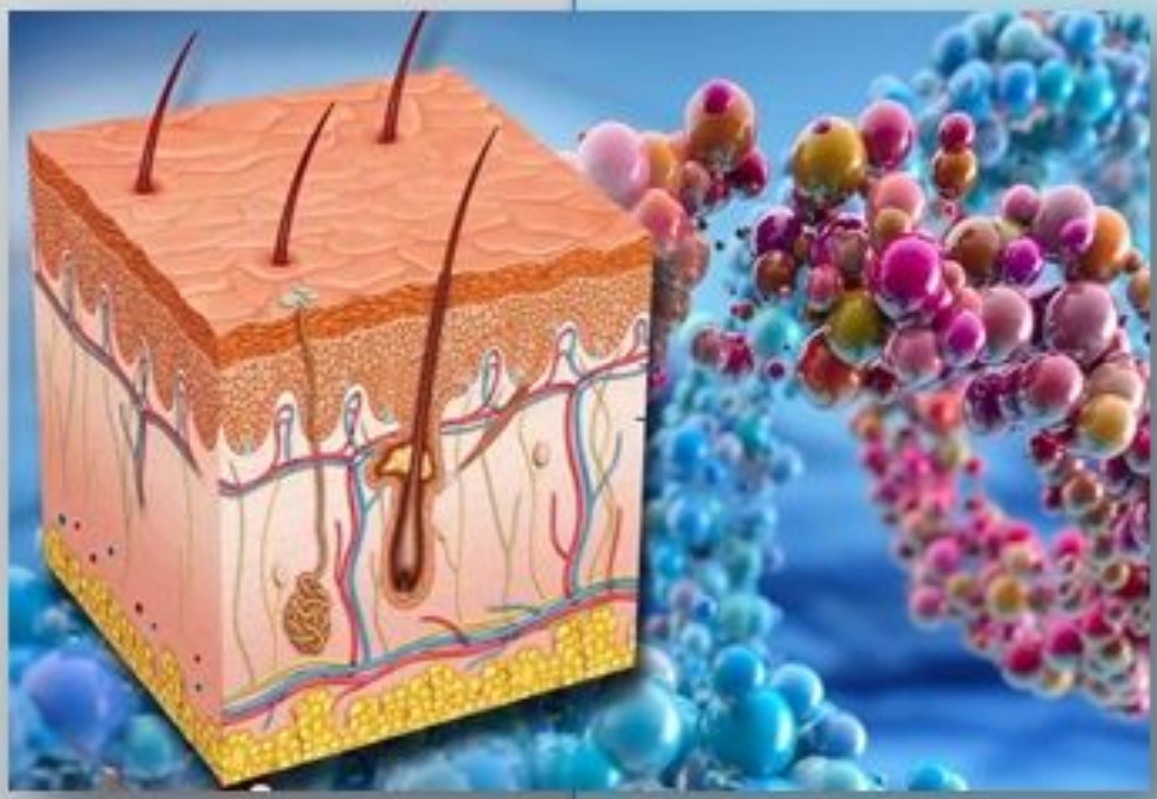
A.B. PAKIRDINOV

LEPRAE HANSEN'S DISEASE. CUTANEOUS LEISHMANIASIS. DERMATOZOONOSES.

STUDY GUIDE



KAFOLAT TAFAKKUR
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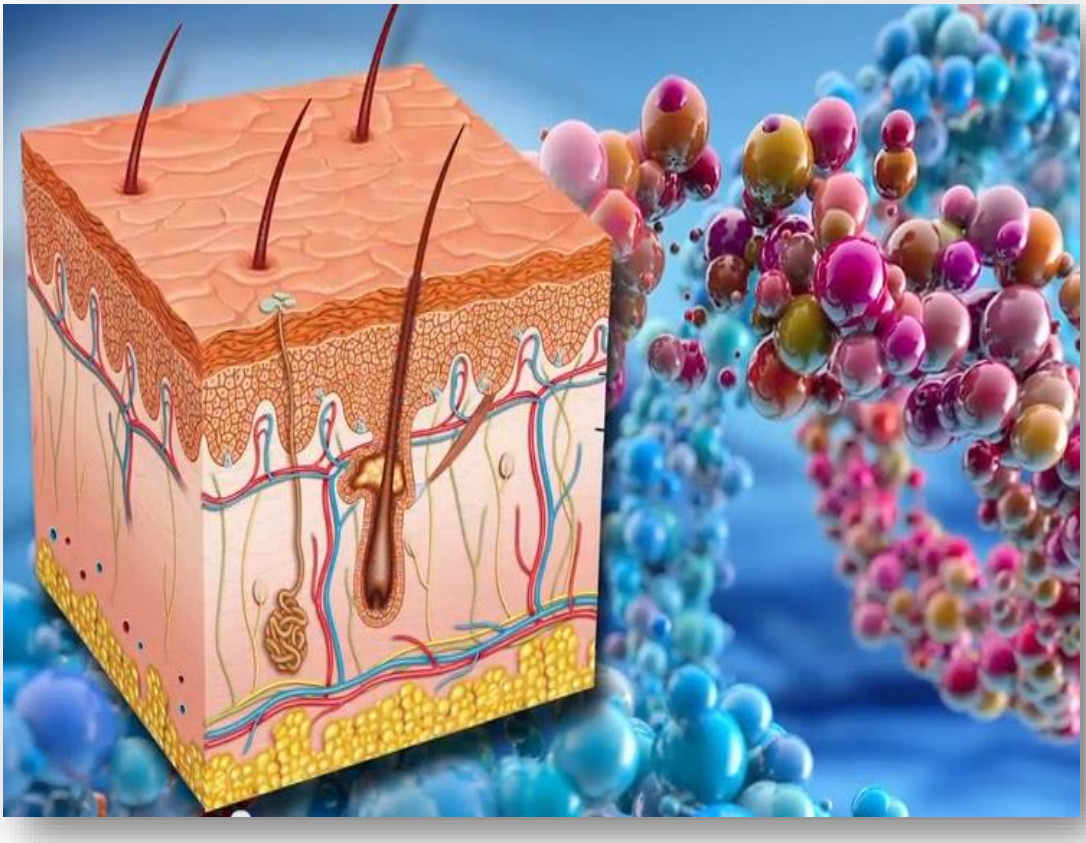

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ANDIJAN – 2024

THE MINISTRY OF HEALTH CARE OF REPUBLIC OF UZBEKISTAN

THE CENTER FOR DEVELOPMENT OF MEDICAL EDUCATION

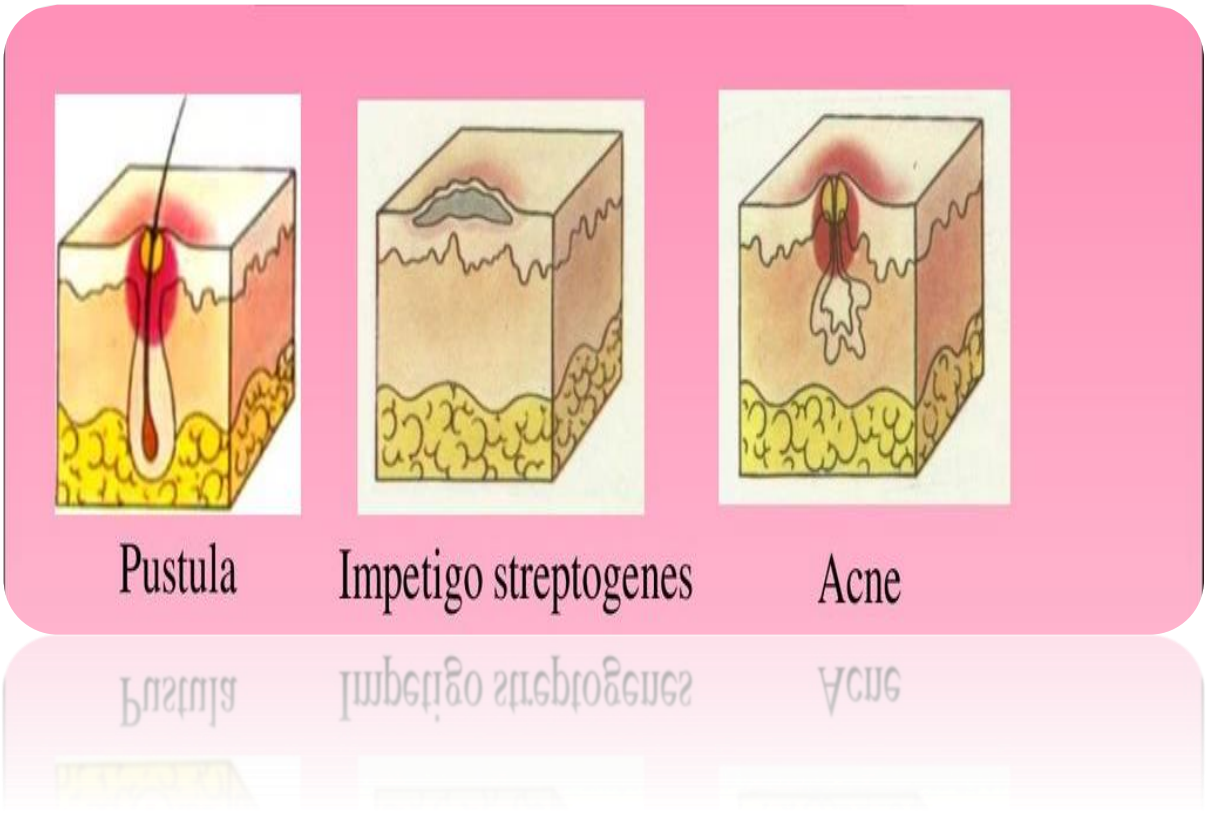
ANDIJAN STATE MEDICAL INSTITUTE

THE DEPARTMENT OF DERMATOLOGY AND VENEREOLOGY

THE DEPARTMENT FACULTY AND HOSPITAL SURGERY

LEPRAE HANSEN'S DISEASE. CUTANEOUS LEISHMANIASIS. DERMATOZOONOSES.

(FOR RESIDENTS, CLINICAL INTERNS, TREATMENT AND PEDIATRICS STUDENTS)



KAFOLAT TAFAKKUR
ANDIJAN – 2024

UDC: 616.5
LBC: 55.8
D36

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Collection of Lectures were reviewed and approved on the internal meeting Protocol: № ___ «__» _____ 2024 year
Professor, Chairman of internal meeting: **A. B. PAKIRDINOV**

Collection of Lectures were reviewed and approved by central methodical committee at Andijan State Medical Institute Protocol № __ «__» ____ 2024 year

Professor: **M.M. MADAZIMOV**

Collection of Lectures were reviewed and approved by Academic Council at Andijan State Medical Institute Protocol № ___ «__» _____ 2024 year
Academic Council Secretary, docent: **N.A. NASRITDINOVA**

ISBN: 978-9910-711-13-8

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LEPRAE HANSEN'S DISEASE

Epidemiology

The World Health Organization (WHO) has committed itself to eliminating Hansen's disease as a public health problem. Elimination (not eradication) is considered as a prevalence of less than 1 case in 10 000 persons in any country. This target was globally met in 2000. The number of new cases of Hansen's disease declined from more than 750 000 in 2001 to 250 000 in 2007. As of 2008, three countries have yet to meet this elimination goal: Brazil, Nepal, and Timor-Leste. Hansen's disease is endemic in certain regions, with 95% of cases for the last two decades reported from 17 countries. Brazil, India, and Indonesia account for 76% of all cases worldwide Although 90% of cases diagnosed in the US are imported, Hansen's disease is endemic in the coastal southeastern US and in Hawaii. In the southeastern US cases may be related to exposure to armadillos, a natural host for the infectious agent.

It is believed that more than 90% of persons exposed to *Mycobacterium leprae* are able to resist infection. In endemic areas, 1.7-31% of the population is seropositive for antibodies to leprosy-specific antigens, suggesting widespread exposure to the bacillus. Around 17% of household contacts of multi- bacillary patients have *M. leprae* which is detectable by polymerase chain reaction (PCR) on skin swabs and 4% in nasal swabs. This clears after the multibacillary patient has been treated with multidrug therapy (MDT) for 2 months. Thus, it appears that while many persons can be transiently infected, they are able to resist overt clinical infection.

There appears to be a genetic basis for susceptibility to acquire Hansen's disease. Monozygotic twins have concordant disease in 60-85% of cases, and dizygotic twins in only 15-25%. Numerous genes have been identified as possibly conferring susceptibility to infection with *M. leprae*. Different genes have been identified in different populations, suggesting there may be multiple genetic causes of susceptibility to infection with *M. leprae*. Tight genetic linkage with the PARK2/ PACRG regulatory region, HLA-DRB1, and lymphotoxin A (LTA+80) has been

detected. *PARK2* is a gene involved in the development of Parkinson's disease, and LTA+80 is a lowproduction lymphotoxin A allele associated with malaria parasitemia.

In adults, cases in men outnumber those in women 1.5:1. Although Hansen's disease occurs at all ages, most cases appearing or acquired in endemic areas present before the age of 35. Patients exposed to armadillos present on average at age 50. The latency period between exposure and overt signs of disease is usually 5 years for paucibacillary cases, and an average of 10 years in multibacillary cases. Infected women are likely to present during or immediately after pregnancy.

The mode of transmission remains controversial. Except for cases associated with armadillo exposure, other cases of Hansen's disease are felt to be the only possible source of infection. Rarely, tatooing or other penetrating injury to the skin can be the route of infection. Multibacillary cases are much more infectious than paucibacillary cases, so the nature of the source case is the most important factor in transmission. Contact is associated with acquiring infection. Household contacts represent 28% of new Hansen's disease patients; they are at 8-10 times greater risk of acquiring disease if the household contact has lepromatous disease, as opposed to only 2-4 times if the contact has tuberculoid leprosy. In 80% of all new cases of Hansen's disease, there is a clear history of social contact with an untreated case of Hansen's disease. By PCR *M. leprae* can be detected on the intact skin by saline washings in up to 90% of multibacillary cases with a high bacterial load (bacterial index [BI] of over 3). Up to 70% of nasal swabs are similarly positive. While the swabs from the patients remain positive after 3 months of MDT, the household contacts swabs become negative, suggesting that the bacilli seen in patients are non- viable and that the risk of transmission is substantially reduced after the index patient is treated. Unfortunately, it may be possible that persons are infectious from their skin or nasal secretions with no clinical evidence of Hansen's disease (multibacillary patients who are not yet symptomatic and without identifiable skin lesions). This may make strategies relying on treatment of contacts of known Hansen's disease ineffective in eradicating the disease. In non-endemic areas transmission

to contacts is very rare, a reassuring fact for the families of patients diagnosed in areas where Hansen's disease is uncommon. The last case of secondary transmission of Hansen's disease in the UK was in 1923.

The infectious agent

All cases of human and animal leprosy are caused by the same organism, *M. leprae.* This is a weakly acid-fast organism that has not been successfully cultured in vitro. It grows best at temperatures (30°C) below the core body temperature of humans. This explains the localization of Hansen's disease lesions to cooler areas of the body and the sparing of the midline and scalp. The organism may be cultivated in mouse footpads and most effectively in armadillos, whose lower body temperature is more optimal for growth of *M. leprae.* Phenolic glycolipid-1 (PGL-1) is a surface glycolipid unique to the leprosy bacillus. In infected tissues, the leprosy bacillus favors intracellular locations, within macrophages and nerves. The genome of the leprosy bacillus has been sequenced and compared to its close relative, the tuberculous bacillus. The genome of *M. leprae* contains only 50% functional genes, apparently the result of significant reductive evolution. Like other intracellular parasites, and in the absence of the ability to share DNA with other bacteria, *M. leprae* has lost many nonessential genes, including those involved in energy metabolism, making it dependent on the intracellular environment for essential nutrients. This may explain the extremely long generation time, 12-14 days, and the inability to culture *M. leprae* in vitro. All *M. leprae* isolates are very homogenous genetically and can be divided into only four genetic variants. These genetic variations are not correlated with virulence.

Diagnosis

A diagnosis of Hansen's disease must be considered in any patient with neurologic and cutaneous lesions. The diagnosis is frequently delayed in the developed world; clinicians do not readily think of Hansen's disease, since they may not have seen it before. In the US, this

diagnostic delay averages 112-2 years. In the UK, in over 80% of cases of Hansen's disease, the correct diagnosis was not suspected during the initial medical evaluations.

Hansen's disease is diagnosed, as with other infectious diseases, by identifying the infectious organism in affected tissue. Because the organism cannot be cultured, this may be very difficult. Skin biopsies from skin or nerve lesions, stained for the bacillus with Fite-Faraco stain, are usually performed in the developed world. In some Hansen's disease clinics, and in the developing world where disease is endemic, organisms are identified in slit smears of the skin. Smears are very specific, but 70% of all patients with Hansen's disease have negative smears. Smears are taken from lesions and cooler areas of the skin, such as the earlobes, elbows, and knees. If organisms are found on skin smears, the patient is said to be multibacil- lary. If the results of skin smears are negative (and there are five or fewer lesions), the patient is called paucibacillary.

Nerve involvement is detected by enlargement of peripheral nerves and lesional loss of sensation. Enlarged nerves are found in over 90% of patients with multibacillary Hansen's disease, and in 75-85% of patients with paucibacillary disease. About 70% of Hansen's disease lesions have reduced sensation, but lesional dysesthesia is not detected in patients with multibacillary disease, the most infectious form.

Serologic tests to detect antibodies against *M. leprae-unique* antigens (PGL-1) and PCR to detect small numbers of organisms in infected tissue have not improved diagnosis. They are universally positive in patients with multibacillary disease, in whom the diagnosis is not difficult. In paucibacillary patients these tests are often negative, and in endemic areas there is a high background rate of positivity of serologic tests. These tests are, therefore, of no real value in the diagnosis of patients with cutaneous Hansen's disease. In pure neural Hansen's disease, however, about 50% of patients are seropositive, and serologic testing might be of use in that setting. Seropositivity might also be used to identify persons in endemic areas at risk of developing Hansen's disease, and chemoprophylaxis could be directed at these persons. Also, seropositivity for antibodies to PGL-1 may be used as a surrogate field

marker for high bacterial load (multibacillary status) and to identify those patients who might require longer therapy to cure their infection. Since PGL-1 antibody tests are best for detecting patients with poor cell-mediated immunity against *M. leprae* and who consequently have high humoral immunity against *M. leprae* and multibacillary disease, there is a need for a diagnostic test to identify those persons who have adequate cell-mediated immunity, but may be at risk of developing paucibacillary Hansen's disease. The lepromin skin test has not served this need, in contrast to tuberculin skin testing. Based on the technology of the T cell interferon (IFN)-y production-based assays for *M. tuberculosis* infection, researchers have identified unique peptides of *M. leprae* and have developed a research IFN-y release assay (IGRA). This was able to detect all paucibacillary cases in a Hansen's disease cohort. In addition, 13/14 household contacts of Hansen's disease patients were positive in this assay. Ideally, in endemic areas, both serological and cell - based assays could be used to detect all patients with Hansen's disease.

Classification

Hansen's disease may present with a broad spectrum of clinical diseases. The Ridley and Jopling scale classifies cases based on clinical, bacteriologic, immunologic, and histopathologic features. In many exposed patients the infection apparently clears spontaneously and no clinical lesions develop. Patients who do develop clinical disease are broadly classified into two groups for the purposes of treatment and for trials that compare treatment strategies. Paucibacillary patients have few or no organisms in their lesions, and usually 3-5 lesions or fewer (for treatment purposes, the finding of acid-fast bacilli by stains or smears classifies a patient as having paucibacillary Hansen's disease). Multibacillary patients have multiple, symmetrical lesions, and organisms detectable by biopsy or smears. The individual's cell-mediated immune response to the organism determines the form Hansen's disease will take in the individual. If the cell- mediated immune response against *M. leprae* is strong, the number of organisms will be low (paucibacillary),

and conversely if this response is inadequate, the number of organisms will be high (multibacillary).

The most common outcome after exposure is probably spontaneous cure. If skin disease does appear, the initial clinical lesion may be a single hypopigmented patch, perhaps with slight anesthesia. This is called indeterminate disease, since the course of the disease cannot be predicted at this stage. The lesion may clear spontaneously or may progress to any other form of Hansen's disease.

The spectrum of leprosy has two stable poles, the tubercu- loid and lepromatous forms. These so-called polar forms do not change; the patient remains in one or the other form throughout the course of the disease. The polar tuberculoid form (called TT), the form of high cell-mediated immunity, is characterized by less than five lesions (often only one) and very few organisms (paucibacillary disease). The patients have strong cell-mediated immunity against the organism. The natural history of many TT leprosy patients is for spontaneous cure over several years. The polar leproma- tous form (called LL) has very limited cell-mediated immunity against the organism, lesions are numerous, and they contain many organisms (multibacillary). Between these two poles is every possible degree of infection, forming the borderline spectrum. Cases near the tuberculoid pole are called borderline tuberculoid (BT), those near the lepromatous pole are called borderline lepromatous (BL), and those in the middle are called borderline borderline (BB). Borderline disease is characteristically unstable, and with time cases move from the TT to the LL pole, a process called downgrading.

Hansen's disease may involve only the nerves. This pure neural disease may be indeterminate, tuberculoid, or leproma- tous (paucibacillary or multibacillary), and is so classified. In Nepal and India, pure neural Hansen's disease may represent as much as 5% of all new cases of Hansen's disease.

Early and indeterminate Hansen's disease

Usually, the onset of Hansen's disease is insidious. Prodromal symptoms are generally so slight that the disease is not recognized until the appearance of a cutaneous eruption. Actually, the first clinical manifestation in 90% of patients is numbness, and years may elapse before skin lesions or other signs are identified. The earliest sensory changes are loss of the senses of temperature and light touch, most often in the feet or hands. The inability to discriminate hot from cold may be lost before pinprick sensibility. Such dissociation of sensibility is especially suspicious. The distribution of these neural signs and their intensity will depend on the type of disease that is evolving.

Often the first lesion noted is a solitary, ill-defined, hypo- pigmented macule that merges into the surrounding normal skin. Less often, erythematous macules may be present. Such lesions are most likely to occur on the cheeks, upper arms, thighs, and buttocks. Examination reveals that sensory functions are either normal or minimally altered. Peripheral nerves are not enlarged, and plaques and nodules do not occur. Histologically, a variable lymphocytic infiltrate (without gran- ulomas) is seen, sometimes with involvement of the cutaneous nerves. Usually, no bacilli, or only a few, are seen on biopsy of this indeterminate form. It is the classification, not the diagnosis, that is indeterminate. Few cases remain in this state; they evolve into lepromatous, tuberculoid, or borderline types, or (if cell-mediated immunity is good) often spontaneously resolve and never develop other signs or symptoms of Hansen's disease.

TUBERCULOID LEPROSY.

Tuberculoid lesions are solitary or few in number (five or less) and asymmetrically distributed. Lesions may be hypopig- mented or erythematous, and are usually dry, scaly, and hairless (Fig. 1). The typical lesion of tuberculoid leprosy is the large, erythematous plaque with a sharply defined and elevated border that slopes down to a flattened atrophic center. This has been described as having the appearance of "a saucer right side up." Lesions may also be macular and hypopig- mented

or erythematous, resembling clinically indeterminate lesions. The presence of palpable induration and neurologic findings distinguishes indeterminate lesions from tuberculoid lesions clinically.

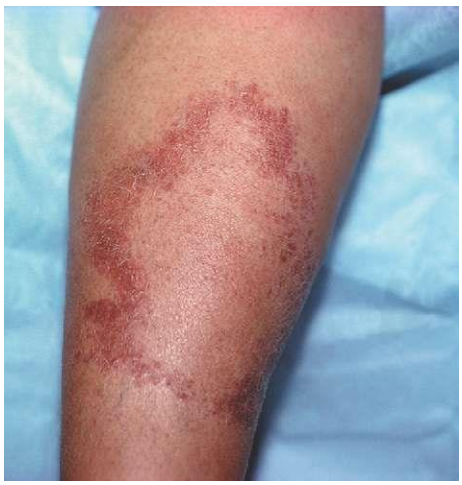


Fig. 1 Tuberculoid leprosy.

The most common locations are the face, limbs, or trunk; the scalp, axillae, groin, and perineum are not involved.

A tuberculoid lesion is anesthetic or hypesthetic and anhid- rotic, and superficial peripheral nerves serving or proximal to the lesion are enlarged, tender, or both. The greater auricular nerve and the superficial peroneal nerve may be visibly enlarged. Nerve involvement is early and prominent in tuber- culoid leprosy, leading to characteristic changes in the muscle groups served. There may be atrophy of the interosseous muscles of the hand, with wasting of the thenar and hypoth- enar eminences, contracture of the fingers, paralysis of the facial muscles, and foot drop. Facial nerve damage dramatically increases the risk for ocular involvement and vision loss.

The evolution of the lesions is generally slow. There is often spontaneous remission of the lesions in about 3 years, or remission may result sooner with treatment. Spontaneous involution may leave pigmentary disturbances.

Borderline tuberculoid leprosy

Borderline tuberculoid lesions are similar to tuberculoid lesions, except that they are smaller and more numerous (Fig. 2). Satellite lesions around large macules or plaques are characteristic.

Borderline leprosy

In borderline leprosy, the skin lesions are numerous (but countable) and consist of red, irregularly shaped plaques. Small satellite lesions may surround larger plaques. Lesions are generalized but asymmetrical. The edges of lesions are not so well defined as the ones seen in the tuberculoid pole. Nerves may be thickened and tender, but anesthesia is only moderate in the lesions.

