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MAL DEL PINTO IN MEXICO*

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SYNOPSIS

This report deals with the geographical distribution, prevalence, epidemiology, etiology, serological, clinical, and histopathological features, and treatment of mal del pinto, or pinta, in Mexico.

Repository penicillin preparations (PAM and Panbiotic) have been found highly effective in the treatment of this endemic, non-venereal treponematosis.

Mal del pinto or pinta is a non-venereal, endemic treponematosis. It is characterized by the presence of cutaneous lesions with marked changes of colour, which ultimately develop into partial or complete depigmentation. These colour changes, which are typical, have given the disease its name.

Geographical Distribution and Prevalence

Pinta is a primitive, tropical disease, and essentially one of the Western Hemisphere, in which it probably existed for many years before the Spanish Conquest.[1] It is prevalent in Mexico, Colombia, Ecuador, Venezuela, and Bolivia, where large regions are affected. It has also been described in smaller, isolated areas in Cuba, Brazil, the Guianas, Guatemala, Honduras, Haiti, the Dominican Republic, and Argentina. Recently, cases that are probably pinta have been reported in other continents, for instance, Africa,[23] Asia,[33] and Oceania.[2]

It is estimated that there are at least 400 000 cases in Colombia [9] and more than half a million in Mexico. According to the Public Health

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Department Census of 1929-31[23] the prevalence for all Mexico is 1.61%. Twelve Federal States are affected, namely, Guerrero, Oaxaca, Mexico, Chiapas, Michoacán, Puebla, Tabasco, Morelos, Nayarit, Veracruz, Colima, and Jalisco. The highest prevalence is found in Guerrero, where approximately 20% of the population is affected.

In Venezuela, the State of Barinas has the highest prevalence and according to Iriarte,[10] 10% of the inhabitants are infected. Ecuador also has a large area where the disease is found, and Leon[15] reported that four States—Napo Pastaza, Pichincha, el Oro, and Loja—show a high prevalence of pinta.

Epidemiology

Distribution

Pinta has no special geographical distribution, contrary to what was previously believed. In Mexico, a few cases are found at high altitudes, but the greatest prevalence is in the lowlands (Balsas river basin). In other countries, such as Ecuador, the disease is found both in the valleys and at altitudes of from 2450 to 2570 metres above sea level. It can occur in small, isolated zones with no special characteristics, as it does, for instance, in Cuba and certain other countries, where the prevalence is quite low.

Climate

Pinta is more prevalent in tropical zones, although it is not confined entirely to them. The disease is found more often in dry areas than in wet ones. Most of the cases in Mexico are found in areas distant from the sea coast.

Environmental conditions

Pinta is prevalent among people of a low socio-economic level, usually living in small villages with inadequate and unsatisfactory sanitary conditions. They frequently live closely crowded together in small huts, several members of the family often sleeping in one bed. In most instances, the disease occurs in people who are undernourished, ill-clad, and bare-footed, and who wash infrequently. By contrast, it rarely attacks those who are clean and the well-clothed, and it seldom occurs in urban communities.

Sex and age

Our study of pinta in Mexico showed that the infection was slightly more common among females than among males. This may be due to the fact that women usually remain at home and come in closer contact with the affected members of their families.

Pinta is essentially a disease of infancy and childhood. There is no evidence for the existence of congenital pinta but most of the patients contract the disease early in life. In a group of 133 pinta patients recently studied by us, the disease occurred at the ages of 1-15 years in 61.6% of the cases. The age distribution was as follows :

Age (years)	*Number of patients*	*Percentage*
1-5	22	16.5
6-10	33	24.8
11-15	27	20.3
16-20	18	13.5
21-30	20	15.1
31-40	7	5.3
41-50	2	1.5
51 or over	4	3.0

Race

Pinta has no predilection for any race, although in Mexico it occurs more frequently in Indians, as the latter usually meet the conditions necessary for acquiring the infection. In Cuba, Brazil, and certain other countries, Negroes are more affected than others.

Transmission

Contact. Pinta is contracted by casual contact. Since the treponeme can not penetrate uninjured skin, the usual port of entry is a minute abrasion or wound of the integument. The primary pinta lesion appears on some part of the body which is habitually exposed, and the disease has a marked tendency to spread among people who wear little clothing, which makes direct contact easier. We have seen two infants infected by their mothers after being held in their arms for long periods during the day. The primary lesions developed on the babies precisely at the site where they were in close and almost continuous contact with active pinta lesions present in the mother.

There are other observations which favour the contact mechanism of infection. Varela & Avila[36] found that 56% of the children of " pinta parents " were affected with the disease. In our studies in the State of Guerrero, Mexico, several facts were noted in this respect. A high proportion (88.9%) of the patients studied had infected relatives living in the same house whereas a low proportion (6.6%) had infected relatives *not* living in the same house. A higher proportion (77.5%) of the disease was noted in house-mates of the pinta patients sleeping in the same beds as the patients than in those (22.5%) sleeping in a different bed.

Congenital. Unlike venereal syphilis, but like yaws, pinta does not produce prenatal infections. It is only on rare occasions that instances of pinta infections have been noted in infants under 6 months of age.

Insects. Leon y Blanco [21] was able to transmit the disease to a volunteer by exposing his excoriated skin to insects recently fed with material containing *Treponema carateum.* It has not, however, been established that these insects serve as true vectors in transmitting the infection. In fact, *Hippelates* naturally infected with *T. carateum* have never been found. As has been conclusively demonstrated in yaws, the treponemes do not invade the salivary glands of the insect and a cycle is not developed, so the only way in which the disease can be transmitted is by the regurgitated material or excreta deposited on the skin after the insect has fed upon secretions of exposed lesions. As in yaws, occasional transmission of pinta by this mechanism can not be excluded, although open lesions are not found in pinta so mechanical passive transmission should be exceedingly rare under the usual conditions.

Etiology

Bacteriology

Pinta is caused by *Treponema carateum,* an organism discovered in 1938 in the lesions of a Cuban patient by Saenz, Grau & Alfonso.[31] Later studies by Leon y Blanco demonstrated the presence of the organism in cases of mal del pinto in Mexico. Under darkfield examination, the electron microscope, and the phase microscope, *T. carateum* appears morphologically identical with the treponeme of syphilis, yaws, and bejel. A few investigators have described minor morphological differences from the various clinical entities; but these observations have not been confirmed by others.

