possibility of direct infection have been exposed to infection by the dust of the floors on which they have slept after occupation by other cases of the disease. A very fruitful source of direct transmission is the school life of the children. Entering a school in the village of Shapaja on the Huallaga, I took twenty-one children of forty present for immediate treatment as secondary cases, and the really bad cases were

absent from school because they could not sit, or write, or walk, or were otherwise incapacitated by the disease.

In a number of cases there is indirect transmission of the disease by insect bite and inoculation of infective material from a case of cuchipe. This gives rise to an itching papule at the site of the bite, followed later by the appearance of the generalised eruption. Very often such a case cannot specify the occasion of the original infection since insect-bites and itching papules are daily occurrences and there was no primary sore noticed.

Transmission by mother to child before birth or by the milk does not appear to occur. In this region nearly every ailment, includion malaria, to which the sucking child is subject, and especially every kind of eczematous eruption, is attributed to the mother's milk. It is therefore not without significance that no such theory is held about cuchipe.

In the present series the proportion of males to females is 2.7 to one, and that is not an unfair estimate of the general condition among adults and children. It is possible to say that no schoolboy in the Huallaga escapes cuchipe, but a proportion



Two groups of schoolboys. Secondary stage and sequelae.

of the girls do. The explanation probably goes no further than the greater liability of the boys to abrasions and contagion one from another in their play.

Yaws as a true pathological entity separate from syphilis is almost a new study, dating from the discovery of its causal organism in 1905. Castellani succeeded in that year in demonstrating from Yaws tissues an organism closely resembling the spirochaete of syphilis, to which he gave the name Treponema pertenue castellani. Its length is 7μ with seven regularly arranged coils, typical of this organism and of the T. pallidum of syphilis, from which it is at present morphologically indistinguishable. It multiplies by increasing in length to 14μ and splitting across. It was first cultivated by Noguchi in ascitic fluid with fresh animal tissue and later by Hata in horse serum under strictly anaerobic conditions. It occurs in the serum exuded on incising a young papule, and is best studied by the method of dark ground illumination. Otherwise where facilities are restricted, it can be recognised by prolonged staining with Giemsa's stain or by making films with Indian ink.

Since the discovery of T.pertenue the greatest advance in the study of the organism and of the etiology of the disease has been the work of Schobl on experimental inoculation of Philippine monkeys. This worker has found in the Philippine monkey an animal highly susceptible to Yaws, showing a variety of clinical lesions produced by inoculation, that are anatomically and clinically identical with the experimental results in human volunteers, as regards both early and late manifestations. (26)

Pathology.

The characteristic lesions are skin lesions, small, raised, suppurative. There is a resemblance of syphilis in the occurrence of an initial lesion at the site of inoculation and later generalisation showing phases that can be compared to secondary and tertiary, though not clearly demarcated.

The primary lesion is known as "cuchipe madre" or mother Yaw by the people in Huallaga, whether they have taken it from the familiar "madre huba" or as I suppose from their own observation of the course of the disease. When it results from inoculation by an insect in healthy skin, it is a single itching papule of 2 cm. diameter. When it

begins in, or breaks down into an ulcer, it leaves after healing under local treatment, a very obvious blue-white scar.

The generalised eruption or secondary manifestations begin with patches described by the patient as "escamosa", dry hard and scaly patches on the skin with fine desquamation, that frequently appear first on the forehead. The rash makes its appearance as a definite eruption, and always the same. It is a crop of little raised spots, which become scaly, raised like a half-nut, bright red in colour, and arranged in little groups. A sero-purulent discharge exudes from the surface of a certain number of these papules, and the others retrocede. Those that remain become covered with a hard scab, circular, greenish-yellow in colour, up to an inch in diameter and standing anything up to half-an-inch above the skin. It is formed by the growth of the papule up from the deep layers of the skin, causing the horny layer to necrose over its summit and to split.

In its fully developed state it resembles nothing more than a limpet fast to a rock. While this is the common lesion, there is a great variety

of forms seen among secondary eruptions. This stage of the disease is rarely if ever found beginning on mucous membrane, though from adjacent skin it frequently affects it, as for instance, at the corners of the mouth and nostrils, and on both male and female genital organs.

The later manifestations beginning while the eruption is in full development in many cases, show most commonly on the soles of the feet and palms of the hands. In these regions there appear a keratosis with fissuring apart from, as well as along with, the bursting of painful Yaws bound down by the tough skin. There may be serpiginous ulcers of cartilage and bone.

Later still, and it may be years after the disappearance of the eruption, although in this series there is one case at twelve years of age, there may occur an ulcerative rhinopharyngitis, which beginning with a chronic ulcer of the nasal cartilage, goes on to destruction of the nasal septum and the formation of granulomatous masses in the pharynx and palate, and almost complete loss of voice.

Fifteen cases of this group are of this nature at various stages and are believed to be cases of Yaws. Tumours of a fibrous nature occur in a few cases in the neighbourhood of joints, and occasionally hot and painful nodes on the long bones and on the phalanges, which remain as non-painful thickenings. There may be a rarefying process in the long bones.

Cases have been described dealing with the evidence for changes in the central nervous system, analagous to those of neuro-syphilis, but never yet in cases in which it has been possible to exclude syphilis.

Primary sore and secondary eruption in same case.

Laja or plantar keratosis.

Keratosis of palm.

Fibrous nodule in region of hip-joint. Same case.

Symptoms and Course.

The clinical course of cuchipe, variable within limits in time, is remarkably constant in character. All cases are seen in one or more of three stages. These are an initial stage when the disease is localised to the "cuchipe madre" or mother Yaw, a later stage when the lesions of the skin demonstrate a generalisation of the infection, and, overlapping this stage and lasting long after it, there are complications and sequelae in untreated cases. This has a noticeable correspondence with the manifestation of syphilis in primary, second and tertiary phases, further emphasised by the close similarity between the causal organisms.

In the case of Yaws, however, one cannot say that there is any clear cut interval between the stages. Actually it is not unknown, to get all three stages in some form present simultaneously in one individual, but it is still true that their appearance in such a case has followed the usual line of progress. Similarly it is not possible to define a narrow fixed period for each stage. The duration of each is variable, especially the third

stage. The first and second stages vary within limits certainly that are not wide, yet vary they do, according to a number of factors difficult to reduce to calculation. They may be comprehended in the mention of the existence of previous disease, such as hookworm infection and anaemia, and of a mode of life low as to hygienic conditions and poor as to nourishment.

Initial Stage.

From the time of infection to the appearance of the primary lesion there is an incubation period that is definitely different for different cases. Here it has resulted within three weeks of infection and it has been seen to develop when the case has been two months away from infection. In the majority of cases there is no notice taken of any constitutional disturbance, either because there is none, or because it passes as a familiar slight attack of terciana (malaria) or of gripe ('flu). A few cases complain of general discomfort similar to that produced by these two causes, and consisting of malestar, slight fever, diarrhoea and pain in the back and the bones.

With or without these symptoms the primary lesion, in those cases where it is perceptible and can be distinguished from numerous sores, appears as a single papule whose diameter is between two and seven centimetres. Whether papule or pre-existing ulcer be the lesion at the site of inoculation, there is invariably a great deal of itching and inflammation, but no induration. There is no part of the body covered by skin on which it may not occur, but a distinct majority of cases get it on the lower part of the leg. This is particularly true of the males, whose bare legs are seldom without a breach of surface continuity owing to their working or walking through forest growth. Women not infrequently get it on the hands and occasionally on the face. Their hands are liable to be the site of inoculation because of the handling of domestic utensils of earthenware, producing abrasions, and the handling of infectious children and clothes producing infection thereof. On the face it probably occurs from fondling infected children.

A primary sore may occur on the mouth of a baby from a sore on the breast of the mother, and

a case has been met with here where the mother got it on the breast from the face of her previously infected baby. In other cases the primary sore has occurred on the back of the neck and even under the lower jaw. One case of cuchipe in this series had the primary lesion on the labium minus, a situation in which it is calculated to be found in one per cent of cases.

When the primary lesion is a papule it is apt to persist throughout the period of the generalised eruption and to be still visible after a year. When it breaks down into an ulcer, or has been imposed on a pre-existing ulcer, it appears to have no tendency to heal nor to increase in size. Under native treatment with caustic applications it heals, leaving invariably a blueish - white scar, a smooth area of some six centimetres by three, that is very noticeable against the dark copper of the healthy skin.

It is usual to write of the primary sore, but it might be more correct, at least in some cases, to write of primary sores, for there are cases that may be judged to present more than one.

Generalised Stage.

From four weeks to a maximum of three months after the appearance of the primary lesion, there breaks out an eruption of the typical cuchipe. The recently published conclusion of Schobl is that the skin is the focus from which the treponemas are disseminated into the surrounding tissues or metastatically into remote parts of the body. The finding of Treponema pertenue in the lymph glands corresponding to active lesions indicates that the route by which the infection becomes generalised is through the lymphatics. (26)

The patient first notices that there is a dryness and scaliness or patches of skin. It is not easily to be noted by sight unless there be a floury desquamation, but both patient and examiner are aware of the patches by touch, and a magnifying glass shows up the scales of desquamating skin. These patches are irregularly scattered over the body, but especially on the forehead, and are more or less circular areas of all sizes.

Within a week there is a tiny papule in each patch, forming a numerous crop all over the body. It is this, the typical early eruption, that has given the name of Framboesia to the disease, but in

Secondary eruption limited to nose and upper lip.

Atypical secondary papules. Case 1.

Case 1. again.

the Huallaga region the raspberry is unknown and this synonym is never heard.

There are cases where the crop takes on the circular form of ringworm and of psoriasis. It may not go beyond the appearance of scaly patches, or it may go beyond papule formation and become a fumigating mass that is here called "verruga".

There are cases where one or more of these variations are present along with the papule crop. In any case the eruption is always itchy. It is sometimes so very itchy that it causes a local subdivision of the disease into "sisu-cuchipe" when the papules are small and very itchy, and "tosino-cuchipe" when they are large and less itchy.

When the papules occur on such parts of the body as the margin of the lip and of the eyelid, near the anus, at the bend of the elbow, and in the inguinal fold, and between the fingers, others practically always develop symmetrically opposite. This suggests that there is a local self-inoculation possible early in the generalised stage. If this is so, there is nothing impossible in the existence of more than one primary sore, and the occurrence of repeated eruptions during the course of the first

one, a thing which is met with clinically.

Unlike the primary sore, the eruption is met with on mucous membranes, but probably in every case by invasion from the muco-cutaneous junction. A particularly nasty appearance in children results when the angles of the mouth, the openings of the nostrils and the margins of the eyelids are covered with dirty rough greenish crusts. The consequences as regards conjunctivitis, obstructed nasal breathing and difficulty in eating are sufficiently serious. Much discomfort also leading to bad habits, arise when the anal and genital regions are the sites of sores, and female children with the papules on the labia suffer considerably from the irritation produced by the urine. It is a little difficult to reconcile this fact with the insensibility of the papule in other parts even to the touch of acid, but possibly the continual scalding and friction on and around the Yaw explain the difference. In any case, there is no doubt of the fact or of its importance as regards the formation of bad habits.

The dirty rough greenish crusts referred to are the later development of the crop of papules, but fortunately are less numerous. All the papules do

not go on to this stage, which is the stage characteristic in the public mind of the disease cuchipe. When each papule has reached a point when it shows a head in the form of a yellow spot of cheesy matter in the centre of its bright red top, it may proceed to dry up and diminish, which is the end of a good part of the eruption, or it may go on to form scabs. In the latter case the horny layer of the surface skin gives way and the papule secretes on its surface a yellow, serous fluid that dries as a cap over the papule. This is increased layer by layer until a thick corrugated crust is formed, as dirty looking a scab as one sees in skin diseases. This is the complete limpet-like lesion.

The persistence of these lesions is very variable. Individually they last a matter of weeks, and cease to increase in size after two to three weeks. When they shrink and drop off they leave a dark stain on the underlying skin which may mark the site years later. They do not leave a scar as an ulcer does. As an eruption the stage of generalisation is over in a year in the majority of cases, but it may pass in as short a time as two

months, or by repeated crops last as long as two years. The common tale with cuchipe in the area of the Huallaga is that, by local application of "piedra lipe" (copper sulphate) and the caustic juice of certain fruits, and the taking of infusions of sarsa or cedar-bark, the disease is cured in a year, but "laja" develops and persists. This indicates complete inactivity on the part of the treatment, since the time is the same in untreated cases, and since all drugs that cure the eruption also cure the foot condition.

This condition of "laja" which defies the herbalists of the Huallaga may be considered as either a late manifestation of the second stage, or as an early sequel. It is a condition of the sole of the foot that may develop along with the eruption, or three, five, nine or twelve years later. It is seen to arise from a typical Yaw on the sole of the foot in a few cases, but so seldom that it must be considered to develop as a skin condition apart from the formation of papules. This is the more obvious from its persistence long after every other sign of Yaws has disappeared, and from its frequent first development long after

Laja. Case 20.

Laja and burst papule at root of great toe.

Case 21.

the papules have cleared up.

The appearance is very much like that of the skin of an old potato, worm-eaten in parts and the outer skin curling up at the edges of fissures. The horny layer of the skin of the soles of the feet is so split and curling back along branching lines of fissures throughout the length of the foot, and circular, shallow holes are found in it, deepening towards their centre, and one to two centimetres in diameter. These latter occur most frequently on the under aspect of the heel and on the ball of the great toe, the pressure areas. In some cases there is only a desquamation of the whole horny layer of the sole of the foot in a multitude of circular scales, about three millimetres in diameters, so numerous and shing as to make the sole of the foot resemble snakeskin. The deeper fissures are not unlike the condition of "hacks" of the hands common in domestic farmworkers in cold weather, and the condition is equally incapacitating. It is without inflammation and its development is so painless as to pass unnoticed, but as an economic factor it is perhaps more important than all the rest of the disease.

When well developed it incapacitates the men for their only work, agriculture and cargo-bearing, because they cannot walk in the forest without suffering and difficulty.

The people of this area care very little for cuchipe, but they fear laja. They have a notion that cuchipe has a personality that listens to and marks with bitter disapproval any expression of dislike to itself, and that it persecutes with malevolent persistence the person who earns that disapproval. Consequently they do not attempt to avoid the contagious victims of the disease lest they offend it. They content themselves with knowing that they can "cure" cuchipe to their own satisfaction in somewhere about a year, but Laja they know they have no hope of curing and for it they seek treatment by injections.

In this region one gets the impression that more than half of all untreated cases of cuchipe develop laja. The present series includes fifty cases of it.

In a few of these cases there is also a desquamation of the skin of the palms, but the patient takes little notice of it, as not causing the same inconvenience.

Throughout this stage of generalisation the Wassermann Reaction is positive.

Complications and Sequelae.

The most terrible condition that has to be considered as a sequel of untreated cuchipe is a destructive ulcerative rhinopharyngitis that resembles the condition described under the name of gangosa as a probable result of Yaws. It has to be distinguished from ulcerative lesions of the same parts due to syphilis, leprosy, leishmaniasis americana, tubercular and malignant ulceration, and blastomycosis.

Here in every case noted it has begun as an ulcer of the nasal septum, not of the palate. Therein it agrees with the description given by Ayuyao of sixty-two cases in the Philippine Islands. (27) It occurs both in children and in adults. Ayuyao's series represents each decade from the first to the sixth. In the present series the youngest is a lad of twelve.

At first and for as long as a year the condition is a dryness and itching with slight dull burning pain, originating in a congested area of the mucous membrane covering the nasal cartilage

on one side. Some of the cases definitely attribute its beginning to the time of the ulcer that was the primary Yaw, and are convinced that they themselves conveyed the infection from ulcer to nose.

