Handbook of Endemic Treponematoses

P. L. Perine, D. R. Hopkins
P. L. A. Niemel, R. K. St. John
G. Causse, G. M. Antal

World Health Organization Geneva

Handbook of Endemic Treponematoses: Yaws, Endemic Syphilis, and Pinta

Peter L. Perine and **Donald R. Hopkins**
International Health Programs Office, Centers for Disease Control, Atlanta, GA, USA

Ronald K. St. John
Pan American Health Organization Washington, DC, USA

Paul L. A. Niemel
Dermatologic Service Paramaribo, Suriname

Georges Causse and **G. M. Antal**
World Health Organization Geneva, Switzerland

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Preface

In spite of a considerable decrease in the prevalence of yaws, endemic syphilis, and pinta as a result of WHO/UNICEF-sponsored national control campaigns during the 1950s and 1960s, these diseases are still endemic in many parts of the world. They are usually found in remote, rural populations that have little or no access to health care and among whom the large-scale treatment activities that are needed are the most difficult to apply. In addition, constant surveillance and active case-finding and case-reporting are essential to the success of control work; these are activities that may be performed by locally-based community health workers, with support and guidance from health services at the district and national levels.

This handbook is intended to be a reference source for health care workers and public health personnel throughout the tropical and subtropical world whose duties include the diagnosis, treatment, and prevention of yaws, endemic syphilis (bejel), and pinta. It is not a comprehensive essay on the biology of the treponemes and does not discuss the pathology of these diseases in detail. It describes briefly the clinical manifestations of each disease, supplementing each description with colour photographs of characteristic lesions. The treatment of the endemic treponematoses is described, with emphasis on the epidemiological methods used to control these diseases. This information should enable health workers to make a correct diagnosis, give the proper treatment, and control (or even eliminate) treponematoses in the population they serve.

Contents

CHAPTER 1

Characteristics and history of the endemic treponematoses

Introduction

The endemic treponematoses—yaws, endemic syphilis (bejel), and pinta—are a group of chronic bacterial infections caused by treponemes. These organisms belong to the family Treponemataceae[1] and the genus *Treponema*. The agents of yaws, endemic syphilis, and pinta are *T. pertenue*, *T. pallidum*, and "*T. carateum*" (invalid)[2], respectively. Man is their only natural host.

Characteristics of treponemes

The treponemes that cause yaws, endemic syphilis, and pinta have identical morphology. Because of their small size and mass, they cannot be seen with an ordinary microscope unless a dark-field condenser is used. They look like thin, silver threads coiled like a corkscrew, and move with a characteristic rapid spinning motion.

The agent of venereal syphilis, also called *T. pallidum*, is identical in almost all respects to the organism that causes endemic syphilis. The difference is that late cardiovascular, neurological, and visceral complications are found with much greater frequency in venereal syphilis than in endemic syphilis. Thus, endemic syphilis is clinically similar to venereal syphilis, but epidemiologically is more closely related to yaws (Table 1).

There are a large number of non-pathogenic species of *Treponema* that are normally present in the mouth and intestinal and genitourinary tracts of man. These organisms are opportunistic pathogens and can stimulate the formation of antibodies that cross-react with the pathogenic treponemes of yaws, endemic syphilis, and pinta. While the avirulent treponemes can be cultured, the pathogenic treponemes do not grow *in*

[1] The other members of the Treponemataceae are *Borrelia* and *Leptospira*, which cause relapsing fever and leptospirosis, respectively.

[2] Bacterial names appearing in quotation marks in the text have no standing in nomenclature since they have not been validated by the International Committee on Systematic Bacteriology.

Table 1. Epidemiological characteristics of treponemal diseases

Epidemiological characteristic	Treponemal disease			
	Venereal syphilis	Endemic syphilis	Yaws	Pinta
Occurrence	sporadic, urban	endemic, rural	endemic, rural	endemic, rural
Geographical distribution	worldwide	South-west Asia, sub-Saharan regions of Africa, Bosnia	Africa, south-east Asia, Western Pacific, South America, Caribbean	Central and South America, Mexico,
Climate in which the disease mostly occurs	all types	arid, warm	humid, warm	semi-arid, warm
Age group with peak incidence (years)	18–30	2–10	2–10	15–30
Transmissibility	high	high	high	low
Mode of transmission:				
Direct (person to person)				
Sexual	usual	no	no	no
Non-sexual	rare	yes	usual	probable
Indirect				
Utensils	rare	usual	rare	unknown
Contaminated fingers	unknown	unknown	probably frequent	unknown
Congenital	occasional	unknown	no	no
Reservoir of infection	adults	children 2–15 years old; contacts in home, school and village; latent cases capable of becoming active	children 2–15 years old; contacts in home, school and village; latent cases capable of becoming active	cases with long-standing skin lesions

vitro. *T. pallidum* and *T. pertenue* are maintained in the laboratory by infecting laboratory animals or by freezing the organisms (at $-70\,^{\circ}C$ or below) in infected tissue or in special solutions.