Laboratory studies in vitro and in vivo have not indicated any consistent variation in the susceptibility to penicillin of the treponemes of venereal syphilis, endemic syphilis, yaws, bejel, or pinta.[13] Clinically, all the entities in the treponematosis group respond to treponemicidal agents, including bismuth, arsenic, penicillin, Aureomycin, Terramycin, dihydrostreptomycin, and the newer broad spectrum antibiotics. Although the clinical response of pinta to penicillin therapy is slower than that of venereal syphilis, endemic syphilis, yaws, and bejel,[30] the darkfield treponemal disappearance time is practically the same in all of them.[30]

Animal inoculation studies have been of special interest. Turner, Hollander & Schaeffer[35] have shown that the syphilis strains, including those from Bosnia, in general produce large indurated lesions, whether inoculations are made into the testes or the skin. The yaws strain, however, has a rather long incubation period with the development of lesions which are less extensive and much less indurated than those produced by the syphilis strain. The bejel strain appears to lie somewhere between the other two in terms of pathogenicity. Although Leon y Blanco & Oteiza [20] have reported on the successful inoculation of pinta treponemes into the scrotum

of rabbits, this observation has not been corroborated by the intensive studies of Varela (personal communication) and Eagle (personal communication). As a result of recent new inoculations, it has been possible to keep one strain alive through the course of three transfers (G. Varela—personal communication).

Transmission experiments

In 1938, Leon y Blanco [16] inoculated himself and other subjects with material containing the treponeme of pinta and successfully produced the initial lesion on the skin, which appeared seven to ten days after the inoculation. Oteiza [27] in his experiments has demonstrated more prolonged incubation periods of up to 61 days. The above-mentioned authors describe the primary lesion as beginning as a small lenticular papule which soon becomes scaly and erythematous. It progresses slowly and after two or three months it is approximately 3 cm in diameter.

Recent studies by our group, carried out in Iguala, Mexico, have shown that it was not possible to transmit pinta by blood transfusion. Four volunteers were transfused with 250-300 ml of citrated blood obtained from four patients with active early pinta. In none of the volunteers, who were followed both clinically and serologically for from one to two years, was it possible to transmit the disease, notwithstanding the fact that all the pinta patients selected for the experiment showed abundant treponemes in their skin lesions. These findings are in agreement with the fact that no accidental case of blood transmission of pinta has so far been reported. Pinta does not affect the liver, kidney, or spleen. The lesions of the cardiovascular and central nervous systems observed in occasional patients have not been proved to be due to the treponeme of pinta. Furthermore, we have not found, in our patients studied in Mexico, any clinical or laboratory evidence of involvement of the cardiovascular or central nervous systems. R. Abarca, of Iguala, Mexico, who has taken X-ray pictures of more than 1000 miners in Mexcala, where almost 50% of the population have pinta, has not been able to find any greater incidence of aortitis in miners with pinta than in the others who are free of the disease (personal communication).

Immunology

Although it is generally agreed that pinta, in its late stage, confers immunity against reinfection and superinfection, there has been some controversy regarding cross-immunity between pinta and syphilis. However, Leon y Blanco [17] has shown that pinta can be successfully inoculated in patients with syphilis and more recent reports indicate that pinta does

not confer immunity to syphilis. In parts of Venezuela, where yaws is common, Briceno Rossi & Iriarte [4] reported on the lack of cross-immunity between pinta and yaws. They have observed pinta lesions in twenty persons who had yaws and approximately the same number of pinta patients who subsequently developed yaws lesions. All these studies seem to indicate that the different strains of treponemes do not confer any appreciable degree of immunity to each other.

Serology

In 1925, Chavarria & Shipley, cited by Strong,[34] erroneously reported that the Wassermann tests in patients with pinta were generally negative. In 1926, however, Menk[22] found that the Wassermann reaction was positive in 74.5% of the patients studied. According to Shattuck,[32] the routine serological tests for syphilis are negative in the primary stage of pinta, whereas, in the secondary stage, these tests are positive in 60% of the patients. In the tertiary stage, positive reactions have been reported, in from 70% to 100% of cases. In the secondary stage, Leon y Blanco [18] obtained 86% and 88% positive reactions, respectively, with the Wassermann complement-fixation and the Kahn flocculation tests. Pardo Castello & Castanedo [23] state : " Further studies have shown that in the first stage serological reactions are negative. It is well into the pintid stage that blood tests become positive in about 80% of the cases; while 100% of those with late manifestations give positive reactions " (page 311). In a review of the literature of various serological tests in pinta, Beerman [3] states that the Kahn test is more likely to be positive than the Wassermann complement-fixation test in the earlier stages and gives reactions of a higher titre in the subsequent stages of the disease. From serological data obtained in the examinations of sera from a group of 157 pinta patients of the State of Guerrero, Mexico, it was noted the serological tests for syphilis are frequently positive in the primary stage. Moerover, the frequency of positivity is even greater in the secondary stage. The results obtained clearly indicate that serological tests begin to give positive reactions from two to four months after the onset of the disease and independently of the stage of the disease. Once these tests become positive, they go on to show a progressive increase in serological titre. The highest titres are obtained in the intermediate type of late case, where it is not uncommon to find 1,024 dils or more. In the primary stage 82% of our patients gave positive reactions, and 97% in the secondary stage. Tables I, II, and III show the serological results obtained. Although a battery of tests was used for the examination of the sera, including the Mazzini and Rein-Bossak quantitative slide flocculation and the Marquez-Rein-Hazay complement-fixation procedures, the tabulations show the results obtained with Rein-Bossak test.

TABLE I. SEROLOGICAL RESULTS IN 11 PATIENTS WITH PRIMARY EARLY PINTA

Duration (months)	Negat-ive	Positive (dils)								
		1	2	4	8	16	32	64	128	total
2	1	1								1
4	1	1								1
6-9					2				1	3
12				1			1		1	3
18								1		1
Total	2									9
		Distribution by Sex								
Female		1		1	1			1	1	5
Male		1			1		1		1	4
Total		2		1	2		1	1	2	9

With the advance of the more purified antigens utilizing cardiolipin, it was hoped that it would be possible to differentiate pinta from syphilis. It was soon found that all the treponemal infections, including pinta, produced positive reactions. In fact, a higher incidence of positivity was obtained with cardiolipin antigens than with the cruder lipoidal antigens, because of the greater sensitivity of the former.

TABLE II. SEROLOGICAL RESULTS IN 71 PATIENTS WITH SECONDARY EARLY PINTA

Duration	Negat-ive	Positive (dils)								
		1	2	4	8	16	32	64	128+	total
3 months	2	2		2	1					5
5-11 months			1	3	5			1	1	11
1- 5 years			4	11	11	1	4	7	11	49
6 + years					2			2		4
Total	2									69
		Distribution by Sex								
Female		2	2	8	10		2	6	6	36
Male			3	8	9	1	2	4	6	33
Total		2	5	16	19	1	4	10	12	69

TABLE III. SEROLOGICAL RESULTS IN 75 PATIENTS WITH LATE PINTA *

Duration	Negat-ive	Positive (dils)								
		1	2	4	8	16	32	64	128+	total
1- 5 years			3	3	9	3	1	1	11	31
5-10 years			2	1		2	1	2	9	17
11-25 years				5		4		3	7	19
26 + years				1	1	1	1		4	8
Total	0									75
	Distribution by Sex									
Female			3	5	6	6	1	3	16	40
Male			2	5	4	4	2	3	15	35
Total			5	10	10	10	3	6	31	75

* Including 52 patients with the intermediate type

Various special laboratory procedures have been devised, with the hope of differentiating syphilis from the other treponemal infections. Among these are the Kahn " verification tests ". Chargin & Rein [6] subjected the sera of 268 patients with pinta to one of the Kahn verification tests. All gave strongly positive reactions with the routine serodiagnostic tests, varying from 4 to 160 units with the Kahn quantitative test. Of these, 225 (83.0%) gave the syphilitic type of reaction; 17 (6.3%) gave the general biological (non-syphilitic) type, and the remaining 26 (9.7%) gave inconclusive results. These results paralled those reported by Escobar.[7]

The euglobulin inhibition procedure devised by Neurath has been found to be of value, by several investigators, in differentiating syphilis from non-syphilitic diseases and conditions. It has not, however, been of any help in differentiating pinta or yaws from syphilis in a series of sera examined in the serological laboratory at New York University.