When ulceration of the septum begins there is no pain, but neither is there any diminishing of normal sensation. The early dryness gives place to a profuse and foul-smelling discharge as the ulcerative process proceeds to destroy cartilage and bone.

First there is perforation of the cartilaginous septum, leaving intact the soft tissue in front from tip of nose to lip. The perforation deepens inwards so that the eroded cartilage presents a deeply concave anterior edge. Both this edge and the whole interior of the nasal cavity are covered with yellow crusts formed of oozing serum and pus. The crusts are easily removed in flakes and the underlying tissues bleed very readily. At the same time granulomatous masses, less vascular in appearance than the normal mucous membrane, having an almost blue-gray tinge, develop on the palate and fauces, without crusts and without causing pain.

The uvula becomes covered with tiny granules and gradually disappears as these come away from tip to base. Swallowing may be difficult and the voice husky. Breathing is interfered with to such an extent that the patient becomes a nuisance to others, especially at night, from the noise of his respiration. Ulceration extends to the upper lip, with the formation of a long, narrow, oval erosion, very shallow, with granulating base and crusts of serous exudate, and apt to bleed at a touch. Within a year of noting the nasal ulcer the septum may be destroyed.

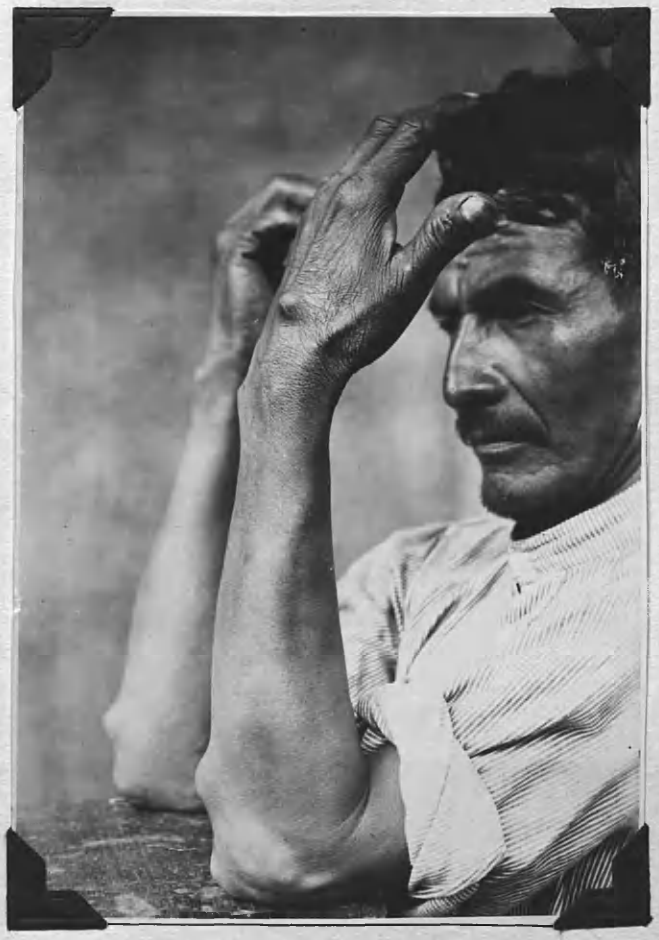
This is a somewhat different picture from that commonly given of gangosa, which describes an ulcer first on the palate and finally only the upper lip spared across the chasm left by the destruction of the roof of the mouth. It is remarkable that for a very long period, when extensive ulceration has taken place inside the nose, a slight redness of the tip, with swelling of the bridge may be all that can be noted externally.

This ulcerative rhinopharyngitis is the most serious sequel that can be ascribed to cuchipe. Next to it is the persistence of chronic ulcers,

commonly on the lower part of the leg, not infrequently on the forearm. They cause little pain but are apt to work deeper insidiously until cartilage and bone are damaged. Where the case is less extreme they still cause very serious damage and incapacity by the extent of contraction of scar tissue.

Not so frequent, less easy to understand and less likely to be reported by the patient, are fibrous tumours that develop in the neighbourhood of joints. They are quite painless, and from their situation are the same as those described as juxta-articular nodules. They occur over the olecranon process of the ulna, at the back of the wrist joint, over the malleoli and on the palm of the hand over the heads of the metacarpals. They vary in size from that of a marble (two such in the palm of the hand in one case) to the size of a golf-ball at the knee, and rarely cause inconvenience. They occur irrespective of age and are encountered even before the secondary eruption has entirely cleared up.

On the other hand there is a sequel in the form of nodule formation that is extremely painful. Swellings, hot and hard, with temperature raised



Juxta-articular nodules. Case 28.

Thickening of first phalanx of middle finger.

Case 25.

Juxta-articular nodules.

and all the appearance of abscess formation below the periosteum, may develop in the long bones of the arm and leg and occasionally of the fingers. Fortunately the acute stage subsides without suppuration, but hard nodes remain.

When this acute inflammation is diffused as an osteitis of the long bones, it may leave permanent deformity of which the extreme example is the sabre deformity of the anterior border of the tibia. A rarefying process is found to be at work in the long bones affected, shown up in X-ray photographs and clinically suggested by the occurrence of spontaneous fractures. Polak in Java found that this lesion could be distinguished from that of tertiary syphilis only by the history and by X-ray examination, when instead of the thickening characteristic of syphilis he found the rarefaction in the cases with a history of Yaws. He has called attention to the consequent difficult of differentiating between the two conditions in the case of young children, because a rarefaction instead of thickening may be found in the case of congenital syphilis. (28)

The condition of symmetrical bony growths on the sides of the nose, described under the name of goundou, has not so far been met with as a result

of cuchipe in this area. In Brazil Araujo in his series described six cases of goundou but with no history of Yaws.

Immunity and Superinfection.

Certain facts in the course of cuchipe are so constant that they are counted on popularly. These are:-

1. There may be successive crops of the papules in the early stage of generalisation.

2. Once this stage has reached the formation of typical crusted cuchipe it goes ahead quietly without exacerbations equal to the first general eruption.

3. When this stage has run its course of six months to a year, it never recurs in the same individual.

These facts if accepted, indicate a probability that superinfection is possible up to the stage of advanced generalisation and that thereafter there is a complete immunity to further attack.

The interference with the due development of the generalised stage by incomplete medical treatment results in relapse. When this occurs many months later, it may or may not be a new infection, but it is never comparable to the first attack in

severity. It appears to be a fair deduction that when the stage of generalisation is interrupted, it leaves the patient with a degree of immunity corresponding to the duration and virulence of his attack, but not completely developed. A case therefore which has been treated and cured in the initial stage will always be liable to reinfection.

In this connection it is of interest to note the four experiments of Lacy and Sellards. (29)

Of four Yaws cases treated with salvarsan, and inoculated six months later with the virus, one developed a typical Yaws lesion and the others were atypical. Again, treated with salvarsan, until all signs had disappeared and the Wassermann reaction was negative, and again inoculated with the virus, the result was the same. The same case developed a typical Yaws lesion. This case which on each occasion proved susceptible to reinfection, had had the disease only three months when first treated, while the others had had it for a much longer time.

Many variations of this controlled experiment are continually met with in practice, in the form of the disappointment of those cases who return cured to their homes only to find the lesions developing

again six months or a year later. Had the second stage in these cases been allowed to go on for a longer time, probably complete immunity would have been developed.

In his animal experiments Schobl, working with the Philippine monkey, has investigated the effects of intradermal inoculation of Yaws material. In the animals which developed only a local Yaw, reinoculation up to the fifth month produced a local lesion containing the treponema. From six months onwards for two and a half years the animals were immune to reinfection. Further, of animals treated in the first two months of the original disease, all were susceptible to reinfection in the seventh month, while those which were treated after the disease had run a longer course were immune. These animals which from the first inoculation developed secondary manifestations were immune from the superinfection as soon as the eruption appeared. (30)

This is better than what occurs in practice with the human subject. The secondary eruption has to be present for some time before immunity is acquired. The time is not the same for all subjects

and is so far undetermined.

Schobl from this study decides that animals could be rendered immune without the appearance of Yaws in the skin, by intradermal inoculation with the treponema, and further experiments to investigate the point brings him to the conclusion that immunity is developed in the subcutaneous tissues, and that it resembles the process of immunisation from small pox by vaccination.

Diagnosis.

The first point in the diagnosis of cuchipe is that of residence in an endemic area or contact with a case of the disease. Thereafter in those cases which present the lesions of the primary and secondary stages, the diagnosis is reduced to a decision between syphilis and cuchipe. In the latter stage of complications and sequelae the matter is more difficult for the possibilities extend to several other conditions. This has one particularly serious aspect in the resemblance of the nasal ulceration to leprosy. As the popular fear of leprosy is only equalled by the dread of phthisis, and a suspected case has to be sent many days' journey to the leper colony at Iquitos, it is a serious matter for the patient.

Diagnostic features of cuchipe.

(a) Initial lesion. A painless but itching granulomatous tumour, inflamed but not indurated, occurring on the lower limbs of a person from an endemic area immediately suggests cuchipe. The size is regularly more than two and up to seven centimetres in diameter. It probably never occurs

on mucous membrane, but may occur on the skin of any part of the body. It may have had its existence as long as three months, but if the lesion is the primary sore of cuchipe, by the end of that period there will be signs of a secondary eruption.

The treponema is found in the serum exuded on scratching lightly the surface of the tumour, preferably near the circumference. The Wassermann reaction at this stage in cases of Yaws is frequently positive but is not constant.

(b) Generalised stage. The typical efflorescent eruption is very constant and is diagnostic. Whether the individual papules be of the larger or smaller type, and although there may be both vegetating and non-vegetating forms varying from forms of roseola and psoriasis to verruga, and at all stages of maturity, yet the irregular distribution of itchy crusted papules is quite definite and characteristic. When the eruption is accompanied as it so frequently is, by the desquamation of the plantar skin, with or without the existence of papules of the soles of the feet, the condition is unquestionably cuchipe. Generally either the primary lesion itself or the scar left on healing,

can be encountered, together with a history of insect bite or pre-existing ulcer at that spot.

(c) Stage of sequelae. Here it is so far impossible to specify any condition that enables one to declare that it is cuchipe and cuchipe only, unless this be accepted in the case of juxta-articular nodes. Even the clear history of a secondary eruption at some period before, does not enable one to put aside the possibility of other causes for bone-changes, chronic progressive ulcers and rhinopharyngitis.

Thickening of the ends of long bones, lower end of tibia and fibula and femur, and the pear-shaped swellings of the phalanges, are similar to the lesions produced by syphilis and tuberculosis.

Chronic ulcers of the limbs not infrequently occur along with varicosity of the veins, so that they might be varicose ulcers.

Ordinary sepsis in the case of many wounds becomes so chronic and prolonged that the resulting ulcer has the same appearance as the sequel to cuchipe. Syphilis produces exactly the same kind of serpiginous punched-out ulcer as that which in cuchipe may go on to destroy cartilage and bone.

These two conditions, bone-changes and ulcers, respond so rapidly to treatment with neosalvarsan, as to enable the diagnosis to be reduced by the effect of treatment, to a decision between cuchipe and syphilis.

It is not so with the most dreaded complication, the ulcerative rhinopharyngitis. Beginning with ulceration of the nasal septum, and later of the upper lip and palate, with granulations of the fauces and pharynx, the condition as encountered here, does not even conform to the usual description of gangosa. It does resemble what Ayuyao in the Philippine Islands describes as tertiary manifestations of Yaws. (27) The other diseases which produce a like result are syphilis, leprosy, tuberculosis, malignant ulceration, leishmaniasis americana, and blastomycosis.

Treatment with neosalvarsan has not the dramatic effect it has in the other forms of cuchipe, so that the matter is not thereby reduced to a decision between syphilis and cuchipe. Antimony tartrate also fails to make much impression, so that it is not possible to decide therefrom in favour of leishmaniasis. To take these six conditions in turn:-

From syphilis this sequel of cuchipe cannot be distinguished except on such ground as the patient's history provides.

From leprosy it can be distinguished. There is no history of contact with obvious leprosy, and it may be noted that the people are not slow but rather over-hasty in suspecting and denouncing leprosy. There are no areas of anaesthesia in the lesion or elsewhere in the body. No acid-fast bacilli are found in the abundant discharge at any stage of the process of ulceration, whereas in leprosy they would be abundant. The Wassermann reaction would not help, being positive in leprosy.

From tuberculosis it may be distinguished by the history, the absence of acid-fast bacilli and of signs of tuberculosis in the lungs or elsewhere, and of reaction to tuberculin. Also the general condition of the patient after years of ulceration is extraordinarily good. One would expect greater emaciation after years of tubercular ulceration.

From malignant ulceration it may be distinguished by microscopic examination of a piece of the tissue and by the limitation of the ulcerative process even after years to the mucous surfaces of nose and mouth.

Ulceration of upper lip in case of ulcerative Rhinopharyngitis. Case 36.

Similar ulceration which got rapidly worse treated with 914, but healed completely with Tartar emetic and Neostibosan.

Also ulceration as extensive as in this condition would, if malignant, surely reduce rapidly and seriously the general condition.

From blastomycosis it may be distinguished by the fact that the tongue is unaffected and by the absence in the discharge of the yeast-like organism of that disease.

From leishmaniasis americana it is exceedingly difficult to distinguish this condition. The only grounds are negatives. There is no response to antimony treatment. There is no ulceration of the tongue. The leishman-donovan body cannot be found after repeated efforts. There have never been described typical cases of leishmaniasis in the area, although the cutaneous disease under the name of uta has long been known up on the sierra. But it is more than possible that it does exist if it were looked for in the Huallaga area also, and even the history of Yaws does not affect the possibility of uta also. Cases of nasal ulceration from infection conveyed from a leg ulcer have been encountered in cases who never had Yaws, and in one case who had the ulcer ten years when he developed cuchipe.

Allegations and observations in support of the identity of syphilis with cuchipe or Yaws.

The confusion which has lasted between Yaws and syphilis since the fifteenth century is reflected in the uncertainty manifested in the publications of these days.

Many writers, and especially North American writers, make no attempt to distinguish them, but deal with the two conditions under the name of treponematosis. They do not suggest that classical syphilis as it may be seen in almost the whole world is likely to be confused with the description of Yaws. They believe that Yaws is a primitive form of syphilis, limited to indigenous races where no treatment has ever modified the development of the disease.

Butler for example, believes that his clinical work in Haiti proves that Yaws is a kind of primitive syphilis. He thinks that what the African slaves brought over to America was the untreated syphilis they got from Europeans. (31)

The resemblance between the conditions is close. The causal organism is morphologically indistinguishable. The clinical course has marked similarity. Each has an initial lesion and after a lapse of some weeks a generalised manifestation concentrated in the skin. Months and years later there are sequelae,

many of which are similar in both conditions. The ulcerativelesions of the later stages are indistinguishable. The Wassermann reaction behaves alike in both. The same treatment with arsenical compounds and with bismuth is dramatically successful in the earlier stages and less effective in the latest stages of both.

In this connection importance has to be given to the reports from many parts of the tropics of the non-existence of classical syphilis in populations where classical Yaws is universal. A striking example is Samoa. Ritchie reports that in Samoa Yaws attacks every child before the age of two, that adults never show primary and secondary lesions, and that syphilis is practically unknown. He concludes that Yaws in childhood gives permanent protection against syphilis. (32)

There is a certain body of opinion from Yaws areas that syphilis is less than elsewhere, markedly less. The present case of cuchipe in the Huallaga area adds a grain of evidence thereto. Syphilis is very rare. In four years I have seen only four cases of primary syphilitic chancre, three of such definite secondary symptoms as eruptions and ulcers

of the mouth, one of ulceration of the pharynx and perforation of the palate with an indefinite history of syphilis, and two of congenital syphilis. Of these ten cases only one came from the endemic cuchipe area. Four from a near village were all due to one untreated case, and the rest were in the town of Moyobamba.