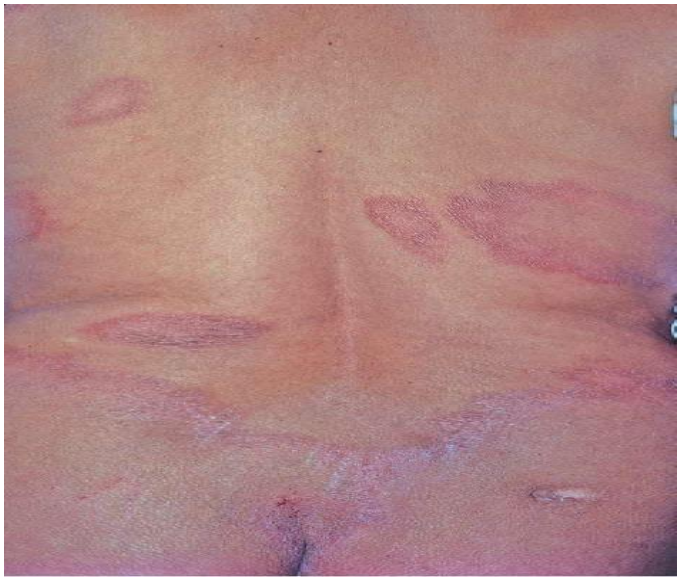


Fig. 2 Borderline tuberculoid leprosy.

Borderline lepromatous leprosy

In borderline lepromatous leprosy, the lesions are symmetrical, numerous (too many to count), and may include macules, papules, plaques, and nodules. The number of small lepromatous lesions outnumbers the larger borderline-type lesions. Nerve involvement appears later; nerves are enlarged, tender, or both, and it is important to note that involvement is symmetrical. Sensation and sweating over individual lesions are normal. Patients usually do not show the features

of fullblown lepromatous leprosy, such as madarosis (loss of the eyebrows), keratitis, nasal ulceration, and leonine facies.

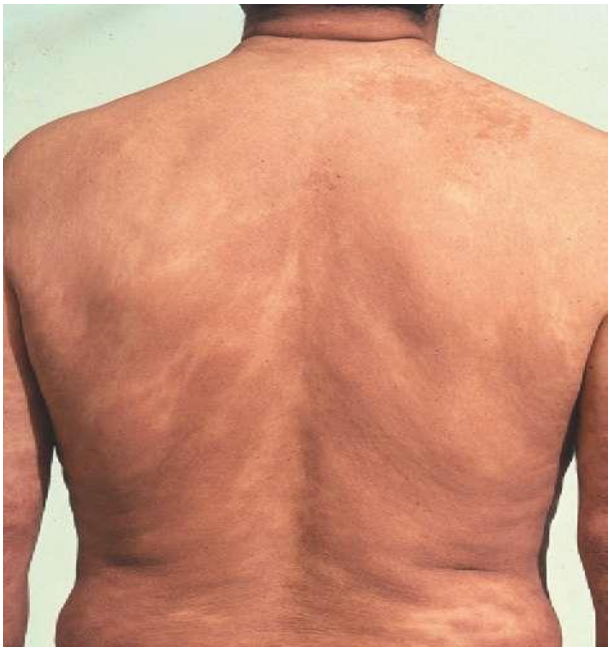


Fig. 3 Lepromatous leprosy.

LEPROMATOUS LEPROSY

Lepromatous leprosy may begin as such or develop following indeterminate leprosy or from downgrading of borderline leprosy. The cutaneous lesions of lepromatous leprosy consist mainly of pale macules (Fig. 3) or diffuse infiltration of the skin.

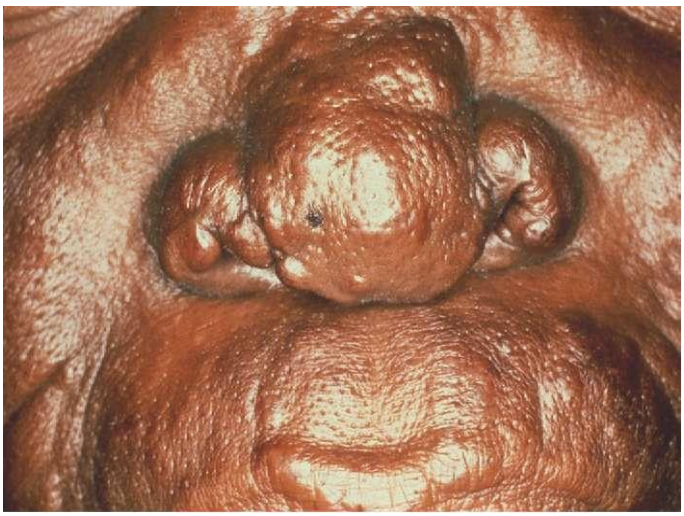


Fig. 4 Lepromatous leprosy.

There is a tendency for the disease to become progressively worse without treatment. Lepromatous leprosy may be divided into a polar form (LLp) and a subpolar form (LL_s); these forms may behave differently.

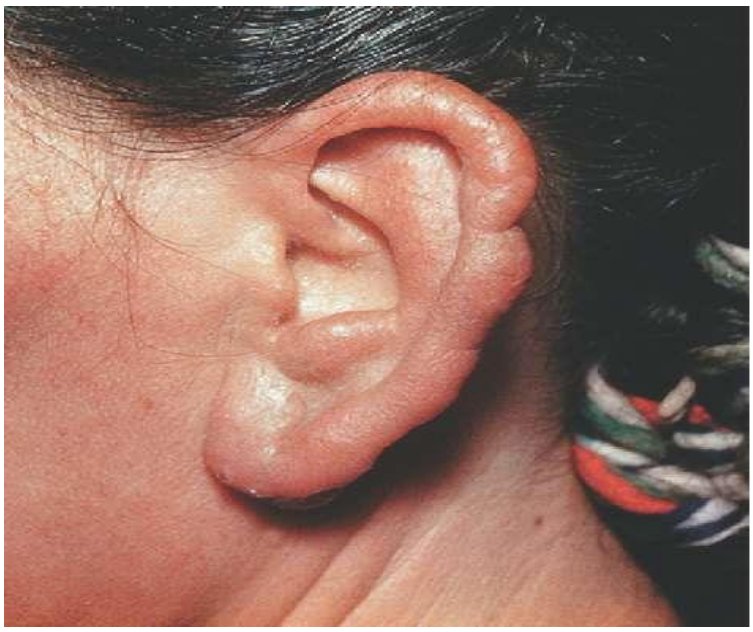
Macular lepromatous leprosy lesions are diffusely and symmetrically distributed over the body. Tuberculoid macules are over the lesions, there is no nerve thickening, and there are no changes in sweating. large and few in number, whereas lepromatous macules are small and numerous. Lepromatous macules are ill defined, show no change in skin texture, and blend imperceptibly into the surrounding skin. There is little or no loss of sensation A slow, progressive loss of hair takes place from the outer third of the eyebrows, then the eyelashes, and finally, the body; however, the scalp hair usually remains unchanged.

Lepromatous infiltrations may be divided into the diffuse, plaque, and nodular types (Fig. 4). The diffuse type is characterized by the development of a diffuse infiltration of the face, especially the forehead, madarosis, and a waxy and shiny appearance of the skin, sometimes described as a "varnished" appearance. Diffuse leprosy of Lucio is a striking form, uncommon except in western Mexico and certain other Latin American areas, where nearly one-third of lepromatous cases may be of this type. This form of lepromatous leprosy is characterized by diffuse lepromatous infiltration of the skin; localized lepromas do not form. A unique complication of this subtype is the reactional state referred to as Lucio's phenomenon (erythema necroticans).

The infiltrations may be manifested by the development of nodules called lepromas. The early nodules are ill defined and occur most often in acral parts: ears (Fig. 5), brows, nose, chin, elbows, hands, buttocks, or knees.

Nerve involvement invariably occurs in lepromatous leprosy, but develops very slowly. Like the skin lesions, nerve disease is bilaterally symmetrical, usually in a stocking-glove pattern. This is frequently misdiagnosed as diabetic neuropathy in the US if it is the presenting manifestation.

Fig. 5 Lepromatous leprosy, enlargement of the earlobe.



HISTOID LEPROSY

Histoid leprosy is an uncommon form of multibacillary leprosy in which skin lesions appear as yellow-red, shiny, large papules and nodules in the dermis or subcutaneous tissue (Fig. 6). Lesions appear on a background of normal skin. They vary in size from 1 to 15 mm in diameter, and may appear anywhere on the body but favor the buttocks, lower back, face, and bony prominences. This pattern may appear de novo, but was mostly described in patients with resistance to dapsone.

Nerve involvement

Nerve involvement is characteristic and unique to Hansen's disease. This neural predilection or neurotropism is a histopathologic hallmark of Hansen's disease. Nerve involvement is responsible for the clinical findings of anesthesia within lesions (paucibacillary and borderline leprosy), and of a progressive "stocking-glove" peripheral neuropathy (lepromatous leprosy).

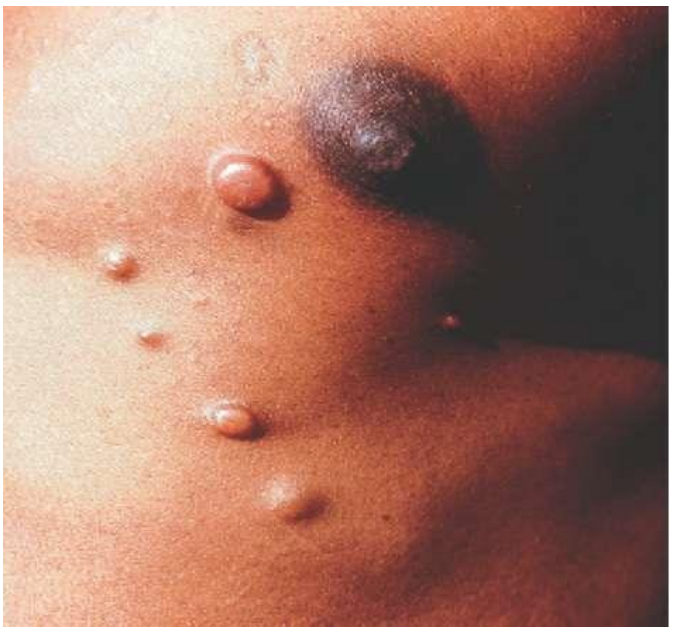


Fig. 6 Histoid leprosy.

The neuropathy is termed "primary impairments" (WHO grade 1). Secondary (or visible) impairments (WHO grade 2) are a consequence of the neuropathy and include skin fissures, wounds, clawing of digits, contrac- tures, shortening of digits, and blindness. Neural damage leads to deformities and in endemic regions results in Hansen's disease being a major cause of "limitations of activity" (formerly called disability) and "restrictions in social participation" (formerly termed handicap). Neuropathy is present in 1.3-3.5% of paucibacillary cases and 7.5-24% of multibacillary cases undergoing MDT. Secondary impairments occur in 3356% of multibacillary cases. Neuropathy may progress, even after effective MDT, and secondary impairments may continue to appear for years as a consequence of the neuropathy. This requires patients with neuropathy to be constantly monitored, even though they are "cured" of their infection.

Nerve enlargement is rare in other skin diseases, so the finding of skin lesions with enlarged nerves should raise the possibility of Hansen's disease. Nerve involvement tends to occur with skin lesions, and the pattern of nerve involvement parallels the skin disease. Tuberculoid leprosy is characterized by asymmetrical nerve involvement localized to the skin lesions. Lepromatous nerve involvement is symmetrical and not associated with skin lesions. Nerve involvement without skin lesions,

called pure neural leprosy, can occur and may be either tuberculoid (paucibacillary) or lepromatous (multibacillary). Nerve disease can be symptomatic or asymptomatic.

Leprosy bacilli may be delivered to the nerves via the perineural and endoneural blood vessels. Once the bacilli transgress the endothelial basal lamina and are in the endo- neurium, they either enter resident macrophages or selectively enter Schwann cells. Damage to the nerves could then occur by several mechanisms:

- obstruction of neural vessels
- vasculitis of neural vessels
- interference with the metabolism of the Schwann cell, making it unable to support the neuron
- immunologic attack on endothelium or nerves
- infiltration and proliferation of *M. leprae* in the closed and relatively nonexpandable endoneural and perineural spaces.

Different and multiple mechanisms may occur in different forms of Hansen's disease and in the same patient over time. The selective ability of *M. leprae* to enter Schwann cells is unique among bacteria. The *M. leprae*-unique PGL-1 phenolic glycolipid, expressed abundantly on the surface of leprosy bacilli, binds selectively to the a2 G module of laminin 2. This a2 chain is tissue-restricted and specifically expressed on peripheral nerve Schwann cells. The binding of *M. leprae* to laminin 2 places it in apposition to the Schwann cell basement membrane when laminin 2 binds to the dystroglycan complex on the Schwann cell membrane. These bound *M. leprae* are endocytosed into the Schwann cells, giving *M. leprae* selective access to the inside of Schwann cells. Other accessory binding molecules may facilitate the binding and endocytosis. The nerves become immunologic targets when they present *M. leprae* antigens on their surface in the context of major histocompatibility (MHC) class II molecules. Schwann cells and hence nerves are usually protected from immunologic attack mediated by the adaptive immune system since they rarely present MHC class II antigens on their surface. In Hansen's disease, expression of these immunologic molecules occurs on the surface of Schwann cells, making them potential

targets for CD4+ cytotoxic T cells. This mechanism may be important in the nerve damage that occurs in type I (reversal) reactions.

The neural signs in Hansen's disease are dysesthesia, nerve enlargement, muscular weakness and wasting, and trophic changes The lesions of the vasomotor nerves accompany the sensory disturbances or may precede them. Dysesthesia develops in a progressive manner. The first symptom is usually an inability to distinguish hot and cold. Subsequently, the perception of light touch is lost, then that of pain, and lastly the sense of deep touch. At times the sensory changes in large Hansen's disease lesions are not uniform because of the variation in the involvement of the individual neural filaments supplying the area. Therefore, the areas of dysesthesia may not conform to the distribution of any particular nerve, nor (except in lepro- matous cases) are they symmetrical.

Nerve involvement affects chiefly (and is most easily observed in) the more superficial nerve trunks, such as the ulnar, median, radial, peroneal, posterior tibial, fifth and seventh cranial nerves, and especially the great auricular nerve. Beaded enlargements, nodules, or spindle-shaped swellings may be found, which at first may be tender. Neural abscesses may form. The ulnar nerve near the internal condyle of the humerus may be as thick as the little finger, round, and stiff, and often easily felt several centimeters above the elbow.

As a result of the nerve damage, areas of anesthesia, paralysis, and trophic disorders in the peripheral parts of the extremities gradually develop. Muscular paralysis and atrophy generally affect the small muscles of the hands and feet or some of the facial muscles, producing weakness and progressive atrophy. Deeper motor nerves are only rarely involved. The fingers develop contractures, with the formation of a claw hand (Fig. 7), and, as the result of resorption of phalangeal bones, fingers and toes become shorter. Ptosis, ectropion, and a masklike appearance occur from damage to the fifth and seventh cranial nerves.

Subsequent to nerve damage ulceration, hyperkeratosis, bullae, alopecia, anhidrosis, and mal perforans pedis can develop. Trophic

ulceration usually manifests as a perforating ulcer on the ball or heel of the foot.

Ocular involvement

Corneal erosions, exposure keratitis, and ulcerations may occur as a result of involvement of the seventh nerve. Specific changes may include corneal opacity, avascular keratitis, pannus formation, interstitial keratitis, and corneal lepromas. The corneal opacities enlarge and finally form visible white flecks called pearls. When (in borderline lepromatous or lep- romatous cases only) the iris and the ciliary body become involved, miliary lepromata (iris pearls), nodular lepromata, chronic granulomatous iritis, and acute diffuse iridocyclitis may result. Of multibacillary patients, 2.8-4.6% are blind at diagnosis and 11% will have a potentially blinding process.

Mucous membrane involvement

The mucous membranes may also be affected, especially in the nose, mouth, and larynx. The nasal mucosa is most commonly involved, and lepromatous patients, if queried, frequently complain of chronic nasal congestion. By far the most common lesions in the nose are infiltrations and nodules. Perforation of the nasal septum may occur in advanced cases, with collapse of the nasal bridge (Fig. 8). Saddle-nose deformities and loss of the upper incisor teeth can occur.

Nodules occurring on the vocal cords will produce hoarseness.

Visceral involvement

In lepromatous leprosy, the body is diffusely involved and bacteremia occurs. Except for the gastrointestinal tract, lungs, and brain, virtually every organ can contain leprosy bacilli. The lymph nodes, bone marrow, liver, spleen, and testicles are most heavily infected. Visceral infection is restricted mostly to the reticuloendothelial system, which, despite extensive involvement, rarely produces symptoms or findings.

Testicular atrophy, with resultant gynecomastia or premature osteoporosis, is an exception.

Secondary amyloidosis with renal impairment may complicate multibacillary leprosy. Glomerulonephritis occurs in more than 5% and perhaps as

many as 50% of Hansen's disease patients, and is not correlated with bacillary load or the presence of erythema nodosum leprosum.

Pregnancy and Hansen's disease

Hansen's disease may be complicated in several ways by pregnancy. As a state of relative immunosuppression, pregnancy may lead to an exacerbation or reactivation after apparent cure. In addition, pregnancy or, more commonly, the period immediately after delivery may be associated with the appearance of reactional states in patients with Hansen's disease.

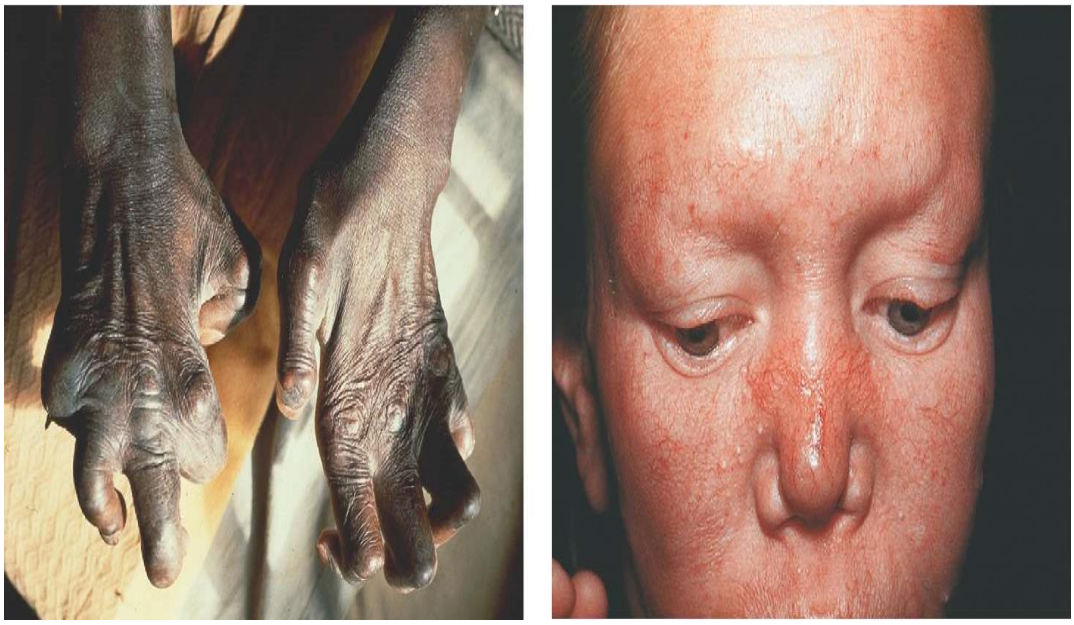


Fig. 7 Claw hand of Hansen's disease.

Pregnant patients with Hansen's disease cannot be given certain medications used to treat Hansen's disease, such as thalidomide, ofloxacin, and minocycline. MDT is tolerated by pregnant women if these restricted agents are avoided. The patient's immune reaction to the leprosy bacillus is a critical element in determining the outcome of infection.

Tuberculoid patients make well-formed granulomas that contain helper T cells, whereas lepromatous patients have poorly formed granulomas and suppressor T cells predominate. The cytokine profile in tuberculoid lesions is that of good cell-mediated immunity with IFN-y and interleukin (IL)-2 being present. In lepromatous patients, these cytokines are reduced and IL-4, 5, and 10, cytokines that downregulate cell- mediated immunity and enhance suppressor function and antibody production, are prominent. Lepromatous leprosy thus represents a classic helper T-cell type 2 (Th2) response to *M. leprae*. Lepromatous patients have polyclonal hypergamma- globulinaemia and high antibody titers to *M. leprae* unique antigens, and may have false-positive syphilis serology, rheumatoid factor, and antinuclear antibodies. Although the cell-mediated immune response of lepromatous patients to *M. leprae* is reduced, these patients are not immune-suppressed for other infectious agents. Tuberculosis behaves normally in patients with lepromatous leprosy.

Histopathology

Ideally, biopsies should be performed from the active border of typical lesions and should extend into the subcutaneous tissue. Punch biopsies are usually adequate. Fite-Faraco stain is optimal for demonstrating *M. leprae*. Because the diagnosis of Hansen's disease is associated with significant social implications, evaluation must be complete, to include evaluation of multiple sections in paucibacillary cases, and consultation with a pathologist experienced in the diagnosis of Hansen's disease can be helpful if the diagnosis is suspected but organ- isms cannot be identified in the affected tissue, especially in paucibacillary disease and reactional states. PCR testing has not been very useful, as it is positive in only 50% of paucibacil- lary cases. The histologic features of Hansen's disease correlate with the clinical pattern of disease. Nerve involvement is characteristic of Hansen's disease, and histologic perineural and neural involvement should raise the possibility of Hansen's disease.

Tuberculoid leprosy

Dermal tuberculoid granulomas, consisting of groups of epithelioid cells with giant cells, are found in tuberculoid leprosy. The granulomas are elongated and generally run parallel to the surface, following neurovascular bundles. The epithelioid cells are not vacuolated or lipidized. The granulomas extend up to the epidermis, with no grenz zone. Lymphocytes are found at the periphery of the granulomas. Acid-fast bacilli are rare. The most important specific diagnostic feature, next to finding bacilli, is selective destruction of nerve trunks and the finding of perineural concentric fibrosis. An S-100 stain may demonstrate this selective neural destruction by demonstrating unrecognizable nerve remnants in the inflammatory foci. Bacilli are most frequently found in nerves, but the subepider- mal zone and arrector pili muscles are other fruitful areas.

Borderline tuberculoid leprosy

The histopathology of the borderline tuberculoid type is similar to that seen in the tuberculoid variety, but epithelioid cells may show some vacuolation, bacilli are more abundant, and a grenz zone separates the inflammatory infiltrate from the overlying epidermis.

Borderline leprosy

In borderline leprosy, granulomas are less well organized, giant cells are not seen, the macrophages have some foamy cytoplasm, and organisms are abundant.

Borderline lepromatous leprosy

In borderline lepromatous lesions, foamy histiocytes, rather than epithelioid cells, make up the majority of the granuloma. Lymphocytes are still present and may be numerous in the granulomas, but are dispersed diffusely within them, not organized at the periphery. Perineural involvement with lymphocyte infiltration may be present. Organisms are abundant and may be found in clumps.

Lepromatous leprosy

In lepromatous leprosy, granulomas are composed primarily of bacilli- and lipid-laden histocytes. These are the so-called lepra cells or foam cells of Virchow. The infiltrate is localized in the dermis and may be purely perivascular or sheetlike and separated from the epidermis by a well-defined grenz zone. Acid-fast bacilli are typically abundant and appear as round clumps (globi). Pure polar lepromatous leprosy differs from the subpolar type primarily in the paucity of lymphocytes in the pure polar form.

Reactional states

Reactions are a characteristic and clinically important aspect of Hansen's disease. Around 50% of patients will experience a reaction after the institution of MDT. In addition to antibiotic therapy, intercurrent infections, vaccination, pregnancy, vitamin A, iodides, and bromide may trigger reactions. Reactions can be severe and are an important cause of permanent nerve damage in borderline patients. Reactional states are frequently abrupt in their appearance, as opposed to Hansen's disease itself, which changes slowly. It is therefore a common reason for patients to seek consultation. In addition, if the patient feels that the chemotherapy is triggering the reaction, he/she will tend to discontinue the treatment, leading to treatment failure.

Reactional states are divided into two forms, called type 1 and type 2 reactions. Type 1 reactions are caused by cell- mediated immune inflammation within existing skin lesions. They generally occur in patients with borderline leprosy (BT, BB, BL). Type 2 reactions are mediated by immune complexes and occur in lepromatous patients (BL, LL).

Type 1 reactions (reversal, lepra, and downgrading reactions)

Type 1 reactions represent an enhanced cell-mediated immune response to *M. leprae,* and commonly occur after treatment is initiated. If the reactions occur with antibiotic chemotherapy, they are called reversal

reactions, and if they occur as borderline disease shifts toward the lepromatous pole (downgrading), they are called downgrading reactions. These two reaction types are clinically identical. Patients in all parts of the borderline spectrum may be affected by type 1 reactions, but these are most severe in patients with borderline lepromatous leprosy who have a large amount of *M. leprae* antigen and therefore have prolonged and repeated reactions during treatment.

Type 1 reactions clinically present with inflammation of existing lesions (Fig. 9). There are no systemic symptoms (such as fever, chills, and arthralgias). Lesions swell, become erythematous, and are sometimes tender, simulating cellulitis. In severe cases, ulceration can occur.

Patients may state that new lesions appeared with the reaction, but these probably represent subclinical lesions that were highlighted by the reaction. The major complication of type 1 reactions is nerve damage.