Data are being accumulated on the results of the Kahn Universal reaction with sera from patients with the various treponemal infections. Although a few preliminary reports seem to indicate that some differences are noted, it is too early to form any definite opinion.

More recently, Nelson and his associates [24, 25] have developed a serological procedure for the detection of a specific antibody in treponemal infections. This specific test has proved to be of tremendous value in differentiating true from false positive reactions. Kahn and his associates [12] tested various strains of *T. pallidum*, *T. pertenue*, and *T. cuniculi* with " standard " pools of sera from animals infected with each of the strains.

These studies indicated a significant immunogenic difference between the syphilis and yaws strains on the one hand and *cuniculi* strains on the other, but no substantial difference between the syphilis and yaws strains tested. However, the studies were limited to a few strains which had been separated from their natural hosts for ten to fifteen years. Similarly, it has not been possible to differentiate the syphilis from the pinta strains of treponeme by this specific procedure (R. A. Nelson Jr.—personal communication).

During the Mexican pinta study,[30] it was noted that the Kahn Standard, the Rein-Bossak, and the Marquez-Rein-Hazay tests gave many zone reactions. This unusual phenomenon has been observed by other investigators with most of the macroflocculation and microflocculation tests. Although such zone reactions are occasionally observed with high-titre syphilis sera and somewhat more frequently with sera from yaws patients, in our experience it occurred most frequently with pinta sera. There was no direct correlation between the incidence of zone reaction and the degree of serological titre. Some pinta sera with relatively low titres gave zone reactions, while others with much higher titres did not. It has been suggested by A. S. Wiener (personal communication) that these zone reactions might be due to a blocking antibody.

Clinical Features

Lesions of pinta are so varied and so intermingled in the course of the disease that classification into sharply delineated stages, as is done with other treponemal diseases, is almost impossible. The classification employed in our studies is as follows :

Early pinta

Primary stage. The first manifestation of the disease is the initial lesion. In our experience with the naturally acquired infection, the development of the primary lesion is similar to that described in experimentally induced infections. We have observed that primary lesions after approximately 15 or 30 days have the appearance of small, lenticular, slightly scaly papules, approximately 1 cm in diameter. In about one to two months these lesions reach a diameter of 2-3 cm, and the morphology changes. The lesions at this stage are usually of three types : erythematous, circinate, or psoriasiform, the last type occurring predominantly in older lesions. The erythematous-scaly lesions are slightly elevated plaques of oval or irregular shape. The circinate lesions are slightly scaly and erythematous, with an annular outline and with slightly elevated borders. The psoriasiform plaque is a scaly, red-salmon or reddish-white, sharply marginated lesion. In all types, but chiefly in the last, the primary lesion may continue

to increase slowly in size and reach sometimes a diameter of 10 cm or more in about one to two years. Frequently, the older lesions are surrounded by smaller satellite lesions (Fig. 1), which may fuse with them and form together a large configurate pattern. Initially, the primary lesion is erythematous, but later, when there is no further increase in size or when the secondary lesions appear, it may become pigmented. This pigmentation varies in shade, and frequently coexists with hypochromic and achromic areas. When the lesion heals there is usually a leukodermic patch at the site where it originally appeared.

The location of the primary lesion, in order of frequency, is as follows: lower extremities, face, neck, upper extremities, chest, loin, and abdomen. Lesions of the lower extremities appear on the legs, dorsum of the feet, ankles, and knees. Lesions frequently occur on the buttocks. Lesions of the face occur on the chin, cheeks, eyelids, and upper lip. Primary lesions of the genitalia and scalp have not been observed in our series of patients.

Secondary stage. Secondary lesions (Fig. 2) develop from one month to one year or more after the appearance of the initial lesion. They are sometimes scarce, only two or three occurring, but they may be numerous. Extensive dissemination, as in syphilis, is a rare occurrence. Primary and secondary lesions may be identical in appearance, being circinate, psoriasiform, or erythematous-scaly plaques. Occasionally, the lesions become secondarily infected and show impetiginization with crusting. By analogy with syphilis, Latapi & Leon y Blanco [14] suggested the term " pintides " for these secondary, disseminated lesions. Pintides appear on the same sites as the primary lesions. The genitalia, the groin, the fossa axillaris, and the scalp are usually not involved.

Initially, pintides are erythematous with some scaling but later they become pigmented, first appearing copper-coloured, then lead-gray, and after some time slate-blue. Although some lesions undergo pigmentation only after several months, others change colour during the first month, the change in colour depending a great deal on the site of the lesion. Lesions of covered parts of the body become pigmented very slowly or not at all, whereas lesions located on uncovered parts become pigmented quite rapidly. In from three months to one year most of the pintides show gradations of depigmentation, centrally, peripherally, or irregularly, in small areas. Often pintides have a mottled appearance caused by alternating patches of erythema, pigmentation, and leukoderma. Finally, the regressing pintides may become completely depigmented. Although this achromia occurs most frequently six months to one year after the appearance of the pintides, it may occur earlier. It is not rare to see leukoderma develop in some patients within three months after the appearance of the secondary lesion (early leukoderma).