Comparing this with experience of general practice in an English seaport, South Shields, where only a tiny fraction of the cases found their way to a private consulting room, I find that I saw more cases of syphilis in a month there than in four years here. It is true that here the Wassermann reaction was not available, but the comparison is with an exactly similar condition at home, namely syphilis that can be diagnosed with some assurance before the test is applied. One fault which might appear to make the comparison valueless can be disregarded. It might be said that a seaport town would show an unduly large number of cases of syphilis, and that a country area ought to be taken for comparison. Even then there is a marked difference, but it has to be noted that no country district at home, and not even the seaport towns,

can compare with this region for the propagation of gonorrhoea. It is a case therefore of excessive prevalence all over the cuchipe area, of gonorrhoea, and therefore of all the necessary facilities for the spread of venereal diseases, and syphilis present, but not prevalent. It is unable apparently to get a footing and propagate itself.

Allegations and observations against the identity of syphilis with cuchipe or Yaws.

The belief that syphilis and Yaws are separate and distinct diseases has had a definite foundation dating from the historic experiments of Charlouis in 1881. He inoculated with syphilis a negro suffering from typical Yaws and there resulted a typical primary syphilitic sore duly followed by the secondary eruption. The belief was strengthened by the work of Castellani in 1905 when inoculation of monkeys established the etiology of Yaws.

It is true that Powell throws doubt on the scientific value of Charlouis' experiments, because they were done in pre-antiseptic days, but Powell himself has reported two cases in which he got syphilis superimposed on Yaws. Since then, many observers have reported cases, as for example

Hanschell. (33)

Manson-Bahr declares, "Antecedent syphilis certainly does not confer immunity to Yaws, nor antecedent Yaws to syphilis". (34)

Macleod, of the London School of Tropical Medicine and Hygiene, makes the assertion even more definite:- "There is no connection between Yaws and syphilis".

Clinically in the cases of cuchipe examined here and in conformity with the descriptions of Yaws lesions published, one is able to indicate certain features of the lesions that seem to be characteristic of the one or of the other disease.

Initial Lesion.

Yaws. Its site is rarely genital (1% of cases), commonly on the lower limbs; never on mucous membrane: always itchy and inflamed but not indurated: diameter two to seven centimetres; if papule persistent; if ulcer slow to heal and leaving a scar, mercury ineffective.

Syphilis. Its site is nearly always genital or on the mucous membrane of the mouth; it is neither itchy nor inflamed but induration is constant and marked; diameter is rarely more than a centi-

metre; it heals spontaneously without leaving a scar; mercury has a curative effect.

Generalised Stage.

Yaws. The efflorescent eruption is typical. Desquamation of plantar skin is confirmatory. The eruption is itchy. Mercury ineffective.

Syphilis. Rarely a crop of paules. More limited distribution. No itching. Frequent lesions (ulcerative) of mucous membranes. Eye complications. Mercury has a curative effect.

Stage of Sequelae.

In this stage it is impossible to tabulate differences. Such late involvement of the nervous system as tabes dorsalis and general paralysis are not known to occur in Yaws nor are they encountered in the cuchipe region. Visceral lesions are being described as occurring in Yaws, but not with the constancy and certainty of the syphilitic effects in liver, heart and aorta.

A very thorough survey of the relationship of Yaws to syphilis is that of Jahnel and Lange. (35) They make a detailed investigation and criticism of

accepted facts and deductions, and show that many of these are insufficiently supported or have been too readily justified. For instance, they find that the evidence does not justify the assertion that Yaws came to South America with the importation of African slaves, and if they are right, then Butler's belief that it was European syphilis that became Yaws in the persons of the African slaves has to be discounted. These writers find that they cannot sustain any theory that considers Yaws as a native tropical form of syphilis, or that it has changed its character in certain races and climates. Accumulating all the available evidence, they give their opinion that where Yaws occurs, Yaws it continues to be, and where syphilis, syphilis, and that only the secondary crop of crusted papules is definitely distinguishable as Yaws and not syphilis.

These are fairly safe conclusions, but it is to be expected that more ample and more accurate evidence will be available when experimental work overcomes its difficulties and avoids its fallacies.

The presence of classical Yaws endemic in a region and the absence from it of classical syphilis may be cause and effect, but the case is not yet

proved. The present position may be summed up as follows:-

1. Yaws and syphilis are two perfectly distinct diseases.

2. There is certain amount of evidence to be confirmed or refuted, that indicates that the immunity of Yaws cases to later Yaws protects a community though not every individual against the spread of syphilis.

The second statement suggests that there is some kinship between the two diseases, and this derives some support from the further work of Jahnel and Lange, in quest of a relationship within the terms of their definite conclusion that Yaws and syphilis are distinct diseases. They used strains of Yaws virus kept in animals to attempt infection of cases of tertiary (neuro) syphilis. Cases of disseminated sclerosis took the disease very slightly. Twenty-five cases of G.P.I. with three different strains of virus, showed no infection whatever, nor did they take when inoculated from the primary lesion of the cases of disseminated sclerosis. This resistance of general paralytics leads the authors to deduce from all the known facts,

a probability that there is a group of related viruses, whose extreme members are classical syphilis and typical Yaws, (that is, Yaws with the typical secondary efflorescence), and that between them are ranged the atypical Yaws and tropical or indigenous native syphilis.

The Wassermann reaction is not a helpful factor in the differential diagnosis between syphilis and Yaws. It is indefinite in the initial stage of Yaws, and markedly positive in the stage of generalisation. It may become negative on treatment or spontaneous healing.

Schobl, from his experimental work makes this statement:- "The reappearance of a positive Wassermann reaction can be produced in healed and cured animals without recurrence of Yaws lesions, and therefore a positive Wassermann reaction does not necessarily mean the existence of Treponema pertenue in the body organism or the animal". (26)

Treatment.

1. Prophylactic.

This has to be based on the fact that the disease spreads by contagion through an abrasion of the skin and not through healthy skin. The ideal would be the isolation of the infected, but since that is never practicable in the circumstances where it is most desirable, an approach to it is made by isolating the lesions of the infected.

This is best secured by the speedy and early treatment of the contagious sores. Thorough treatment is what should be aimed at, but the expense may be prohibitive, or there may not be sufficient time available to carry out in each village the repeated treatments necessary to complete cure. When this is the case, there is no question that prophylaxis is very efficiently achieved by the amount of treatment on one occasion that suffices to eliminate the active secondary cases. If this could be done throughout an area like the Huallaga region, down the river village by village, a very valuable restriction of the spread of the disease would be produced. Todd reports on the value of Halarsol in this connection, as giving useful prophylaxis at a

tenth of the cost of the salvarsan derivatives. (36)

Apart from medicinal treatment as a principal prophylactic measure, the simple isolation of the contagious lesion is to be secured by dressing the sores with antiseptic ointments, of which the easiest to make on the spot is one of the combinations of zinc oxide and boracic acid. Especially important is it that this should be attended to in the schools. It would be better prophylaxis to have the secondary cases among children admitted to school under special vigilance, for the purpose of having their sores dressed as they will never be at home, than simply to forbid their attendance.

This isolation of the infection can never be complete. It is therefore of equal importance to protect the wounds and abrasions of the non-infected, both against direct contact with Yaws lesions and against inoculation by flies. This entails an effort to educate the people to an understanding of the need for dressing their ulcers, and for using the touch of tincture of iodine or of crude alcohol that would prevent every second scratch received in the forest from going on to form a chronic ulcer.

The mode of infection indicates that all the

measures of general hygiene need to be taught and employed. There is need of war on flies and instruction against over-crowding at night. There is need too, to do away with that fear of offending the personality of cuchipe to the extent of not allowing the infected and the healthy to sleep together.

These points simply mean measures against dirt and darkness and bad ventilation in the huts, which the people use only as places to sleep in. Their days they spend in the open, bathed in water and in sunshine. In the huts the infection remains in the dusty surface of the earthen floor. The only effective proceeding in many cases is to burn the old huts, and have all huts white-washed as to walls, and hammered firm or bricked as to floor, so that a daily sweep-out, never dreamt of before, could be insisted on.

Further defence against Yaws is provided by every measure that improves the individual standard of health. One of the first of these is the treatment of hookworm infection and its anaemia.

2. Curative.

The prophylactic measures that refer to the general condition of the patient are a first necessity, also in curative treatment. The dressing of sores, treatment of concurrent disease, abundant nourishing food, and tonic medicines, are together an important element in securing a speedy cure by specific treatment, and in helping to eliminate the debilitating effects of the disease and its complications.

Yaws has been hailed as one of the diseases in tropical medicine where the qualified medical man scores a public success over the curandero or quack specialist in this region in herbal treatments. The latter's stand-by in cuchipe is sarsa, taken in infusions for many weeks, with local caustic applications of vegetable juice (jagua) or of copper sulphate.

The treatment does nothing to shorten the course of the disease. The medical man, on the contrary, certainly has in the arsenical compounds prepared for the treatment of syphilis, a treatment whose effects are most dramatic, especially in the most clamant stage of the disease, the secondary eruption, and in the most incapacitating and most

persistent stage, the keratosis of the feet. Yet one is driven to doubt whether these drugs have been getting a fair chance in the treatment of Yaws, because one finds that disappearance of the secondary rash on administration of the dose recommended in the text books, while often synonymous with curation of the disease, is not invariably so. 0.9 gm. of neosalvarsan into the vein of an adult in the full-blown eruption of cuchipe, will clear up the urgent symptoms as no other drug in any other disease will do, but it does not always guarantee a complete cure. Any chance that the terrible rhinopharyngitis already described, can occur in a case insufficiently treated, is reason enough to make one desire more than the disappearance of the rash.

There is no doubt that neosalvarsan can be so administered as to give complete cure of Yaws or cuchipe, in all but an infinitesimal number of cases that may be called resistent to all arsenical medication. One such case there is in this small series, and Heinemann describes two in Javanese - a boy of seven who resisted eight injections of 0.2 gm. neosalvarsan, and a woman who did not improve after six injections of 0.45 gm. (37)

Here in the case of a man of 22, with only five of the crusted papules, injections of 0.45 gm., 0.6 gm., and 0.6 gm. were necessary to cause slight improvement, but one lesion on the forehead and one in the axilla still refused to yield after further injections of 0.75 gm., 0.75 gm., and 0.9 gm. Nine months later he had a crippling condition of laja on both feet, and bismostab cleared it up.

These cases are so few and far between that they do not affect the estimation of neosalvarsan as the best drug in the treatment of Yaws. As an intravenous injection it will always need particular care, and it may present difficulties of administration in children, but there is only one real objection and one real reason for wanting anything better, and that is the cost of it.

Cuchipe is a disease of poor people at a low cultural level, and frankly indifferent to their own condition as long as it is not painful. Repugnance to the loathesomeness of a Yaws eruption is not sufficiently strong with them to stimulate them to the effort or sacrifice required to pay a high price for treatment, as they certainly would for phthisis.

Only a Government able and willing to spend lavishly can enter on an efficient Yaws campaign armed with 914, and in the many tropical areas where the treatment of Yaws is a small part of the responsibility sustained by missions alone, there are but few of the latter able to afford it so abundantly and so easily as not to feel urgent need of a cheaper, effective treatment. In this case a considerate Department of Public Health provided the neosalvarsan with which treatment was done.

As a substitute mercury naturally would be first thought of, but here the close similarity between syphilis and Yaws is broken, and so much so that, were it not waste of time, mercury's inactivity in Yaws might be used to distinguish between the two diseases. Mercury is no use in Yaws.

At present the substitute on trial is that drug which is superseding mercury in the treatment of syphilis, as being more effective and less toxic. Bismuth was introduced for the treatment of syphilis nine years ago, and its good results have caused it to be tried in Yaws. They have caused also the appearance of a swarm of different preparations from which there still has to emerge one superior to all others and comparable to neosalvarsan.

In the present series the treatment has been with neosalvarsan, but twenty cases have been treated with Bismostab, a Boots' preparation of metallic bismuth in glucose.

Treatment with Neosalvarsan.

The drug is easily soluble in water and should be given intravenously. Only with the greatest reluctance and in circumstances of special difficulty should it ever be given intramuscularly in oil. As an intravenous injection it needs continual wariness and strict aseptic precautions. Distilled water is not available for many workers who have to treat Yaws, but perfectly sound results, without a single case for regret, are got over a large series by the use simply of boiled and filtered water. Patients who suffer from nephritis are not good cases for the treatment, and all anaemic and cardiac cases must get it with caution, and preferably after an endeavour to improve their condition.

The injection should be given bearing in mind the fact that the most experienced doctor may find that the solution is being injected outside the vein when he had no reason to doubt that the needle was inside. It is better to make several needle

punctures that will be forgotten a moment later, than to risk injecting a quantity of a solution that will produce necrosis of the soft tissues, sloughing and ulceration, or at best a very painful swelling of the arm with constitutional disturbance.

In babies the matter is difficult. It is usually impossible to define a vein and impossible to get a child to remain still the necessary time. Neosalvarsan in these cases is better replaced with other preparations. The intramuscular injection in oil will give the curative effect, but at best it causes painful swelling and fever that may last many days, and at worst a deep abscess may result, however sterile the injection.

Children take the drug excellently. An occasional patient within a few moments of the injection feels dizziness with trembling, cold sweat and darkening of the sight. There may be profuse salivation and "the taste of the injection" in the mouth. Even these symptoms may be avoided by giving the injection lying down. A rare case experiences, later in the day of the injection, a feverish reaction not unlike "catheter fever", but the condition passes in an hour or two. More serious

is the arsenical keratosis which may occur apparently as an idiosyncrasy when therapeutic doses have been applied. This requires treatment with sodium thiosulphate. The great majority of cases suffer no inconvenience whatever from the injection.

For cuchipe neosalvarsan is best given in three doses at intervals of a week, a smaller dose first. Secondary lesions and the plantar keratosis are drying up within five days after the first injection, at ten days they are soft blue-red marks on the skin with no scabs, and when the third injection is given there are practically no lesions left.

In children two doses are usually sufficient. Of adults a number not infrequently assume that two are sufficient, when they see the improvement in their condition and consider the difficulties of prolonging for a week the expense of life in the town.

For children under five, the dose given in sterile oil into the gluteal muscle should be 0.15 gm. repeated a week later, a total of 0.3 gm. From five to ten, given intravenously, the total dose is 0.3gm. to 0.6 gm. according to the development of the child. From ten to fifteen the total may be 1 gm. but in the

smaller children a total of 0.3 gm. should first be applied and later treatment regulated by the occurrence of a relapse. A good series in those about the age of puberty is 0.3 gm., 0.3 gm., and 0.45 gm. In adults the series of three injections ranges from a total of 1 gm. up to 3 gm. according to the patient's condition.

A man in good general condition can receive a first injection of 0.9 gm. which may be considered a maximum single dose, without inconvenience, but better treatment is to give him the series 0.6 gm., 0.75 gm., 0.9 gm. An adult can receive a total dosage of 3.15 gm. or the series of six graduated injections at weekly intervals over six weeks.

In nearly all cases of secondary cuchipe the third injection, which is the largest dose, and the costliest, appears almost superfluous even to the patient who get it for nothing. In the absence of facilities for getting the Wassermann reaction as a check on treatment, clinical experience indicates the foregoing as the minimum of treatment with which one can be satisfied - namely, clinical cure and an extra dose beyond it. Only the following up of cases for years will show whether this gives security against the sequelae.