The treponemes of yaws, pinta, and the different types of syphilis are closely related. Infection with one organism provides partial protection against infection by another, which indicates that they share common antigens. There is no laboratory test that can distinguish these treponemes from one another. *T. pallidum* and *T. pertenue* cause different lesions when inoculated into rabbits and hamsters, but this has no practical significance. "*T. carateum*", on the other hand, produces lesions only in man and higher apes.

The most notable characteristic of the pathogenic treponemes is their tendency to cause a chronic infection that progresses by stages of

clinically apparent disease. Two stages are usually recognized: early and late. Each stage may present lesions that differ in location and morphology. In yaws and endemic syphilis, only the lesions of the early stage are infectious, and may recrudesce during the first 5 years of latency and serve as a source for new cases in the community.

The close relationship between the pathogenic treponemes suggests that they have a common ancestor. A popular theory speculates that a single treponemal disease originated in primitive man in equatorial Africa. It was transmitted by social contact, and over the millennia, it spread the world over, following man's migrations. This disease changed its characteristics according to place, race and climate, giving rise first to pinta and then to yaws and endemic syphilis. According to this "unitarian" theory, a mutation caused the organism of endemic syphilis to become more virulent, which led to the appearance of venereal syphilis in Europe in the late 15th century.

Whatever their origin, the endemic treponematoses were until recently among mankind's most common afflictions. In the land mass between the Tropics of Cancer and Capricorn, these infections constituted a vast public health problem. Although seldom, if ever, fatal, the treponematoses caused serious public health, social and economic problems in the communities in which they occurred.

History of epidemiology and control programmes

The first effective drugs for the treatment of yaws and venereal and endemic syphilis were the arsenicals, which were discovered by Dr Paul Ehrlich in 1910. They remained the drugs of choice until penicillin became widely available in the 1940s. Unfortunately, these drugs had serious toxic side-effects. It was necessary to give arsenicals by a series of injections over a period of several weeks to achieve a cure. In some areas the prevalence of clinical yaws did decrease after treatment of all active cases with arsenicals and other metal therapy. However, this did not eliminate yaws from the population because it was not then appreciated that treatment was also necessary for the patient's symptomless contacts who had incubating or latent infections.

The remarkable curative power of benzylpenicillin (penicillin G) in venereal syphilis was demonstrated in 1943, and shortly thereafter in yaws, endemic syphilis, and pinta. The need to give several injections of benzylpenicillin as well as its high cost limited the use of the drug for the treatment of the endemic treponematoses until the late 1940s, when improved technology lowered manufacturing costs and led to the development of inexpensive, long-acting penicillin preparations. These long-acting, repository benzylpenicillin preparations—namely, penicillin aluminium monostearate (PAM) and benzathine benzylpenicillin—were very effective against the endemic treponematoses when given in a single intramuscular injection.