FIG. 1. PSORIASIFORM PLAQUE WITH SATELLITE IN PRIMARY STAGE OF EARLY PINTA

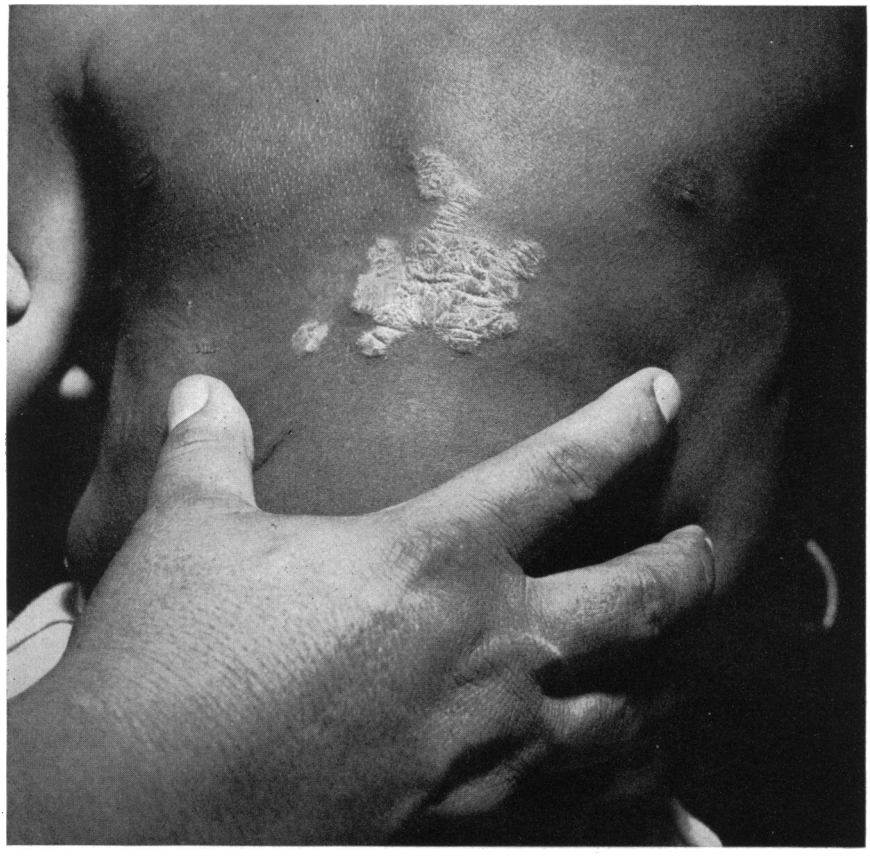


FIG. 2. LARGE PSORIASIFORM PINTIDE IN SECONDARY STAGE OF EARLY PINTA

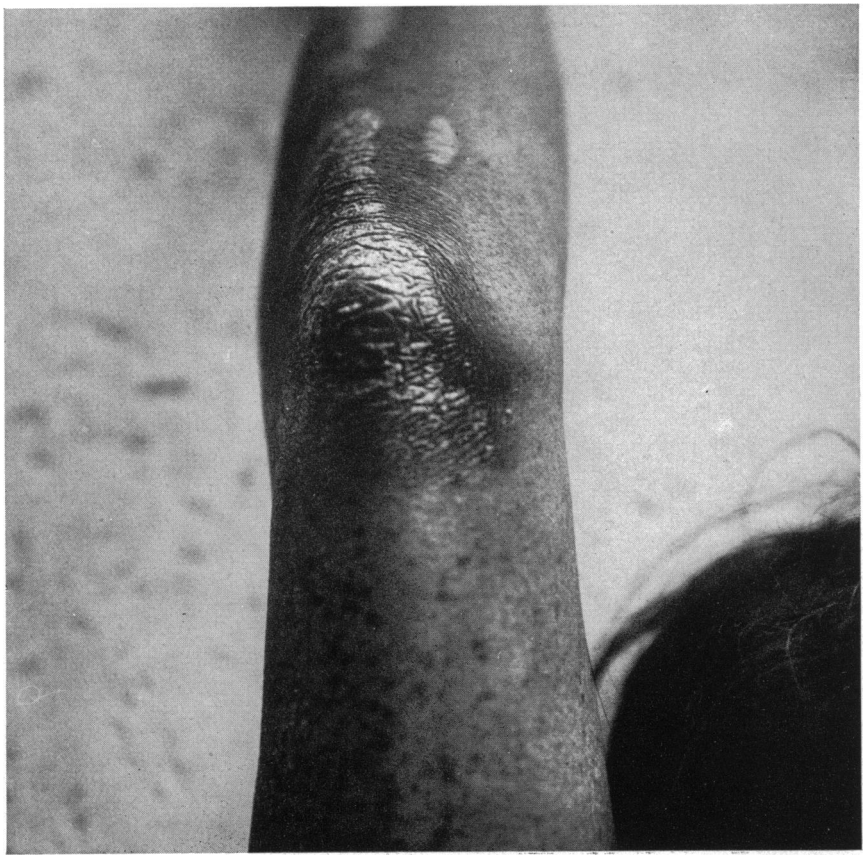


FIG. 3. DYSCHROMIC AND LEUKODERMIC LESIONS IN LATE PINTA

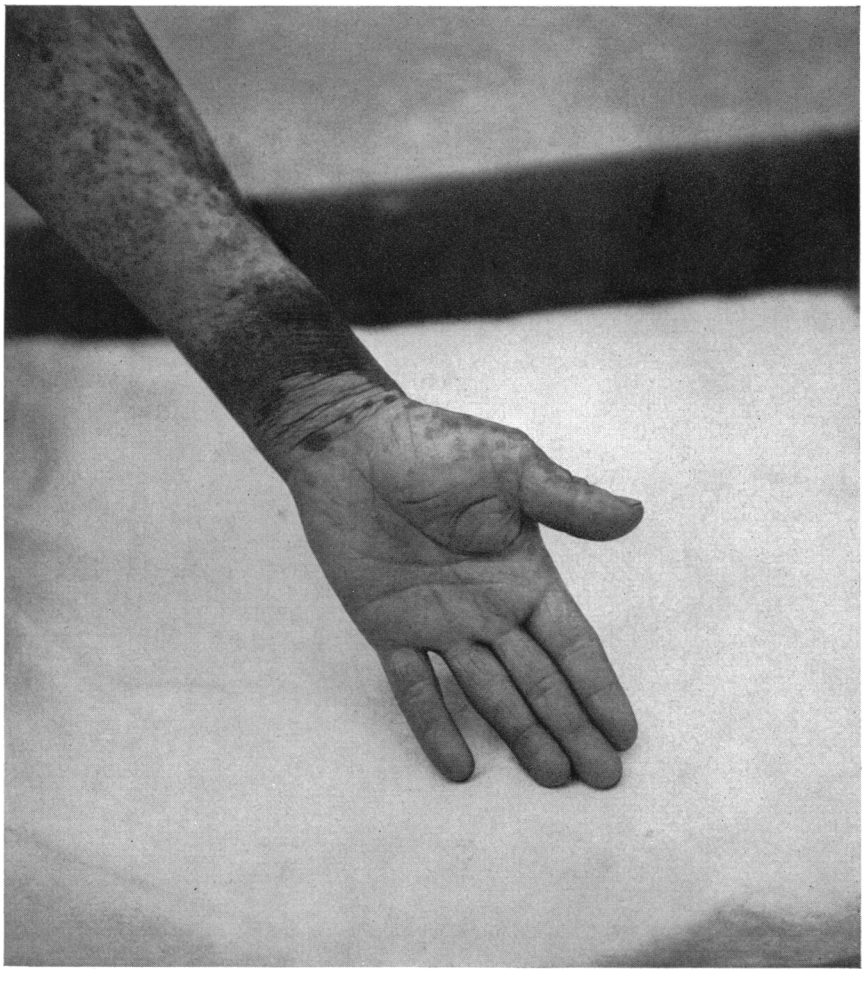
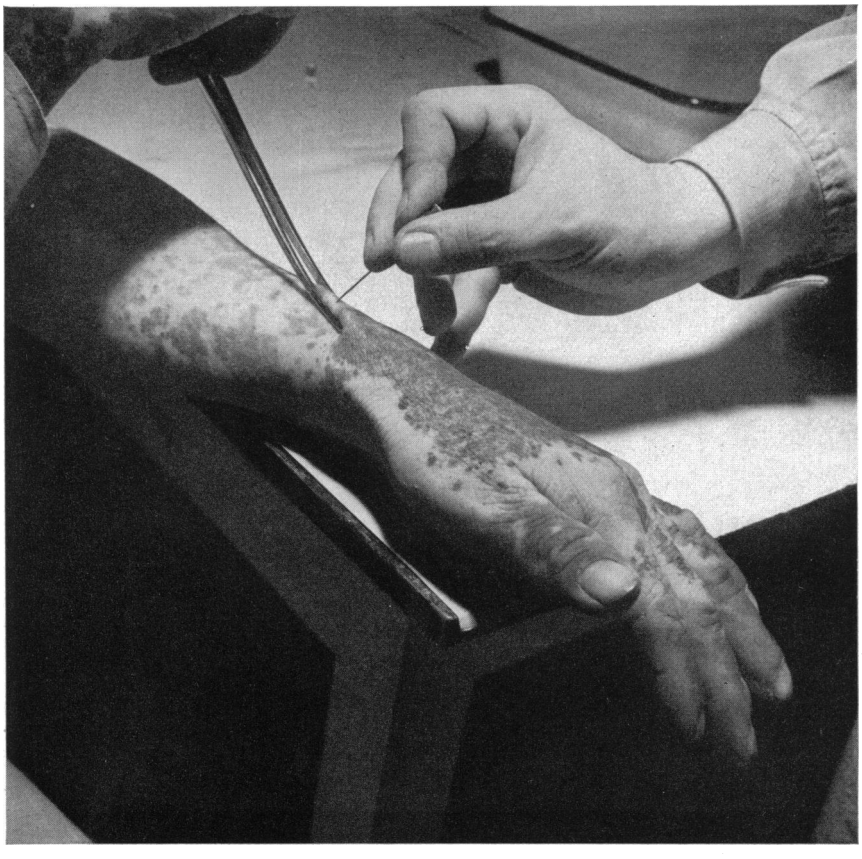