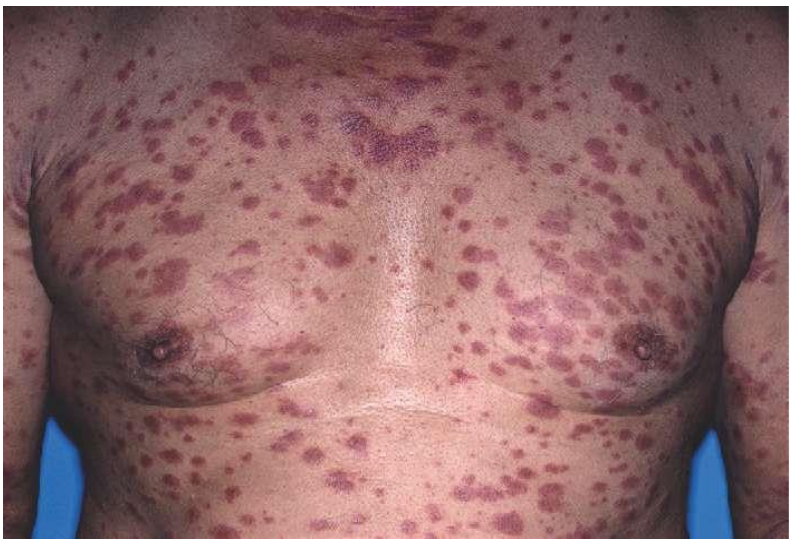


Fig. 9 Type I reaction.

As the cell-mediated inflammation attacks *M. leprae* antigen, any infected tissue compartment can be damaged. Because bacilli are preferentially in nerves, neural symptoms and findings are often present. Reversal reaction occurring within a nerve may lead to sudden loss of nerve function and to permanent damage to that nerve. This makes type 1 reactions an emergency. In this setting, affected nerves are enlarged and tender. In other patients, the neuritis may be subacute or chronic and of limited acute symptomatology, but may still result in severe nerve

damage. Histologically, skin lesions show perivascular and perineural edema and large numbers of lymphocytes. Severe reactions may demonstrate tissue necrosis. Bacilli are reduced.

Type 2 reactions (erythema nodosum leprosum)

Erythema nodosum leprosum (ENL) occurs in half of patients with borderline lepromatous or lepromatous leprosy, 90% of the time within a few years of institution of antibiotic treatment for Hansen's disease or during pregnancy. ENL is a circulating immune complex-mediated disease. As such, in contrast to type 1 reactions, it can result in multisystem involvement and is usually accompanied by systemic symptoms (fever, myalgias, arthralgias, anorexia). Skin lesions are characteristically erythematous, subcutaneous, and dermal nodules that are widely distributed (Fig. 10).

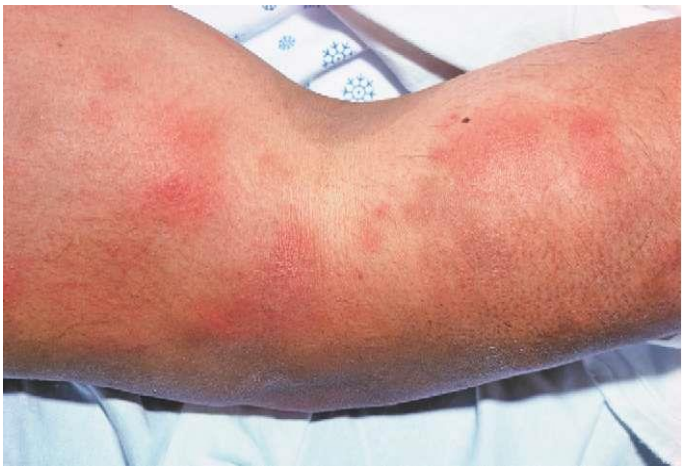


Fig. 10. Erythema nodosum leprosum.

They do not occur at the sites of existing skin lesions. Severe skin lesions can ulcerate. Unlike classic erythema nodosum, lesions are generalized and favor the extensor arms and medial thighs.

ENL is a multisystem disease and can produce conjunctivitis, neuritis, keratitis, iritis, synovitis, nephritis, hepato- splenomegaly, orchitis, and lymphadenopathy. The intensity of the reaction may vary from mild to severe and it may last from a few days to weeks, months, or even years. Histologically, ENL demonstrates a leukocytoclastic

vasculitis. Laboratory evaluation will reveal an elevated sedimentation rate, an elevated C-reactive protein, and a neutrophilia.

Lucio's phenomenon

Lucio's phenomenon is an uncommon and unusual reaction that occurs in patients with diffuse lepromatous leprosy of the "la bonita" type, most commonly found in western Mexico. Some consider it a subset of ENL, but it differs in that it lacks neutrophilia and systemic symptoms. It is not associated with institution of antibiotic treatment as is ENL, but it is commonly the reason for initial presentation in affected patients. Purpuric macules evolve to bullous lesions that rapidly ulcerate, especially below the knees (Fig. 11).

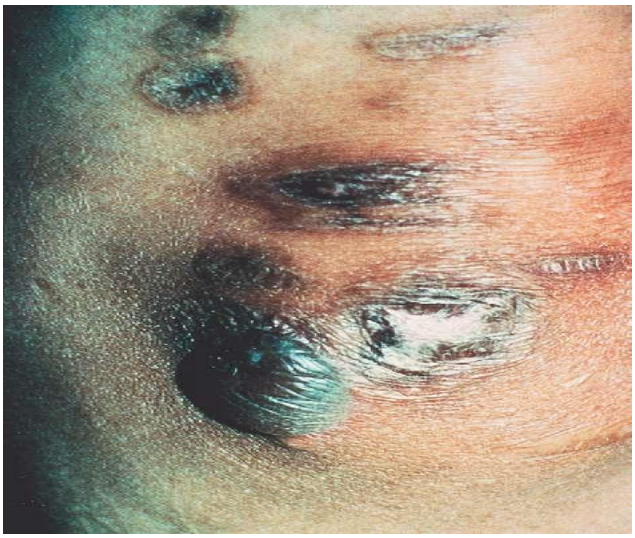


Fig. 11. Lucio's phenomenon, early bullous lesions.

They may be painful, but may also be relatively asymptomatic. Histologically, bacilli are numerous, and in addition to being in the dermis, are seen within blood vessel walls with thrombosis of mid-dermal vessels resulting in cutaneous infarction. Fever, splenomegaly, lymphadenopathy, glomerulonephritis, anemia, hypoalbu- minemia, polyclonal gammopathy, and hypocalcemia can be associated. If the patient is diagnosed early, before significant metabolic and infectious complications occur, the outcome is favorable.

Treatment

Before 1982, dapsone monotherapy was the standard treatment for Hansen's disease, and while it was effective in many patients, primary and secondary dapsone-resistant cases occurred. In addition, multibacillary patients required lifelong treatment, which had inherent compliance problems. To circumvent these problems and shorten therapeutic courses, WHO proposed MDT. This has been very effective in treating active cases of Hansen's disease. The number of antibiotics used and the duration of treatment are determined by the bacterial load the patient exhibits. This can be assessed by slit skin smear, where finding any bacilli classifies the patient as multibacillary. On skin biopsy the same criterion is used, i.e. finding any bacilli identifies the patient as multibacillary. The number of lesions constitutes the "field" classification system, and patients are classified as having 1 lesion, 2-5 lesions in one anatomic region (paucibacillary), or over 5 (multibacillary). This classification can result in undertreatment of patients with few lesions, but who are actually multibacillary. Three other reasons can result in undertreatment of patients:

- failure or inability to do a skin biopsy
- classifying patients with more than five lesions as "tuberculoid" and hence "paucibacillary"
- failure to understand that, although the patient has histologic and clinical features of "tuberculoid" disease, organisms are identified on skin biopsy and hence he/she requires treatment for multibacillary disease.

All patients with more than five lesions and those with organisms identified on skin biopsy should be treated for multibacillary Hansen's disease. Failure may also result from noncompliance, drug resistance, relapse after apparent clinical and bacteriologic cure, and persistence. Persisters are viable organisms that, by mouse footpad testing, are sensitive to the antimicrobial agents given but persist in tissue despite bactericidal tissue levels in the patient. They are usually found in macrophages or nerves. These persisters correlate with relapse occurring 6-9 years following MDT. Since relapses may occur many years after

MDT, where adequate healthcare resources exist, multibacillary patients should be followed annually to examine for evidence of relapse, reaction, or progression of neuropathy.

There are several different MDT recommendations, but only two are given here-those recommended by the Public Health Service for patients in the US and those recommended by WHO. Because dapsone resistance is less common in the US, and effective compliance programs can be developed to enhance monotherapy, dapsone monotherapy may still be considered after MDT in the US. For paucibacillary cases (no organisms found on skin smears or skin biopsy; five lesions or less; indeterminate and tuberculoid leprosy) in the US, the recommendation is 600 mg/day of rifampin and 100 mg/day of dapsone for 12 months. Paucibacillary patients who relapse with paucibacillary disease are treated with an appropriate regimen for multibacillary disease. In the US, multibacillary cases receive 100 mg/day of dapsone, 50 mg/day of clofazimine, and 600 mg/day of rifampin, or a standard WHO regimen (see below) for 2 years (Fig. 12). For multibacillary patients who refuse clofazimine, 100 mg of minocycline or 400 mg/day of ofloxacin may be substituted. Clarithromycin, 500 mg/day, may also be used in treatment regimens. Multibacillary relapses, whether the initial diagnosis was paucibacillary or multibacillary disease, should have a mouse footpad sensitivity study carried out, and be treated with an appropriate multidrug regimen for 2 years, followed by daily life-long dapsone or clofazimine, depending on sensitivity testing. The WHO-recommended protocols are shorter and cheaper than those recommended in the US. There is concern that the reduction of MDT from 2 years to 1 year may lead to increased numbers of relapses, especially among patients with high bac- illary loads (BI over 4 on skin smear).

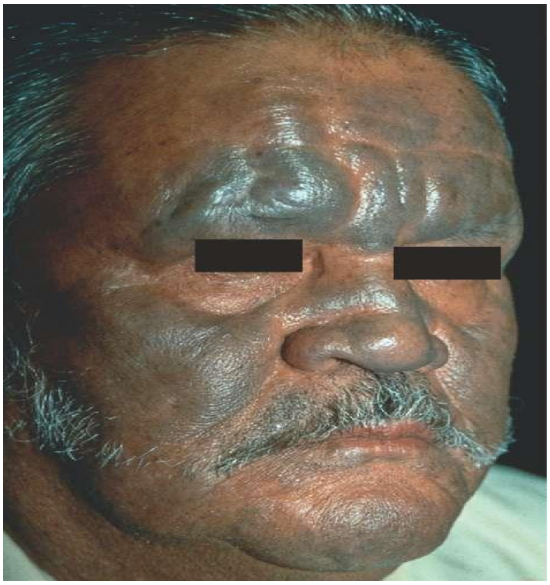


Fig. 12 Lepromatous leprosy with discoloration secondary to clofazimine.

The WHO recommendation for paucibacillary disease (no bacilli on smears or biopsy; five or fewer lesions; indeterminate and tuberculoid patients) is 600 mg of rifampin under supervision once a month for 6 months and 100 mg/day of dapsone for 6 months, unsuper- vised, with completion of the treatment within 9 months.

For single-lesion paucibacillary disease a single dose of 600 mg of rifampin, 400 mg of ofloxacin, and 100 mg of minocycline (ROM), all at one time, is given. This one-dose ROM treatment is less effective than the 6-month regimen for paucibacillary disease. Multibacillary patients (BT, BB, BL, and LL; more than five lesions; any bacilli seen on smears or biopsies) are treated with rifampin, 600 mg, and clofazimine, 300 mg, once a month under supervision, with dapsone, 100 mg/day, and clofaz- imine, 50 mg/day. Treatment is for 12 months. For patients intolerant of clofazimine, an alternative regimen is rifampin, 600 mg, ofloxacin, 400 mg, and minocycline, 100 mg, all once monthly for 24 doses. An alternative for the patient intolerant or resistant to rifampin or dapsone is clofazimine, 50 mg, ofloxacin, 400 mg, and minocycline, 100 mg, daily for 6 months, followed by 18 months of clofazimine, 50 mg daily, plus either ofloxacin, 400 mg/day, or minocycline, 100 mg/ day. At the end of treatment, visible skin lesions are often still present, especially with the WHO short-duration treatments. Paucibacillary lesions tend to clear 1-2

years after the 6-month treatment course. In the US, treatment could be continued until skin lesions are clear, even if the recommended duration of treatment has been passed. With short-duration MDT, it is very difficult to distinguish clinical relapse (failure of treatment) from late type 1 reactions causing skin lesions to reappear. Pathologic examination (biopsy) or an empiric trial of prednisone for several months may be considered in these cases.

There is significant disagreement regarding the effectiveness of the 1- or 2-year WHO-recommended MDT regimens. Relapse rates for multibacillary patients treated with MDT for 1 or 2 years have been reported to be as high as 7-20% overall, and 13-39% with BI of 4 or greater at diagnosis. Based on this information, patients with BL/LL disease with a BI of 4 or greater are at greatest risk for relapse, and should be treated beyond the 1-year recommended period, with treatment continued until smear negativity.

Once neurologic complications have occurred, patients with Hansen's disease should be offered occupational therapy. This should include training on how to avoid injury to insensitive skin of the hands and feet. Special shoes may be required. Ocular complications are frequent, and an ophthalmologist with specific skill in treating patients with Hansen's disease is an invaluable member of the treatment team.

Management of reactions

Even though reactions may appear after drug treatment is instituted, it is not advisable to discontinue or reduce anti- leprosy medication because of these. In mild reactions-those without neurologic complications or severe systemic symptoms or findings-treatment may be supportive. Bed rest and administration of aspirin or nonsteroidal anti-inflammatory agents may be used.

Type 1 reactions are usually managed with systemic corticosteroids. Prednisone is given orally, starting at a dose of 40-60 mg/day. Neuritis and eye lesions are urgent indications for systemic steroid therapy. Nerve abscesses may also need to be surgically drained

immediately to preserve and recover nerve function. The corticosteroid dose and duration are determined by the clinical course of the reaction. Once the reaction is controlled, the prednisone may need to be tapered slowly - over months to years. The minimum dose required and alternate-day treatment should be used in corticosteroid courses of more than 1 month in duration. Clofazimine appears to have some activity against type 1 reactions and may be added to the treatment in doses of up to 300 mg/day if tolerated. Cyclosporine can be used if steroids fail or as a steroid- sparing agent. The starting dose would be 5-10 mg/kg. If during treatment the function of some nerves fails to improve while the function of others normalizes, the possibility of mechanical compression should be evaluated by surgical exploration. Transposition of the ulnar nerve does not seem to be more effective than immunosuppressive treatment for ulnar nerve dysfunction.

Thalidomide has been demonstrated to be uniquely effective against ENL and is the treatment of choice. Thalidomide is a potent teratogen and should not be given to women of child- bearing potential. The initial recommended dosage is up to 400 mg/day in patients weighing more than 50 kg. This dose is highly sedating in some patients, and patients may complain of central nervous system side effects, even at doses of 100 mg/ day. For this reason, such a high dose should be used for only a brief period, or in milder cases treatment may be started at a much lower dose, such as 100-200 mg/day. In cases in which there is an acute episode of ENL, the drug may be discontinued after a few weeks to months. In chronic type 2 reactions, an attempt to discontinue the drug should be made every 6 months. Systemic corticosteroids are also effective in type 2 reactions, but long-term use may lead to complications. Clofazimine in higher doses (up to 300 mg/day) is effective in ENL, and may be used alone or to reduce corticosteroid or thalidomide doses. The combination of pentoxifylline, 400800 mg twice a day, and clofazimine, 300 mg/day, can be used in ENL when thalidomide cannot be used or to avoid the use of systemic steroids to manage severe ENL. Pentoxifylline alone is inferior to steroids and thalidomide, but can be considered in milder

cases. Tumor necrosis factor (TNF) inhibitors, specifically infliximab, have been reported to be effective in treating recurrent ENL.

Lucio's phenomenon is poorly responsive to both corticosteroids and thalidomide.

Prevention

Because a defect in cell-mediated immunity is inherent in the development of Hansen's disease, vaccine therapies are being tested. Bacillus Calmette-Guerin (BCG) vaccination alone provides about 34-80% protection against infection, In the UK, BCG immunization is given to household contacts under the age of 12. Vaccines have been produced and are effective. It is unclear if they will be needed except in the areas of highest endemicity, as MDT has been effective in reducing the prevalence of disease. Since 80% of patients have contact with multi- bacillary patients, prevention depends on treating active multibacillary patients and examining exposed persons on an annual basis to detect early evidence of infection. Prophylactic antibiotic regimens have been used in such exposed patients and demonstrate a reduction in new Hansen's disease cases by more than 50% in the first 2 years. Interestingly, patients who had less contact with the source patient benefited more. In the UK, close contacts under the age of 12 whose source case was lepromatous are given rifampin, 15 mg/kg once a month for 6 months. Several trials of chemoprophylaxis in whole endemic regions (once-yearly MDT with single-dose rifampin, minocycline, and clofazimine) have shown early promise and may be useful in hyperendemic regions.

PARASITIC INFESTATIONS AND BITES

The major groups of animals responsible for bites, stings, and parasitic infections in humans belong to the phyla Arthropoda, Chordata, Cnidaria (formerly Coelenterata), Nemathelminthes, Platyhelminthes, Annelida, and Protozoa. Vector-borne disease continues to be a major worldwide public health threat. Mosquito-borne diseases, such as malaria, West Nile fever, and equine encephalitis, present risks for the resident population as well as travelers. Tick-borne diseases include Lyme disease,

Rocky Mountain spotted fever, ehrlichiosis, tick-borne relapsing fever, tularemia, babesiosis, and Colorado tick fever. Children and those who work outdoors are at higher risk for contracting arthropod-borne diseases. Protection of children is complicated by the potential toxicity of agents used as repellents. This chapter will review parasitic diseases and the major causes of bites and stings, as well as strategies for prevention.

PHYLUM PROTOZOA

The protozoa are one-celled organisms, divided into classes according to the nature of their locomotion. Class Sarcodina organisms move by temporary projections of cytoplasm (pseudopods); class Mastigophora by means of one or more flagella; and class Ciliata by short, hairlike projections of cytoplasm (cilia). Class Sporozoa have no special organs of locomotion.

Class Sarcodina Amebiasis cutis

Entamoeba histolytica is an intestinal parasite transmitted by the fecal-oral route or by sexual contact. Cutaneous ulcers usually result from extension of an underlying amebic abscess; the most common sites are the trunk, abdomen, buttocks, genita- lia, or perineum. Those on the abdomen may result from hepatic abscesses. Penile lesions are usually sexually acquired. Most lesions begin as deep abscesses that rupture and form ulcerations with distinct, raised, cordlike edges, and an ery- thematous halo approximately 2 cm wide. The base is covered with necrotic tissue and hemopurulent pus containing amebae. These lesions are from a few centimeters to 20 cm wide. Without treatment, slow progression of the ulcer occurs in an increasingly debilitated patient until death ensues. Patients may also present with fistulae, fissures, polypoid warty lesions, or nodules. Deep lesions are more likely to be associated with visceral lesions.

The sole manifestation of early amebiasis may be chronic urticaria. An estimated 10 million invasive cases occur annually, most of them in the tropics. Infection may be asymptomatic, or bloody diarrhea and hepatic abscesses may be present. In the US, the disease occurs chiefly in

institutionalized patients, world travelers, recent immigrants, migrant workers, and men who have sex with men (MSM). The histologic findings are those of a necrotic ulceration with many lymphocytes, neutrophils, plasma cells, and eosi- nophils. E. histolytica is found in the tissue, within blood and lymph vessels. The organism measures 50-60 |m in diameter, and has basophilic cytoplasm and a single eccentric nucleus with a central karyosome.

The organism is frequently demonstrable in fresh material from the base of the ulcer by direct smear. Culture of the protozoa confirms the diagnosis. Indirect hemagglutination test results remain elevated for years after the initial onset of invasive disease, whereas the results of gel diffusion precipitation tests and counterimmunoelectrophoresis become negative at 6 months. This property can be used to test for recurrent or active disease in persons coming from endemic areas. When the perianal or perineal areas are involved, granu- loma inguinale, lymphogranuloma venereum, deep mycosis, and syphilis must be considered. In chronic urticaria, fresh stool examinations by a trained technician are necessary.

The treatment of choice is metronidazole (Flagyl), 750 mg orally three times a day for 10 days. Abscesses may require surgical drainage.

Other ameba. Amebas of the genera Acanthamoeba and Balamuthia may also cause skin lesions in infected hosts. These organisms are ubi- quitous in the environment and are found in soil, water, and air. Granulomatous amebic encephalitis is the most common manifestation of infection with these amebas. In the case of Acanthamoeba, invasive infections are nearly always in immunocompromised individuals, including those with acquired immunodeficiency syndrome (AIDS) and organ transplant patients, although Acanthamoeba can also involve the cornea in those who use homemade contact lens solution. Disseminated lesions present as pink or violaceous nodules that then enlarge, suppurate, and form ulcers with a necrotic eschar (Fig. 13). Other findings include fever, nasal congestion or discharge, epistaxis, cough, headaches, lethargy, altered mental status, and seizures. In patients infected with Acanthamoeba who have disease of the central nervous system (CNS),

death is nearly universal within days to weeks. The organisms are visible on skin biopsy and culture is definitive. In patients without CNS involvement, the mortality rate is 75%, with successfully treated cases often managed with a combination of 5-fluorocytosine and sulfadiazine.

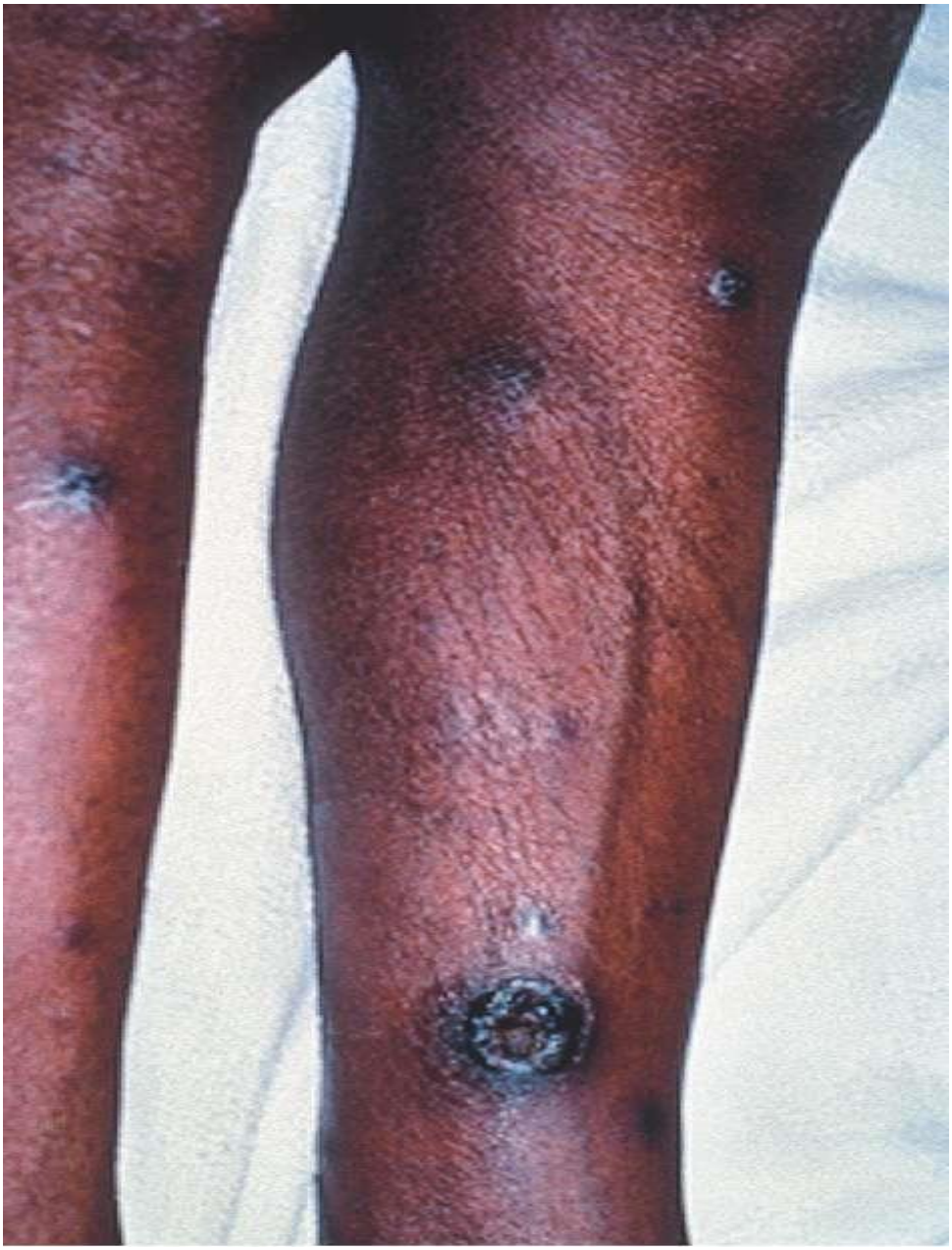


Fig. 13 Disseminated acanthameba in HIV disease.