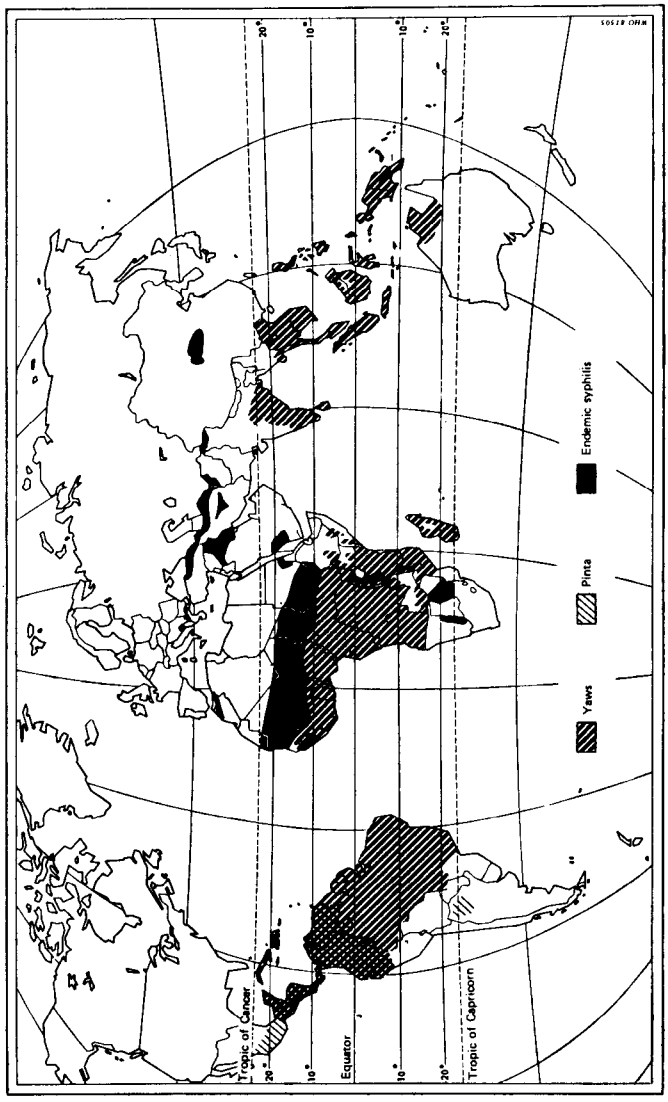

Fig. 1. Geographical distribution of the endemic treponematoses in the early 1950s

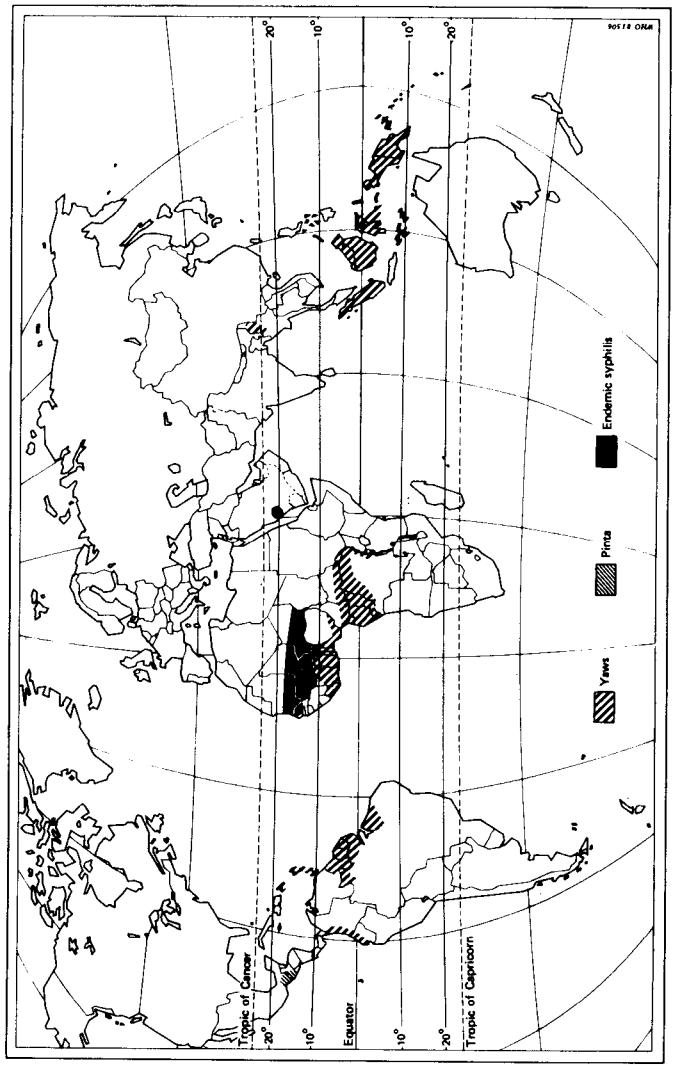

Fig. 2. Geographical distribution of the endemic treponematoses in the early 1980s

Yaws control campaigns using PAM or benzathine benzylpenicillin in Haiti, Indonesia and Jamaica were remarkably successful in lowering the prevalence of the active form of the disease. These campaigns also established the epidemiological concept that penicillin treatment was necessary for asymptomatic household contacts and presumed latent cases, in order to abolish the reservoir of infection.