Of 108 cases treated on these lines with neosalvarsan, five only are known to have relapsed after two years. All of the five had relapsed within six months of treatment and in each case, the relapse consisted in a very slight re-appearance of the secondary papules. Three cleared up and have remained clear with an additional dose of neosalvarsan, one with four injections of bismostab and one with infusions of sarsa, which probably means spontaneously.

Of tertiary cases, apart from rhinopharyngitis, there cleared up on this treatment, three cases of chronic serpiginous ulcers and four of juxta-articular nodes. Of the latter one had secondary papules and two plantar keratosis as well as the nodes.

Gangosa, or ulcerative rhinopharyngitis, does not respond to neosalvarsan as do the other conditions, an additional reason for desiring thorough cure in the early stages. By giving the full course of six injections from 0.15 gm. to 0.9 gm. the progress of the disease is checked, but a second series is necessary after six weeks rest. This is so in cases where the history as to syphilis is as negative as the history of Yaws is definite.

In the following table are omitted the cases of rhinopharyngitis belonging to the present study. Also are omitted the only two cases of primary lesions which were treated and followed up. Both were between 10 and 15 years of age, the one being cured with 0.3 gm. and the other with 1.05 gm., neither having shown secondary eruption three years later.

The table gives the treatment of 108 cases of which 58 were principally secondary papules, 42 laja, and 8 later lesions apart from rhinopharyngitis.

		Lesions.			
Age Group.	Total Dose.	Sec.	Kerat.	Tert.	Relapsed.
Birth - 10 years.	0.3 gm.	9	4	0	1
	0.45 gm.	1	0	1	0
	0.6 gm.	2	0	0	0
10 - 15	0.3 gm.	9	9	0	1
	0.45 gm.	3	1	0	0
	0.6 gm.	2	0	0	1
	0.75 gm.	2	0	0	0
	0.9 gm.	1	0	0	0
	1.05 gm.	1	0	0	0
15-30	0.75 gm.	4	1	0	0
	0.9 gm.	4	7	1	0
	1.05 gm.	2	3	1	0
	1.2 gm.	2	3	1	0
	1.35 gm.	2	4	1	0
	1.5 gm.	1	4	0	0
	1.95 gm.	3	3	2	0
	2.25 gm.	1	0	0	0
	3.00 gm.	0	0	1	0
	4.05 gm.	1 (resistent)		0	0

		Lesions.			
	Total Dose.	Sec.	Kerat.	Tert.	Relapsed.
Over 30	0.75 gm.	1	0	0	1
	0.9 gm.	1	0	1	0
	1.35 gm.	3	3	0	0
	1.5 gm.	1	0	0	0
	2.25 gm.	2	0	0	0

The need for a better treatment than that with neosalvarsan has been felt in two ways. These are the drawbacks of intravenous injection for large numbers, and the cost. The first inconvenience appears to be met by the preparation myosalvarsan, suitable for injection either intramuscularly or subcutaneously.

Lissner reports thirty three cases so treated with results equal to those got with neosalvarsan. (38) The greater drawback of cost remains as it was.

Before going on to the consideration of bismuth therapy in Yaws, three of the arsenical preparations under trial must be mentioned. These are Stovarsol, Treparsol and Halarsol.

Stovarsol. Is acetyl-oxy-amino-phenyl-arsenic acid, formerly used as an adjuvant to emetine in intractable

amoebiasis. It is found to be effective in Yaws. Bouffard considers that it solves the very real difficulty of treatment of young children. Having used it in over 9,000 cases in two years, he recommends for infants three tablets on each of two successive days, increased to four for children between eight and fifteen, and to four on three successive days for older patients. He had five per cent relapses. (39).

Treparsol. Tried on a small scale, also by the mouth, was given to adult cases of Yaws, 0.25 gm. to 1 gm. per day for four successive days in two or more successive weeks. Clinical cure was got by total doses varying from four to fifteen grams but the number of cases was small. (40)

Halarsol. Is reported on by Todd and Chesterman, in the Belgian Congo. They maintain strongly that in Halarsol we have a drug which can be sold at the same price as neosalvarsan, whose dose is only one tenth of the latter, and whose effects are equally dependable. In a series of 240 cases up to August 1928, Halarsol was used in 2.5 per cent solution put up in 2 cc. ampoules. Clinical cure was obtained

with 0.5 cc. to 2 cc. (12 mg. to 50 mg.) repeated after three or four days. 0.1 gm. cures an adult of foot Yaws, and 0.025 gm. cures a baby of the secondary eruption. It is injected either intramuscularly or intravenously. Only one case of poisoning occurred when 12 cc. were given in one dose to a woman with bad secondary Yaws. The symptoms were headache and vomiting which lasted three days.

The use of Halarsol in the prophylaxis of Yaws in villages, clearing up the contagious secondary lesions by one or two visits without thorough individual treatment, is claimed in this report to be preferable to courses of bismuth. (41)

Bismuth in the treatment of Yaws.

Bismuth was introduced nine years ago in the treatment of syphilis as a substitute for mercury, and has increased its claims as time has proved that it is both more effective and less toxic than the other. It was the natural thing to try it also in Yaws, in which mercury has no effect. Bismuth is definitely active in Yaws. It is unlike mercury in that it is not absorbed either by the skin in

inunction nor by the intestine when taken by the mouth, in a degree sufficient to be so used in syphilis or Yaws.

The method of administration is by intramuscular injection. It has the disadvantage of being toxic in over-dosage, and the safe dose is so variable in individuals and an over-dose so close to the effective curative dosage that the greatest vigilance is needed in its use. This disadvantage is increased by the necessity for administering bismuth treatment over considerable periods, during which it is not easy to get a uniform rate of absorption.

To quote Lomholt, Copenhagen:- "The essential thing in all bismuth treatment must be to secure a uniform and regular absorption. Otherwise a sudden strong absorption may bring a dangerous intoxication; or on the contrary a lack of absorption may cause a deficiency of the therapeutic effect. For this very reason the internal and percutaneous administration of bismuth must be left out of the question". (42)

The effects of over-dosage with bismuth, whether by a single massive dose or by prolonged administration, are similar to those produced by mercury. A blue line on the gums develops in all intensive

bismuth treatment, but the danger point is reached when soreness of the gums and excessive salivation are complained of. This may go on to a bad gingivitis and stomatitis with fetor, and in cases of pyorrhoea the ulceration may be dangerously severe.

Intravenous injection of bismuth salts has been tried and given up because the rapid elimination called for too frequent injections, and because a severe trigeminal neuralgia was caused.

Hypodermic injection is very painful and the bismuth is apt to be depositied, so that absorption is both slow and irregular, and abscess formation is common.

Intramuscular injection is the method in use, and the site to be preferred is the gluteal muscles, in their upper and outer part, about four finger-breadths below the crest of the ilium. The two sides should be used alternately. The usual dose for an adult is 0.2 gm. of bismuth metal in 1 cc. to 2 cc. of fluid. 0.4 gm. is still within the margin of safety, and it is scaled down for children according to body weight.

The effect in Yaws can be counted on with a great many of the preparations now offered for this treatment. Many bismuth preparations will, with

three or four injections at weekly intervals, clear up the generalised Yaws eruption. The need at the moment is for one preparation which will definitely excel the others, and give not merely a good, but the maximum curative effect available from bismuth. What is being sought is the most rapid and regular absorption with the minimum of pain, and it is the case that the more rapid the absorption, the greater must be the pain, because of the greater reaction of injured tissues. With all intramuscular injections of bismuth there is a certain amount of immediate absorption, then the damaged tissues begin to encapsulate the deposit of bismuth, and the rate of absorption slows down, but continues for long periods.

From an encapsulated deposit of the drug there may result at an unexpected time a sudden absorption, which may be the cause of symptoms of over-dosage during a course of injections of therapeutic doses.

In the search for the ideal preparation, quickly and steadily absorbed, but painless in its application, there are on trial many different salts of bismuth put up in different fluids. General conclusions with regard to them may be quoted from the same paper by Lomholt. (42)

"(a) Watery solutions are effective but somewhat painful and troublesome because they require frequent injection.

(b) Oily suspensions are almost painless but their absorption is somewhat slow and therefore often rather irregular. Preference should be given to the compounds that are not quite insoluble in water. Bismuth salicylate seems to be one of the best.

(c) Oily solutions are almost painless but not specially rapidly absorbed. Their therapeutical power is reported by many to be good.

(d) Watery suspensions are absorbed rather quickly and are therefore slightly painful. Preference should be given to compounds of restricted solubility. The oxychloride possesses the qualities of absolute purity and stability. With particles of a size 3μ to 5μ it is almost painless and very powerful, specially good on account of its reliability and effectiveness".

Lomholt in the treatment of syphilis divides the various compounds into groups according to their rate of solubility.

Metallic bismuth, the carbonate, oxide, and oxychloride, he puts in a group of very restricted solubility, and he quotes Biro Istvan as showing that with metallic bismuth in 10 per cent in oil (sorbismol) only 6 per cent was eliminated in the urine and faeces in thirty days after the series of injections.

The preparation "Bismostab" as used in a few cases of cuchipe in this series is a 20 per cent suspension of finely divided metallic bismuth in 5 per cent glucose solution. There has been no chance to measure the elimination rate and only clinical results are available. These indicate that bismostab fulfils admirably the condition of painlessness, and that absorption is steady but not very rapid.

Lomholt's second group is formed of the hydroxide, the subnitrate, and the oleate of bismuth, slightly more soluble but still of slow absorption rate.

The third group consists of organic compounds, less slowly and more regularly absorbed. Potassium sodium-bismuth-tartrate, the "trepol" that was the first preparation used by Levaditi, he finds at a

disadvantage because it varies in bismuth content and rate of absorption. Iodoquinate has to be given in large doses, and both this compound and Bismo-yatren B. irritate the tissues too much. Bismuth salicylate has not these drawbacks and is considered the best of the group.

Of preparations on trial in the treatment of Yaws mention may be made of reports on four.

Bismuth-sodium-potassium-tartrate.

Franklin reporting 4,473 cases of Yaws from the Gold Coast finds this drug efficacious and cheap. He gave a total of 14 grains in doses of 1.5 grains deep subcutaneously. It is less effective than neosalvarsan and not effective in late Yaws. (43)

Boase in Uganda, using the same salt intramuscularly found the natives objecting to the pain. For primary lesions he prefers neosalvarsan. (44)

Acheson, reporting 2,279 cases in Northern Rhodesia got good results using three injections into the gluteal muscles of 4 grains each in 20 minims of water at five-day intervals. (45)

Bismuth Subnitrate.

Van Hoorde reports a series of cases treated by four weekly intramuscular injections of a ten

per cent suspension of bismuth subnitrate in oil, in doses of 4 cc. The results were good. Lesions cleared up quickly, and little pain or induration was caused. One case developed gingivitis. (46)

Oxy-iodo-gallate of bismuth. - "Airol".

Portois, after giving 7,000 injections of Airol, claims for it cheapness combined with effectiveness, as measured by the production of a negative Wassermann reaction, almost as great as neosalvarsan. In 1,000 cases there were five cases of gingivitis, with doses of 1 cc. to 4 cc. at weekly intervals over ten weeks, of a solution of 20 gms. Airol triturated with 100 cc. each of glycerine and water. A further advantage is the liberation of a small quantity of iodine which enables the user to dispense with sterilisation of the mixture. (47)

Bisnene.

This compound has been prepared as a safe intravenous injection for Yaws cases. It is a bismuth analogue of urea-stibamine containing 50 per cent bismuth. It has been tried in a few cases and causes the disappearance of the secondary eruptions with four injections of 0.1 to 0.15 gm. at weekly intervals. (48)

Bismostab in the treatment of cuchipe.

Bismostab, prepared by Boots' Pure Drug Company, is a sterile 20 per cent suspension of finely divided bismuth metal in five per cent glucose solution, so that 1 cc. of bismostab contains 0.2 gm. of bismuth metal. Details are here given of ten cases selected from a group treated with bismostab to the point of clinical cure and some months without relapse.

The dose recommended by the makers is 0.5 cc. to 1 cc. or of the metallic bismuth 0.1 gm. to 0.2 gm. It is found that this dose is rather small for cuchipe cases and to adults doses of 1 cc. to 2 cc. were given.

Ten selected Cases.

A. Cases of Primary Lesion Alone.

A baby of 2½ years with a primary sore just above the knee. 0.6 cc. of Bismostab (0.12 gm. bismuth metal) was given into the gluteal muscles on one occasion. The lesion began to dry within a week and the edges to grow in. In this condition the child was taken away. Seen eight months later she still had the sore, now a shallow ulcer 2 cm. by

1 cm. but no secondary eruption had occurred. Stovarsol by the mouth cleared it up.

A woman of 35 with a primary lesion on the leg in front of the ankle got four injections of 1 cc., 1.5 cc., 2 cc., 1.5 cc. at four day intervals to a total of 6 cc. or 1.2 gm. The lesion did not change and neosalvarsan was used with immediate effect. There was some stomatitis which cleared up with Thiostab.

B. Cases of Secondary Cuchipe.

1. With Primary Lesion still unhealed.

A girl of 18 with secondary papules on face and body and primary sore on leg, got five injections at intervals of 4, 6, 7 and 7 days of 1 cc., 1 cc., 1 cc., 2 cc., 2 cc. to total 7 cc. (1.4 gm.) With the second the papules began to dry and with the fourth had disappeared. The primary sore only healed after the fifth. No blue line nor gingivitis.

A lad of 18 with secondary papules, on face and body and primary sore on leg. Four injections spread over three weeks, 1 cc., 1 cc., 1.5 cc., 1.5cc. to total 5 cc. (1 gm.) Secondary papules began to heal with second, but plantar keratosis and primary sore needed two more. Blue line with third but no gingivitis.

2. Secondary Eruption Only.

Boy of seven with secondary papules on face, body and feet got four injections at weekly intervals of 0.5 cc., 0.6 cc., 0.6 cc., 0.6 cc. to total 2.3 cc. (0.46 gm.) Improvement was slow but definite. To permit of his going away, treatment was finished with 0.3 gm. neosalvarsan intravenously. No gingivitis.

Girl of 8 with secondary papules on face and all over body. Got four injections of 1 cc. each at intervals of four days to total of 4 cc. (0.8 gm.) Healing began with the second and was almost complete with the third, when a blue line on the gums developed. With the fourth the lesions disappeared. Slight gingivitis was cured with one injection of 0.3 gm. Thiostab.

Lad of 18 with secondary papules on face and body got two injections of 1.5 cc. and 2 cc. at four days interval to total 3.5 cc. (0.7 gm.) The lesions dried up and he did not wait for more. No gingivitis.

3. In addition to neosalvarsan.

A girl of 13 with secondary papules on face and body got 0.6 gm. neosalvarsan in two doses.

Eight months later she had papules round the mouth. 0.3 gm. neosalvarsan in one dose healed these. A month later she again had papules, now on the perineum. At six day intervals she got four injections bismostab of 0.6 cc. each to total 2.4 cc. (0.48 gm.) Lesions began to dry within the second and disappeared with the fourth. No gingivitis, but blue line. No recurrence six months later.

Man of 22 with secondary papules on face and axilla. He got a total of 4.05 gm. neosalvarsan over a period of three months. Nine months later he had severe plantar keratosis. He then got bismostab at intervals of a week, three injections of 2 cc. to total 6 cc. (1.2 gm.) Keratosis healed with third. No gingivitis. No later information.