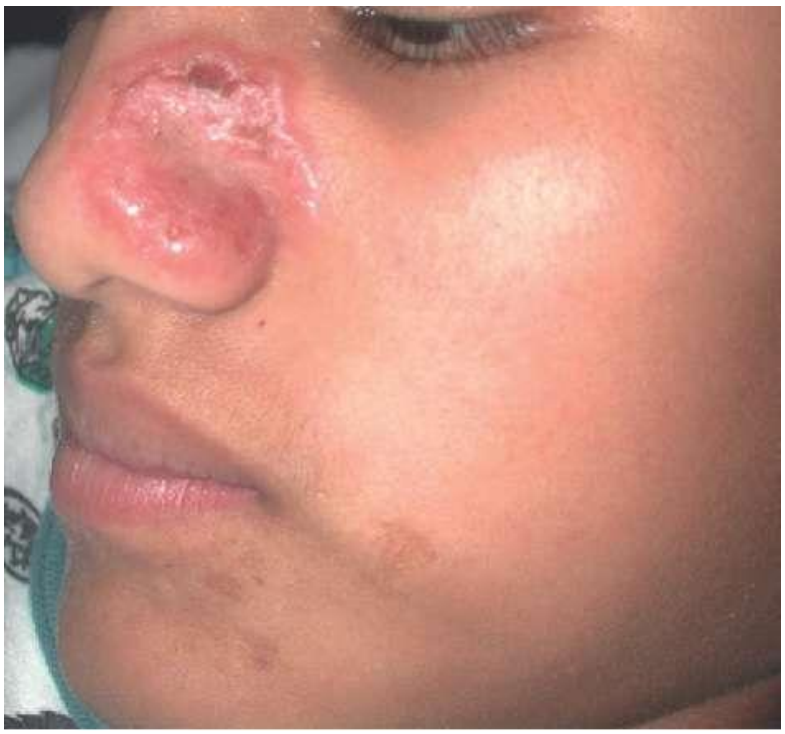


Fig. 14 Balamuthia infection.

In patients infected with Balamuthia mandrillaris, involvement of the central face is typical and pentamidine is favored for treatment (Fig. 14). Chlorhexidine topically and surgical debridement are local adjunctive measures that may prove beneficial.

Class Mastigophora

Organisms belonging to this class are known as flagellates. Many have an undulating membrane with flagella along their crest.

Trichomoniasis

Trichomonas vulvovaginitis is a common cause of vaginal pruritus, with burning and a frothy leukorrhea. The vaginal mucosa appears bright red from inflammation and may be mottled with pseudomembranous patches. The male urethra may also harbor the organism; in the male it causes urethritis and prostatitis. Occasionally, men may develop balanoposthi- tis. Erosive lesions on the glans and penis or abscesses of the median raphe may occur. Neonates may acquire the infection during passage through the birth canal, but they require treatment only if symptomatic or if colonization lasts more than 4 weeks. As this is

otherwise nearly exclusively a sexually transmitted disorder (STD), Trichomonas vulvovaginitis in a child should prompt suspicion of sexual abuse.

Trichomoniasis is caused by Trichomonas vaginalis, a colorless pyriform flagellate 5-15 |m long. T. vaginalis is demonstrated in smears from affected areas. Testing by direct immunofluorescence is sensitive and specific, and PCR analysis is now available.

Metronidazole, 2 g in a single oral dose, is the treatment of choice. Alternatively, 500 mg twice a day for 7 days may be given. Patients should be warned not to drink alcohol for 24 h after the last dose because of the disulfiram-type effects of this medication. Male sex partners should also be treated. The use of metronidazole is contraindicated in pregnant women, and clotrimazole, applied intravaginally at a dosage of 100 mg a night for 2 weeks, may be used instead.

LEISHMANIASIS

Cutaneous leishmaniasis, American mucocutaneous leishma- niasis, and visceral leishmaniasis (kala-azar), which includes infantile leishmaniasis and post-kala-azar dermal leishmania- sis, are all caused by morphologically indistinguishable protozoa of the family Trypanosomidae, called Leishmania (pronounced leesh-may-nea). The clinical features of these diseases differ and they have, in general, different geographic distributions. The reason for the variable clinical manifestations may reside with the diversity of the organism, the immune status of the patient, and the genetic ability to initiate effective cell-mediated immune response to the specific infecting organism. It is known that the antigen-specific T-cell responses, which lead to the production of interferon (IFN) and interleukin (IL)-12, are important for healing of the lesions and the induction of lifelong, species-specific immunity to reinfection that results after natural infection. Both CD4 and CD8+ lymphocytes appear to be active in the immune response. IL-10-producing natural regulatory T cells may play a role in the downregulation of infection-induced immunity.

Cutaneous leishmaniasis

There are several types of lesion. All tend to occur on exposed parts, as all are transmitted by the sandfly. Old World leishmaniasis manifests mainly in the skin and has also been called Baghdad boil, Oriental sore, leishmaniasis tropica, Biskra button, Delhi boil, Aleppo boil, Kandahar sore, and Lahore sore. Mild visceral disease may occur. Skin lesions of New World infection have been termed uta, pian bois, and bay sore or chiclero ulcer. Clinical feres

In Old World leishmaniasis, lesions may present in two distinct types. One is the moist or rural type, a slowly growing, indurated, livid, indolent papule (Fig. 15), which enlarges in a few months to form a nodule that may ulcerate in a few weeks to form an ulcer as large as 5 cm in diameter. Spontaneous healing usually takes place within 6 months, leaving a characteristic scar. This type is contracted from rodent reservoirs such as gerbils via the sandfly vector. The incubation period is relatively short—1-4 weeks. The dry or urban type has a longer incubation period (2-8 months or longer), develops much more slowly, and heals more slowly than the rural type.

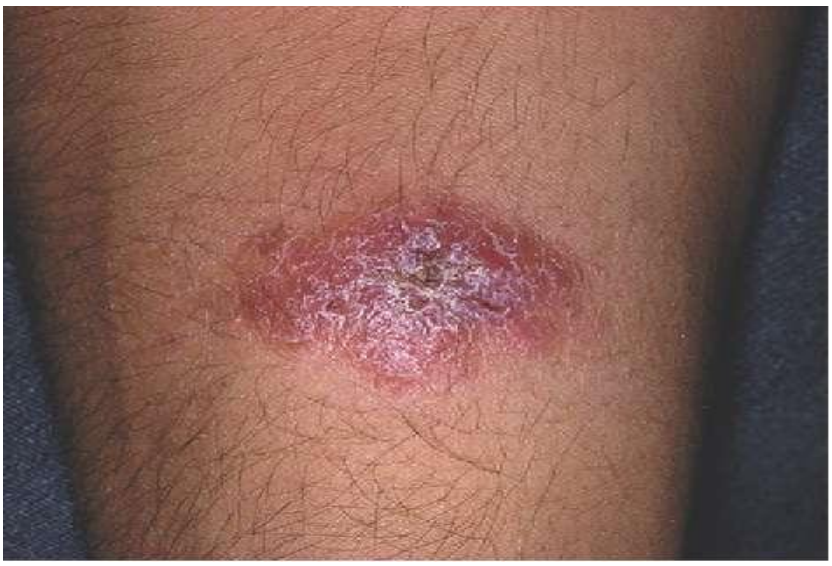


Fig. 15 Old World leishmaniasis.

Rarely, after the initial or "mother" lesion is healed, at the borders of the healed area, a few soft red papules may appear that are covered with

whitish scales and have the "apple jelly" characteristics of granulomatous diseases such as lupus vul- garis.

These spread peripherally on a common erythematous base and are the lupoid type. This is also known as leishma- niasis recidivans and occurs most commonly with the urban type of disease, caused by Leishmania tropica. New World disease may also induce purely cutaneous lesions, of varied morphology. The primary papule may become nodular, ver- rucous, furuncular, or ulcerated, with an infiltrated red border (Fig. 16). Subcutaneous peripheral nodules, which eventually ulcerate, may signal extension of the disease.

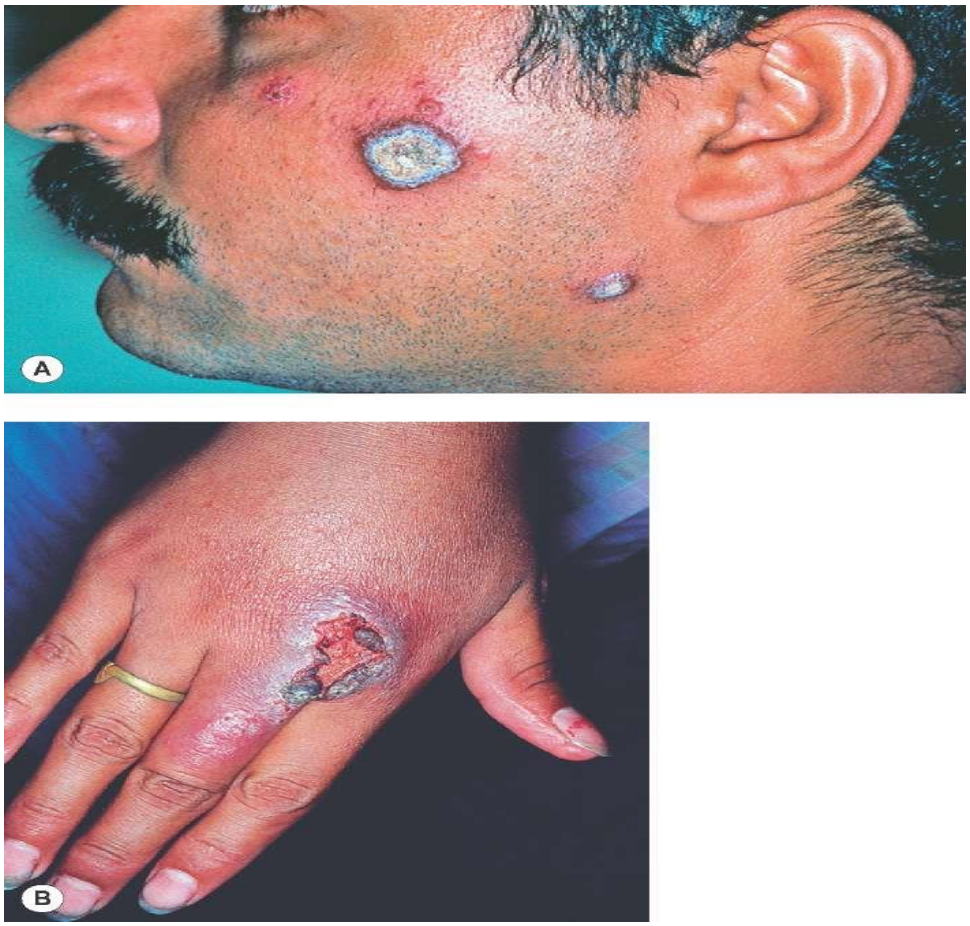


Fig. 16 A and B, New World leishmaniasis

A linear or radial lymphangitic (sporotrichoid) pattern may occur with lymphadenopathy, and the nodes may rarely yield organisms. Facial lesions may coalesce and resemble erysipelas. Recidivans lesions are unusual in the New World form of disease. In Yucatan and Guatemala, a

subtype of New World disease exists: the chiclero ulcer. The most frequent site of infection is the ear (Fig. 17).

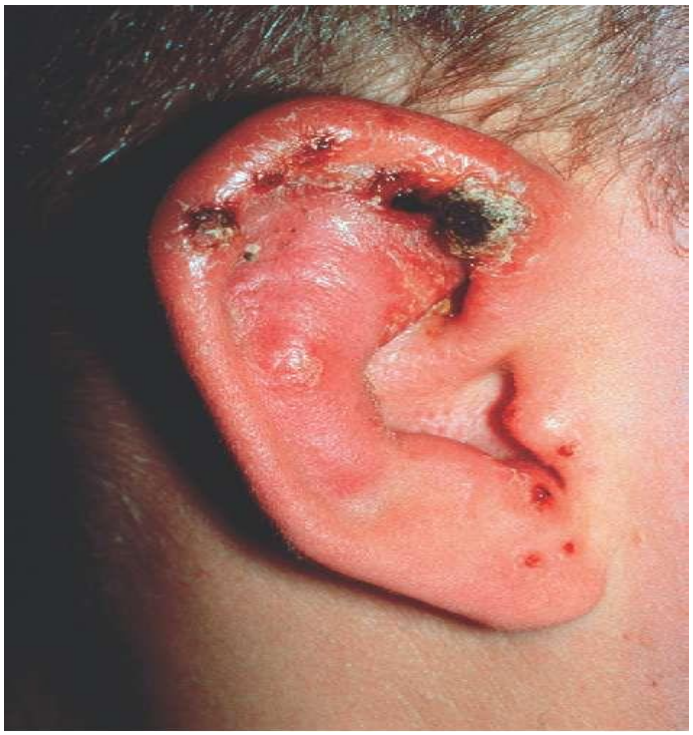


Fig. 17 Chiclero ulcer in leishmaniasis.

The lesions ulcerate and occur most frequently in workers who harvest chicle for chewing gum in forests, where there is high humidity. This form is a more chronic ulcer that may persist for years, destroying the ear cartilage and leading to deformity.The etiologic agent is Leishmania mexicana and the sandfly vector, Lutzomyia flaviscutellata. Uta is a term used by Peruvians for leishmaniasis occurring in mountainous territory at 1200-1800 m above sea level. The ulcerating lesions are found on exposed sites and mucosal lesions do not occur. Disseminated cutaneous leishmaniasis may be seen in both New and Old World disease. Multiple nonulcerated papules and plaques, chiefly on exposed surfaces, characterize this type. The disease begins with a single ulcer, nodule, or plaque from which satellite lesions may develop and disseminate to cover the entire body. The disease is progressive and treatment is usually ineffective. It is characterized by anergy to the organism. This type of leishmaniasis must be differentiated from lepromatous leprosy, xanthoma tuberosum, paracoccidi- oidal granuloma, Lobo's disease, and malignant lymphoma.

Etiologic factors

L. tropica, Leishmania major, Leishmania aethiopica, and Leishmania infantum, the cause of Mediterranean visceral leishmaniasis, may cause cutaneous leishmaniasis. Purely cutaneous leish- maniasis is also caused by several species present in the New World. L. mexicana does not induce mucosal disease. Leishmania braziliensis guyanensis produces cutaneous disease, as does Leishmania braziliensis braziliensis and Leishmania braziliensis panamensis; however, the latter two may also result in muco- cutaneous disease.

Epidemiology

Cutaneous leishmaniasis is endemic in Asia Minor and to a lesser extent in many countries around the Mediterranean. Iran and Saudi Arabia have a high occurrence rate. In endemic areas, deliberate inoculation on the thigh is sometimes practiced so that scarring on the face—a frequent site for Oriental sore—may be avoided. Purely cutaneous lesions may also be found in the Americas. In the US, leishmaniasis is largely restricted to South Texas, although rare reports of human cutaneous disease have occurred as far north as Pennsylvania, and visceral leishmaniasis in immunosuppressed humans is being recognized as an emerging infection in areas not previously thought to be endemic for the disease.

Pathogenesis

The organism has an alternate life in vertebrates and in insect hosts. Man and other mammals, such as dogs and rodents, are the natural reservoir hosts. The vector hosts are Phlebotomus sandflies for the Old World type and Phlebotomus perniciosus and Lutzomyia sandflies for New World cutaneous leishmania- sis. After the insect has fed on blood, the flagellates (lepto- monad, promastigote) develop in the gut in 8-20 days, after which migration occurs into the mouth parts; from here trans- mission into humans occurs by a bite. In humans, the flagella are lost and a leishmanial form (amastigote) is assumed.

Histopathology

An ulcer with a heavy infiltrate of histiocytes, lymphocytes, plasma cells, and polymorphonuclear leukocytes is seen. The parasitized histiocytes form tuberculoid granulomas in the dermis. Pseudoepitheliomatous hyperplasia may occur in the edges of the ulcer. Numerous organisms are present (mostly in histiocytes), which are nonencapsulated and contain a nucleus and a paranucleus. Wright, Giemsa, and monoclonal antibody staining may be helpful in identifying the organisms. The organisms are seen within histiocytes and often line up at the periphery of a vacuole like the bulbs surrounding a movie marquee. Polymerase chain reaction (PCR) primers are available for a variety of species. PCR is more sensitive than microscopy, but less sensitive than culture.

Diagnosis

In endemic areas, the diagnosis is not difficult. In other localities, cutaneous leishmaniasis may be confused with syphilis, yaws, lupus vulgaris, and pyogenic granulomas. The diagnosis is established by demonstration of the organism in smears. A punch biopsy specimen from the active edge of the ulcer is ideal for culture. It can be placed in Nicolle-Novy-MacNeal (NNN) medium and shipped at room temperature. Parasites can also be cultured from tissue fluid. A hypodermic needle is inserted into the normal skin and to the edge of the ulcer base. The needle is rotated to work loose some material and serum, which is then aspirated. A culture on NNN medium at 22-35°C (71.6-95°F) is recommended to demonstrate the lep- tomonads. As expected, PCR is the most sensitive diagnostic test for cutaneous leishmaniasis.

Treatment

Spontaneous healing of primary cutaneous lesions occurs, usually within 12-18 months, shorter for Old World disease. Reasons to treat a self-limited infection include avoiding disfiguring scars in exposed areas, notably the face; avoiding secondary infection; controlling disease in the

population; and failure of spontaneous healing. In the diffuse cutaneous and recidivans types, the disease may persist for 20-40 years if not treated.

In areas in which localized cutaneous leishmaniasis is not complicated by recidivans or sporotrichoid forms, or by muco- cutaneous disease, treatment with such topical modalities as paromomycin sulfate 15% plus methylbenzethonium chloride 12%, ketoconazole cream under occlusion, cryotherapy, local heat, photodynamic therapy, and laser ablation, or with intra- lesional sodium stibogluconate antimony or emetine hydro- chloride may be effective and safe.

In the setting of Old World cutaneous leishmaniasis, some data suggest that intramuscular meglumine antimoniate in combination with intralesional meglumine antimoniate may be superior to intralesional therapy alone. A meta-analysis of studies of Old World cutaneous leishmaniasis concluded that pentamidine was similar in efficacy to pentavalent antimonials and both were superior to the other agents studied. Since then, a Pakistani study concluded that itraconazole was more effective and more economical, and had fewer side effects than meglumine antimoniate in both wet and dry types of cutaneous leishmaniasis. It should be noted that the number of patients was relatively small, and other studies have been disappointing. Oral fluconazole and zinc sulfate have been used to treat L. major. A similar meta-analysis of studies of New World cutaneous leishmaniasis concluded that meglu- mine might be the best agent in its class. Azithromycin has been used in New World disease, but is inferior to antimonials. Perilesional injections of IFN-y have also been reported to be effective but are expensive.

In patients who are immunosuppressed or who acquire infection in areas where mucocutaneous disease may occur, systemic therapy is recommended. As with topical treatment, many alternatives have been reported to be effective. Sodium antimony gluconate (sodium stibogluconate) solution is given intramuscularly or intravenously, 20 mg/kg/day in two divided doses for 28 days. It can be obtained from the Centers for Disease Control (CDC) Drug Service (Atlanta, GA 30333). Repeated courses may be given. Antimony n-methyl glutamine

(Glucantime) is used more often in Central and South America because of its local availability.

Other systemic medications reported to be effective include fluconazole, 200 mg per day for 6 weeks, ketoconazole, dapsone, rifampicin, and allopurinol. Some of these have not been subjected to controlled clinical trials, as is true of most topical treatments. The recidivans and disseminated cutaneous types may require prolonged courses or adjuvant IFN therapy. Amphotericin B may be used in antimony- resistant disease. Lipid formulations of amphotericin B are highly effective in short courses but are expensive. Liposomal amphotericin B may be especially helpful for L. braziliensis and L. guyanensis infections. Intramuscular pentamidine is also used for L. guyanensis cutaneous leishmaniasis, because this infection is resistant to systemic antimony. Miltefosine is being used for cutaneous disease in Colombia and Bolivia. It may prove to be the treatment of choice for diffuse cutaneous leish- maniasis and post-kala-azar dermal leishmaniasis. It is less toxic than most other available agents and its use is likely to increase in all forms of leishmaniasis, but some studies have shown it to be ineffective in L. major and L. braziliensis infections. Control depends chiefly on the success of antifly measures taken by health authorities and personal protection with protective clothing, screening, and repellents. Vaccines are being investigated but are not available.

MUCOCUTANEOUS LEISHMANIASIS

(leishmaniasis americana, espundia)

Clinical features

The initial infection, which occurs at the site of the fly bite, is a cutaneous ulcer. Secondary lesions on the mucosa usually occur at some time during the next 5 years (Fig. 18). The earliest mucosal lesion is usually hyperemia of the nasal septum with subsequent ulceration, which progresses to invade the septum and later the paranasal fossae. Perforation of the septum eventually takes place. For some time the nose remains unchanged externally, despite the internal destruction. At first, only a dry

crust is observed, or a bright red infiltration or vegetation on the nasal septum, with symptoms of obstruction and small hemorrhages. Despite the mutilating and destructive character of leishmaniasis, it never involves the nasal bones. When the septum is destroyed, the nasal bridge and tip of the nose collapse, giving the appearance of a parrot beak, camel nose, or tapir nose.

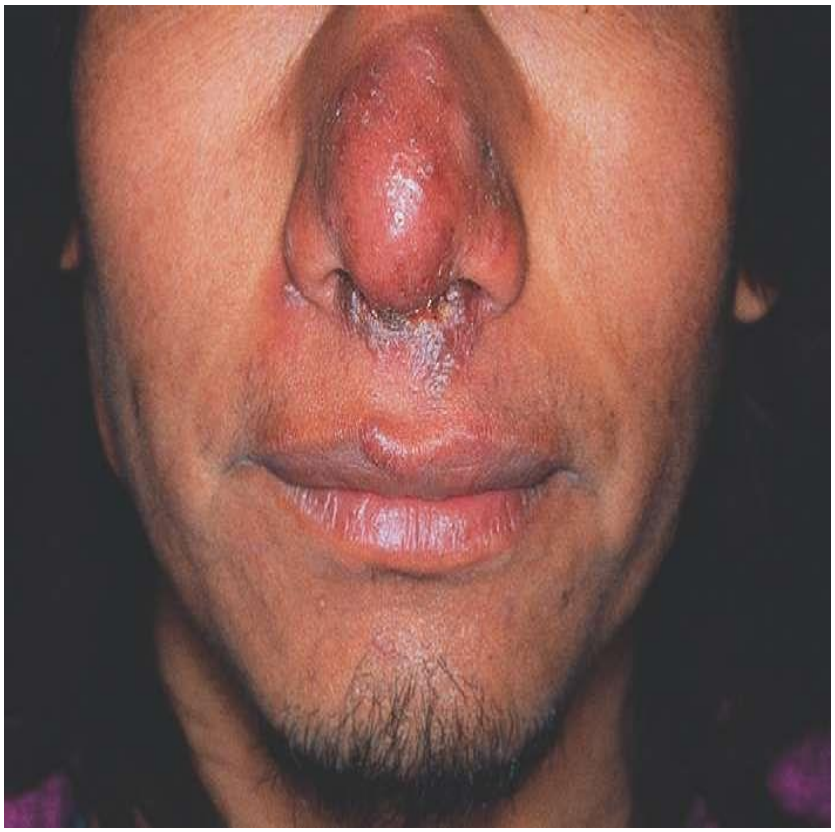


Fig. 18 Mucocutaneous leishmaniasis.

It is important to recall that the four great chronic infections (syphilis, tuberculosis, Hansen's disease, and leishmaniasis) have a predilection for the nose. The ulcer may extend to the lips (Fig. 19) and continue to advance to the pharynx, attacking the soft palate, uvula, tonsils, gingiva, and tongue. The eventual mutilation is called espundia. Two perpendicular grooves at the union of the osseous palate and soft tissues, in the midst of the vegetative infiltration of the entire pharynx, are called the palate cross of espundia.

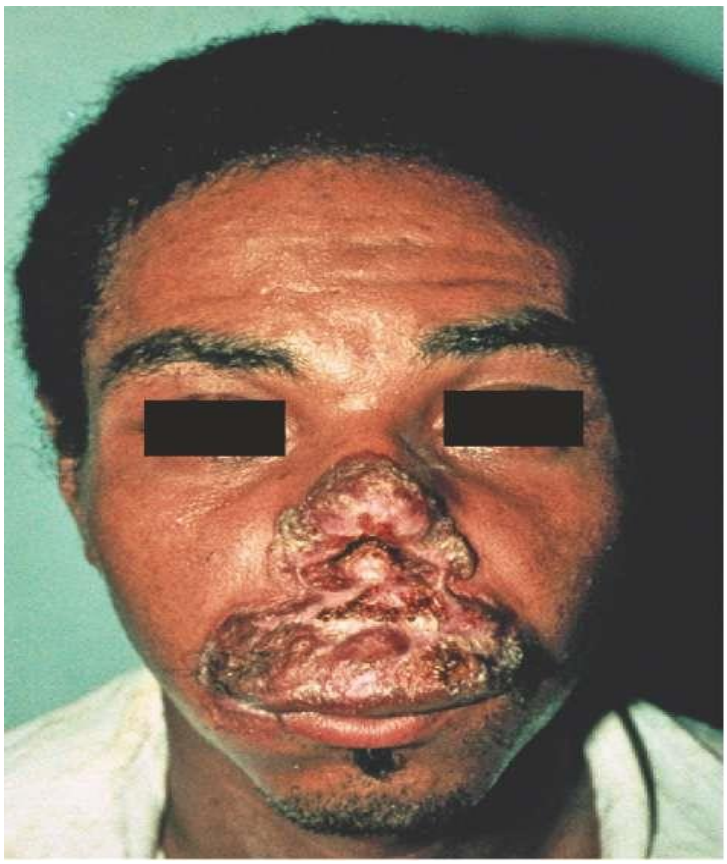


Fig. 19 Severe destructive mucocutaneous leishmaniasis.