In 1948, WHO, together with UNICEF, established a global yaws control programme based on the premise that mass penicillin treatment, if carefully planned and carried out, would result in a significant reduction in the incidence of infectious cases, which could then be kept to a minimum by thorough case-finding and preventive measures. Because yaws is so closely related clinically and epidemiologically to endemic syphilis, and to a lesser extent to pinta, mass penicillin treatment was later extended to include these infections.

Mobile teams were formed to give penicillin treatment to yaws patients and their contacts. Where the prevalence of cases with active lesions was 10% or greater, penicillin was given to the entire community; where the prevalence was between 5 and 10%, penicillin was given to patients, household contacts, and all children under 15 years of age; where the prevalence was less than 5%, only active cases and household contacts were treated. Follow-up surveys of treated communities were deemed essential in order to prevent reinfection of the community and to detect and treat: (*a*) cases that may have been missed; (*b*) those in whom the treatment had failed; and (*c*) infected immigrants. The case-finding techniques used in these surveys included house-to-house searches by "yaws scouts"—a technique later used with great success in the smallpox eradication programme. Mass campaigns were organized and coordinated to create ever-enlarging yaws-free areas. Every effort was made to integrate post-campaign yaws surveillance into the permanent health service of the community where such existed. Experienced mobile teams were assigned to groups of health posts to follow up all new active cases of the disease.

The problems facing the yaws control programmes were enormous. About half of the 400 million people living in the tropical belt between the Tropics of Cancer and Capricorn were likely to be exposed to yaws during their lifetime (Fig. 1). Most of these people lived in the warm, humid, rural parts of Africa, America, south-east Asia, Australia and the neighbouring Pacific islands, and the Indian subcontinent. Up to 80% of those exposed were infected, and at any given time, up to 20% of those infected had clinical yaws. Approximately 10% of those infected with yaws were invalids because of late crippling lesions or were severely disfigured.

Foci of endemic syphilis were present in Afghanistan, North Africa, southern Africa, south-west Asia, China and Europe. The largest concentration of cases was in south-west Asia and the sub-Saharan regions of Africa. The estimated prevalence of clinical disease ranged from 3% to 5% of the population, but the incidence of late destructive lesions was much higher than that found in yaws.

Pinta was confined to the western hemisphere, and in the 1950s, there were an estimated one million cases in Central America, northern South America, and Mexico.

In the 1960s, in many countries the mobile teams that conducted the yaws treatment campaigns were dismantled or given other assignments and, although an effort was made to incorporate yaws control into the primary health care system, there was little active case-finding or prophylactic treatment of contacts. This led to the persistence or resurgence of endemic foci, from where the infection is again spreading, thus threatening the gains made by previous mass-treatment campaigns. This applies particularly to areas of western and central Africa and, to a lesser extent, to Asia.

Over the past 10 years, the trends in the incidence of the endemic treponematoses have differed according to the particular disease and the geographical region. Pinta continues to decrease in prevalence and is at present restricted to a few areas of Central America, Colombia, and southern Mexico, although only limited surveillance has been done in the past decade (Fig. 2).

Endemic syphilis has also decreased in prevalence in the world as a whole, but foci of infection persist in Africa and south-west Asia. A recent survey found thousands of cases of early endemic syphilis in Mali, Mauritania, Niger, and Upper Volta. This suggests that today endemic syphilis may be a much greater problem in sub-Saharan Africa (Sahel) than it was formerly.

Yaws has shown the greatest changes in regional prevalence since the mass treatment campaigns. In South America only scattered foci of active yaws persist. Previously heavily infected countries such as Brazil and Suriname are almost yaws-free, and in other areas such as Colombia, Ecuador, French Guiana, and Guyana only a few dozen or hundred cases are reported annually. However, there is little active case-finding in these countries. In south-east Asia, yaws still exists in Indonesia and Papua New Guinea.

Africa remains the main reservoir of yaws in the world. Several patterns of yaws prevalence are evident. In many countries, e.g., Ivory Coast and Nigeria, clinical cases of yaws are declining owing to a combination of improved rural health care and improved standards of living. In other countries, yaws has increased to levels approaching those of the pre-campaign era. An example is Ghana, where premature curtailment of surveillance by mobile medical field units and economic difficulties have contributed to the recrudescence of the disease.

Yaws is underreported in most African countries since the disease occurs predominantly in remote rural areas or among isolated tribes, such as the Pygmies in the Central African Republic, the Republic of Cameroon, and Zaire. Finally, countries that have achieved good control over endemic treponematoses are constantly under the threat of importation of these diseases from nearby areas. Without renewed control programmes, the gains made by the mass treatment campaigns of 20 years ago will soon be lost in some African countries.