FIG. 4 DYSCHROMIC AND LEUKODERMIC LESIONS IN LATE PINTA



This figure also shows the method used for obtaining serum for darkfield demonstration of *Treponema carateum*.

FIG. 5. EXTENSIVE AREAS OF LEUKODERMA AND DYSCHROMIA IN LATE PINTA

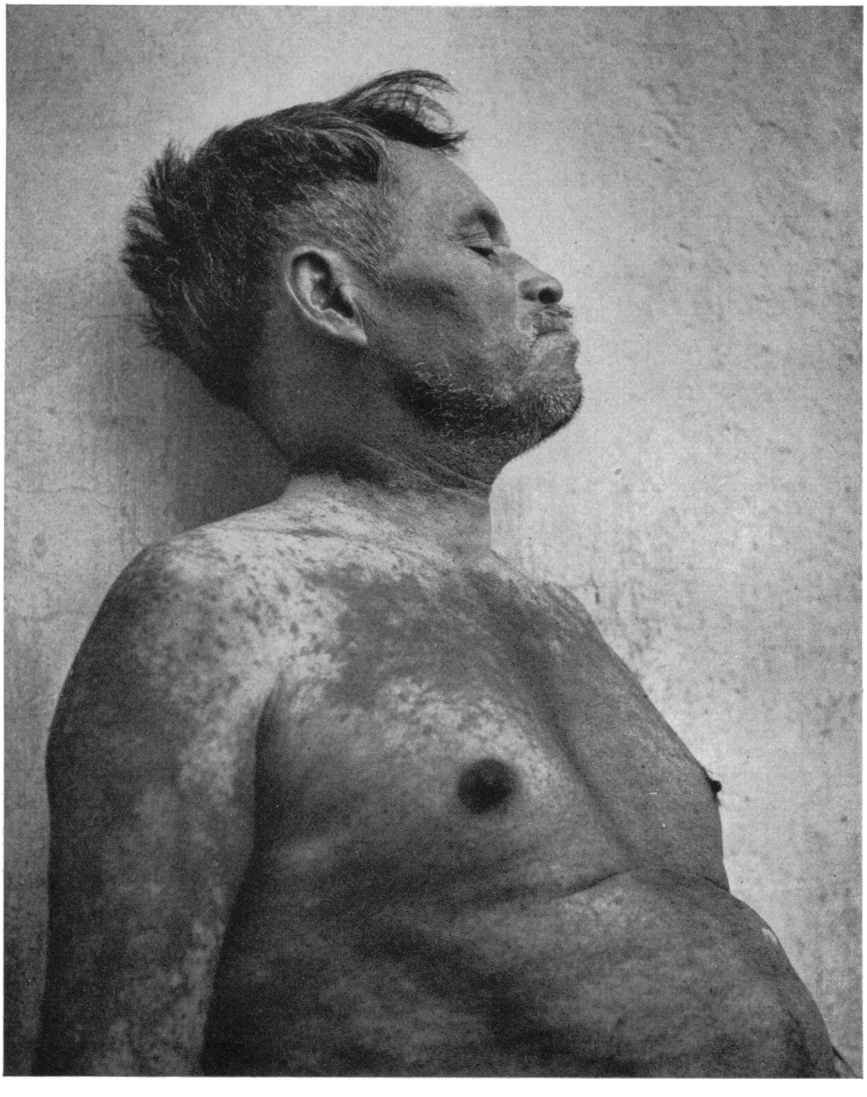