Only in exceptional cases does American leishmaniasis invade the genital or ocular mucous membranes. The frequency of mucous membrane involvement is variable. In Yucatan and Guatemala, it is an exception; in other countries, such as Brazil, it may occur in 80% of cases.

Etiologic factors

Mucocutaneous leishmaniasis is caused by L. braziliensis braziliensis and L. braziliensis panamensis. Leishmania has two forms: the nonflagellated form or leishmania, which is found in the tissues of humans and animals susceptible to the inoculation of the parasite; and the flagellated form or leptomonad, which is found in the digestive tract of the vector insect (Lutzomyia in mucocutaneous disease) and in cultures. The typical morphology of leishmania, as found in vertebrates, is round or oval, usually with one extremity more rounded than the other, measuring 2-4 |m x 1.5-2.5 |m, with cytoplasm, nucleus, and blepharoplast or kinetoplast.

Epidemiology

Mucocutaneous leishmaniasis is predominantly a rural and jungle disease. It most often occurs in damp and forested regions. The disease can be contracted at any time of the year, but the risk is highest just after the rainy season. All ages and races, and both sexes are equally affected. Epidemics parallel the El Nino cycle.

Histopathology

In the ulcerous type, marked irregular acanthosis and sometimes pseudoepitheliomatous hyperplasia can be found. The dermis shows a dense infiltration of histiocytes, lymphocytes, and plasma cells. In new lesions some neutrophils are observed. Large Langhans giant cells or typical tubercles are occasionally seen. Numerous organisms are present (mostly in histiocytes), which are nonencapsulated and contain a nucleus and a para- nucleus. Wright, Giemsa, and monoclonal antibody staining may be helpful in identifying the organisms. In patients with granulomatous infiltrates containing intracellular parasites within histiocytes, leishmaniasis is one of several diseases to be considered, including rhinoscleroma, histoplasmosis, gran- uloma inguinale, Chagas' disease, Penicillium marneffei infection, and toxoplasmosis. Touch smears stained with Giemsa are helpful in many cases of cutaneous and mucocutaneous leishmaniasis.

Laboratory findings

Leishmania is demonstrated in the cutaneous and mucous membrane lesions by direct smears or cultures. In biopsy material stained with Wright stain, intracellular and extracellular organisms are seen with typical morphology of two chromatic structures: nucleus and parabasal body. In later mucosal lesions the scarcity of parasites makes identification difficult. The culture is done on NNN medium for leptomonads.

Prophylaxis

Although it is impractical to eliminate the insect vector, it is still the only valid measure for the control of this prevalent disease. Effective vaccines are not available.

Treatment

Treatment is the same as described for cutaneous leishmania- sis, except that antimony resistance is common in mucocutane- ous disease. Combination therapy using antimonials with drugs such as rifampin or azithromycin, or adding immuno- modulators such as IFN-y, IL-2, or imiquimod may result in cure. Amphotericin B treatment may be necessary.

VISCERAL LEISHMANIASIS
(kala-azar, dumdum fever)

Clinical features

The earliest lesion is the cutaneous nodule or leishmanioma, which occurs at the site of the initial sandfly inoculation. Kala- azar, meaning "black fever," acquired its name because of the patchy macular darkening of the skin caused by deposits of melanin that develop in the later course of the disease. These patches are most marked over the forehead and temples, peri- orally, and on the mid-abdomen.

The primary target for the parasites is the reticuloendothe- lial system; the spleen, liver, bone marrow, and lymph nodes are attacked. The incubation period is 1-4 months. An intermittent fever, with temperatures ranging from 39° to 40°C (102-104°F), ushers in the disease. There are hepatospleno- megaly, agranulocytosis, anemia, and thrombocytopenia. Chills, fever, emaciation, weight loss, weakness, epistaxis, and purpura develop as the disease progresses. Susceptibility to secondary infection may produce pulmonary and gastrointestinal infection, ulcerations in the mouth (cancrum oris), and noma. Death occurs about 2 years from onset in untreated individuals.

Most infections are subclinical or asymptomatic. In patients with AIDS, papular and nodular skin lesions may occur. Dermatofibroma-type or Kaposi sarcoma-like brown to purple nodules are most commonly reported, although random biopsies of normal skin will reveal organisms; therefore, clinical correlation is necessary to attribute skin findings to Leishmania specifically.

Etiologic factors

L. donovani spp. donovani, infantum, and chagasi cause visceral leishmaniasis and are parasites of rodents, canines, and humans. They are nonflagellate oval organisms some 3 mm in diameter, known as Leishman-Donovan bodies. In the sandfly it is a leptomonad form with flagella.

Epidemiology

L.d. donovani causes visceral leishmaniasis in India, with the major reservoir being humans and the vector being Phlebotomus argentipes. L.d. infantum occurs in China, Africa, the Near East and Middle East, and the Mediterranean littoral, where the major reservoirs are dogs, and Phlebotomus perniciosus and Phlebotomus ariasi are the vectors of the Mediterranean type. American visceral leishmaniasis is caused by L. donovani chagasi and is transmitted by the sandfly Lutzomyia longipalpis. American visceral leishmaniasis principally affects domestic dogs, although explosive outbreaks of the human infection occur sporadically, when the number of L. longipalpis builds up to a high level in the presence of infected dogs. Canine visceral infections with L. infantum have been reported in foxhounds in various parts of the United States and Canada.

Diagnosis

Leishman-Donovan bodies may be present in the blood in individuals with kala-azar of India. Specimens for examination, in descending order of utility, include spleen pulp, sternal marrow, liver tissue, and exudate from lymph nodes. Culturing on NNN medium may also reveal the organisms.

Treatment

General supportive measures are essential. Pentavalent antimony has long been the drug of choice. In areas of drug resistance, amphotericin B is usually effective, but it is expensive and toxic, and requires intravenous administration. Miltefosine is an oral alkyl-phosphocholine analog that has proven as effective as amphotericin B in some trials. It is often used to treat visceral disease in India and Ethiopia. Mixed infections involving both Leishmania and Trypanosoma cruzi are becoming increasingly common in Central and South America because of overlapping endemic areas. Amiodarone has been used as an unconventional antiparasitic drug in this setting in addition to standard therapy.

Post-kala-azar dermal leishmaniasis

In kala-azar, the leishmanoid (amastigote) forms may be widely distributed throughout apparently normal skin. During and after recovery from the disease, a special form of dermal leishmaniasis known as post-kala-azar dermal leishmaniasis appears. This condition appears during or shortly after treatment in the African form, but its appearance may be delayed up to 10 years after treatment in the Indian form. It follows the treatment of visceral leishmaniasis in 50% of Sudanese patients and 5-10% of those seen in India. There are two constituents of the eruption: a macular, depigmented eruption found mainly on the face, arms, and upper part of the trunk; and a warty, papular eruption in which amastigotes can be found. Because it may persist for up to 20 years, these patients may act as a chronic reservoir of infection. This condition closely resembles Hansen's disease. High concentrations of IL-10 in the blood of visceral leishmaniasis patients predict those who will be affected by post-kala-azar dermal leishmaniaisis. Miltefosine may become the drug of choice.

Viscerotropic leishmaniasis

Twelve soldiers developed systemic infection with L. tropica while fighting in Operation Desert Storm in Saudi Arabia. None had symptoms of kala-azar, but most had fever, fatigue, malaise, cough, diarrhea, or

abdominal pain. None had cutaneous disease. Diagnostic tests yielded positive results on bone marrow aspiration; lymph node involvement was also documented. Treatment with sodium stibogluconate led to improvement.

Human trypanosomiasis

Three species of trypanosome are pathogenic to humans: Trypanosoma gambiense and Trypanosoma rhodesiense in Africa, and Trypanosoma cruzi in America. The skin manifestations are usually observed in the earlier stages of the disease as evanescent erythema, erythema multiforme, and edema, especially angioedema. In the early stage of African trypanosomiasis, a trypanosome chancre may occur at the site of a tsetse fly bite. Then erythema with circumscribed swellings of angioedema, enlargement of the lymph nodes, fever, malaise, headache, and joint pains ensue. In the West African (Gambian) form, the illness is chronic, lasting several years, with progressive deterioration, whereas the East African (Rhodesian) form is an acute illness, with a stormy, fatal course of weeks to months. The Rhodesian form is more often associated with cutaneous signs. Annular or deep erythema nodosum-like lesions are frequent manifestations (Fig. 20). Lymphadenopathy is generalized, but frequently there is a pronounced enlargement of the posterior cervical group (Winterbottom's sign).

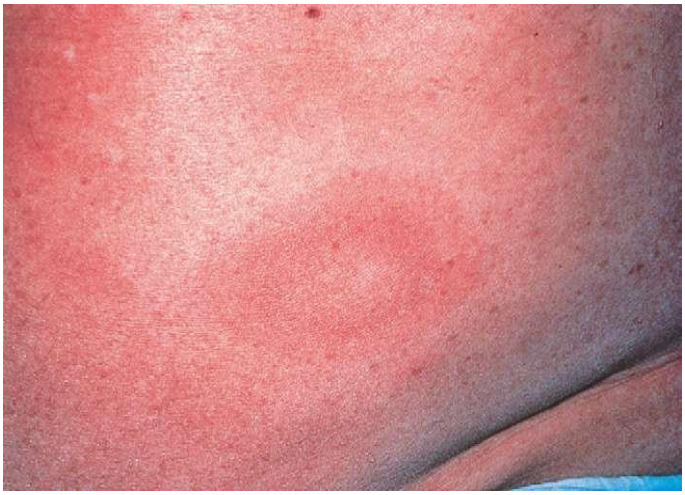


Fig. 20 African trypanosomiasis.

In American trypanosomiasis (Chagas' disease), similar changes take place in the skin. The reduviid bug (kissing bug, assassin bug) (Fig. 21) usually bites at night, frequently at mucocutaneous junctions, where the bug's infected feces are deposited when it feeds. The unsuspecting sleeping person rubs the feces into the bite and becomes infected. If the bite of the infected bug occurs near the eye, Romana's sign develops; this consists of unilateral conjunctivitis and edema of the eyelids, with an ulceration or chagoma in the area. The bite of a "kissing bug" becomes markedly swollen and red, whether trypanosomes are involved or not. Acute Chagas' disease is usually a mild illness consisting of fever, malaise, edema of the face and lower extremities, and generalized lymph-adenopathy. Skin lesions occurring in this phase include nodules at the site of inoculation, disseminated nodules, or morbilliform and urticarial lesions. In chronic Chagas' disease, which occurs in 10-30% of infected persons years to decades later, the heart (myocarditis, arrhythmias, thromboembolism, and cardiac failure) and the gastrointestinal system (mega- esophagus and megacolon) are the most commonly involved organs. During the remaining infected but asymptomatic indeterminate phase, patients may transmit the disease through transfusion. When such patients become immunosuppressed (with AIDS or organ transplantation), reactivation skin lesions may occur.

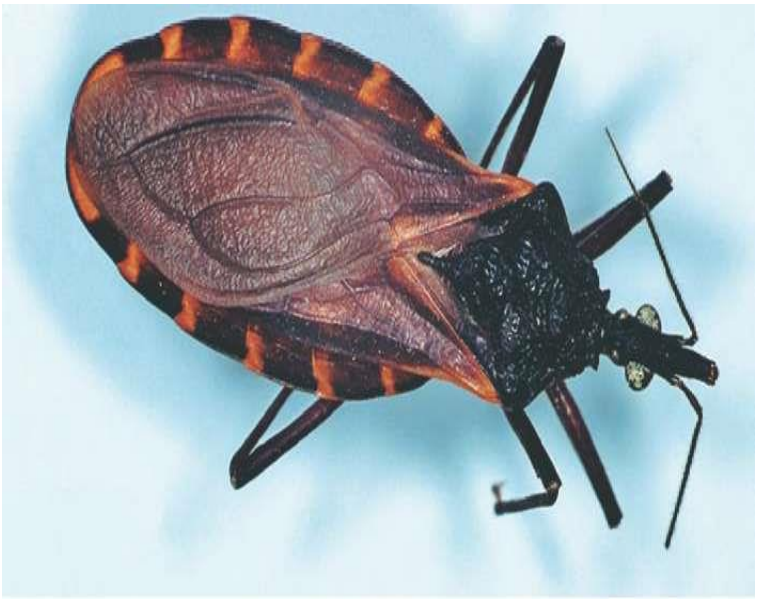


Fig. 21 Triatome reduviid bug.

Rhodesian trypanosomiasis is endemic among the cattle- raising tribes of East Africa, with the savannah habitat of the vectors determining its geographic distribution. Wild game and livestock are reservoir hosts, in addition to humans. The tsetse fly, Glossina morsitans, is the principal vector.

For Gambian trypanosomiasis, humans are the only vertebrate host and the palpalis group of tsetse flies is the invertebrate host. These flies are found close to the water, and their fastidious biologic requirements restrict their distribution, and thus that of the disease. Incidence is seasonal, with humidity and temperature being determining factors. The highest incidence is in males aged 20-40 years in tropical areas of West and Central Africa.

Chagas' disease is prevalent in Central and South America from the US to Argentina and Chile; the highest incidence is in Venezuela, Brazil, Uruguay, Paraguay, and Argentina. Approximately 29% of all male deaths in the 29-44-year-old age group in Brazil are ascribed to Chagas' disease.

Before CNS involvement has occurred in the Rhodesian form, suramin, a complex, non-metal-containing, organic compound, is the treatment of choice. When the CNS is involved, melarsoprol is the drug of choice. Pentamidine isethionate is the drug of choice for the Gambian disease. Eflornithine appears to be a good alternative to melarsoprol for second- stage West African trypanosomiasis. For American trypano-somiasis, treatment is of limited efficacy. Nifurtimox and benznidazole clear the parasitemia and reduce the severity of the acute illness. There is a high incidence of adverse effects, however. Although benznidazole reduces parasite load during the acute phase, it does not prevent chronic cardiac lesions. Ruthenium complexation improves bioavailability of benz- nidazole and has the potential to improve outcomes. Conservative treatment is the typical approach to the patient with congestive heart failure from Chagas myocarditis, but recent data suggest that clomipramine, a tricyclic anti- depressant that inhibits Trypanosoma

cruzi's trypanothione reductase, improves the course of cardiac disease in animal models. Gastrointestinal complications may be treated surgically.

Class Sporozoa

Hair growth and exfoliative dermatitis have also been observed. The differential diagnosis of congenital toxoplasmosis is the TORCH syndrome (toxoplasmosis, rubella, cytomegalovirus, and herpes simplex). In acquired toxoplasmosis, early skin manifestations consist of cutaneous and subcutaneous nodules, and macular, papular, and hemorrhagic eruptions. These may be followed by scarlatiniform desquamation, eruptions mimicking roseola, erythema multiforme, dermatomyositis or lichen planus, as well as exfoliative dermatitis. As a rule, the exanthem is accompanied by high fever and general malaise.

Diagnosis of acquired toxoplasmosis is of special importance to three groups of adults: healthy pregnant women concerned about recent exposure; adults with lymphadenopathy, fever, and myalgia, who might have some other serious disease, such as lymphoma; and immunocompromised persons, such as patients with AIDS, in whom toxoplasmosis might be fatal. It is the most common cause of focal encephalitis in patients with AIDS and this may be accompanied by a widespread papular eruption.

T. gondii is a crescent-shaped, oval, or round protozoan that can infect any mammalian or avian cell. The disease is often acquired through contact with animals, particularly cats. Reservoirs of infection have been reported in dogs, cats, cattle, sheep, pigs, rabbits, rats, pigeons, and chickens. The two major routes of transmission of T. gondii in humans are oral and congenital. Meats consumed by humans may contain tissue cysts, thus serving as a source of infection when eaten raw or undercooked. There is no evidence of direct human-to-human transmission, other than from mother to fetus.

The diagnosis cannot be made on clinical grounds alone. It may be established by isolation of T. gondii; demonstration of the protozoa in tissue sections, smears, or body fluids by Wright or Giemsa stain;

characteristic lymph node histology; and serologic methods. In the setting of bone marrow transplantation, the organism has caused interface dermatitis, creating the potential for misdiagnosis as graft versus host disease. A combination of pyrimethamine (Daraprim) and sulfa- diazine acts synergistically and forms an effective treatment. Dosages and total treatment time vary according to the age and immunologic competence of the infected patient.

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Hair growth and exfoliative dermatitis have also been observed. The differential diagnosis of congenital toxoplasmosis is the TORCH syndrome (toxoplasmosis, rubella, cytomegalovirus, and herpes simplex). In acquired toxoplasmosis, early skin manifestations consist of cutaneous and subcutaneous nodules, and macular, papular, and hemorrhagic eruptions. These may be followed by scarlatiniform desquamation, eruptions mimicking roseola, erythema multiforme, dermatomyositis or lichen planus, as well as exfoliative dermatitis. As a rule, the exanthem is accompanied by high fever and general malaise.

Diagnosis of acquired toxoplasmosis is of special importance to three groups of adults: healthy pregnant women concerned about recent exposure; adults with lymphadenopathy, fever, and myalgia, who might have some other serious disease, such as lymphoma; and immunocompromised persons, such as patients with AIDS, in whom toxoplasmosis might be fatal. It is the most common cause of focal encephalitis in patients with AIDS and this may be accompanied by a widespread papular eruption.

T. gondii is a crescent-shaped, oval, or round protozoan that can infect any mammalian or avian cell. The disease is often acquired through contact with animals, particularly cats. Reservoirs of infection have been reported in dogs, cats, cattle, sheep, pigs, rabbits, rats, pigeons, and chickens. The two major routes of transmission of T. gondii in humans are oral and congenital. Meats consumed by humans may contain tissue cysts, thus serving as a source of infection when eaten raw or

undercooked. There is no evidence of direct human-to-human transmission, other than from mother to fetus.

The diagnosis cannot be made on clinical grounds alone. It may be established by isolation of T. gondii; demonstration of the protozoa in tissue sections, smears, or body fluids by Wright or Giemsa stain; characteristic lymph node histology; and serologic methods. In the setting of bone marrow transplantation, the organism has caused interface dermatitis, creating the potential for misdiagnosis as graft versus host disease.

A combination of pyrimethamine (Daraprim) and sulfa- diazine acts synergistically and forms an effective treatment. Dosages and total treatment time vary according to the age and immunologic competence of the infected patient.

PHYLUM CNIDARIA

The cnidarians include the jellyfish, hydroids, Portuguese man-of-war, corals, and sea anemones. These are all radial marine animals, living mostly in ocean water. When a swimmer's skin contacts these organisms, they release a toxin through small spicules.

Toxoplasmosis

Toxoplasmosis is a zoonosis caused by a parasitic protozoan, Toxoplasma gondii. Infection may be either congenital or acquired. Congenital infection occurs from placental transmission. Abortion or stillbirth may result. However, a full-term child delivered to an infected mother may have a triad of hydrocephalus, chorioretinitis, and cerebral calcification. In addition, there may be hepatosplenomegaly and jaundice. Skin changes in toxoplasmosis are rare and clinically nonspecific. In congenital toxoplasmosis, macular and hemorrhagic eruptions predominate. Blueberry muffin lesions, reflecting dermatoerythropoiesis, may be seen. Occasionally, abnormal.

Portuguese man-of-war dermatitis

Stings by the Portuguese man-of-war (Physalia physalis in the Atlantic, or the much smaller Physalia utriculus or "bluebottle" in the Pacific) are characterized by linear lesions that are ery- thematous, urticarial, and even hemorrhagic. The forearms, sides of the trunk, thighs, and feet are common sites of involvement. The usual local manifestation is sharp, stinging, and intense pain. Internally, there may be severe dyspnea, prostration, nausea, abdominal cramps, lacrimation, and muscular pains. Death may occur if the areas stung are large in relation to the patient's size.

The fluid of the nematocysts contains toxin that is carried into the victim through barbs along the tentacle. The venom is a neurotoxic poison that can produce marked cardiac changes. Each Portuguese man-of-war is a colony of symbiotic organisms consisting of a blue to red float or pneumatophore with a gas gland, several gastrozooids measuring 1-20 mm, reproductive polyps, and the fishing tentacles bearing the nemato- cysts from which the barbs are ejected. The hydroid is found most frequently along the southeastern Florida coastline and in the Gulf of Mexico, and on windward coasts throughout the mid-Pacific and South Pacific. Safe Sea, a barrier cream, has been reported as being effective at preventing jellyfish stings off the coast of Florida, but studies of barrier creams in general have been mixed.

Jellyfish dermatitis

This produces lesions similar to those of the Portuguese man- of-war, except that the lesions are not so linear (Fig. 22). Immediate allergic reactions occur infrequently as urticaria, angioedema, or anaphylaxis. Delayed and persistent lesions also rarely occur.

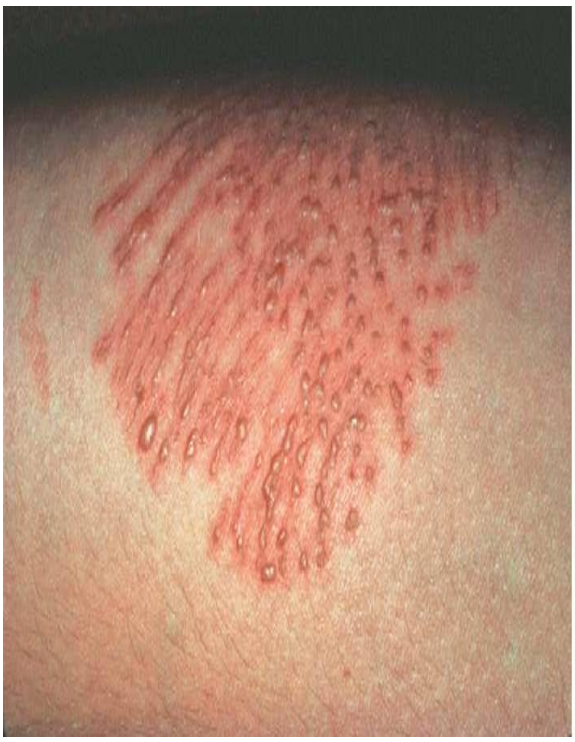

Fig. 23 Seabather's eruption. **Fig. 22 Jellyfish sting.**

The Australian sea wasp, Chironex fleckeri, which is colorless and transparent, is the most dangerous of all, with a sting that is often fatal. Another sea wasp, Carybdea marsupialis, much less dangerous, occurs in the Caribbean. Rhopilema nomadica, common in the Mediterranean, has been reported to cause severe delayed dermatitis.

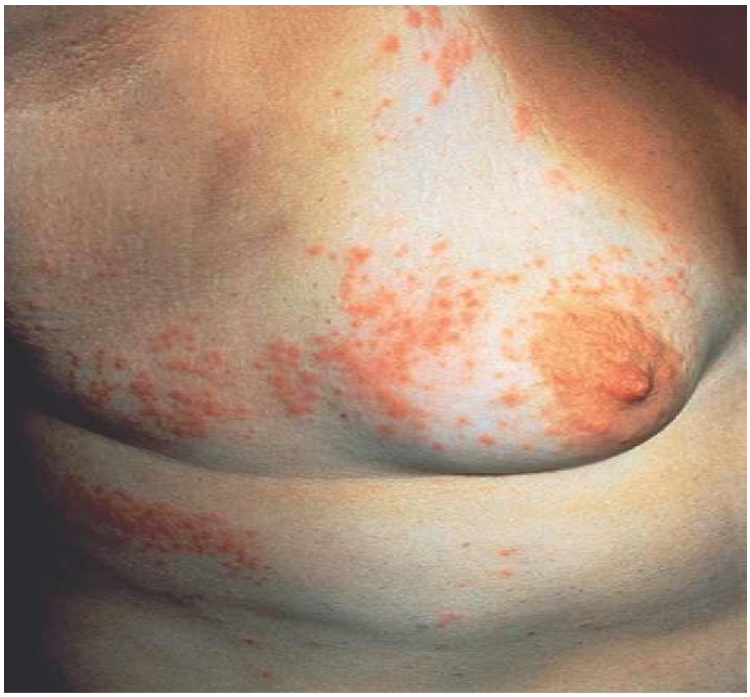

Fig. 24 Sea anemone.

Seabather's eruption is an acute dermatitis that begins a few hours after bathing in the waters along the coast of the Atlantic. It affects covered areas of the body as cnidarian larvae become entrapped under the bathing suit and the nematocyst releases its toxin because of external pressure. Thus, the buttocks and waist are affected primarily, with the breast also involved in women (Fig. 23). Erythematous macules and papules appear and may develop into pustules or vesicles. Urticarial plaques are also present in a smaller number of patients. Crops of new lesions may occur for up to 72 h, and the eruption persists for 10-14 days on average. It is quite pruritic. Outbreaks in Florida are usually caused by larvae of the thimble jellyfish, Linuche unguiculata, which patients report as "black dots" in the water or their bathing suits. The larvae of the sea anemone, Edwardstella lineata, caused one epidemic of seabather's eruption in Long Island, New York. This organism also has nematocysts; thus, the mechanism of the eruption is the same as with the jellyfish-induced eruption. It is likely that different cnidarian envenomations in different waters produce a similar clinical picture. Other reports focus on spring plants, dinoflagellates, protozoans, or crustaceans as potential causes. Since trapping of cnidarian larvae with their nematocysts or other toxic or irritant substances under the bathing suit accounts for this eruption, seabathers who take off their bathing suit and shower soon after leaving the water may limit it.