CHAPTER 2

Yaws

In areas where yaws has long been endemic, there are names for it in the local language or dialect. Some of its synonyms are: *pian* (French); *framboesia* (German, Dutch); *buba* (Spanish); *bouba* (Portuguese).

Causative agent

The organism responsible for yaws is *Treponema pertenue*. It is identical in appearance to *T. pallidum* (the organism that causes venereal and endemic syphilis) and "*T. carateum*" (the cause of pinta). *T. pertenue* does not cause congenital infections because it cannot cross the placenta. It produces lesions in the skin, bone, and cartilage, but not in deeper tissues or organs. Like other pathogenic treponemes, it is easily killed by drying, exposure to oxygen, and elevated temperature. The organism multiplies very slowly (once every 30–33 hours) in man and experimentally infected animals. It does not grow in culture.

Occurrence

Yaws occurs primarily in the warm, humid, tropical areas of Africa, Central and South America, the Caribbean and the equatorial islands of south-east Asia. In the endemic areas where wet and dry seasons alternate, clinical manifestations and the prevalence of infectious yaws lesions increase during the rainy season.

Reservoir

Children aged 2–15 years and latent cases serve as the reservoir of infection. A yaws-like treponeme (the so-called "*T. fribourg–blanc*" (invalid)) has been isolated from west African monkeys and baboons, but its significance for human yaws is unknown.

Mode of transmission

Yaws is transmitted by direct (person-to-person) non-sexual contact with the exudate or serum from infectious yaws lesions (early or relapse papules, papillomata, ulceropapillomata, or macules). Late yaws lesions (deep ulcers, gangosa, bone, and hyperkeratotic palmar and plantar lesions) are not infectious. Indirect transmission by insects and contaminated utensils (fomites) is generally of limited significance.

The spread of yaws may be facilitated by crowding and poor community sanitation. The lack of water and soap for bathing and washing and of shoes and clothing for children between the ages of 5 and 15 years are said to favour yaws transmission.

Course of infection

The clinical course of a hypothetical case of yaws is as follows. The initial or primary papule, sometimes called the mother yaw, appears on the skin at the site of entry of *T. pertenue* after an incubation period of 9–90 days (average, 21 days). The site of entry is often a pre-existing abrasion, laceration or insect bite. During the incubation period the organism multiplies at the infection site, invades subcutaneous lymphatics, and spreads through the bloodstream.

The yaws papule enlarges to become an early papilloma or framboesioma; it is very rich in treponemes. This lesion usually lasts 3–6 months. It may heal spontaneously before the appearance of the first crop of early secondary yaws lesions, thereby creating a brief period of latency.

The early secondary yaws lesions may appear on the skin near the initial lesion or elsewhere in the body, including bone and cartilage. These lesions result from autoinoculation and from the spread of *T. pertenue* systemically. Each crop of early secondary lesions may persist for more than 6 months; the lesions heal spontaneously, and do not leave scars unless they become ulcerated and secondarily infected by certain other bacteria. The disease then enters a non-infectious latent period, which may last the lifetime of the patient.

The state of latency can be interrupted at any time by the reappearance or relapse of infectious yaws lesions. These relapses tend to occur at intervals for up to 5 years after infection. Relapsing lesions tend to be localized to the periaxillary, perianal, or circumoral areas. The total duration of infectiousness for an untreated yaws patient, including relapses, is probably of the order of 12–18 months.

Late, active yaws lesions are often destructive and develop in as many as 10% of cases; these lesions may develop early in the course of the infection, but they more usually appear several years after the initial infection.

Types of yaws lesion

Yaws produces a great variety of skin, bone and joint lesions (the terms used to describe or modify the description of skin lesions are defined in the glossary presented in Annex 1). The cutaneous yaws lesions have a number of common characteristics:

— Early lesions are often pruritic, and scratching facilitates both spread of the infection to other areas of the body by autoinoculation and the transmission of the disease within the community.
— The early lesions tend to occur in crops, which often overlap with one another.
— Mixed (polymorphous) forms of lesions are often present in the same patient;
— A change in climate may influence the number and morphology of yaws lesions. In the dry season fewer lesions are present and they tend to be of the macular type; papillomata tend to retreat to the more humid areas of the body surface such as axillae and anal folds.
— Induration is not a common feature of early yaws lesions.