4. Secondary Eruption with Bone Changes.

Boy of seven with last of secondary eruption on sole of foot and on one cheek. Swelling of first phalanx of middle finger of right hand and of lower end of left fibula. He got bismostab at four day intervals in doses of 1 cc. to total of 4 cc. (0.8 gm.) The papules healed after the second. After the fourth both thickenings of bone were notably less and

all pain gone. Blue line on gums but no gingivitis.

To get further effect on the bone swellings 0.15 gm. neosalvarsan was injected intravenously one month later. The swellings became scarcely noticeable but did not entirely disappear.

From the small number of cases observed one may form an idea of the value of bismostab in the treatment of Yaws.

1. It is remarkably painless. In no case was there either pain or induration.

2. It is absorbed steadily if not rapidly. The doses at four day intervals necessary to dry the secondary lesions are already efficacious by the time the blue line is apparent or the warning of increased salivation developing. Children take it well.

3. Secondary papules begin to dry with the second injection and take longer in the healing process than with neosalvarsan. With bismostab treatment lasts nearly three weeks.

4. It is less effective with the primary lesion than with the secondary, and much less effective with it than is neosalvarsan.

5. Plantar keratosis responds to bismostab but less rapidly than to neosalvarsan.

6. In the one case observed it had a surprisingly rapid effect on bone changes in the case of a boy of seven.

7. Bismostab will sometimes complete the cure of a case that persists or relapses with neosalvarsan.

8. Bismostab is easier to give to infants than neosalvarsan.

The position of bismuth treatment of Yaws at the moment, whatever preparation be used, is that it is a useful help to neosalvarsan, but that it does not at all replace it.

It can be used to reduce the total cost of treatment.

It is good where intravenous neosalvarsan is impossible to administer or contra-indicated.

It offers good hope of providing within a reasonable time a dependable and definite treatment.

It is less effective than neosalvarsan even though it clears up excellently the secondary eruption, and it has still the disadvantage that its toxic effects are close upon the curative effects. There is not enough margin.

Group of cases at all stages from Pachisa on tributary of River Huallaga. Many painted with caustic vegetable juice "jagua".

Clinical Section.

The following notes on cases of cuchipe seen in the area of the Huallaga River serve to illustrate many of the facts noted in the preceding sections. The cases have been selected from a total of two hundred and forty-two, made up as follows:-

Total number of cases examined..... 242.

Males - 177. Of these under 15 years - 76.

Females - 65. Of these under 15 years - 36.

Proportion of males to females - 2.7 to 1.

Stage of Disease.

Initial stage or primary sore.....	11
Secondary eruption alone or with primary.	115
Secondary eruption with keratosis.....	10
Secondary eruption with other lesions.... (J.A.N. and bone lesions)	2
Plantar keratosis alone.....	69
Juxta-articular nodules.....	7
Chronic ulcers.....	13
Ulcerative rhinopharyngitis.....	15
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The notes on the selected cases are arranged in the following order:-

Group 1. Ten cases of the typical secondary eruption as it is seen continually and commonly coming for treatment.

Group 2. Eleven cases of plantar keratosis (laja), of which eight were without other lesions, two in combination with the secondary eruption, and one in combination with both the secondary eruption and juxta-articular nodules.

Group 3. Three cases of the initial stage or primary sore.

Group 4. One case of the secondary eruption along with bone lesions.

Group 5. Six cases of later lesions, of which three were juxta-articular nodules and three were chronic ulcers.

Group 6. Four sets of family groups consisting of two, three, three and five members.

Group 7. Three cases of ulcerative rhinopharyngitis.

The first group is illustrative of the disease in its most familiar manifestation. It brings out the following points:-

Common history of onset.
Home and school circumstances.
The absence of influence of age and sex on the liability to contagion.
The variety of lesions in the generalised eruption, and
The contentment of the patient on seeing the eruption disappear with one or two injections of neosalvarsan, so that he does not wait for more than the drying of the papules.

The second group illustrates the serious handicap to agricultural workers and cargo-bearers of the crippling foot lesions. It shows how these lesions may appear along with the eruption and persist for years after it, or how they may develop years after the eruption has disappeared, as in a girl of 19 who had the eruption at the age of six.

Both these groups show the rapid response to neosalvarsan and the less rapid but sure response to Bismostab,

The third group describes the primary sore in an infant and in the mother of infected children.

The case in group four with one case included in the second group (Case 21), shows how the secondary eruption and the keratosis may not only run into each other but may be combined with such later manifestations as juxta-articular nodules and bone-changes.

The fifth group illustrates the commonest late results when none of the earlier lesions persist, juxta-articular nodules and chronic serpiginous ulcers.

The sixth group, in which are included some of those already described, give some idea of the way in which the disease pervades the households in the endemic region, whether these be of the poorer type or of the better class whose children are exposed to infection in school.

The seventh group is very much open to discussion and is a study in itself. A rhinopharyngitis beginning invariably on the nasal septum, attacking the pharynx and fauces, sparing the hard palate and not sparing the upper lip, is not typical gangosa. It may well be Leishmaniasis. Leishmaniasis americana in the form of uta occurs in the nearest sierra region six days journey away, and in the form of espundia in the central region entirely out of touch with this area. It has never been described in the Huallaga area, but I have recently got a cure in several cases of chronic ulcers of the leg and of espundia-like lesions of the lip, nose and throat which had resisted neosalvarsan, with preparations of antimony, tartar emetic and neostibosan.

There are numerous cases of this type of ulcerative rhinopharyngitis in the villages of the

Huallaga. They have no local name for it, though strangely enough they have learnt to call it syphilis, which it is not and which they actually do not know at all in its other and earlier manifestations. The commonest history connects its onset with the period of cuchipe, but there are cases with no history of cuchipe whose story is that there was a chronic ulcer of the leg from which infection was transferred by the fingers to the nose. Three cases with typical history and lesions are described, but the diagnosis is not made between cuchipe and Leishmaniasis except to say that the evidence of the history is suggestive of the origin from cuchipe.

Only those cases are described in which there was absolutely no history of syphilitic sores or other signs of syphilis.

1. Cases of secondary eruption alone or with primary sore.

Case 1. (124) With two photographs, (page 44).

Girl of eight years old, born and brought up in Saposoa, capital of the province of Huallaga. Lives with father, mother, four sisters and one brother. One sister died at four years old, a year ago. House thatched, two rooms, walls cane and mud-plaster, floor earth. Parents sleep in one room, children in the other in pairs, in beds off the floor. Family not of the very poorest. Family history of cuchipe. Father had it years ago. Mother has just developed a cuchipe madre (Case 23,) Brother aged 7 brought the disease from school to the house over a year ago. He was "cured" with sarsa and copper sulphate. (Case 24, bone lesions with secondary lesions six months after cure) From him a younger sister was infected, with whom slept the present case.

Patient's history. Six months ago a scratch in the skin of the left popliteal space persisted and formed a crusted sore which increased to the size of a five-shilling piece. About two months later

papules appeared on the dorsal aspect of the forearm over the olecranon process, and in steady succession on the fingers of the right hand, on the foot, toes, face and trunk. She felt no symptoms of constitutional disturbance and was not at any time inclined to stay in bed. Some papules healed and disappeared while new ones kept coming out. Examination of patient. Mentally a bright child, but of very poor physical development, thin, narrow-chested, anaemic. Hair notably thin, dry and hard, the opposite of what is almost general among girls here, whose hair is thick and glossy.

The stool showed the usual ova of hookworm, ascaris and trichiuris. No other abnormality apart from the following eruption:-

A crop of raised papules, some like a half nut with crusted yellow-green top, some semi-circular raised, crusted ridges, some soft, reddish without crusts and of the size of a pea, scattered over face, body, upper and lower extremities, to the number of thirty-four lesions. Scars of healed lesions show on the thigh, the fingers, and the dorsal aspect of elbow and wrist. The lesions are situated:-

Above right eyebrow, just below orbital ridge of left eyebrow; right side upper lip above angle of mouth; four covering area between lower lip and point of chin; on neck over hyoid bone; two in front above anterior fold of right axilla; one in similar relation to left axilla; two inches above left nipple; on abdominal wall three inches above umbilicus; four on pubis; one inner aspect each thigh, one behind anus; in each popilteal space, (the left a psoriasis-like lesion the still unhealed primary sore); internal malleolus, instep and ball of great toe of left foot; two in the lumbar region; one behind the right ear, one on the pinna and one on the scalp; and on the first, second and third fingers of the right hand.

The primary sore still remains as the crusted ridge round the healed centre of the sore in the left popliteal space.

The sores on the fingers, especially one large green crusted lesion on the anterior aspect of the middle finger of the right hand, make the holding of the pen almost impossible.

The sores on the pubis and behind the anus are a source of continual misery from the itching.

Treatment.

1. General. Kept in separate room along with her brother, also a Yaws case. Poor condition improved by anthelmintic purge (carbon tetrachloride) and a tonic of Ferri et Ammon. Cit. and Arsenic, along with nourishing food at regular hours.

2. Specific.

Drug..... Bismostab.

Application.. Intramuscular injection in the gluteal region.

Dosage..... 1 cc., 1 cc., 1 cc., 1 cc., to total of 4 cc. or 0.8 gm.

Interval..... Four days.

Result..... With second injection lesions began to dry. With third a blue line appeared on the gums. With fourth the lesions had disappeared. There was some gingivitis for which one injection of 0.3 gm. Thiostab (Sod. Thiosulph.) was given.
A month later the girl was most healthy in appearance, robust and of good colour. Three months later no relapse.

Case 2. (119)

Youth of 18, born and brought up in the village of Jepelacio, at about 2,700 feet. Cuchipe was last taken there by Case 9. Two or three cases have occurred in the year since then. Work is agriculture; home conditions poorest.

Family history of cuchipe. None of the family have had it.

Patient's history of cuchipe. Had an ulcer on inner side of left leg resulting from an infected scratch in the forest in March 1930. In August a sore developed on inner side of sole of right foot midway between toes and heel, and by September the whole sole of the foot had numerous papular sores that made walking painful. Then sores appeared on face, forehead, lips and back. The palms of the hands began to peel in little circular patches. He remembered being in company of Case 9. but could not account for infection.

Examination of patient. Normally developed youth in good general condition. Some degree of anaemia due to ankylostomiasis. No abnormality apart from the cuchipe eruption.

On inner side of left leg a granulating ulcer with thickened edges and dirty greyish base, 1½ inches by 1 inch.

On forehead eight reddish papules, size of a pea; several more on cheeks; two at left angle of mouth; in the scapular region five lesions, papular, larger than those on face, and covered with hard, greenish crust, older lesions than those on face;

sole of right foot covered with circular holes of the outer skin with two hard swellings similar to the lesions on the back but not crusted. Sole of left foot normal. Palms of both hands covered with the tiny circular holes of the superficial skin left by desquamation. This was painless.

Treatment.

Drug..... Bismostab.

Application.. Intramuscular injection in gluteal region.

Dosage..... 1 cc., 1 cc., 1½ cc., 1½ cc. to total 5 cc., or 1 gm.

Intervals.... 5 days, 10 days, 5 days.

Result..... With second injection papules began to dry. After third remained primary ulcer improved. After fourth all lesions healed Blue line on gums with third. No gingivitis. Three months later no relapse.

Case 3. (72)

Girl of 13 born and brought up in Tabalosos in Province of San Martin. Numerous cases of cuchipe in school. Brother also infected. (Case 4)

Patient's history of cuchipe. An insect bit her on inner side of left leg. An ulcer formed, lasted some weeks and healed. She was brought to Moyobamba, three days journey immediately afterwards, and ten days later a crop of papules began to appear. The

first lesions were on the anterior aspect of both arms. Ten days later more developed on the fingers. Thereafter they came out in both axillae; on the neck, at the corners of the eyes and mouth and in the openings of the nostrils, and at the back of the knees and legs. She had no general symptoms, but suffered from the constant itch, the watering of the eyes, and the soreness of all movements that opened the mouth. Also she suffered morally from the scorn and epithets of the Moyobamba school children.

Examination of patient. A normal girl in every way except for the recent eruption of cuchipe. The papules were large, like limpets in shape and crust, forming a greenish-black mass at both angles of the mouth, on the eyebrows and filling the nostrils. In the axillae and on the legs were this same type. On the arms and fingers smaller and more shrivelled.

Treatment and Relapses.

1. Drug..... Neosalvarsan.

   Application.. Intravenous.

   Dosage..... 0.3 gm., 0.3gm., to total 0.6 gm.

   Interval..... One week.

   Result..... Whole eruption had disappeared a fortnight later.

Relapse..... Eight months later four secondary papules on face, round mouth, heavily crusted.

2. Drug..... Neosalvarsan.

Dose..... 0.3 gm. on one occasion.

Result.....Lesions dried up completely.

Relapse..... One month later two secondary papules in anal cleft, one behind anus and one in front. Miserable from itch and burning on micturition.

3. Drug..... Bismostab.

Application. Intramuscular in gluteal region.

Dosage..... 0.6 cc., 0.6 cc., 0.6 cc., 0.6 cc. to total 2.4 cc., or 0.48 gm.

Interval.... 6 days.

Result..... Lesions disappeared after third injection. No blue line nor gingivitis. No recurrence six months later.

Case 4. (73)

Boy of 7. Brother of preceding. History and lesions similar to sister's. Face equally badly affected.

Treatment.

Drug..... Neosalvarsan.

Application. Intravenous.

Dosage..... 0.15 gm. on one occasion.

Result..... Lesions disappeared in a fortnight. No sign of recurrence fifteen months later. Father avoided further treatment.

Case 5. (94)

Boy of 12 from Indian village of Sisa, province of San Martin.

History of primary sore under the lower jaw. No information about its cause.

A month later the secondary eruption came out over face and trunk and when seen he was a typical case of the crusted papules.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.3 gm. on one occasion.

Result.....Eruption cleared up in a fortnight. Returned to his village. Seen there ten months later had keratosis of both feet. Repeated same dose of neosalvarsan and condition cleared up.

Case 6. (114)

Man of 50 living for years in Moyobamba. Work agriculture. House and living the poorest.

Patient's history of cuchipe. Injured the skin over the crest of the tibia by a bruise in January 1930. An ulcer formed as often before. In May he had three days slight fever and "pains in the bones". Itching and swelling began in the region of the ulcer. A crust formed over it and he treated it with simple

Case 6.

dressings. In July he had an itchy, scaly patch over the eyebrow, followed by similar patches on lip, chin, neck and hands. By the end of July there was a fully developed secondary eruption.

Examination of patient. Man in normal condition with usual intestinal helminthic infection. The cuchipe eruption was of the bigger lesions, thickly crusted, and limited at the time of treatment to the face, neck, chest and fingers. These last had made his work difficult as he could not grip the machete to cultivate.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.9 gm. on one occasion.

Result..... Lesions cleared up in ten days. No sign of recurrence thirteen months later. Did not accept invitation for further treatment.

Case 7. (123)

Man of 18. From Saposoa, capital of the Province of Huallaga. Mother, three sons, and two daughters live in thatched house of two rooms. The other two males and one daughter have had Yaws. Boy of 12 brought it to the house from school two years before.

Patient's history of cuchipe. Got a scratch over left ankle in the forest, and an ulcer formed in April 1930. Healed with simple dressings. In June he suffered severe "pains in the bones" and the secondary papules appeared on the neck, face and body.

Examination of patient. Eruption of small papules, few of them being crusted. Some on the face, but the back from the neck down covered profusely. Numerous in the lumbar region.

Treatment.

Drug..... Bismostab.

Application.. Intramuscular in gluteal region.

Dosage..... 1½ cc., 2 cc., to total 3½ cc., or 0.7 gm.

Interval..... 3 days.

Result..... Eruption dried up by tenth day. Did not continue treatment. Blue line on gum without gingivitis. No recurrence two months later.