Hydroid, sea anemone, and coral dermatitis

Patients contacting the small marine hydroid, Halecium, may develop a dermatitis. The organism grows as a 1 cm-thick coat of moss on the submerged portions of vessels or pilings. Sea anemones (Fig. 24) produce reactions similar to those from jellyfish and hydroids. Coral cuts (Fig. 25) are injuries caused by the exoskeleton of the corals, Milleporina. They have a reputation for becoming inflamed and infected, and for delayed healing. The combination of implantation of fragments of coral skeleton and infection (since the cuts occur most commonly on the feet) probably accounts almost entirely for these symptoms. Detoxification as

soon as possible after the injury is advisable for all these types of sting or cut.

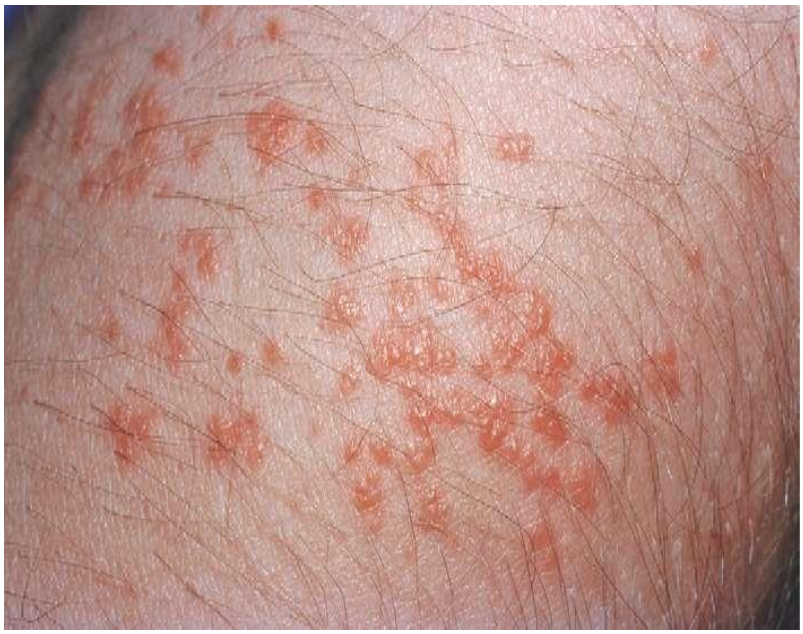

Fig. 25 Coral cuts.

Treatment of stings and cuts

Hot water immersion may be an effective remedy for many stings, but scald injuries must be avoided. Undischarged nematocytes may be removed with sea water, but never with fresh water, as this may cause them to discharge. Pacific Chironex (box jellyfish) nematocytes should always be inactivated with 5% acetic acid (vinegar) when it is available, but Pacific Physalia (bluebottle) nematocytes may discharge on contact with vinegar. Large visible tentacles may be removed with forceps in a double-gloved hand. Remaining nematocysts may be removed by applying a layer of shaving cream and shaving the area gently. Meat tenderizer may cause tissue damage and has been shown to be no better than placebo in some studies.

Pressure dressings and abrasion will worsen the envenoma- tion. Topical anesthetics or steroids may be applied after decontamination. Systemic reactions may occur through either large amounts of venom or a previously sensitizing exposure from which anaphylaxis may result, and systemic treatment with epinephrine, antihistamines, or corticosteroids may be needed. Specific antivenin is available for the box jellyfish,

Chironex fleckeri. This should be administered intravenously to limit myonecrosis. MgSO4 may also be of value in the setting of box jellyfish envenomation. Recurrent jellyfish reactions have shown partial responses to tacrolimus ointment 0.1%.

Sponges and bristleworms

Sponges have horny spicules of silicon dioxide and calcium carbonate. Some sponges produce dermal irritants, such as halitoxin and okadaic acid, and others may be colonized by Cnidaria. Allergic or irritant reactions may result. Bristleworms may also produce stinging. All of these may be treated by first using adhesive tape to remove the spicules, then applying vinegar soaks, as described above, and finally, applying topical corticosteroid agents.

Sea urchin injuries

Puncture wounds inflicted by the brittle, fragile spines of sea urchins, mainly of genus Diadema or Echinothrix, are stained blue-black by the black spines and may contain fragments of the spines. The spines consist of calcium carbonate crystals, which most commonly induce an irritant reaction with pain and inflammation of several days' duration. Foreign-body or sarcoid-like granulomas may develop, as may a vesicular hypersensitivity reaction, 10 days after exposure. Injuries by spines of the genus Tripneustes have been reported to cause fatal envenomation, but this genus is not found on US coasts.

Starfish also have thorny spines that can sting and burn if they are stepped on or handled. Several different types of stinging fish also produce puncture wounds. Stingrays, scor- pionfish, stonefish, catfish, and weaverfish may cause such envenomations.

These wounds should be immersed in nonscalding water (45°C [113°F]) for 30-90 min or until the pain subsides. Calcified fragments may be visible on x-ray evaluation, with fluoroscopy guiding extraction of spines, especially on the hands and feet. Sea urchin spines have been effectively removed using the erbium:YAG laser. Debridement and pos-

sibly antibiotic therapy for deep puncture wounds of the hands and feet are recommended. There is a specific antivenin for stonefish stings.

Seaweed dermatitis

Although this is caused by a marine alga and not by an animal, it deserves mention with other problems associated with swimming or wading. The dermatitis occurs 3-8 h after the individual emerges from the ocean. The distribution is in parts covered by a bathing suit: scrotum, penis, perineum, and peri- anal area. The dermatitis is caused by a marine plant, Lyngbya majuscula Gomont. It has been observed only in bathers swimming off the windward shore of Oahu, Hawaii. Seabather's eruption, clamdigger's itch, and swimmer's itch must be differentiated from seaweed dermatitis caused by marine algae. Prophylaxis is achieved by refraining from swimming in waters that are turbid with such algae. Swimmers should shower within 5 min of swimming. Active treatment in severe cases is the same as for acute burns.

Dogger Bank itch

Dogger Bank itch is an eczematous dermatitis caused by the sea chervil, Alcyonidium hirsutum, a seaweed-like animal colony. These sea mosses or sea mats are found on the Dogger Bank, an immense shelflike elevation under the North Sea between Scotland and Denmark.

PHYLUM PLATYHELMINTHES

Phylum Platyhelminthes includes the flatworms, of which two classes, trematodes and cestodes, are parasitic to humans. The trematodes, or blood flukes, parasitize human skin or internal organs. The cestodes are segmented, ribbon-shaped flatworms that inhabit the intestinal tract as adults and involve the subcutaneous tissue, heart, muscle, and eye in the larval form. This is encased in a sac that eventually becomes calcified.

Class Trematoda Schistosome cercarial dermatitis

Cercarial dermatitis is a severely pruritic, widespread, papular dermatitis caused by cercariae of schistosomes for which humans are not

hosts (the usual animal hosts are waterfowl and rodents, such as muskrats).

The eggs in the excreta of these animals, when deposited in water, hatch into swimming miracidia. These enter a snail, where further development occurs. From the snail, the free- swimming cercariae emerge to invade human skin on accidental contact. The swimming, colorless, multicellular organisms are a little less than a millimeter long. Exposure to cercariae occurs when a person swims or, more often, wades in water containing them. They attack by burrowing into the skin, where they die. The species that causes this eruption cannot enter the bloodstream or deeper tissues.

After coming out of the water, the bather begins to itch and a transient erythematous eruption appears, but after a few hours, the eruption subsides, together with the itching. Then, after a quiescent period of 10-15 h, the symptoms recur, and erythematous macules and papules develop throughout the exposed parts that were in the water. After several days the dermatitis heals spontaneously. There are two types: the freshwater swimmer's itch, and the saltwater marine dermatitis or clam digger's itch. It is not communicable.

Various genera and species of organism have been reported from various locations worldwide. An outbreak of cercarial dermatitis was reported from Delaware in 1991 in which the avian schistosome, Microbilharzia variglandis, was implicated as the causative organism. Schistosoma spindale cercaria caused a recent epidemic in southern Thailand.

Thoroughly washing, then drying with a towel after exposure can prevent the disease. Rubbing with alcohol is an additional preventive measure advocated by some. Snail populations can be controlled or waterfowl may be treated with medicated feedcorn to destroy the adult schistosomes and prevent outbreaks of swimmer's itch.

Visceral schistosomiasis (bilharziasis)

The cutaneous manifestation of schistosomiasis may begin with mild itching and a papular dermatitis of the feet and other parts after swimming in polluted streams containing cercariae. The types of schistosome causing this disease can penetrate into the bloodstream and eventually inhabit the venous system, draining the urinary bladder (Schistosoma hae- matobium) or the intestines (Schistosoma mansoni or Schistosoma japonicum). After an asymptomatic incubation period, there may be a sudden illness with fever and chills, pneumonitis, and eosinophilia. Petechial hemorrhages may occur.

Cutaneous schistosomal granulomas most frequently involve the genitalia, perineum, and buttocks. The eggs of S. haematobium or S. mansoni usually cause these bilharziomas. Vegetating, soft, cauliflower-shaped masses, fistulous tracts, and extensive hard masses occur; these are riddled by sinuses that exude a seropurulent discharge with a characteristic odor. Phagedenic ulcerations and pseudoel- ephantiasis of the scrotum, penis, or labia are sometimes encountered. Histologically, the nodules contain bilharzial ova undergoing degeneration, with calcification and a eosinophils, and occasional giant cells. In some cases, eventual malignant changes have been noted in chronic lesions. Animal studies have shown a moderate Th1 response to parasite antigens in most tissues, but a strong Th2 response that propagates fibrogenesis within the liver. Infrequently, ectopic or extragenital lesions may occur, mainly on the trunk. This is a papular eruption tending to group in plaques and become darkly pigmented and scaly. A severe urticarial eruption known as urticarial fever or Katayama fever is frequently present along with an S. japoni- cum infection; it occurs with the beginning of oviposition, 4-8 weeks after infection. This condition occurs mainly in China, Japan, and the Philippines. In addition to the urticaria, fever, malaise, abdominal cramps, arthritis, and liver and spleen involvement are seen. This is felt to be a serum sicknesslike reaction.

Preventive measures include reducing infection sources, preventing contamination by human excreta of snail-bearing waters, control of snail

hosts, and avoiding exposure to cercaria-infested waters. Prophylactic measures are constantly sought to control one of the world's worst parasitic diseases, but as yet none has been found to be practical. For both S. haematobium and S. mansoni, praziquantel (Biltricide), 40 mg/kg orally for each of two treatments in 1 day, is the treatment of choice. S. japonicum treatment requires 60 mg/kg in three doses in 1 day. Schistosomicides exhibit toxicity for the host as well as for the parasite, and the risk of undesirable side effects may be enhanced by concomitant cardiac, renal, or hepatosplenic disease.

Cysticercosis cutis

The natural intermediate host of the pork tapeworm, Taenia solium, is the pig, but under some circumstances humans act in this role. The larval stage of T. solium is Cysticercus cellulosae. Infection takes place by the ingestion of food contaminated with the eggs, or by reverse peristalsis of eggs or proglottides from the intestine to the stomach. Here the eggs hatch, freeing the oncospheres. These enter the general circulation and form cysts in various parts of the body, such as striated muscles, brain, eye, heart, and lung.

In the subcutaneous tissues, the lesions are usually painless nodules that contain cysticerci. They are more or less stationary, usually numerous, and often calcified, and are therefore demonstrable radiographically. Pain and ulceration may accompany the lesions. The disease is most prevalent in countries in which pigs feed on human feces. It may be confused with gumma, lipoma, and epithelioma. A positive diagnosis is established solely by incision and examination of the interior of the calcified tumor, where the parasite will be found. Fine needle aspiration has also been used to establish the diagnosis.

Albendazole or praziquantel is effective; however, the status of the CNS, spinal, and ocular involvement needs to be thoroughly assessed prior to treatment. The length of therapy and use of concomitant corticosteroids depend upon the location of the cysts. None of the

regimens clears the calcified parasites, however, which need to be surgically removed.

Sparganosis

Sparganosis is caused by the larva of the tapeworm Spirometra. The adult tapeworm lives in the intestines of dogs and cats. This is a rare tissue infection occurring in two forms. Application sparganosis occurs when an ulcer or infected eye is poulticed with the flesh of an infected intermediate host (such poultices are frequently used in the Orient). The larvae become encased in small nodules in the infected tissue. Ingestion sparganosis occurs when humans ingest inadequately cooked meat, such as snake or frog, or when a person drinks water that is contaminated with Cyclops, which is infected with plerocercoid larvae. One or two slightly pruritic or painful nodules may form in the subcutaneous tissue or on the trunk, breast, genitalia, or extremities. Cerebral disease may also occur. Diagnosis is usually made via excision of the nodule, although noninvasive imaging has also been used.

Humans are the accidental intermediate host of the Sparganum, which is the alternative name for the plerocercoid larva. Treatment is surgical removal or ethanol injection of the infected nodules (Fig. 26). This may be difficult because of the swelling and extensive vascularity.

Echinococcosis

Echinococcosis is also known as hydatid disease. In humans, infection is produced by the ova reaching the mouth from the hands, in food, or from containers soiled by ova-contaminated feces from an infected dog. This leads to Echinococcus granulo- sus infestation of the liver and the lungs. Soft, fluctuating, semitranslucent, cystic tumors may occur in the skin, sometimes in the supraumbilical area as fistulas from underlying liver involvement. These tumors become fibrotic or calcified after the death of the larva.

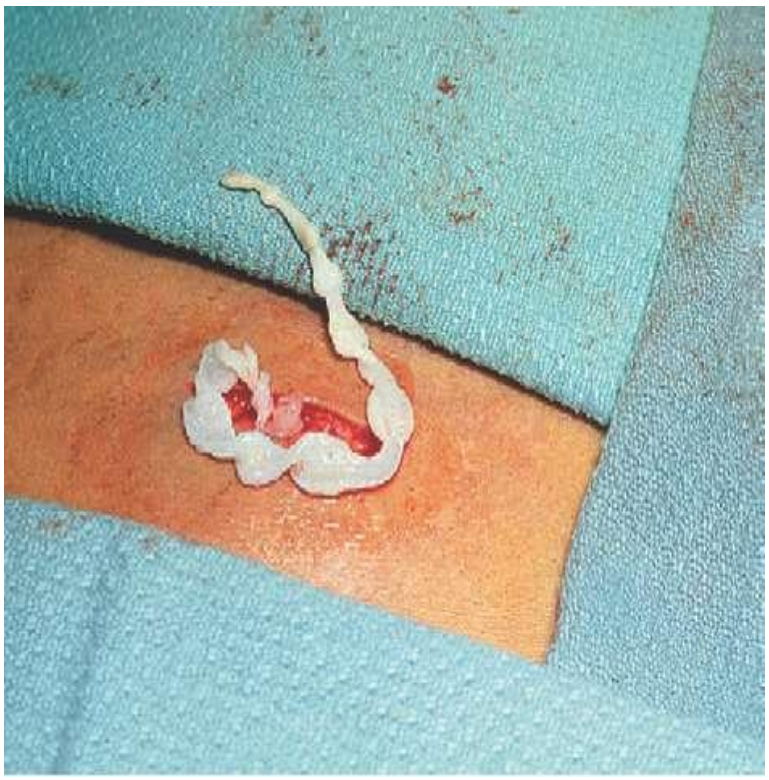

Fig. 26 Sparganosis.

Eosinophilia, intractable urticaria and pruritus, and even acute generalized exanthematous pus- tulosis may be present. Such reactive findings may be present as skin manifestations of many of the helminthic infections, including other types of tapeworm. The treatment is excision, with care being taken to avoid rupturing the cyst. Albendazole combined with percutaneous drainage may also be used. Hymenolepis nana is a cosmopolitan dwarf tapeworm endemic in the tropics, which may cause a treatment-resistant pruritic papular eruption associated with eosinophilia. Stool specimens for ova and parasites are definitive and praziquantel is curative.

PHYLUM ANNELIDA LEECHES

Leeches, of the class Hirudinea, are of marine, freshwater, or terrestrial types. After attaching to the skin, they secrete an anticoagulant, hirudin, and then engorge themselves with blood. Local symptoms at the site of the bite may include bullae, hemorrhage, pruritus, whealing, necrosis, or ulceration. Allergic reactions, including anaphylaxis, may result. Leeches may be removed by applying salt, alcohol, or vinegar, or

by use of a match flame. Bleeding may then be stopped by direct pressure or by applying a styptic pencil to the site.

Leeches may be used medicinally to salvage tissue flaps that are threatened by venous congestion. However, Aeromonas infection, anetoderma, and pseudolymphoma may be complications of their attachment.

PHYLUM NEMATHELMINTHES

Phylum Nemathelminthes includes the roundworms, both free-living and parasitic forms. Multiplication is usually outside the host. Both the larval and adult stages may infect humans.

Class Nematoda

Enterobiasis (pinworm infection, seatworm infection, oxyuriasis)

The chief symptom of pinworm infestation, which occurs most frequently in children, is nocturnal pruritus ani. There is intense itching accompanied by excoriations of the anus, perineum, and pubic area. The vagina may become infested with the gravid pinworms. A pruritic papular dermatosis of the trunk and extremities may be observed infrequently. Restlessness, insomnia, enuresis, and irritability are but a few of the many symptoms ascribed to this exceedingly common infestation. Oxyuriasis is caused by the roundworm Enterobius vermicu- laris, which may infest the small intestines, cecum, and large intestine of humans. The worms, especially gravid ones, migrate toward the rectum and at night emerge to the perianal and perineal regions to deposit thousands of ova; then the worm dries and dies outside the intestine. These ova are then carried back to the mouth of the host on the hands. The larvae hatch in the duodenum and migrate into the jejunum and ileum, where they reach maturity. Fertilization occurs in the cecum, thus completing the life cycle. Humans are the only known host of the pinworm, which probably has the widest distribution of all the helminths. Infection occurs from hand-to-mouth transmission, often from handling soiled clothes, bedsheets, and other

household articles. Ova under the fingernails are a common source of auto- infection. Ova may also be airborne and collect in dust that may be on furniture and the floor. Investigation may show that all members of the family of an affected person also harbor the infection. It is common in orphanages and mental institutions, and among people living in communal groups. Rarely is it feasible to identify a dead pinworm in the stool. Diagnosis is best made by demonstration of ova in smears taken from the anal region early in the morning before the patient bathes or defecates. Such smears may be obtained with a small eye curette and placed on a glass slide with a drop of saline solution. It is also possible to use Scotch tape, looping the tape sticky-side out over a tongue depressor and then pressing it several times against the perianal region. The tape is then smoothed out on a glass slide. A drop of a solution containing iodine in xylol may be placed on the slide before the tape is applied to facilitate detection of any ova. These tests should be repeated on 3 consecutive days to rule out infection. Ova may be detected under the fingernails of the infected person. Albendazole, 400 mg, mebendazole, 100 mg, or pyrantel pamoate, 11 mg/kg (maximum 1 g) given once and repeated in 2 weeks, is effective. Personal hygiene and cleanliness at home are important. Fingernails should be cut short and scrubbed frequently; they should be thoroughly cleaned on arising, before each meal, and after using the toilet. Sheets, underwear, towels, pajamas, and other clothing of the affected person should be laundered thoroughly and separately.

HOOKWORM DISEASE

(ground itch, uncinariasis, ancylostomiasis, necatoriasis)

The earliest skin lesions (ground itch) are erythematous macules and papules, which in a few hours become vesicles. These itchy lesions usually occur on the soles, toe webs, and ankles; they may be scattered or in groups. The content of the vesicles rapidly becomes purulent. These lesions are produced by invasion of the skin by the Ancylostoma or Necator larvae, and precede the generalized symptoms of the disease by 2 or 3 months. The cutaneous lesions last less than 2 weeks before the larvae continue their human life cycle. There may be as high as 40%

eosinophilia around the fifth day of infection. The onset of the constitutional disease is insidious and is accompanied by progressive iron-deficiency anemia and debility. During the course of the disease urticaria often occurs. The skin ultimately becomes dry and pale or yellowish.

Hookworm is a specific communicable disease caused by Ancylostoma duodenale or Necator americanus. In the soil, under propitious circumstances, they attain the stage of infective larvae in 5-7 days. When they come into accidental contact with bare feet, these tiny larvae (which can scarcely be seen with a small pocket lens) penetrate the skin and reach the capillaries. They are carried in the circulation to the lungs, where they pass through the capillary walls into the bronchi. They move up the trachea to the pharynx and, after being swallowed, eventually reach their habitat in the small intestine. Here they bury their heads in the mucosa and begin their sexual life.

Hookworm is prevalent in most tropical and subtropical countries, and is often endemic in swampy and sandy localities in temperate zones. In these latter regions the larvae are killed off each winter, but the soil is again contaminated from human sources the following summer. N. americanus prevails in the western hemisphere, Central and South Africa, South Asia, Australia, and the Pacific islands.

The defecation habits of infected individuals in endemic areas are largely responsible for its widespread distribution, as is the use of human feces for fertilization in many parts of the world. In addition, the climate is usually such that people go barefoot because of the heat or because they cannot afford shoes. Infection is thereby facilitated, especially through the toes. Finding the eggs in the feces of a suspected individual establishes the diagnosis. The ova appear in the feces about 5 weeks after the onset of infection. The eggs may be found in direct fecal films if the infection is heavy, but in light infections it may be necessary to resort to zinc sulfate centrifugal flotation or other concentration methods. Mixed infections frequently occur.

Albendazole, 400 mg once, or mebendazole, 100 mg twice a day for 3 days or 500 mg once, or pyrantel pamoate, 11 mg/ kg (maximum 1 g) each day for 3 days, is effective. Prophylaxis is largely a community problem and depends on preventing fecal contamination of the soil. This is best attained by proper sanitary disposal of feces, protecting individuals from exposure by educating them about sanitary procedures, and mass treatment through public health methods.

Nematode dermatitis

Miller et al described a patient who developed a persistent widespread folliculitis caused by Ancylostoma caninum. It was apparently acquired by his lying in grass contaminated by the droppings of his pet dogs and cats. A biopsy revealed hookworm larvae within the hair follicle. Oral thiabendazole was curative.

CREEPING ERUPTION (larva migrans)

Creeping eruption is a term applied to twisting, winding linear skin lesions produced by the burrowing of larvae. People who go barefoot on the beach, children playing in sandboxes, carpenters and plumbers working under homes, and gardeners are often victims. The most common areas involved are the feet, buttocks, genitals, and hands.

Slight local itching and the appearance of papules at the sites of infection characterize the onset. Intermittent stinging pain occurs, and thin, red, tortuous lines are formed in the skin. The larval migrations begin 4 days after inoculation and progress at the rate of about 2 cm/day. However, they may remain quiescent for several days or even months before beginning to migrate. The linear lesions are often interrupted by papules that mark the sites of resting larvae (Fig. 27). As the eruption advances, the old parts tend to fade, but sometimes there are purulent manifestations caused by secondary infection; erosions and excoriations caused by scratching frequently occur. If the progress of the disease is not interrupted by treatment, the larvae usually die in 2-8 weeks, with resolution of the eruption, although rarely it has been reported to persist

for up to 1 year. At times, the larvae are removed from the skin by the fingernails in scratching. Eosinophilia may be present.

Loeffler syndrome, consisting of a patchy infiltrate of the lungs and eosinophilia as high as 50% in the blood and 90% in the sputum, may complicate creeping eruption. The majority of cases in the US occur along the southeast coast and are caused by penetration by the larvae of a cat and dog hookworm, Ancylostoma braziliense. It is acquired from body contact with damp sand or earth that has been contaminated by the excreta of dogs and cats.

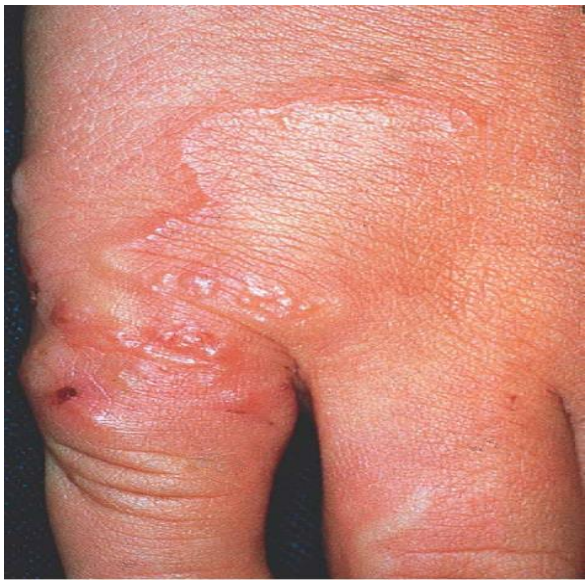

Fig. 27 Cutaneous larva migrans.

The larvae of A. caninum, which also infests the dog and the cat, rarely produce a similar dermatitis. The diagnosis is typically made clinically, although biopsy may sometimes demonstrate the organism and even dermoscopy has been used.

Ivermectin, 200 |g/kg, generally given as a single 12 mg dose and repeated the next day, or albendazole, 400 mg/day for 3 days, is an effective treatment. Criteria for successful therapy are relief of symptoms and cessation of tract extension, which usually occurs within a week. Topical thiabenda- zole, compounded as a 10% suspension or a 15% cream used four times a day, will result in marked relief from pruritus in 3 days, and the tracts become inactive in 1 week. Topical met- ronidazole

has also been reported to be effective. Another condition, not to be confused with this helminthic disease, which also is called creeping eruption (or sandworm, as it is known in South Africa, particularly in Natal and Zululand), is caused by a small mite about 300 |m long that tunnels into the superficial layers of the epidermis.

Gnathostomiasis

Migratory, intermittent, erythematous, urticarial plaques characterize human gnathostomiasis. Each episode of painless swelling lasts from 7-10 days and recurs every 2-6 weeks. Movement of the underlying parasite may be as much as

cm/h. The total duration of the illness may be 10 years. Histopathologic examination of the skin swelling will demonstrate eosinophilic panniculitis. The clinical manifestation has been called larva migrans profundus.