FIG. 6. DIFFUSE AREAS OF PIGMENTATION ON THE FACE IN LATE PINTA

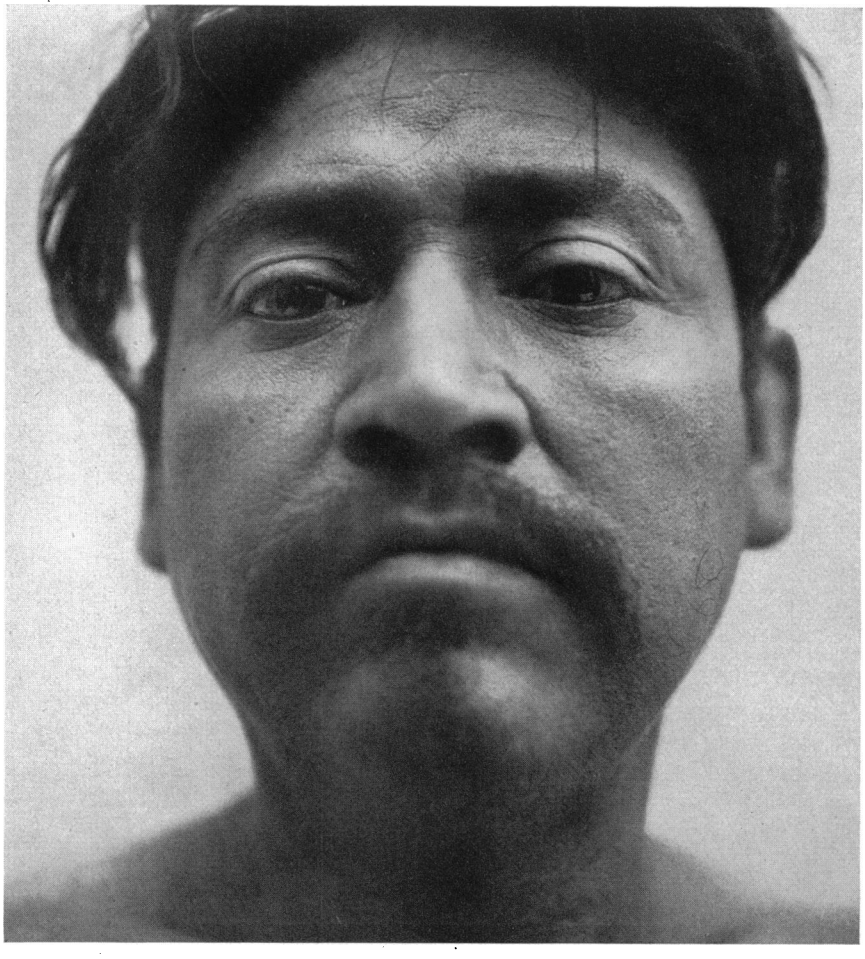


FIG. 7. LARGE POLYCHROMIC AND KERATOTIC PLAQUE IN THE INTERMEDIATE TYPE OF LATE PINTA

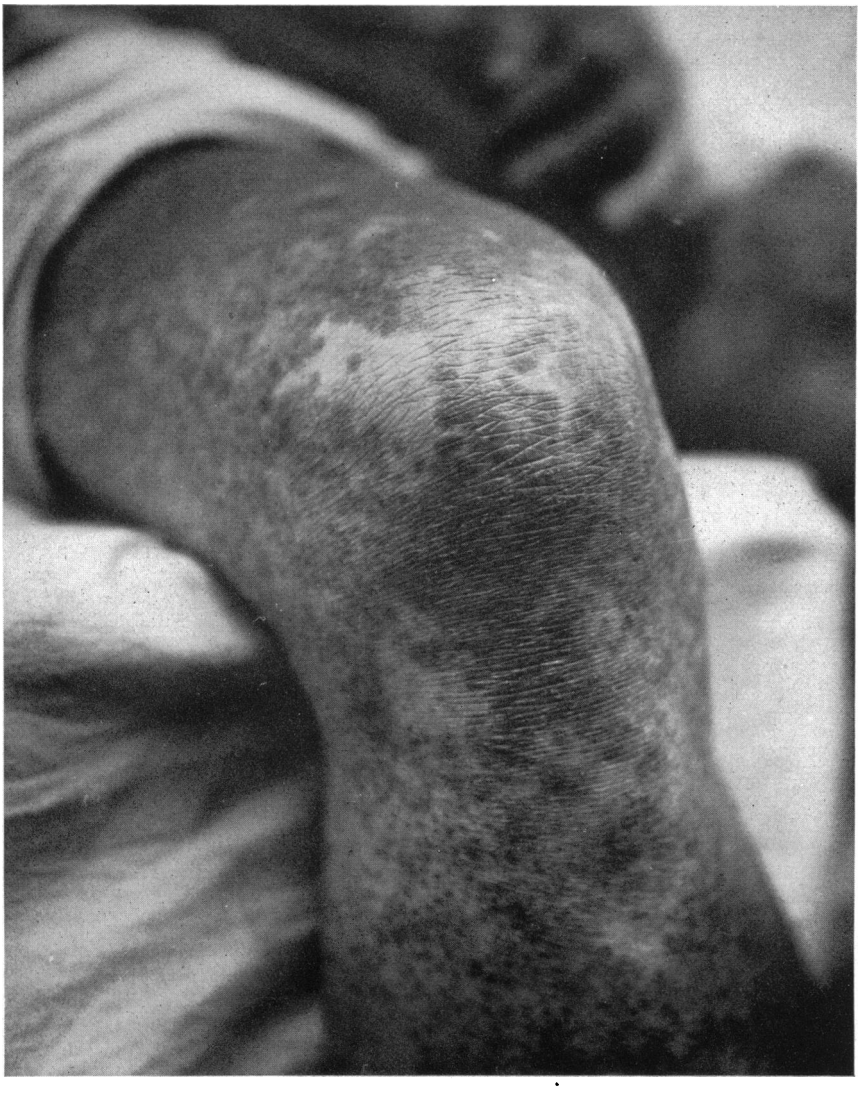
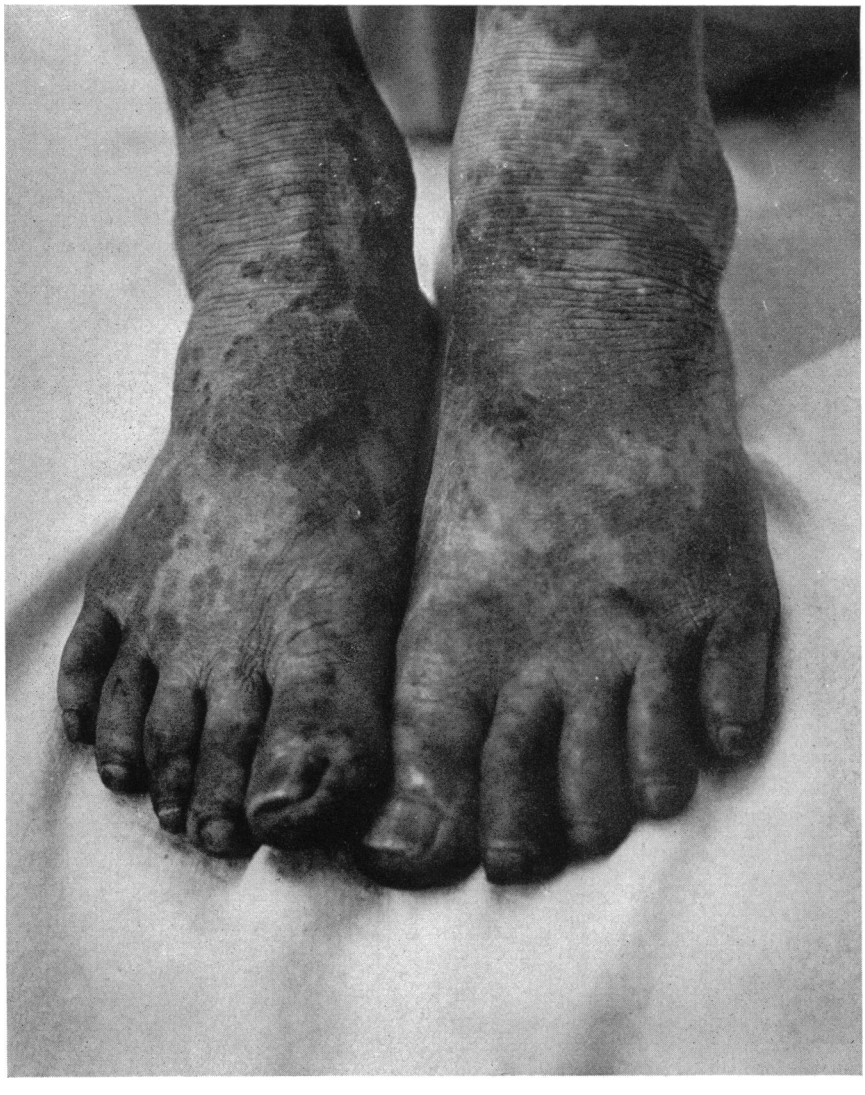