Case 8. (120)

Girl of 18 from Indian village of Sisa. Of well-to-do family. Wears shoes and stockings. Older brother had Yaws eight years ago.

Patient's history of cuchipe. In July 1930 an inflamed swelling developed from an insect-bite above the external malleolus of the left leg. It opened into an ulcer and increased to about 1 inch by ½ inch. In September tiny papules appeared on the face and thereafter on the trunk and limbs. No constitutional disturbance.

Examination of patient. A perfectly normal, healthy young woman, exceptionally well dressed for a cuchipe case.

October 1930. On the face, principally on forehead and cheek, a number of small red papules, size of a pea. On the neck and on the scapular region a crop of similar papules. Above the external malleolus of the left leg a granulating ulcer with thickened edges and dark red base, shallow.

Treatment.

Drug..... Bismostab.

Application. Intramuscular in gluteal region.

Dosage..... 1 cc., 1 cc., 1 cc., 2 cc., 2 cc., to total of 7 cc., or 1.4 gm.

Intervals... 4 days, 6 days, 7 days, 7 days.

Result..... With second injection papules began to disappear. With fourth all papules gone but primary ulcer still in process of healing. With fifth all healed. No blue line nor gingivitis. No recurrence three months later.

Case 9. (65)

Man of 46 resident in Roque, two days from Moyobamba and some 200 feet lower. Occupation agriculture.

Patient's history of cuchipe. In June 1929 developed a sore at the root of the nail of the middle finger of the right hand. It became crusted. He took four bottles of Elixir Nogeira, called also Elixir 914. In July an eruption of papules came out first on the face and then on the chest, arms, legs and trunk. He calls it "sisu-cuchipe" because it is very itchy.

Examination of patient. A middle-aged man in poor physical condition. Anaemia due to ankylostome infection.

A crop of thickly crusted papules with the hard greenish tops of fully-developed cuchipe over the face, chest, abdomen, back and buttocks. Primary sore still a crusted tumour at the root of the nail of the middle finger of the right hand. A fungating mass of papules round the anus.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.75 gm., 0.75 gm., to total 1.5 gm.

Interval..... 1 week.

Result..... By day of second injection eruption had practically disappeared. It had disappeared entirely before the end of the fortnight, and he did not present himself for third injection. No recurrence seventeen months later.

Case 10. (82)

Girl of 13 from poor village of Chulluyaco. Cuchipe all over the village. Living conditions the poorest, i.e. for bed a skin on the floor of the hut, and all sleeping in one room.

Patient's history of cuchipe. In November 1929 she had on the sole of the left foot at the root of the toes, the wound made by the ulcerating cut of a pique or chigger. The wound did not heal as on other occasions, but granulations formed with itching and inflammation. In January an eruption of papules appeared on the chest and arms.

Examination of patient. January 1930. Poorly developed girl infested with ankylostomes, anaemic and badly nourished. The typical cuchipe secondary eruption well developed on the chest, in the axillae and on the arms. A dirty granulating ulcer under the middle toes of the left foot.

Treatment.

1. General. Anthelmintic purge, iron and arsenic tonic, and nourishing food.

2. Specific.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.3 gm., 0.45 gm. to total 0.75 gm.

Interval..... 1 week.

Result..... The eruption had all disappeared before the end of the fortnight. She returned to her village. No recurrence a year later.

2. Group of cases of plantar keratosis.

A. Without other lesions - eight cases.

Case 11. (113)

Man of 28, brother of case No. 8. In good circumstances and has not gone barefoot for eight years.

Patient's history of cuchipe. In 1921 had a cuchipe madre or primary sore on one of his toes. Two months later the secondary eruption began to appear and his body became "bathed" in it. With the usual local treatment the eruption disappeared in a little more than a year. He used infusions of sarsa and caustic applications of copper sulphate ("piedra lipe") and a vegetable juice of the colour

of ink, jagua.

One year later "laja" or keratosis developed on the soles of both feet although he had worn shoes all the year. At the time of examination it had persisted eight years, and was persistently painful.

Examination of patient. A well developed, well nourished, and well dressed young man, with no abnormality except on the soles of the feet. The soles of both feet were completely covered with small circular scales of desquamating skin, producing the appearance of fish scales, and except for the colour suggestive of snake skin. The colour was that of normal clean skin. The scales could be picked or rubbed off, leaving whole skin below without bleeding. This new skin showed linear markings indicating the beginning of another period of fissuring.

Treatment. Patient had only one day at his disposal in Moyobamba.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.9 gm. on one occasion.

Result..... In three weeks all desquamation ceased. Discomfort disappeared at once. Seven months later no recurrence.

Case 12. (95)

Lad of 16 from Saposoa capital of Huallaga. Schoolboy in poor circumstances with hookworm anaemia.

Patient's history of cuchipe. From a leg ulcer the secondary eruption of cuchipe appeared a year before examination. Treated with sarsa and caustics. Disappeared after a year. During its existence the soles of both feet were the sites of several papules, and the skin became so fissured that he could hardly walk.

Examination of patient. The dark circular stains left on the skin by recently dried secondary papules of cuchipe were evident. No lesion remained except on the soles of the feet. Both were covered with circular patches of the size of a sixpence, where the skin seemed to have been punched out in its superficial layers, the edges curling back, the centre deeper than the periphery. Among these patches ran longitudinal and radiating shallow fissures.

Treatment.

Drug..... Bismostab.

Application.. Intramuscular into gluteal region.

Dosage..... 0.6 cc., 1 cc., 1 cc., 1 cc., 0.6 cc., to total 4.2 cc. or 0.84 gm.

Intervals.... One week between every two injections.

Result..... Improvement in the third week. Condition cleared up by fifth injection. Blue line on gum but no gingivitis. No recurrence nine months later.

Case 13. (97)

Man of 38 from the town of Balsapuerta on the river a week above Iquitos.

Patient's history of cuchipe. A year and a half before examination he became covered with cuchipe after having a sore for some time on the back of his neck, from insect bite. The eruption cleared up in about nine months with sarsa and caustics. Since then he had suffered from laja of both feet and could not carry cargoes.

Examination of patient. Dark stain size of half a crown still visible on the back of his neck where the primary sore had been. No other lesions except on the soles of both feet. The superficial plantar skin, especially on the under surface of the heel and on the ball of the great toe, showed the same circular patches and fissures as were noted in the preceding case.

Stains left after healing of secondary eruption.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.6 gm. on one occasion.

Result..... Condition cleared up in a week. Went away. No relapse in six months.

Case 14. (96)

Little Indian boy adopted by Peruvian family as a child after a conflict in which the baby got left behind. Supposed to be about eleven years old.

Patient's history of cuchipe. None available. Present owner brought him for the foot condition.

Examination of patient. The dark copper coloured skin of the body showed no marks of cuchipe lesions. The lighter coloured soles of the feet were so covered with desquamating patches and fissures that the boy could only walk with difficulty. None of these patches was raised like a papule but all were of the shallow punched-out or wormeaten appearance.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.3 gm. on one occasion.

Result..... Condition cleared up in a week. Eleven months later no recurrence.

Case 15. (50)

Man of 30 from Balsapuerta.

Patient's history of cuchipe. Seven months before examination there began a slight secondary eruption of cuchipe, which consisted in all of some six papules, and which lasted only six months. As the papules disappeared, laja developed on the soles of both feet, and a similar condition on the palms of both hands.

Examination of patient. No body lesions nor scars visible. On the soles of both feet three or four circular desquamating patches without fissures. Tiny circular desquamating scales on the palms.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.6 gm. on one occasion.

Result..... Condition of both palms and soles healed in a week. No later information.

Case 16. (53)

Man of 20 from town of Lamas, provice of San Martin.

Patient's history of cuchipe. Six years before examination he had had the secondary eruption of

cuchipe following on a chronic ulcer of the leg. A year before examination, and four years after the disappearance of the papules, laja developed on both feet. Walking became painful and difficult.

Examination of patient. No body lesions except on soles of feet. Whole plantar surface, from heel to toes, wormeaten in circular patches with curling edges like the skin of an old potato.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.6 gm. on one occasion.

Result..... Condition healed in a week. No later information.

Case 17. (111)

Man of 30 from Lamas.

Patient's history of cuchipe. Eight years before examination he had had the secondary eruption of cuchipe, beginning with an illness like malaria. Ever since that time he has suffered continuously and been often incapacitated for work by laja of both feet.

Examination of patient. Exactly similar to preceding case.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.9 gm. on one occasion.

Result.....Condition healed in a week.
No recurrence six months later.

Case 18. (69)

Girl of 19 from Pachisa, a poor village on a tributary of the Huallaga.

Patient's history of cuchipe. Had cuchipe in childhood. Does not remember details except that she and her brothers and sisters were all "bathed" in it at the same time. They were treated with sarsa and copper sulphate. At the age of 18 in Moyobamba her feet developed laja, and she had difficulty in doing her work as a domestic servant, especially in carrying the water pitcher on her head, because of the discomfort of walking.

Examination of patient. No body lesions except the irregular desquamation and the fissuring of the skin of the soles of both feet.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.3 gm., 0.45 gm., to total of 0.75 gm.

Interval.....One week.

Result..... The condition had disappeared when seen one month later. There was no recurrence after sixteen months.

B. Plantar keratosis with the secondary eruption - two cases.

Case 19. (112)

Man of 20 from Saposoa, province of Huallaga. Patient's history of cuchipe. In February 1930 he became aware of a sore on the inner side of the right foot that was persisting longer than these usually did. A week later the secondary cuchipe eruption was coming out on the face and body. He was treating himself with sarsa when laja developed on both soles and both palms. Then he came for treatment, because he knew that while he could cure his cuchipe, he could not cure his laja. Examination of patient. A raised red granulating tumour of about an inch diameter on inner margin of right foot midway between heel and toes, not crusted as was the primary sore. Crusted papules of the generalised eruption each the size of a shilling and well raised from the skin, were evident in both axillae, on the chest, the arms and forearms. On the palms tiny circular scales of desquamating skin; on the soles the typical larger circular holes in the superficial skin.

Treatment.

Drug.....Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.6 gm., 0.75 gm. to total of 1.35 gm.

Interval..... One week.

Result..... Lesions all healed in fortnight. No later information.

Case 20. (66)

Man of 22 resident for three years in Sisa.

Patient's history of cuchipe. In May 1929 had a chronic leg ulcer. In August the secondary cuchipe eruption appeared on the forehead, and some papules on neck and chest.

Examination of patient. Seen in October 1929 two months after appearance of eruption. Only a few papules, small, not thickly crusted. There was no laja.

Treatment and relapses.

1. Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.45 gm., 0.6 gm., 0.6 gm., to total of 1.65 gm.

Intervals.... One week between each two injections.

Result..... All lesions except one papule at root of hair on forehead dried up.

2. Drug..... Neosalvarsan.

Dosage..... 0.75 gm., 0.75 gm., to total now of 3.15 gm.

Intervals.... From last three weeks - 1 week.

Result..... Went away without lesions.

Relapse..... Two months later lesion on same spot on brow.

3. Drug..... Neosalvarsan.

Dosage..... 0.9 gm., making total of 4.05 gm.

Result..... Lesion cleared up at once.

Relapse..... Nine months later laja very severe on left foot, and of less degree on right foot.

4. Drug..... Bismostab.

Application.. Intramuscular into gluteal region.

Dosage..... 2 cc., 2 cc., 2 cc., to total of 6 cc. or 1.2 gm.

Intervals.... 7 days, 7 days.

Result..... Laja cleared up after third injection. Blue line on gum but no gingivitis. No later information.

C. Plantar keratosis with secondary eruption and juxta-articular nodules.

Case 21. (64)

Man of 30 from Saposoa, province of Huallaga. Patient's history of cuchipe. Eight months before examination the secondary eruption followed on a chronic leg ulcer. While the eruption existed he found himself incapacitated for walking in the forest by the development of laja of both feet. Some weeks before examination two firm, painless swellings appeared on the dorsal aspects of the wrist joints.

Examination of patient. The typical crusted papules of a secondary eruption of some months duration were seen on the forehead, chest, arms and buttocks.

The soles of the feet showed general desquamation and fissuring with the addition of a painful burst papule under the heel and another at the root of the great toe on its plantar aspect.

On the dorsum of each wrist over the medial part of the joint was a small round swelling, firm but not bony to the touch, slightly movable, more fibrous to the touch than a ganglion, and painless to the patient. The size was that of half an ordinary marble.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.6 gm. on one occasion.

Result..... Within a week papules dried up, both on body and soles of feet. Laja all desquamated and left healthy skin. Nodules distinctly smaller. Patient did not wait further treatment. No later information.

3. Group of cases of primary sore - three cases.

Case 22. (108)

Baby girl of 2½ years from village of Juan Guerra on river Huallaga.

Patient's history of cuchipe. Child was brought by the mother who had a fully developed cuchipe eruption over shoulder, back and face. Three weeks before examination the child had an itching, inflamed spot like a pimple on the internal aspect of the right thigh three finger-breadths above the knee. It persisted and the child was fretful and feverish, continually scratching the lesion.

Examination of patient. No other lesion than the one inside the right thigh. A raised, raw, red and granulating tumour, 3 cm. long and 2 cm. wide. Surrounding skin inflamed.

Treatment.

1. Drug..... Bismostab.

Application.. Intramuscular in gluteal region.

Dosage..... 0.6 cc., on one occasion - 0.12 gm.

Result..... Lesion began to dry within a week. Edges began to grow in. In this condition mother went away from Moyobamba with baby.

Seen in her home village eight months later the child still had the sore, now a shallow ulcer 2 cm. by 1 cm. on the same site, but no secondary eruption had occurred.

2. Drug..... Stovarsol.

Application.. Tablets by mouth.

Dosage..... 3 tablets of 0.25 gm. on each of two successive days.

Result..... Healed lesion in a fortnight.

Case 23. (126)

Woman of 35 from Saposoa, province of Huallaga. Patient's history of cuchipe. Came with her two children to have them treated for cuchipe. Cases 1. and 25. Same family history. While they were undergoing treatment she complained of a sore which she had had since before the hourney, some three weeks in all. An insect bit her in front of the right ankle. A small, raised sore resulted and was

Patient's history of cuchipe. In November 1930 a sore developed on inner side of right foot near the ankle. Numerous cases of cuchipe in village. Sore at first raised tumour, opened into an ulcer under treatment with caustics. Walking became impossible.

Examination of patient. Seen in her village in January 1931 there was no sign of secondary cuchipe eruption. The patient could not use the right foot for walking and hopped along with the use of a pole, keeping the foot off the ground. The lesion was a circular, shallow ulcer with raised margins and red granulating base, size of half a crown. There was no induration of surrounding tissues but considerable itching.

Seen in Moyobamba whither she was carried in February, three weeks later, there was evident the very earliest stage of the secondary eruption of cuchipe on the fingers.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.75 gm., 0.75 gm., 0.9 gm., total 2.4 gm.

Intervals.... One week.

Result..... In the first week the signs of a developing eruption disappeared entirely and it progressed no further. The primary ulcer dried up and the edges began to grow in. With the second injection this closing went on rapidly to complete healing.

4. One case of lesion of bones (tertiary) in combination with the secondary eruption.

Case 25. (125)

Son of Case 23. and brother of Case 1. 7 years. Patient's history of cuchipe. One year before examination when at school he had an ulcer on the left ankle. It lasted several months and healed, leaving a glossy scar of 1 inch diameter.

During the existence of the ulcer papules of cuchipe came out all over his body, but especially on hands and lips. The eruption was accompanied by "pains in the bones". The eruption was beginning to die down when persistent pain and heat began in the middle finger of the right hand and in both ankles. Then at these three sites swelling began.