The nematode Gnathostoma dolorosi or spinigerum is the cause; most cases occur in Asia or South America. Eating raw flesh from the second intermediate host, most commonly freshwater fish, in such preparations as sashimi and ceviche, allows humans to become the definitive host. Eating raw squid or snake is another less common exposure. As the larval cyst in the flesh is digested, it becomes motile and penetrates the gastric mucosa, usually within 24-48 h of ingestion. Symptoms then occur as migration of the parasite continues. Surgical removal is the treatment of choice, if the parasite can be located. This may be combined with albendazole, 400 mg/day or twice a day for 21 days, or ivermectin, 200 |g/kg/day for 2 days.

Creeping eruption in several reports from Japan has been found to be caused by a newly recognized causative parasite of the nematode superfamily Spiruroidea. Eating raw squid was associated with the onset of long, narrow lesions that were pruritic, linear, and migratory. Surgical removal is necessary; chemotherapy has been largely unsuccessful. Data regarding ivermectin are mixed.

Larva currens

Intestinal infections with Strongyloides stercoralis may be associated with a perianal larva migrans syndrome, called larva currens, because of the rapidity of larval migration (currens means "running" or "racing"). Larva currens is an autoinfec- tion caused by penetration of the perianal skin by infectious larvae as they are excreted in the feces. An urticarial band is the prominent primary lesion of cutaneous strongyloidiasis. Strongyloidiasis, like the creeping eruption secondary to it, is often a chronic disease; infections may persist for more than 40 years. Approximately one-third of patients infected are asymptomatic.

Signs and symptoms of systemic strongyloidiasis include abdominal pain, diarrhea, constipation, nausea, vomiting, pneumonitis, urticaria, eosinophilic folliculitis, and a peripheral eosinophilia. The skin lesions originate within 30 cm of the anus and characteristically extend as much as 10 cm/day.

Fatal cases of hyperinfection occur in immunocompromised patients. In such patients the parasite load increases dramatically and can produce a fulminant illness. Widespread petechiae and purpura are helpful diagnostic signs of disseminated infection and chronic urticaria is a possible presenting sign. Periumbilical ecchymoses may appear as if they were caused by a thumbprint.

Administration of ivermectin, 200 |g/kg/day for 2 days, or thiabendazole 50 mg/kg/day in two doses (maximum 3 g/day) for 2 days, is the treatment of choice. Immuno- suppressed hosts may be treated with thiabendazole, 25 mg/kg twice a day for 7-10 days.

There are free-living strongyloides known as Pelodera that can produce a creeping eruption also. Jones et al reported a case of widespread follicular, erythematous, dome-shaped papules and pustules that began within 24 h of working under a house. This eruption persisted for 1 month before presentation. Scraping the lesions revealed live and dead larvae of the free-living soil nematode, Pelodera strongyloides. Treatment with oral thiabendazole led to resolution.

DRACUNCULIASIS

(Guinea worm disease, dracontiasis, medina worm)

Guinea worm disease is now limited to remote villages in several sub-Saharan African countries. It is caused by Dracunculus medinensis and is contracted through drinking water that has been contaminated with infected water fleas in which Dracunculus is parasitic. In the stomach, the larvae penetrate into the mesentery, where they mature sexually in 10 weeks. Then the female worm burrows to the cutaneous surface to deposit her larvae and thus causes the specific skin manifestations. As the worm approaches the surface, it may be felt as a cordlike thickening and forms an indurated cutaneous papule. The papule may vesiculate and a painful ulcer develops, usually on the leg. The worm is often visible. When the parasite comes in contact with water, the worm rapidly discharges its larvae, which are ingested by water fleas (Cyclops), contaminating the water. The cutaneous lesion is usually on the lower leg, but it may occur on the genitalia, buttocks, or arms (Fig. 28). In addition to the ulcers on the skin, there may be urticaria, gastrointestinal upsets, eosinophilia, and fever. The disease may be prevented by boiling drinking water, providing safe drinking water through boreholes, or filtering the water through mesh fibers.

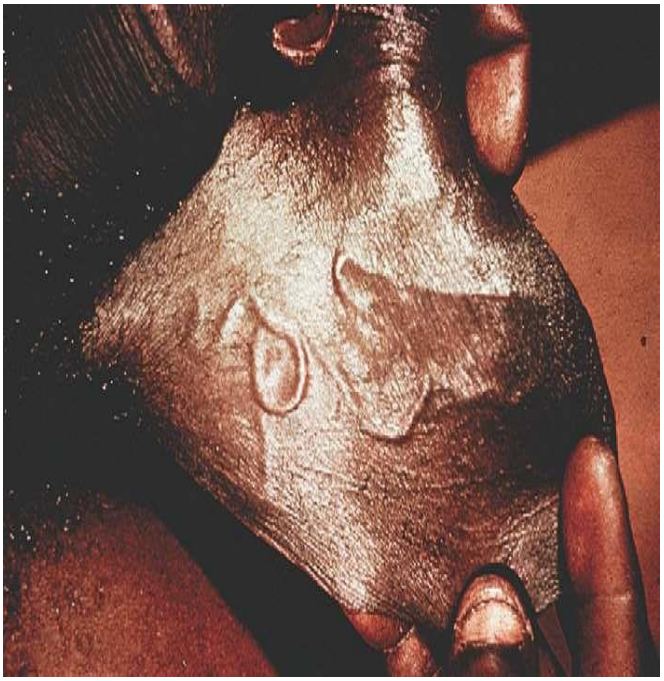

Fig. 28 Dracunculiasis.

Native treatment consists of gradually extracting the worm a little each day, with care not to rupture it; in the event of such an accident, the larvae escape into the tissues and produce fulminating inflammation. Surgical removal is the treatment of choice. Metronidazole, 500 mg/day, resolves the local inflammation and permits easier removal of the worm. Immersion in warm water pro motes emergence of the worm. Global eradication is within our grasp, and Guinea worm disease may become a historical footnote.

FILARIASIS

Elephantiasis tropica (elephantiasis arabum)

Filariasis is a widespread tropical disorder caused by infestation with filarial worms of Wuchereria bancrofti, Brugia malayi, or Brugia timori species. It is characterized by lymphedema, with resulting hypertrophy of the skin and subcutaneous tissues, and by enlargement and deformity of the affected parts, usually the legs, scrotum, or labia majora. The disease occurs more frequently in young men than in women.

The onset of elephantiasis is characterized by recurrent attacks of acute lymphangitis in the affected part, associated with chills and fever (elephantoid fever) that last for several days to several weeks. These episodes recur over several months to years. After each attack the swelling subsides only partially, and as recrudescences supervene, thickening and hypertrophy become increasingly pronounced. The overlying epidermis becomes stretched, thin, and shiny, and over the course of years, leathery, insensitive, and verrucous or papil- lomatous from secondary pyogenic infection. There may be a dozen or more attacks in a year.

In addition to involvement of the legs and scrotum, the scalp, vulva, penis, female breasts, and arms are at times affected, either alone or in association with the other regions. The manifestations vary according to the part involved. When the legs are attacked, both are usually affected in a somewhat symmetrical manner, the principal changes occurring on the posterior aspects above the ankles and on the dorsa of the feet. At first, the thickening may be slight and associated with edema that pits on

pressure. Later, the parts become massive and pachydermatous, the thickened integument hanging in appos- ing folds, between which there is a fetid exudate (Fig. 29).

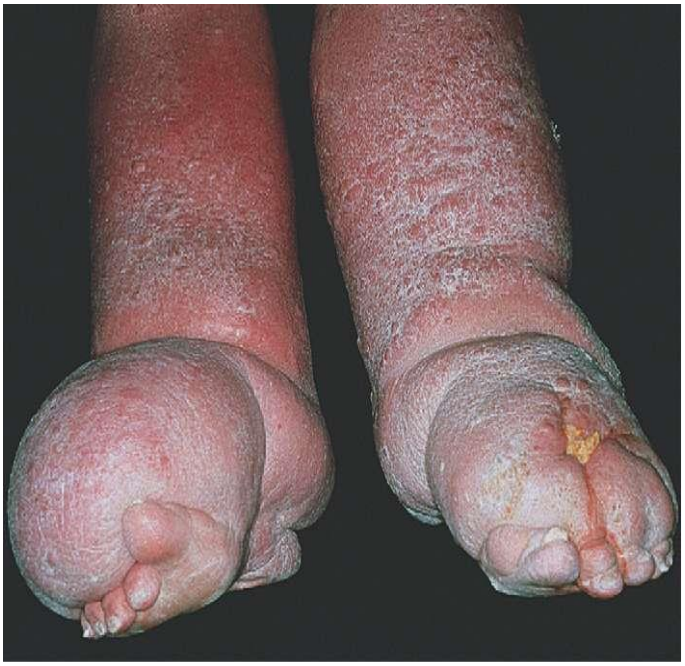

Fig. 29 Filarial elephantiasis.

When the scrotum is affected, it gradually reaches an enormous size and the penis becomes hidden in it. The skin, which at first is glazed, is later coarse and verrucous, or, in far- advanced cases, ulcerated or gangrenous. Resistant urticaria may occur. Filarial orchitis and hydrocele are common. A testicle may enlarge rapidly to the size of an apple and be extremely painful. The swelling may subside within a few days, or the enlargement may be permanent. As a result of obstruction and dilation of the thoracic duct or some of its lower abdominal tributaries into the urinary tract, chyle appears in the urine, which assumes a milky appearance. Lobulated swellings of the inguinal and axillary glands, called varicose glands, are caused by obstructive varix and dilatation of the lymphatic vessels. Filaria are transmitted person to person by the bites of a variety of mosquitoes of the Culex, Aedes, and Anopheles species. The adult worms are threadlike, cylindrical, and creamy white. The females are 4-10 cm long. Microfilarial embryos may be seen coiled each in its own membrane near the posterior tip. Fully grown, sheathed microfilariae are 130-320 m long. The adult worms live in the lymphatic

system, where they produce microfilariae. These either remain in the lymphatic vessels or enter the peripheral bloodstream. An intermediate host is necessary for the further development of the parasite. It is important to realize that infestation by the filaria is often asymptomatic, and elephantiasis usually occurs only if hundreds of thousands of mosquito bites are suffered over a period of years, with episodes of intercurrent streptococcal lymphangitis. Filariasis was endemic in the considerable Samoan population of Hawaii for half a century, and only one case of elephantiasis has occurred among this group.

Search for the microfilariae should be made on fresh cover- slip films of blood (collected at night), urine, or other body fluid, and examined with a low-power objective lens. Calcified adult worms may be demonstrated on x-ray examination, and ultrasound can detect adult worms. At times, adult filariae are found in abscesses or in material taken for pathologic examination. Specific serologic tests and a simple card test for filarial antigen are available. The prognosis in regard to life is good, but living becomes burdensome unless the condition is alleviated. Diethylcarbamazine, in increasing doses over a 14-day period, is the treatment of choice. This regimen clears microfilariae but not adult worms. A single dose of ivermectin may also be effective. Doxycycline kills the intracellular symbiotic bacteria, Wolbachia. This leads to long-term sterility of adult female worms. It is being studied to determine its place in the treatment of both bancroftian filariasis and onchocerciasis. A worldwide effort to eliminate these diseases is under way. Surgical operations have been devised to remove the edema- tous subcutaneous tissue from the scrotum and breast. Prophylactic measures consist of appropriate mosquito control. Diethylcarbamazine has been effective in mass prophylaxis and if a trip of over 1 month is planned to areas with endemic W. bancrofti and extensive exposure to mosquitoes is likely, taking 500 mg/day for 2 days each month is recommended.

LOIASIS

(loa loa, Calabar swelling, tropical swelling, fugitive swelling)

Infection with Loa loa is often asymptomatic. In infected persons, the parasite develops slowly and there may even be an interval of as much as 3 years between infection and the appearance of symptoms, although the usual interval is 1 year. The first sign is often painful, localized, subcutaneous, nonpit- ting edema called Calabar or fugitive swelling (Fig. 30 A). These are one or more slightly inflamed, edematous, transient swellings, usually about the size of a hen's egg. They usually last a few days and then subside, although recurrent swellings at the same site may eventually lead to a permanent cystlike protuberance. These swellings may result from hypersensitiv- ity to the adult worm or to materials elaborated by it. Eosinophilia may be as high as 90% and often is between 60% and 80%. The filariae may be noticed subcutaneously in the fingers, breasts, eyelids, or submucosally under the conjunctivae. The worm may be in the anterior chamber of the eye, the myocardium, or other sites. It has a predilection for loose tissues such as the eye region, the frenum of the tongue, and the genitalia. The wanderings of the adult parasite may be noticed because of a tingling and creeping sensation. The death of the filaria in the skin may lead to the formation of fluctuant cystic lesions.

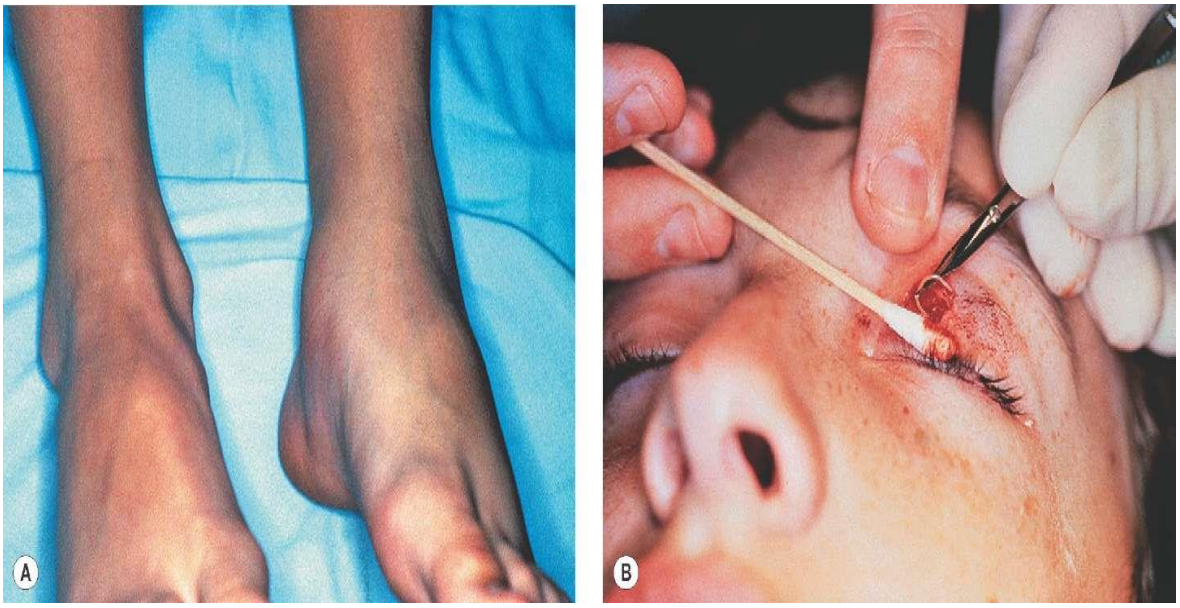

Fig. 30 A and B, Loiasis.

Loiasis is widely distributed in West and Central Africa, where it is transmitted by the mango fly, Chrysops dimidia or Chrysops silacea. This fly bites only in the daytime. Humans are the only important reservoir for the parasite. The observation of the worm under the conjunctiva, Calabar swellings, and eosinophilia establish the diagnosis. Demonstration of the characteristic microfilariae in the blood during the day is possible in only some 20% of patients. Specific serologic tests are available, and luciferase immunoprecipitation systems can provide rapid diagnostic results with improved sensitivity and specificity compared with enzyme-linked immunosorbent assays (ELISA).

Removal of the adult parasite whenever it comes to the surface of the skin is mandatory (Fig. 30 B). This must be done quickly by seizing the worm with forceps and placing a suture under it before cutting down to it. Worms that are not securely and rapidly grasped may escape into the deeper tissues.

Diethylcarbamazine kills both adults and microfilariae, and is given in increasing doses for 21 days. In regions in which onchocerciasis and loiasis are both endemic and ivermectin is used in a community-based elimination strategy for onchocer- ciasis, simultaneously infected patients with a high Loa loa load have a greater risk of serious side effects. If ivermectin treatment of these patients is undertaken, proper monitoring and appropriate supportive treatment should be available in anticipation of this risk. Diethylcarbamazine is an effective chemo- preventive, using 300 mg/week in temporary residents of regions of Africa where Loa loa is endemic.

Onchocerciasis

The skin lesions are characterized by pruritus, dermatitis, and onchocercomas. The dermatitis is variable in its appearance and probably relates to chronicity of infection, age of the patients, geographic area in which it was acquired, and relative immune responsiveness. Early in the course of the infection an itchy papular dermatitis may occur, and in

visitors who acquire the infection this may be localized to one extremity (Fig. 31).

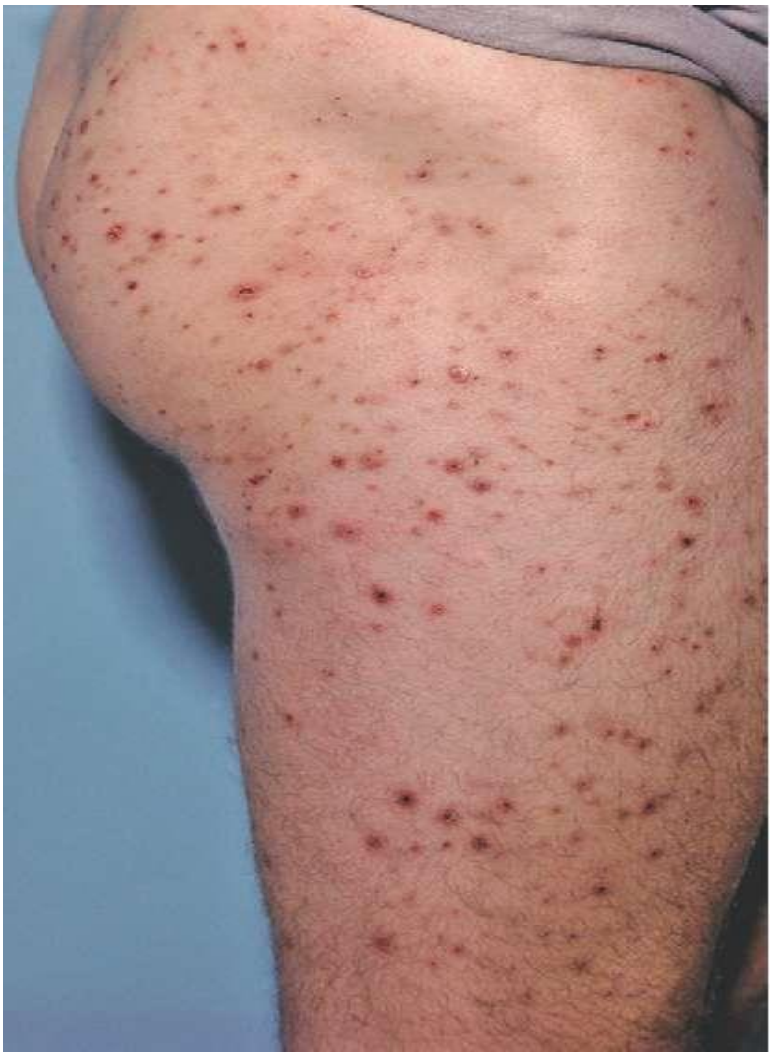

Fig. 31 Early onchocerciasis.

In Central America, papules may appear only on the head and neck area. This unusual localization of insect bite-appearing papules with excoriations may lead to the diagnosis in travelers returning to their home countries.

As time passes, the dermatitis becomes chronic and remains papular; however, thickening, lichenification, and depigmen- tation occur (Fig. 32). Later, atrophy may supervene. When the depigmentation is spotted, it is known as leopard skin; when the skin is thickened, it is called elephant skin. When local edema and thickened, wrinkled, dry dermatitic changes predominate, it is sometimes called lizard skin.

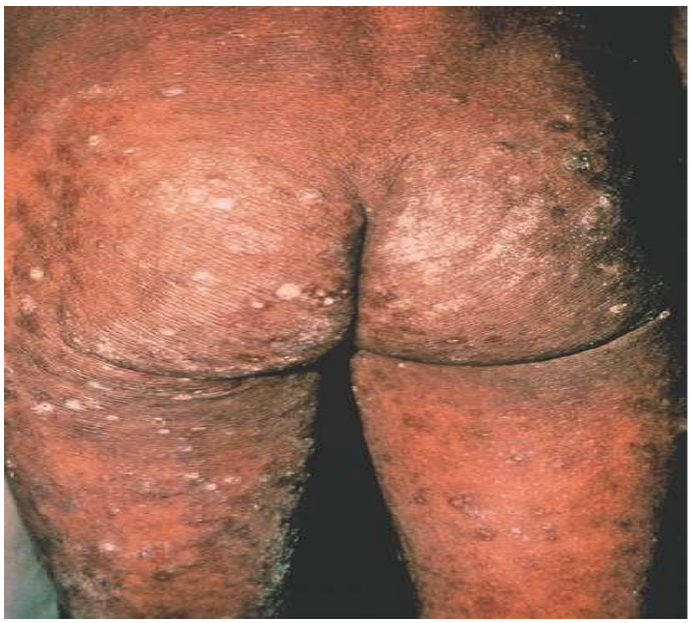

Fig. 32 Onchocerciasis.

In Saudi Arabia, Yemen, and East Africa, a localized type of onchocerciasis exists called sowda, which is Arabic for "black." It is characterized by localized, pruritic, asymmetrical, usually darkly pigmented, chronic lichenified dermatitis of one leg or one body region. It is also known as the chronic hyperreactive type, and an association with antidefensin antibodies suggests a reason for this enhanced reactivity against the parasite.

After a time, firm subcutaneous nodules, pea-sized or larger, develop on various sites of the body. These nodules are onchocercomas containing myriad microfilariae. These occur in crops, are frequently painful, and their site varies. In parts of Africa, where natives are wholly or nearly unclothed, the lesions occur on the trunk, axillae, groin, and perineum. In Central and South America, the head, especially the scalp, is the usual site of involvement. Firm, nontender lymphadenopathy is a common finding in patients with chronically infected onchocerciasis. "Hanging groin" describes the loose, atrophic skin sack that contains these large inguinal nodes (Fig. 33).

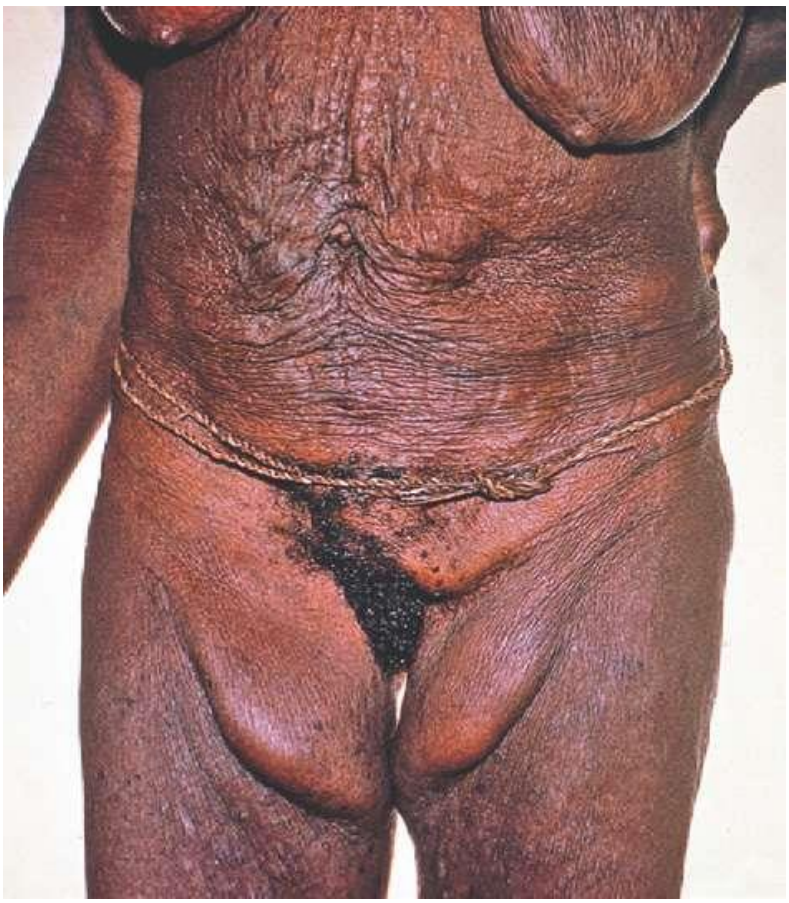

Fig. 33 Onchocerciasis.

In about 5% of affected persons, serious eye lesions arise late in the disease, gradually leading to blindness.

Onchocerciasis is caused by Onchocerca volvulus, which is transmitted to humans by the bite of the black fly of the genus Simulium. It breeds in fast-flowing streams. When the black fly bites, it introduces larvae into the wound. The larvae reach adulthood in the subdermal connective tissue in about 1 year. Then millions of the progeny migrate back into the dermis and the aqueous humor of the eye.

Onchocerciasis occurs in Africa on the west coast, in the Sahara, Sudan, and the Victoria Nile division, where it is known as river blindness. In Central and South America, this disease is to be found in Guatemala, Brazil, Venezuela, and southern Mexico.