FIG. 8. POLYCHROMIC AND KERATOTIC LESIONS IN THE INTERMEDIATE TYPE OF LATE PINTA



Pintides may recur, either early (1 to 2 years) or late (10 years or more) in the course of the disease. Recurrent pintides may appear on the same site as the original lesions, but they are usually less numerous and frequently larger, sometimes reaching a diameter of 10 cm or more. Although they may be psoriasiform or circinate, they usually occur as erythematous scaly plaques with ill-defined borders. This type sometimes becomes keratotic, especially when located on the legs, knees, ankles, wrists, elbows, or loin. In some instances, new erythematous recurrent plaques intermingle with the pigmented and leukodermic areas resulting from the original pintides, so that diffuse, extensive, polychromic areas are formed, sometimes arranged on the extremities in sleevelike fashion. It is difficult to classify such patients since they have secondary and late pinta lesions at the same time (intermediate type). Recurrent pintides undergo the same regressive achromic changes as noted on the original disseminated lesions.

A very interesting finding in some cases of pinta is the presence of extensive areas of melanosis probably due to photosensitization. These patchy or diffuse areas of pigmentation are independent of the pinta lesions and resemble other types of melanosis due to photosensitization.[11, 26] The exposed areas of the body such as the face, neck, and to a lesser degree the backs of the hands, forearms, and arms, are most frequently involved. As these darkly pigmented areas merge with pigmented secondary or late lesions, it is nearly impossible to distinguish them from the active lesions. In fact, pigmentation of secondary and late lesions may be produced by the same mechanism of photosensitization.

Late pinta

Leukoderma represents the terminal stage of the disease. However, classification of this stage is also extremely difficult since it does not necessarily reflect the duration of the disease, but rather the rate of regression to the achromic phase. This may occur as early as three months following the onset, yet we have observed many patients with this achromia in whom there were also concomitant recurrent pintides for many years. Thus, some patients may present the late stage with achromic lesions in a few months, while other patients may continue to develop recurrent secondary lesions for many years. The late changes proceed in an irregular fashion, allowing an intermingling of all varieties of dyschromia, hypochromia, and achromia (Fig. 3-8). The dyschromic lesions appear chiefly on the face and with less frequency on the hands, wrists, forearms, legs, and feet. The hypochromic lesions appear on the thighs, legs, buttocks, forearms, arms, back, chest, and loin, whereas the achromic areas appear over bony prominences (elbows, feet, knuckles, wrists, knees, and ankles). In pinta of long duration, poikiloderma-like atrophic changes may occur, usually on the forearms, back of the hands, and legs.

Leukoderma or " white pinta " represents the terminal stage of the disease, either as a result of adequate therapy of old cases or even without treatment in those patients who become " spontaneously cured " after many years.

Histopathology

In contradistinction to other treponematoses, where clear-cut histopathological differences between one stage and the other are found, in pinta such differences are minimal. It is difficult to differentiate between the various stages, since the differences are more closely related to the duration of the disease and the age of the lesions than to a particular clinical stage—primary, secondary, or tertiary.

Early pinta

Primary and secondary lesions show similar histopathological pictures. At first, there is moderate acanthosis, slight spongiosis with a moderate inflammatory infiltrate in the upper portion of the dermis. The infiltrate, which is located chiefly around the dilated blood vessels, is made up primarily of lymphocytes with some histocytes, plasma-cells, and neutrophils. At this early stage, the pigmentary changes are minimal, which accounts for the erythematous colour of the lesions. As the lesions become older, there is some evidence of mild hyperkeratosis and some parakeratosis especially in the psoriasiform type. Hasselmann [8] has discovered other lesions which are characterized by the presence of lichen planus-like changes consisting of hyperkeratosis, granulosis, and some liquefaction degeneration of the basal cell layer. Keratotic follicular plugging may also be present. The lichen planus-like changes are more frequently found in cases of long duration or in recurrent secondary lesions.

Pigmentary changes are characteristic of the older lesions and, as described by Leon y Blanco,[19] consist of a decrease of melanin in the basal cell layer with a deposit of pigment in the dermis. Hasselmann [8] also described the decrease or absence of pigment in the deeper strata of the rete Malpighii with a deposit of pigment in the dermis, either in clumps or around the blood vessels. In a few instances, however, increase of pigment is found, both in the basal and the dendritic cells with intermingled areas of decreased and increased melanin.

Although there is some exocytosis in pinta lesions, intra-epidermal abscesses, as in yaws, are not found.[8] In contradistinction to syphilis the vessels of the dermis do not show proliferation or obliteration of their lumina. At most, the nuclei of the cells of the intima may occasionally appear prominent and enlarged.

Late pinta

Late intermediate or dyschromic lesions show changes similar to those described above. The leukodermic ones are characterized by the disappearance of the pigment in the epidermis. Few inflammatory changes are present.

In cases of very long duration poikiloderma-like atrophic lesions may be found, consisting of atrophy of the epidermis with thinning of the rete pegs, dilatation of the superficial vessels in the dermis, liquefaction degeneration of the basal cell layer, degeneration of the collagen, and destruction of the elastic fibres. Hair follicles and sebaceous glands are absent in such cases.

As Leon y Blanco has demonstrated, treponemes are found in the epidermis and dermis in early pinta, but only in the epidermis and pilosebaceous follicles in the later stages.

Treatment

Various preparations of arsenic, bismuth, and mercury have been used since Menk in Colombia and Gonzalez Herrejon in Mexico suggested the possibility that pinta was a spirochaetosis similar to syphilis and yaws. Variable results were obtained with the use of these preparations. Pardo Castello & Castanedo [28] and Varela & Avila [36] agreed that Mapharsen was efficacious for early lesions but was of no value in producing repigmentation of hypochromic lesions or in reversing positive serological reactions, which became negative in a few patients only.