Examination of patient. The boy is poorly developed, and has the usual hookworm infection and anaemia more severely than his sister. Walks with difficulty and limping badly, doubling up his right foot in strong plantar flexion and eversion. This he does to save himself from the pain of pressure on a burst chuchip papule of the size of a marble on the inner side of the under surface of the heel in line with the internal malleolus. No other skin lesions are present, except one psoriasis-like semi-circle on the right cheek and the scar of the primary sore evident as a glossy stain on the left ankle.

The middle finger of the right hand has a pear-shaped swelling involving the whole first phalanx and the inter-phalangeal joint. The swelling is very obvious, is hard but not inflamed, and the aching pain of which the boy complains is not increased by pressure.

The lower end of the left fibula has a marked thickening continuous below with the external malleolus. This thickening is definitely in the bone and of the same character as that in the finger.

Treatment.

1. General. Anthelmintic, tonic and nourishment.

2. Specific.

A. Drug..... Bismostab.

Application.. Intramuscular in gluteal region.

Dosage..... 1 cc., 1 cc., 1 cc., 1 cc., to total of 4 cc., or 0.8 gm.

Intervals.... 4 days.

Result..... With second injection the papule was drying up. By fourth the bone swellings were noticeably less than in the fibula, being practically indistinguishable. Pain gone. Blue lines on gums, but no gingivitis.

B. Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.15 gm. on one occasion.

Result..... Given one month after the other treatment to get further effect on the phalangeal swelling. A fortnight later it was also scarcely noticeable but did not entirely disappear.

The first effect of treatment was the immediate cessation of the aching pain in these bones with the first injection of Bismostab.

Thickening of distal end of fibula above left external malleolus. Case 25.

5. Group of cases of later lesions only - 6 cases.

A. Juxta-articular nodules - 3 cases.

Case 26. (59)

Woman of 35 from Saposoa, province of Huallaga. Patient's history of cuchipe. Not definite as to dates or number of years. She had cuchipe all over the body following on a chronic ulcer of the leg. For several years thereafter she suffered from laja of the soles of the feet. Then she found swellings developing over the left knee and both elbows. A few months later she came for treatment.

Examination of patient. No signs of the secondary eruption had persisted. The soles of the feet had typical desquamating patches and fissures.

Below the left knee anteriorly, over the ligament of the patella, there was a firm, fibrous tumour, not freely movable over the ligament, of the size of a half-golfball.

Over the olecranon process of the left ulna a similar tumour, but smaller, flatter and somewhat nodular.

Over the olecranon process of the right ulna a tumour slightly larger than, but otherwise exactly similar to, that over the left olecranon process.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.45 gm., 0.45 gm., 0.6 gm., to total of 1.5 gm.

Intervals.... One week.

Result..... All the lesions, laja and nodules, disappeared completely, and eighteen months later there was no further development.

Case 27. (102)

Man of 23 from Balsapuerta.

Patient's history of cuchipe. Had a generalised eruption several years before examination. Cleared up spontaneously. Then a painless swelling developed over the left elbow.

Examination of patient. No other lesion than a firm fibrous tumour over the crest of the ulna posteriorly three finger-breadths below the tip of the olecranon. Size was like three-quarters of a golfball, character irregular and nodular.

Treatment.

Drug.....Neosalvarsan.
Application.. Intravenous.

Dosage..... 0.3 gm., 0.6 gm., to total 0.9 gm.

Interval..... One week.

Result..... Tumour disappeared within fortnight.

Case 28. (122)

Man of 54 from Tarapoto, province of San Martin. Patient's history of cuchipe. In 1923 he had cuchipe papules on the dorsum of the left foot and on the hands. These persisted for two years, but no more came out on the body. Then on each fore-arm and on the back of the hand tumours appeared and increased slowly in size.

Examination of patient. One inch below each olecranon process and just under the skin a tumour like a complete marble, firm, fibrous and unfixed to the skin. A similar tumour, but smaller, over second meta-carpal one inch distal to wrist joint on back of left hand. No pain on pressure and no inflammation. No other lesion. The patient's main complaint and motive for seeking treatment is that he has continual "pains in the bones" ever since the tumours developed.

Treatment.

Drug..... Neosalvarsan.

Application Intravenous.

Dosage..... 0.9 gm. on one occasion.

Result..... Pains ceased. Nodules were visibly smaller when he went away. No later information.

5. B. Chronic (tertiary) ulcers - 3 cases.

Case 29. (11)

Woman of 35. Came with husband suffering from laja after secondary eruption, and boy of 3 covered with secondary eruption.

Patient's history of cuchipe. Husband brought cuchipe to the house in Balsapuerta three years before. She got infected, the primary sore occurring on the left arm. The secondary eruption cleared up after a year, but the primary sore and one secondary papule opened into ulcers on the left arm. These were slowly extending and deepening.

Examination of patient. No lesions of cuchipe except on the left arm. Above the elbow on the internal aspect of the arm were two ulcers. One extended from one inch above the external condyle for two and a half inches upwards. The other extended from the level of the middle of the first for two inches up the arm, being placed posteriorly to the first. Both were of width, three quarters of an inch, and in depth had gone into the muscles but had not exposed bone. The edges raised and thickened the base a dirty grey colour and discharging pus.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.6 gm. on one occasion.

Result..... With antiseptic dressings daily the ulcers had healed in a fortnight so as to dispense with bandaging. Two years later no sign of recurrence.

Case 30. (84)

Man of 29 from Saposoa, province of Huallaga.

Patient's history of cuchipe. Two years before examination an insect-bite on the dorsum of the left foot became a small tumour and broke down into an ulcer a month later. Two months later the secondary eruption of cuchipe appeared on the fingers, face and body. A second ulcer developed on the external aspect of the left leg a hand-breadth above the external malleolus. The eruption passed in a year and for nine months he had only the persistent ulcer on the left leg, refusing to heal. Then laja developed.

Examination of patient. No other lesions than a slight degree of laja on the soles of the feet, and a bad leg ulcer in the position described. Its shape was elongated, and the long diameter of two

and a half inches in the long axis of the limb. Width over an inch. Depth half an inch. Edges hard and raised giving a punched-out appearance. Base a dirty grey surface discharging pus.

Treatment.

Drug..... Neosalvarsan.

Application.. Intravenous.

Dosage..... 0.75 gm., 0.75 gm., to total of 1.5 gm.

Interval..... One week.

Result..... The ulcer had healed and the laja had disappeared at the end of a fortnight. Six months later no recurrence.

Case 31. (104)

Man of 25 from Lasam, province of San Martin.

Patient's history of cuchipe. Had the eruption of cuchipe for several months, clearing up a year before examination. One papule on the inner margin of the right foot did not clear up but formed an open sore, crippling him.

Examination of patient. Only the one lesion present. On the inner margin of the right foot at the level of the head of the first metatarsal, an ulcer extending from the dorsal to the plantar aspect of the foot. Length two inches in transverse axis of foot. Width one and a half inches in the

long axis of the foot. Bone not exposed. Edges raised and hard. Base grey and discharging pus.

Treatment.

Drug..... Neosalvarsan.

Application... Intravenous.

Dosage..... 0.9 gm. on one occasion.

Result..... Ulcer healed after a fortnight. No later information.

6. Some family groups. - 6 cases.

Case 32. (107 and 108.

Mother of 39 years of age and baby of 2½. From Juan Guerra province of San Martin.

History. The mother had primary sore on one of the toes. A month later the secondary eruption came out on face and shoulders. Five weeks later the baby developed an itching papule on internal aspect of right thigh. (described as Case 22.) Three weeks later came for treatment.

Treatment. The mother cleared up with one intravenous injection of Neosalvarsan 0.75 gm. and had no recurrence eight months later. The baby got 0.6 cc. Bismostab intramuscularly and was taken away immediately. Eight months later, seen in her village the sore was still unhealed, but no secondary papules

had developed. Healed with Stovarsol three tablets on each of two successive days.

Case 33. (124, 125, 126)

Mother and two children. These have been described in detail separately as cases 23, 1 and 25.

History. The boy of 7 (case 25) brought the disease to the house from school a year before and infected a younger sister. By the latter it was communicated to Case 1, a girl of 8, who slept with her. At the time of the examination the mother had a primary sore in front of the right ankle. The girl was in the stage of a generalised eruption. The boy had one papule still on the foot, and thickening of bone in the middle finger of the right hand and in both fibulae at the distal extremity.

Case 34. (10, 11, and 12)

Father 37 years, mother 35 years and male child 3 years.

History. The man brought cuchipe to the house three years before examination. While he was covered with papules, the wife developed a primary sore on the left arm above the elbow, and the secondary eruption came out. Both cases cleared up, the man remaining with laja, and the woman with

two persistent ulcers of the arm. (case 29)

Two and a half years after the first appearance of the disease in the house, the child, born just at that time, developed a sore on the knee. At the time of examination six months later, the eruption "bathed" the body, fingers and face. The mouth was in a distressing condition. Both lips were covered with a cluster of crusted papules which encroached on the mucous membranes.

Treatment.

Man..... 0.75 gm. Neosalvarsan intravenously on one occasion. Condition cleared up at once.

Woman.... 0.6 gm. Neosalvarsan intravenously on one occasion. Ulcers healed in a fortnight.

Child.... Drug..... Neosalvarsan.

Application.. Intramuscular into gluteal region in sterile olive oil.

Dosage..... 0.15 gm., 0.15 gm., to total 0.3 gm.

Interval..... One week.

Result..... Intravenous medication impossible in this case and no other drug available, Neosalvarsan in oil was used. The eruption improved with the first and disappeared with the second injection. The injections did not cause abscess formation, but did cause much

pain and feverishness with redness and induration at the sites of injection. No recurrence two years later.

Case 35. (13, 14, 15, 16 and 17.)

Mother aged 28 and four children, aged 11, 10, 4 and 2.

History. The child of two got a primary sore in the region of the mouth, and at the time of examination had the generalised eruption. The children got their primary sores at school, the boy of 10 being first to bring the infection to the house. The sequence thereafter they could not explain, and at the time of examination, the mother and the three older children had all lost the secondary papules and were suffering from laja. The mother and the boy of four were so crippled by it as to be scarcely able to walk.

Treatment.

Mother... Neosalvarsan 0.6 gm. on one occasion. Condition cleared up. Within two months she had a repetition of secondary papules to total of 12 on body. These disappeared when she took sarsa. Nothing since.

Girl of 11... 0.3 gm. Neosalvarsan on one occasion. Healed.

Boy of 10.... 0.3 gm. Neosalvarsan repeated a week later. Healed.

Boy of 4..... 0.3 gm. Neosalvarsan in oil intramuscularly in gluteal region repeated after a fortnight.

Healed. Pain and induration at sites of injection but no abscess formation.

Boy of 2... 0.15 gm. in the same way repeated after a fortnight. Same result.

7. Three cases typical of fifteen of rhino-pharyngitis of debatable origin.

Case 36. With photograph, page 63.

Man of 28, from the village of Juanjui in the province of Huallaga. Agricultural worker of the poorest class.

History of case. Lived in good health till four years before. Then he got an ulcer on the dorsum of the left foot that persisted for 1½ years. An eruption of cuchipe then occurred all over the body and face, but only after the ulcer had healed with applications of arsenic powder. The cuchipe was treated with the usual infusions of sarsa and caustic vegetable juices, and in six months began to disappear. At the time of the eruption he became aware of a soreness and burning of the left side of the nasal septum, at first dry, later with profuse discharge and finally with foul pus. When the ulcer of the septum had made a hole through it and the discharge came from both sides, over a year before the examination, he found a sore developing on his upper lip with bleeding. Then the

same soreness occurred on swallowing and his voice began to get husky. His general condition became poor from the difficulty in eating, the inability to work for his food and continual attacks of fever. Examination of case. On external examination the patient had the appearance of wasting, the physical development very poor. His face had an unusual high colour of the cheeks, like the cheeks of a case of mitral lesion of the heart. The nose was reddened and slightly swollen at the end. The upper lip was noticeably swollen and crusted and bleeding.

A general examination showed him to have no condition to be noted as abnormal beyond some bronchitis and a poor heart action without valvular lesions. Nothing abnormal was found in the examination of the spleen, liver and kidney. There was no sign detected of tubercular disease active in the lungs.

Examination of the nose and mouth. The bridge of soft tissue joining the end of the nose to the centre of the upper lip remained intact, but inside the nose the cartilaginous septum had been

ulcerated away, and only the concave edge of the bony septum presented inside the cavity. The mucous membrane of the cavity was in a state of chronic inflammation and discharging profuse bad smelling pus. The floor of the nasal cavity was not perforated.

The upper lip was occupied from anterior to posterior margin by a shallow ulcer 1½ inches long. (See photograph) with greenish-yellow crusts, and bled freely on removal of the crusts. The upper gum at the roots of the teeth was ulcerated without crusts and bled easily. The lower lip and gum were unaffected. The hard palate anteriorly was unaffected, but the soft palate and the fauces were covered with tiny granules. The uvula in its lower part had disappeared and the remaining part was also covered with these granules, the whole presenting the appearance of granulation and ulceration, and the free end of the uvula firmly adherent to the posterior pharyngeal wall. The tonsils were small and covered with the same granules. It was not possible to examine the vocal chords, but the voice was completely husky and the tone a harsh whisper.

There was absolutely no loss of sensation. The discharge from the nose, from the surface of the lip and the exudation from scarification of the mucous membrane of the nose and lip, the fluid expressed from a piece of the granulating process of the fauces, and the sputum were all examined microscopically.

Using Giemsa's stain for treponemas (Manson-Bahr) no treponema were found. With Leishman's stain no Leishman-Donovan bodies were found. With Ziehl-Neelson's process and the Gram's method, no acid fast bacilli nor Gram positive bacilli suggestive of the organisms of tuberculosis or leprosy were found. Staphylococci, streptococci, and different Gram negative bacilli were the only organisms found.

Diagnosis. Failure to find the causal organism in this case excludes leprosy and in conjunction with the absence of signs in the lungs, excludes tuberculosis.

There was no history suggestive of syphilis. There is a very definite history of Yaws, in immediate relationship to the commencement of the rhinopharyngitis. Failure to find the causal organism is against it, but the laboratory facilities were very limited.

There remains the question of "uta" or espundia, leishmaniasis americana. This condition occurs in an area five thousand feet higher up, over the cordillera (13,000 feet) in the sierra. It has not been described in the Huallaga, but that fact does not mean that it does not occur.

The skin ulcers of Leishmaniasis have not been met with among the cases that come up to Moyobamba, all chronic ulcers so far yielding easily to simple antiseptic treatment or to Neosalvarsan. But some cases have occurred of a similar nasal ulceration to this, less advanced, equally negative as regards finding the causal organism, and with absolutely no history of Yaws. Yet, if this condition were Leishmaniasis the causal organism would be found by repeated and careful search in a number of cases. Between Yaws and syphilis there is only the history, negative for syphilis and from an area where syphilis in its other manifestations is excessively rare, directly positive for Yaws.

In favour of a diagnosis of Yaws there is the residence in an endemic area, the history of recent infection, the absence of specific treatment during

infection. The lesion differs from the usual description of gangosa especially in the attacking of the upper lip and the non-perforation of the hard palate, the nasal septum being first to go.

One expected that treatment would help the diagnosis, and with Neosalvarsan an immediate improvement occurred.

The nasal discharge became less, and the lip began to heal. The voice remained husky. The improvement did not continue. Antimony was tried in the only form available at the time, intravenous injections of tartar emetic 0.4 gm. twice weekly for twenty four injections, a total of .96 gm.

There was no improvement with this treatment beyond the effect secured with Neosalvarsan.

When he returned to his village the ulcerative process was seen not to have advanced from the beginning of treatment six months before, but healing had not occurred.