Despite the variety of yaws lesions, in endemic areas the disease can usually be accurately diagnosed on the basis of clinical findings alone.

Constitutional symptoms such as fever and malaise are not significant in yaws. The lymph nodes draining cutaneous lesions are frequently enlarged and tender, but they do not suppurate. Nocturnal bone pain and tenderness of the tibial shaft and other long bones due to periostitis are common in early yaws.

The nomenclature and classification of yaws lesions are given in Table 2.

Differential diagnosis

Diseases commonly confused with yaws are as follows:

— *Impetigo*. A common skin infection of children caused by streptococci or staphylococci (Fig. 40 and 41).
— *Tinea versicolor* (pityriasis versicolor). A superficial skin infection caused by the fungus, *Malassezia furfur*, characterized by fawn-coloured scaling macules or patches on shoulders, chest, upper back and abdomen (Fig. 42).
— *Molluscum contagiosum*. A viral disease of the skin producing pink or white papules with a prominent central core, which may appear anywhere on the body (Fig. 43).
— *Scabies*. Infestation of human skin by *Sarcoptes scabiei*, producing cutaneous papules or vesicles caused by the burrowing into the skin of the mite. Lesions are prominent around finger webs and the anterior surfaces of elbows and wrists. Scabies is frequently accompanied by severe itching (Fig. 44 and 45).

Table 2. Classification of yaws lesions

Early yaws lesions	*Examples*	*Infectiousness*[a]
Initial lesions	papilloma (Fig. 3)	+ + +
Papillomata	papillomata (Fig. 4, 5, 6, 7, 8, 9, 10)	+ + +
	serpiginous papilloma (Fig. 11)	
	ulceropapillomata (Fig. 12, 13, 14)	
Macules	squamous macules (Fig. 15 and 16)	+
	palmar (Fig. 17), plantar (Fig. 18)	
Maculopapules	maculopapulomatous (Fig. 19)	+ +
	mucocutaneous (Fig. 20)	
Papules	squamous micropapules (Fig. 21)	+ +
Micropapules	polymorphous (Fig. 22)	+ +
Nodules	Fig. 23	+
Plaques	Fig. 24	+
Hyperkeratosis	plantar (Fig. 25, 26, 27)	–
	palmar (Fig. 28)	
Bone and joint lesions	polydactylitis (Fig. 29)	–
	osteoperiostitis (Fig. 30 and 31)	–
Late yaws lesions		
Hyperkeratosis	Fig. 26, 27, 28 (hyperkeratotic lesions may be similar in both late and early yaws)	–
Nodular	scars (Fig. 32)	–
Ulcerated nodular	gangosa (Fig. 33, 34, 35);	–
Plaques	osteoperiostitis (Fig. 36);	–
Bone and joint	sabre tibia (Fig. 37); gondou (Fig. 38); monodactylitis (Fig. 36)	–
Juxta-articular nodules	Fig. 39	–

[a] – = not infectious; + = infectious; + + = very infectious; and + + + = highly infectious.

— *Lichen planus*. A chronic inflammatory disease of unknown etiology characterized by flat-topped, shiny papules with a characteristic violet hue (Fig. 46).

— *Tropical ulcer* (ulcus tropicum). A painful ulcer that usually occurs on the lower limbs in the humid tropics. It is caused by a mixed infection with "*Treponema vincentii*", *Fusobacterium nucleatum* and other bacteria. In contrast to yaws ulcerations, tropical ulcers have well-defined edges, a purulent base, and may penetrate into tendons and bone (Fig. 47).

— *Plantar warts* (verruca plantaris). A tender, flat wart on the sole of the foot caused by a papovavirus; may be confused with plantar papilloma (Fig. 48).

— *Tungiasis* (jiggers). Plantar lesions caused by the burrowing of the female sand-flea, *Tunga penetrans* (Fig. 49).

— *Cutaneous leishmaniasis*. An indurated, usually solitary nodule or chronic ulceration caused by *Leishmania* species (Fig. 50).

— *Leprosy*. The lesions of both lepromatous and tuberculoid forms of leprosy caused by *Mycobacterium leprae* may be mistaken for yaws; however, anaesthesia is never caused by yaws (Fig. 51).
— *Psoriasis*. This chronic, hereditary skin disease may sometimes be mistaken for yaws. Its distinctive lesions are red macules covered almost to their edges by whitish or silvery lamellated scales. It usually involves the knees, elbows, trunk, and scalp (Fig. 52 and 53).