Zozaya, Varela & Castro Estrada,[37] in 1947, treated several cases of pinta in Mexico with penicillin. Later, Rein et al.,[30] in the first Mexican mass study of pinta, treated a group of 665 pinta patients of the State of Guerrero, Mexico, and demonstrated the possibility of a satisfactory clinical and serological response by the use of a single dose of 1,200,000 units of procaine penicillin G in oil with 2% aluminium monostearate (PAM). Since that time, this repository penicillin, as well as the broad spectrum antibiotics (Terramycin, Aureomycin, streptomycin, chloramphenicol) have been employed in many thousand of cases. Although the broad spectrum antibiotics have been effective, the response is slower and the darkfield disappearance time of treponemes from the lesions is longer than with penicillin. Recently, a new penicillin salt (*N,N'*-dibenzylethylenediamine dipenicillin G) has been introduced for the treatment of syphilis.[5] Due to its extremely low solubility in water, penicillin serum levels prolonged over longer periods of time than with PAM can be obtained.

Rein and his associates [29] have reported on the value of a new combination of three penicillin salts (Panbiotic [a]) in the treatment of treponemal

TABLE IV. CLINICAL AND SEROLOGICAL TREATMENT RESULTS WITH PAM AND PANBIOTIC

	Number treated	Number re-examined after 2 years	Results	
			cured	improved
PAM series (665 cases)			clinical	
Stage of disease :				
primary	20	16	16	—
secondary	231	151	104	47
late	414	183	74	91
total	665	350		
			serological	
Serological testing		332	65	179
Panbiotic series (92 ca			clinical	
Stage of disease :				
primary	5	3	3	
secondary	49	35	34	
late	38	30	23	
total	92	68		
			serological	
Serological testing		57	10	45

diseases. A single dose of 2 ml in aqueous suspension provides 300 000 units of potassium penicillin G, 300 000 units of procaine penicillin G, and 600 000 units of *N,N'*-dibenzylethylenediamine dipenicillin G. It was conceived by Buckwalter, who felt that the variations in solubility of each penicillin salt when administered as a single intramuscular injection should provide an initial high blood concentration within an hour, an intermediate blood concentration for 24 to 36 hours, and a prolonged blood concentration for at least 15 days or longer in the majority of patients. The clinical and serological results obtained in a series of 665 pinta patients treated with PAM and 92 patients treated with Panbiotic are given in Table IV.[b] All patients who were available or could be found were subjected to clinical and serological re-examination.

a Bristol Laboratories, Inc., Syracuse, N.Y., USA

b The first series of cases was treated with PAM ; several years later a new series was treated with Panbiotic, when this new repository type of penicillin became available.

RÉSUMÉ

Le mal del pinto est une tréponématose endémique non vénérienne, caractérisée par des lésions cutanées avec dyspigmentation partielle ou totale. Elle existe principalement en Amérique centrale et en Amérique du Sud ; des cas ont été signalés en Afrique, en Asie et en Océanie.

Cette étude concerne plus particulièrement le Mexique, où l'on estime à un demi-million le nombre des cas. La prévalence maximum (20%) s'observe dans l'Etat de Guerrero. La maladie n'a pas de distribution géographique nette. Au Mexique, on trouve quelques cas en haute altitude, mais la plupart se rencontrent dans les terres basses. Elle est plus fréquente dans les zones tropicales sèches. La maladie est répandue parmi les couches les moins favorisées de la population, dans les petits villages ayant de mauvaises conditions d'hygiène, avec une légère prédominance chez les femmes. Le mal del pinto frappe surtout les enfants (61,6% des cas s'observent dans les groupes d'âge de 1-15 ans). Il se transmet par contact, à la faveur d'une éraflure ou d'une blessure cutanée, d'autant plus facilement que le corps est moins protégé par des vêtements et que la promiscuité, dans les habitations, est plus étroite. Le mal del pinto n'est pas une affection congénitale ; on ne l'a observé qu'exceptionnellement chez les enfants de moins de six mois. La transmission passive, par les déjections d'insectes s'étant nourris sur les sécrétions des lésions, quoique possible, ne joue pas de rôle dans l'épidémiologie de la maladie.

Le mal del pinto est causé par *Treponema carateum*, morphologiquement semblable aux tréponèmes de la syphilis, du pian et du béjel. Comme ces derniers, il est sensible à l'arsenic, au bismuth, au mercure et aux antibiotiques. Bien que la réponse clinique à la pénicilline soit plus lente que dans le cas de la syphilis, le tréponème disparaît du sang, après traitement, aussi vite que les agents des autres tréponématoses. L'inoculation expérimentale à l'homme ainsi que la transmission par transfusion de sang ont donné des résultats positifs. La maladie n'affecte ni le foie, ni la rate, ni les reins, ni les systèmes nerveux et cardiovasculaire. Il n'existe pas d'immunité croisée appréciable entre les divers tréponèmes, agents de la syphilis, du pian et du mal del pinto.

Il est difficile de délimiter les stades successifs de développement de la maladie, comme on le fait pour les autres tréponématoses. Les premières manifestations (phase récente primaire) sont des papules lenticulaires légèrement écailleuses qui atteignent 3 cm de diamètre après 2-3 mois et 10 cm en 1-2 ans ; elles peuvent confluer. Elles sont localisées — par ordre de fréquence — aux extrémités inférieures, au visage, au cou, aux membres supérieurs, au thorax, à l'abdomen. Un mois après l'apparition de la lésion initiale, surviennent des lésions secondaires qui peuvent ressembler aux lésions primaires. Les lésions disséminées ont été appelées « pintides », par analogie avec les syphilides. D'abord de couleur cuivrée, puis plombée, elles deviennent bleu-ardoise — la pigmentation étant plus rapide sur les parties découvertes du corps — puis elles se décolorent progressivement.

La leucodermie représente le stade final de la maladie, qu'il s'agisse de guérison survenant spontanément ou à la suite du traitement. Elle peut coïncider avec l'existence de pintides colorées récurrentes.

Après avoir décrit l'histopathologie de la maladie, les auteurs discutent le traitement. L'arsenic, le bismuth et le mercure ont été employés avant l'introduction des antibiotiques. Dès 1947, le mal del pinto a été traité par la pénicilline. Dans la première campagne systématique effectuée au Mexique, des résultats satisfaisants ont été obtenus avec une injection unique de 1 200 000 unités de PAM. D'autres antibiotiques à spectre d'activité étendu ont été utilisés avec succès. Récemment, une nouvelle préparation, le Panbiotic, réunissant trois sels de pénicilline (pénicilline potassique, PAM, sel de *N*-*N*'dibenzyléthylènediamine de la bipénicilline G) a donné des résultats encourageants. La combinaison de ces trois types de pénicilline ayant des solubilités différentes, assure une pénicillinémie élevée dès la première heure après l'injection et une concentration efficace durant 15 jours et plus.

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