Case 37.

Man of 35, from village of Pachisa far up the river Huallaga.

History of case.

When ten years old he had an ulcer on the inner aspect of the calf of the left leg, which lasted a year and healed with dressings of caustic juices, leaving a scar still distinguishable. When the ulcer was six months old the eruption, typical of cuchipe, came out on the chest, neck, forehead, feet, buttocks and limbs, lasted over six months and was cured with sarsa and caustic juices. When he was seventeen, six years later, and with no known cause, there began an ulcer of the right side of the nasal septum. At first there was a dryness and burning, then formation and discharge of crusts, and then abundant purulent discharge. He was accepted for army service and served the stipulated three years. For some twelve years the nasal condition continued as a continual purulent discharge, but his general health was excellent. Five years ago his voice began to get husky, and he found discomfort in the throat. On the upper lip, within the red margin, the surface became sore, bleeding and crusted, a year ago. Recently the gums of the upper jaw on the inner surface at the root of the teeth began to bleed easily and to waste without pain. No history of syphilis, and

had a clean bill of health during his army service.

Examination of case. Unlike the preceding case the general appearance is robust. Externally the face shows only a slight thickening of the upper lip. The nose externally appears normal.

A systematic examination showed no abnormal condition, but rather everything in good order.

Examination of the nose and mouth. Again the bridge of soft tissue joining the end of the nose to the centre of the upper lip had remained intact, and inside the nose the cartilaginous septum had been ulcerated away, so that the concave free margin of the bony septum presented inside the cavity. The interior of the nasal cavity was in a state of chronic inflammation and there was a foul purulent discharge. The floor of the nasal cavity was not perforated.

On the upper lip there was an ulcer of much less severity than in the preceding case, measuring an inch by ¼ inch and quite superficial, only the mucous membrane being destroyed. It had no crusts. There was redness and suppuration of the gum round the roots of the upper teeth so that the teeth were becoming uncovered towards the sockets.

The condition of the pharynx differed superficially from that of the preceding case in that the red angry look of the whole fauces was not there. Instead, the mucous membrane of the fauces was of a grey-blue colour, and small granulomatous masses covered the soft palate and narrowed the opening of the pharynx. The uvula and the tonsils had entirely disappeared, and the mucous membrane of the lateral and posterior pharyngeal wall was covered with the same small granules as in the preceding case, similar in all but the absence of the bright red colour.

The voice again was husky but not reduced entirely to a whisper. There was no loss of sensation.

The same examination of the discharge from nose and mouth and from the granulations was made, with the same negative result.

Diagnosis. Again the possibilities to be considered are syphilis, Yaws, tuberculosis, leishmaniasis, malignant disease, blastomycosis and leprosy.

Tuberculosis and leprosy are excluded by the absence of an acid fast bacillus in the discharges, and by the absence of signs in the lungs in the one case and of loss of sensation in the other.

Blastomycosis is excluded by the nature of the

lesion and the absence of the organism in the discharges.

Malignant disease with a history of eighteen years since the nasal ulceration began would not be expected to have advanced so far locally, leaving the general condition as good as in this robust patient. Microscopical examination of the tissue was not possible.

The evidence for syphilis and for Yaws from the nature of the lesion is equal. The history is not entirely dependable, but it is definite and clear for Yaws and quite absent for syphilis.

The question of leishmaniasis is again most difficult. The Leishman-donovan body was not found after repeated search.

The diagnosis again appears to lie between Yaws, syphilis and leishmaniasis, with the evidence in favour of the first.

Treatment entirely failed to clinch the diagnosis.

Neosalvarsan in a series of six injections to a total of 3.15 gm. made no apparent change in the condition. Tartar emetic in doses of .04 gm. twice weekly for twenty injections to a total of 0.8 gm. had no better effect. He recently returned to his village no better.

Case 38.

Man 35, born and lived till 18 in sierra in region where there is dermal leishmaniasis. History of case. Went in good health to Iquitos, stayed a year, and then came to Saposoa in the endemic Yaws area for five years. Spent three years in a rubber working part of the Huallaga also cuchipe region twelve days from Saposoa, and came back to Saposoa. A year later, or ninth year in the area he developed cuchipe.

The primary sore appeared on the internal malleolus of the right foot and lasted two years. Six months after its appearance the secondary eruption came out all over the body, in a form so severe that he says only the palms of the hands escaped. After a year with the usual treatment by sarsa and caustics it passed off. The primary sore healed last leaving a whitish scar. Thus, five years ago he was apparently well.

Four years ago a small blister formed behind the internal malleolus of the right foot close to the site of the primary sore. He cannot say if it was exactly on the same site. It healed, and in a month appeared again and became a little open sore

which remained so for six months while he went on working. Then it began to grow rapidly in what he calls "verruga" form, a mass of little growths like the formation of the head of a cauliflower. It was painful and to sleep he rested the sore heel upon the other sound one. The same sore developed on the left foot on the outer side of the heel. There was a foetid discharge. The tumour on the right foot reached the size of a small cabbage by the accumulation of small growths.

Two years ago a quack shaved off a large part of one tumour, without anaesthetics or dressing, "letting the blood run down the street drain". The place healed with a glossy white scar two square inches in area.

One year ago he began to have excessive salivation and pain on swallowing, and a month later his voice got husky. Dry burning of the septum of the nose was followed by ulceration and purulent discharge.

Examination of case. An unusually big, strong and well nourished man. Systematic examination revealed nothing to note.

Examination of the nose and mouth. The bridge of soft tissue joining the end of the nose to the

centre of the upper lip had remained intact. Half the nasal septum (cartilage) was ulcerated away and the free edge presented a concave shape as left by the perforation of the end of the cartilage. Much purulent discharge. No perforation of the roof of the mouth.

There was no ulceration of the lip, and no lesion of the soft palate. The uvula had disappeared and the posterior part of the soft palate and pharynx was a mass of granulomatous growth, narrowing seriously the pharyngeal opening. There was no redness or inflammation and no ulceration. Laryngeal examination was not possible.

Examination of the feet. On both feet, extending from internal to external malleolus, a fungating mass of tumour growth. A greasy, purulent discharge dripped from both and the odour was foetid. The tumours bled easily on touching. Above that, on the right foot an area of white, smooth scar where the tumour had been cut.

The tumour on the left foot was in three small masses, that on the right was in a group of one large and two small masses. The large mass was as big as an orange. There was no loss of sensation but considerable pain.

Diagnosis. In this case there is nothing to suggest Yaws, but the history of its close relationship to the onset of the tumour growth which preceded the rhinopharyngitis, and the resemblance of the nasal and buccal condition to the preceding cases.

As before microscopical examination of the fluid discharges was negative.

If leprosy, tuberculosis, syphilis and blastomycosis be excluded on the same grounds as in the two preceding cases, there are left Yaws, leishmaniasis and malignant disease. The latter again is not apparent in the unusually good condition of the patient.

Considering leishmaniasis, he was brought up in a region where it is reported, but thirteen years after leaving it he had no sign of it. On the other hand, there is no reason to feel sure that the endemic Yaws region in which it developed is not also a site of leishmaniasis americana. Against it are the two points that the organism could not be found, and that a series of thirty-eight injections of tartar emetic of 0.2 gm to 0.4 gm. each over a period of twenty-five weeks had no visible effect on the condition. Neither had 3.15 gm. of

Neosalvarsan. To relieve the foot condition one great mass of the right foot growth was cut off using a local anaesthetic. It had the consistence of soft cartilage, almost cheesy rather than fibrous, and bled very profusely. Healed well.

With the injections of Neosalvarsan the foul discharge from the feet became less and the offensive odour disappeared.

The throat became less painful and swallowing much freer. This was maintained while tartar emetic was being administered, but no further improvement was obtained with either treatment.

He returned to his village intending to come back for further treatment and for the surgical removal of the masses on the feet.

This is almost certainly diffuse cutaneous leishmaniasis of the feet and consequently probable espundia of nose and pharynx, which might mean that the other 14 cases of ulceration of nasal septum are also leishmaniasis and that there is no gangosa among them.

Fungating tumour of heel after partial removal. Case 38.

Probably cutaneous Leishmaniasis complicating clinical picture.

Summary.

This paper treats in detail of Yaws as it is found under the name "El Cuchipe" in the corner of the montana or forest region of Peru, drained by the River Huallaga, the department of San Martin.

Cuchipe is regarded as pian or boubas or Yaws which has invaded the region by coming up river from Brazil. The condition is defined as a chronic, contagious disease, characterised by its beginning with a single cutaneous sore and by the appearance, within a variable short period of itching papules which are granulomatous and thickly crusted. The paper is based on two hundred and forty two cases.

Reference is made to the history of Yaws in an endeavour to trace the development of our scanty knowledge of the disease as it increased from the fifteenth century, onwards. The history of its entry into new countries is reported, noting the fact that Garrison concedes to Yaws the honour of opening the field of modern Tropical Medicine.

The etiology of Yaws is discussed with special reference to the findings in connection with cuchipe. The general geographical distribution is

described. In the area under consideration it is noted how a rise in level from 1,200 feet to 2,500 feet with a corresponding fall in temperature from 28°C. to 22°C. produces a dramatic check on the power of Yaws to establish and propagate itself. It is found that age has no influence on liability to infection, but that the proportion of males to females affected is about 2.5 to 1, for reasons connected solely with liability to abrasions of the skin. The mode of infection is described under the two forms of direct and indirect transmission.

The emergence of Yaws as a true pathological entity distinct from syphilis by Castellani's demonstration of the causal organism and by Schobl's inoculation experiments is mentioned. The causal organism is described, and the principal pathological lesions are detailed as they affect chiefly the skin in an initial and a generalised stage, and also in the later manifestations affecting other organs.

The typical course of the disease is described in full under three divisions. The first is up to the formation of the mother-yaw, and is definite. The second is the stage of generalised eruption and

it may overlap the latest stage of complications and sequelae. The primary sore is described in detail. Different types of secondary eruption are noted, and special emphasis is laid on the constant occurrence of plantar keratosis.

The later lesions attributed to Yaws are ulcerative rhinopharyngitis, juxta-articular nodes, osteitis of long bones, and chronic serpiginous ulcers. These are described in detail.

The question of immunity and superinfection is discussed.

The principal diagnostic features of cuchipe are enumerated in the three stages. The resemblance to syphilis is discussed and examined in detail.

It is found that the efflorescent papular eruption is the only stage of Yaws that is definitely distinguishable. The points of difference in the primary lesions of both conditions are tabulated.

The allegations and observations for and against the identity of the two diseases are examined. In this connection mention is made of the apparent absence of classical syphilis in the endemic regions of typical Yaws, and the Huallaga area cited as an additional example.

The differential diagnosis of the sequelae is given as far as possible for each, the case of Leishmaniasis americana in its form of espundia being the most serious difficulty. Leprosy, tubercular and malignant ulceration and blastomycosis are considered in relation to the rhinopharyngitis. It is noted that this sequel begins on the nasal septum and does not spare the upper lip.

The treatment of Yaws is considered in detail, under the heads of prophylactic and curative. Prophylaxis centres round the prevention of contamination of skin abrasions and the hygienic measures for combating the disease are indicated. The use of drugs in prophylaxis, by administering enough to whiten the secondary eruption without complete cure, is mentioned in connection with a report on the use of halarsol by workers in Africa. In curative treatment the use of neosalvarsan is first considered fully, and details are given of its use in one hundred and ten cases of cuchipe, two primary and one hundred and eight of other stages presented in a table of age-group and total dosage. The cases of rhinipharyngitis are dealt with apart from this table.

Reports on other arsenical compounds are quoted, namely Stovarsol, Treparsol and Halarsol.

Bismuth treatment of Yaws is fully discussed and reports quoted on several preparations of bismuth under trial. Treatment of ten cases of different stages of cuchipe with metallic bismuth in glucose, being the Boots' preparation Bismostab, is described in detail.

Clinical notes are given of cases typical of each stage and of combined stages of the disease to bear out the preceding findings. Full notes are given of three cases of ulcerative rhinopharyngitis to indicate the difficulty of deciding whether they are Yaws or Leishmaniasis americana.

Conclusions.

1. The disease known as cuchipe in the montana of Peru is Yaws and conclusions formed from its study are applicable to Yaws.

2. The etiology of Yaws is affected by climate and altitude, to the extent that at 2,500 feet and 22°C. its propagation suffers a dramatic check in comparison with 1,200 feet and 28°C.

3. Infection is by the route of skin abrasion, is never by mucous membrane, and may be by direct or indirect transmission from an infective lesion to the abrasion.

4. Age has no influence on liability to infection, and sex only as far as the male sex is more exposed to wounds and abrasions in agricultural workers and cargo-bearers. Race has no effect.

5. The disease develops in three stages, an initial stage, a stage of generalisation, and in a proportion only of untreated cases, a stage of complications and sequelae.

6. In the Huallaga area the most serious incapacity is that produced by "laja" or plantar keratosis in more than half of all untreated cases.

This condition is apart from the bursting of secondary papules bound down by the plantar skin and develops at any time from the time of the eruption up to ten and more years afterwards. It is persistent.

7. The secondary eruption passes in about a year. Sequelae may begin before it has disappeared or may develop years later.

8. Juxta-articular nodules, chronic ulcers, and thickening of bones are definitely complications of Yaws.

9. Typical gangosa is not encountered in the Huallaga area, but a chronic ulcerative rhinopharyngitis beginning on the nasal septum and not sparing the upper lip, is met with in cases with definite and recent Yaws history. The condition is not definitely proved to be Yaws and might conceivably be Leishmaniasis americana, though the latter has not been described in the montana but in the sierra of Peru.

10. The fully developed secondary eruption produces permanent immunity to the skin lesions. Cases treated after the eruption has lasted several months are immune. Cases treated in the initial

or early generalised stage are liable to relapse but the relapse is of very slight degree.

11. The efflorescent eruption of papules in the generalised stage is the only period of the disease that is definitely distinguishable from syphilis. The primary sore is usually distinguishable. The later lesions are not distinguishable except on the history.

12. Although the lesions in all but the second stage are of close resemblance, the evidence is that Yaws and syphilis are two distinct diseases. There is evidence for a relationship between them, in the work of Jahnel and Lange, on the lines of a group of related viruses whose extreme members are classical syphilis and efflorescent Yaws.

13. The case of cuchipe in the Huallaga gives a certain amount of support to this idea of relationship between distinct conditions, by adding one more to reported cases, where the presence of endemic Yaws in a region coincides with the absence of classical syphilis, or with its inability to spread in otherwise favourable conditions.

14. In the treatment of Yaws prophylaxis by hygienic measures is important and should be secured by enlisting the help of the school authorities. Prophylactic treatment by single doses of effective drugs is worth doing where full treatment cannot be given.

15. Cure of Yaws can be got with arsenical compounds and with bismuth, but not with mercury.

16. Neosalvarsan is superior to every other drug at present, and has fewer drawbacks than bismuth. The objections to it are (1) its cost, and (2) the inconvenience of intravenous injection in certain cases. It must be given in doses beyond simple clinical cure of secondary eruption. It is rapidly effective in all stages of the disease except in the ulcerative rhinopharyngitis, and in it it is a deterrent.

17. Bismuth is definitely effective in Yaws, but is slower than Neosalvarsan. It can only be given intramuscularly. The objections to it are (1) the toxic effects are too close to the curative effects. (2) Its effect is marked only in the eruption. It is much less effective in the stage

of the primary Yaw and of the sequelae.

18. Bismostab is an excellent method of administering bismuth. It is painless. It is absorbed steadily and with sufficient rapidity. It clears up the secondary eruption in a fortnight to three weeks.

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