The presence of eosinophilia, skin lesions, and onchocerco- mas with ocular lesions is highly suggestive in endemic areas. Frequently, the microfilariae may be found in skin shavings or dermal lymph, even when

no nodules are detectable. The scapular area is the favorite site for procuring specimens for examination by means of a skin snip. This is performed in the field or office by lifting the skin with an inserted needle and then clipping off a small, superficial portion of the skin with a sharp knife or scissors. The specimen is laid in a drop of normal saline solution on a slide, covered with a coverslip, and examined under the microscope. The filariae wriggle out at the edges of the skin slice.

Specific serologic and PCR-based diagnostic tests from blood and skin biopsies are available. Other filarial parasites can be detected in similar systems. When patients suspected of having onchocerciasis were given a single oral dose of 50 mg of diethylcarbamazine, a reaction consisting of edema, itching, fever, arthralgias, and an exacerbation of pruritus was described as a positive Mazzotti test reaction, which supported the diagnosis of onchocerciasis. The reaction may be related to Wolbachia organisms within the worms.

Onchocercomas may be surgically excised whenever feasible. Ivermectin as a single oral dose of 150 g/kg is the drug of choice. Skin microfilaria counts remain low at the end of 6 months' observation. Ivermectin should be repeated every 6 months to suppress the dermal and ocular microfilarial counts. More frequent dosing does not appear to reduce microfilarial counts further.

Doxycycline kills the intracellular symbiotic bacteria, Wolbachia. It is being tested for long-term effects and determination of its place in the treatment of onchocerciasis and ban- croftian filariasis. If there is eye involvement, prednisone, 1 mg/kg, should be started several days before treatment with ivermectin. Moxidectin and emodepside also appear promising as alternative drugs. There are community-based treatment protocols that have the objective of eliminating onchocerciasis from endemic areas. Severe reactions may occur in patients simultaneously infected with Loa loa.

Trichinosis

Ingestion of Trichinella spiralis larva-containing cysts in inadequately cooked pork, bear, or walrus meat may cause trichinosis. It usually causes a puffy edema of the eyelids, redness of the conjunctivae, and sometimes urticaria or angioedema associated with hyperpyrexia, headache, erythema, gastrointestinal symptoms, muscle pains, and neurologic signs and symptoms. Ten percent of patients develop a bilateral, asymptomatic hand swelling that is especially prominent over the digits, and erythema along the perimeters of the palms and volar surfaces of the digits, which progresses to desquamation. In 20% of cases a nonspecific macular or petechial eruption occurs and splinter hemorrhages are occasionally present. Eosinophilia is not constant, but may be as high as 80%. In the average patient, eosinophilia begins about 1 week after infection and attains its height by the fourth week.

The immunofluorescence antibody test has the greatest value in establishing early diagnosis. The bentonite floccula- tion test, ELISA, and other serologic tests are limited by their inability to detect infection until the third or fourth week.

Diagnosis is confirmed by a muscle biopsy that demonstrates larvae of Trichinella spiralis in striated muscle. Unfortunately, trichinae cannot usually be demonstrated unless eosinophilic vasculitis and granulomas have been described on biopsy. A 2 mm-thick slice of the muscle biopsy may be compressed between two glass slides to demonstrate the cysts.

The condition is treated with albendazole, 400 mg twice a day for 14 days. Corticosteroidal agents are effective as a means of controlling the often severe symptoms and should be given at doses of 40-60 mg/day.

Pneumocystosis

Pneumocystis jirovecii (formerly carinii) has features characteristic of both protozoa and fungi. It is an opportunistic infection, occurring primarily as a pulmonary infection in AIDS patients. Extrapulmonary involvement is uncommon and usually occurs in the reticuloendothelial

system. Skin findings may occur. At least half of reported cases are of nodular growths in the auditory canal, with the remainder having nonspecific pink to skin-colored papules and nodules that may ulcerate. On biopsy, the dermis contains foamy material within which Giemsa-positive organisms are identified. Cutaneous botryomycosis caused by combined Staphylococcus aureus and Pneumocystis jirovecii has been reported in the setting of HIV infection. A 3-week course of trimethoprim-sulfamethoxazole combination is the treatment of choice. In combined infections, all pathogens require treatment.

PHYLUM ARTHROPODA

This phylum contains more species than all the other phyla put together. The following classes are of dermatologic significance: Myriapoda, Insecta, and Arachnida. Mosquitoes, flies, ticks, and fleas transmit diseases throughout the world. Bites and stings are always prevalent, but increase dramatically after natural disasters such as hurricanes and flooding.

Prevention of arthropod-related disease

Mosquitoes remain the most important vectors of arthropod- borne disease, and mosquito control programs are an essential component of the public health efforts of many states. Insect repellents are effective in preventing disease transmission and are especially important during travel to areas where vector-borne disease is endemic. Most are based on DEET (N,N-diethyl-3-methylbenzamide, previously called N,N- diethyl-m-toluamide). DEET has been tested against a wide range of arthropods, including mosquitoes, sandflies, ticks, and chiggers. The American Academy of Pediatrics recommends concentrations of 30% or less in products intended for use in children. As this represents a major market share for these products, many formulations that comply with the recommendation are available. Some evidence suggests that children do not have a higher incidence of adverse reactions when compared to adults, but even in adults there have been occasional reports of neurotoxicity. High concentrations of DEET can also produce erythema and irritation or

bullous eruptions. Extended-release products reduce the need for repeated application, and appear to minimize the risk of complications. Overall, DEET has a good safety record in widespread use. Picaridin (KBR 3023) is a piperidine-derived repellent ingredient that is also effective against a range of arthropods. In some studies, it has been shown to be less irritating than DEET while providing comparable efficacy. The best studies for the evaluation of repellents are field trials that involve a range of arthropods. Arm box studies are still performed, but must be interpreted with caution. In a well-designed arm box study, soybean oil (Bite Blocker for Kids) performed reasonably well, and was second only to DEET in efficacy. Citronella did not perform well, and citronella candles have little documented efficacy. In contrast, neem oil is an effective mosquito repellent that is used in many areas of the world that are endemic for malaria. Geraniol candles demonstrate some efficacy, but only in the area immediately surrounding the candles. Repellency drops significantly at a distance of even 2 m. Candles with geraniol are twice as effective as those with linalool and five times as effective as those with citronella. IR3535 (ethyl butyl acetyl aminopropionate) in a variety of formulations has also demonstrated good efficacy against mosquitoes. Complete protection times in field trials ranged from 7.1 to 10.3 hours.

Travelers to malaria-endemic areas should follow CDC guidelines for malaria prophylaxis. They should also avoid night-time outdoor exposure and use protective measures such as repellents and bed netting. The anopheline mosquitoes that carry malaria tend to bite at night, so bed nets and screens are important measures. Mosquitoes that carry dengue mostly bite during the day. Repellents play a greater role in protection against dengue, as it is more difficult to limit daytime outdoor activity. Mosquito control programs depend largely on drainage of stagnant water and spraying of breeding areas. In developing countries, water barrels may be stocked with fish or turtles to consume mosquito larvae. Both can soil the water and the relative risks must be evaluated. In some studies, the risk has clearly favored stocking the barrel. Mosquito traps, including the Mosquito Magnet, have been shown to be effective for the control of mosquitoes in limited areas. Generally, mosquitoes fly upwind to bite, and

downwind to return to their resting area. Mosquito traps must be positioned between the breeding and resting areas, and the area to be protected. Mosquito traps commonly use CO2, heat, and chemical attract- ants. Some Culex mosquitoes are repelled by octenol, and the manufacturer may provide guidelines for areas where the attractant should not be used.

Prevention of disease from ticks and chiggers

Tick-borne diseases include rickettsial fevers, ehrlichiosis, Lyme disease, babesiosis, relapsing fever, and tularemia. Most require a sustained tick attachment of more than 24 h for effective transmission, and frequent tick checks with prompt removal of ticks is an important strategy for the prevention of tick-borne illness. Unfortunately, tick inspections frequently fail to identify the tick in time for prompt removal. Some data suggest that adult ticks are found and removed only 60% of the time within 36 h of attachment. Nymphal ticks are even more difficult to detect, and may be removed in as few as 10% of patients within the first 24 h. Because of this, repellents and acaricides remain critical for preventing tick-borne illness. Permethrin has cidal activity against a wide range of arthropods. Some North African Hyalomma ticks are resistant to per- methrin, and may exhibit a paradoxical pheromone-like attachment response when exposed to the agent, but permeth- rin performs very well with other species of tick, as well as mosquitoes and chiggers. It can be used to treat clothing, sleeping bags, mosquito netting, and tents. Permethrin-treated clothing, used in conjunction with a repellent, provides exceptional protection against bites in most areas of the world. Permethrin has a good record of safety, although there is a report of congenital leukemia with 11q23/MLL rearrangement in a preterm female infant whose mother had abused permeth- rin because of a pathologic fear of spiders. Permethrin can induce cleavage of the MLL gene in cell culture, providing a plausible link between the agent and the leukemia. It should be emphasized that permethrin in this case was not used according to the manufacturer's instructions, and the theoretical risk of carcinogenicity should be weighed against the very real risk of death from

arthropod-borne disease. Cardiac gly- cosides have also been used topically as acaricides and have performed well in limited studies. Ixodes scapularis is the major North American vector for Lyme disease, human granulocytic ehrlichiosis, and human babesiosis. A Lyme vaccine was marketed in the US, but proved to be a commercial failure and was voluntarily withdrawn from the market. Prevention of Lyme disease now centers on prevention of tick attachments and on prompt tick removal. Back yards and recreational areas adjacent to wooded areas have higher rates of tick infestation. Tick numbers can be reduced by deer fencing, removal of leaf debris, application of an acaricide, and the creation of border beds with wood chip mulch or gravel. Bait boxes and deer feeding stations have been devised that are capable of delivering a topical acaricide while the animal feeds. Parasitic wasps control tick numbers in nature, but wasp populations may fluctuate, and investment in wasp control may be a risky venture compared with other forms of tick control. Other natural forms of tick control have been investigated, as they have the potential to become self-sustaining in the environment, at least for a period of time. Fungi and nematodes show some promise. In southern states, fire ants control tick populations by eating tick eggs.

Prevention of flea-borne illness

Fleas are important vectors of plague and endemic typhus. They may also be vectors of cat-scratch disease. Lufenuron is a maturation inhibitor that prevents fleas from breeding. It is commonly used in oral and injectable forms for the prevention of flea infestation in cats and dogs. Fipronil is used topically for the prevention of flea and tick infestation. Other agents in use include imidacloprid, selamectin, and nitenpyram. House sprays often include pyrethroids or pyriproxyfen. Powdered boric acid may be helpful for the treatment of infested carpets or floor boards. A knowledgeable veterinarian and an exterminator should be consulted.

Class Myriapoda

Morphologically and genetically, the class Myriapoda is distinct from other groups of arthropod. This group contains the centipedes and

millipedes. Both are capable of producing significant skin manifestations. Centipede bites (Chilopoda). Centipede bites are manifested by paired hemorrhagic marks that form a chevron shape caused by the large paired mouth- parts. The bite is surrounded by an erythematous swelling (Fig. 34) that may progress into a brawny edema or lymphangitis. Locally, there may be intense itching and pain, often associated with toxic constitutional symptoms. Most centipede bites run a benign self-limited course, and treatment is only supportive.

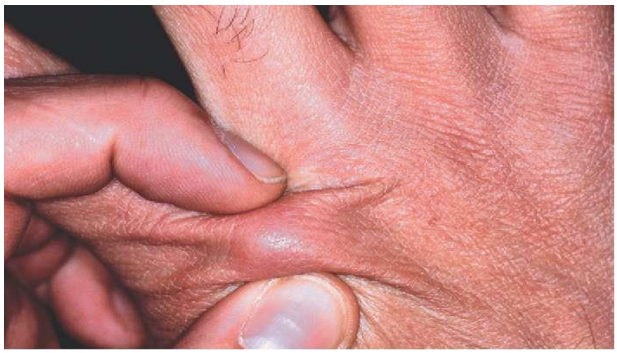

Fig. 34 Centipede bite.

Children are often bitten when they try to handle centipedes. As some species of Scolopendra in the western US will attain a length of 15-20 cm, the child may describe it as a snake. Recognition of the characteristic chevron shape is important to avoid inappropriate treatment with snake antivenin. In the eastern US, the common house centipede, Scutigera coleoptrata, does not bite humans. Scolopendra subspinipes, in Hawaii, inflicts a painful bite. As exotic species appear more commonly at pet stores and swap meets, envenomation by them will become more common.

In some tropical and subtropical areas, centipede bites account for about 17% of all envenomations (compared to the 45% caused by snakes and 20% by scorpions). Most bites occur at home and involve an upper extremity. Local pain and edema occur in up to 96% of patients, depending on the species involved. Treatment is largely symptomatic. Rest, ice, and elevation may be sufficient, but topical or intralesional anesthetics may be required in some cases. Tetanus immunization should be considered if the patient has not been immunized within the past 10 years.

Centipede bites can result in Wells syndrome, requiring topical or intralesional corticosteroids. Rarely, bites may produce more serious toxic responses, including rhabdomyolysis, myocardial ischemia, proteinuria, and acute renal failure. These have been reported following the bite of Scolopendra heros, the giant desert centipede. Although centipedes have sometimes been found in association with corpses, injuries from the centipede tend to be postmortem and are rarely the cause of death. Ingestion of centipedes by children is usually associated with transient, self-limited toxic manifestations.

Millipede burns (Diplopoda)

Some millipedes secrete a toxic liquid that causes a brownish pigmentation or burn when it comes into contact with skin. Burns may progress to intense erythema and vesiculation. Millipedes may be found in laundry hung out to dry, and millipede burns in children have been misinterpreted as signs of child abuse. Recognition of the characteristic curved shape of the burn can be helpful in preventing misdiagnosis. Some millipedes can squirt their venom and ocular burns are reported. Washing off the toxin as soon as possible will limit the toxic effects. Other treatment is largely symptomatic.

Diplopods (Fig. 35) have evolved a complex array of chemicals for self-defense. Some primates take advantage of these chemicals. Two millipede compounds, 2-methyl-1,4- benzoquinone and 2-methoxy-3-methyl-1,4-benzoquinone, demonstrate a repellent effect against Aedes aegypti mosquitoes. Tufted and white-faced capuchin monkeys anoint themselves with the secretions to ward off mosquitoes. Effective commercial repellents are available for human use and millipede juice is not recommended.

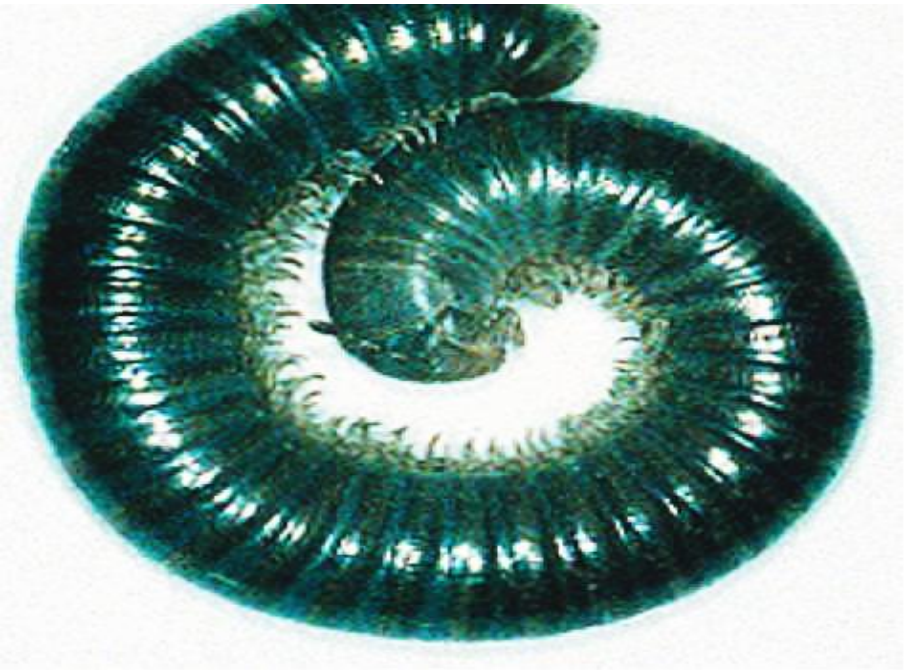

Fig. 35 Millipede.

Class Insecta Order Lepidoptera

Order Lepidoptera includes butterflies, moths, and their larval forms, caterpillars. Severe systemic reactions have occurred as the result of ingestion of some caterpillars, and with some species the sting alone can produce severe toxicity. Lonomia achelous, found in Latin America, can cause a fatal bleeding diathesis. The Spanish pine caterpillar, Thaumetopoea pityo- campa, causes both dermatitis and anaphylactoid symptoms. Pine caterpillars are also an important cause of systemic reactions in China and Israel. The tussock moth, Orgyia pseudo- tsugata, causes respiratory symptoms in forestry workers in Oregon.

Caterpillar dermatitis

Irritation is produced by contact of the hairs with the skin. Toxins in the hairs can produce severe pain, local pruritic erythematous macules, and wheals, depending on the species. If the hairs get into the clothing, widespread persistent dermatitis may result. Not only the caterpillars, but also their egg covers and cocoons commonly contain stinging hairs. In the US the most common caterpillars of medical importance are the brown-tail moth caterpillar (Nygmia phoeorrhoea), puss caterpillar (Megalopyge opercularis) (Figs 36 and 37), saddleback caterpillar (Sibine stimulae)

(Fig. 38), io moth caterpillar (Automeris io), crinkled flannel moth caterpillar (Megalopyge crispata), Oklahoma puss caterpillar (Lagoa crispata), Douglas fir tussock moth caterpillar (Orgyia pseudo- tsugata), buck moth caterpillar (Hemileuca maia), and flannel moth caterpillar (Norape cretata).

Fig. 36 Puss caterpillar

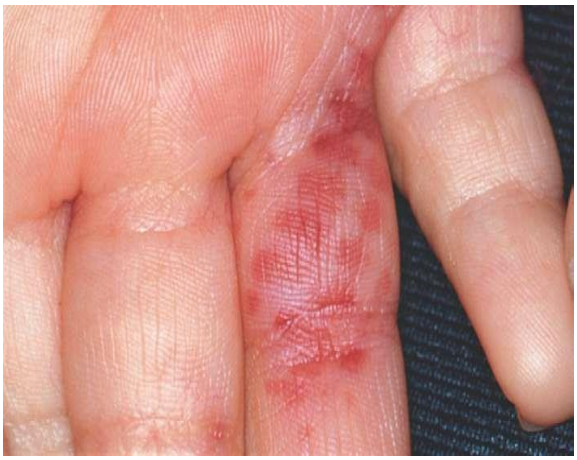

Fig. 37 Characteristic railroad track purpura of a puss caterpillar sting.

The hairs of the European processionary caterpillar (Thaumetopoea processionea) are especially dangerous to the eyes, but ophthalmia nodosa (a papular reaction to embedded hairs) can be seen with a wide variety of caterpillars and moths. Airborne procession- ary caterpillar hairs have caused large epidemics of caterpillar dermatitis.

Moth dermatitis

Moth dermatitis may be initiated by the hairs of the brown-tail moth (Euproctis chrysorrhoea), goat moth (Cossus cossus), puss moth (Dicranura vinula), gypsy moth (Lymantria dispar), and Douglas fir tussock moth (Hemenocampa pseudotsugata). In Latin America, the moths of the genus Hylesia are most frequently the cause of moth dermatitis. Severe conjunctivitis and pruritus are the first signs, and may persist for weeks aboard ships that have docked in ports where the moth is common. Caripito itch is named after Caripito, Venezuela, a port city where the moth is found. Korean yellow moth dermatitis is caused by Euproctis flava Bremer.

Topical applications of various analgesics, antibiotics, and oral antihistaminics are of little help. Topical or oral cortico- steroids are sometimes helpful, as is scrubbing and tape stripping of skin. Contaminated clothing may need to be discarded if dermatitis persists after the clothing is washed.

Order Hemiptera

The true bugs belong to the order Hemiptera. The order includes bedbugs, water bugs, chinch bugs, stink bugs, squash bugs, and reduviid bugs (kissing bugs, assassin bugs). The latter are vectors of South American trypanosomiasis. In most true bugs, the wings are half sclerotic and half membranous, and typically overlap. In bedbugs, the wings are vestigial.

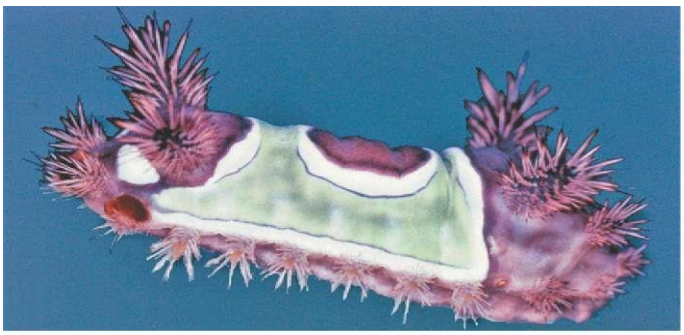

Fig. 38 Saddleback caterpillar.

Fig. 39 Bedbug.

Cimicosis (bedbug bites)

Bedbugs have flat oval bodies and retroverted mouthparts used for taking blood meals (Fig. 38). Cimex lectularius is the most common species in temperate climates, and Cimex hemipterus in tropical climates. Both are reddish brown and about the size of a tick. C. hemipterus is somewhat longer than C. lectularius. They breed through a process referred to as traumatic insemination, where the male punctures the female and deposits sperm into her body cavity. Bedbugs hide in cracks and crevices, then descend to feed while the victim sleeps. It is common for bedbugs to inflict a series of bites in a row ("breakfast, lunch, and dinner").

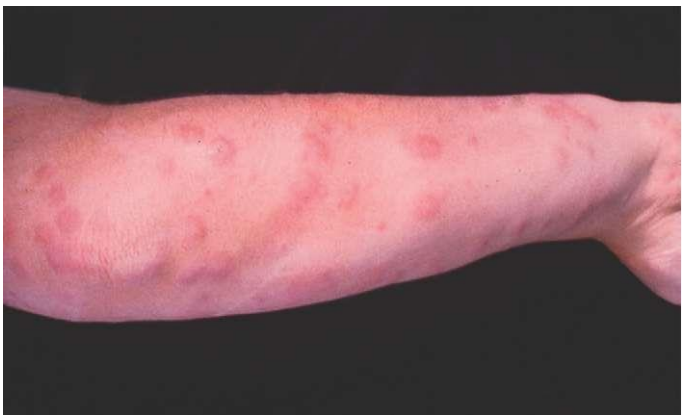

Fig. 40 Bedbug bites.

Bites may mimic urticaria, and patients with papular urticaria commonly have antibodies to bedbug antigens. Bullous and urticarial reactions occur (Fig. 40). The incidence is rising in the US, and in some refugee camps, almost 90% of residents suffer from bedbug bites. Bedbugs are suspected vectors for Chagas' disease and hepatitis B, although data are sparse.

Bedbugs often infest bats and birds, and these hosts may be responsible for infestation in houses. Management of the infestation may require elimination of bird nests and bat roosts. Cracks and crevices should be eliminated, and the area treated with an insecticide such as dichlorvos or permethrin. As most insecticides have poor residual effect on mud bricks, wood, and fabric, frequent retreatment may be necessary. Microencapsulation of insecticides enhances persistence. Permethrin-impregnated bednets have been shown to be effective against bedbugs in tropical climates.

Reduviid bites.

Triatome reduviid bugs (kissing bugs, assassin bugs, conenose bugs) descend on their victims while they sleep, and feed on an exposed area of skin. The bite is typically painless, although the bugs are capable of producing a more painful defensive bite. Swelling and itching occur within hours of the bite (Fig. 41).

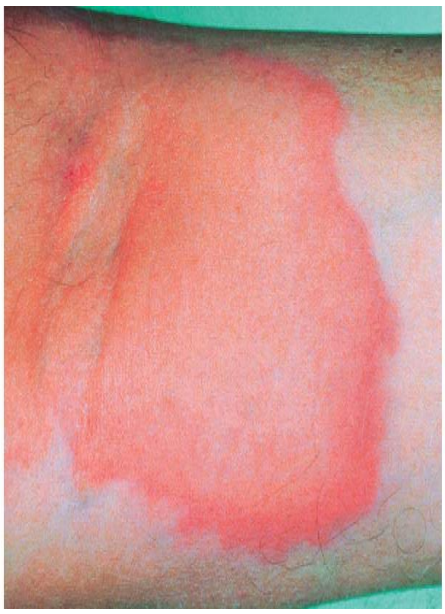

Fig. 41 Triatome bite **Fig. 42 Crab louse**

Many Latin American species have a pronounced gastrocolic reflex and defecate when they feed. Romana's sign is unilateral eye swelling after a night-time encounter with a triatome bug. Trypanosoma cruzi is transmitted by the feces and rubbed into the bite. American trypanosomiasis can produce heart failure and megacolon. Triatome bugs infest thatch, cracks, and crevices, and infestation is associated with poor housing conditions. In nonendemic areas, bites are sporadic, and are often followed by a red swelling suggestive of celluli- tis. Anaphylaxis has also occurred. Arilus cristatus, the wheal bug, is widely distributed and has an extremely painful defensive bite but it is not known to carry disease.

ORDER ANOPLURA

Pediculosis

Three varieties of these flattened, wingless insects infest humans: Pediculus humanus var. capitis (the head louse), P. humanus var. corporis (the body louse), and Phthirus pubis (the pubic or crab louse) (Fig. 42). Rarely, zoonotic lice or louse-like psocids will cause infestation.

Pediculosis capitis

Pediculosis capitis is more common in children, but occurs in adults also. Patients present with intense pruritus of the scalp, and often have

posterior cervical lymphadenopathy. Excoriations and small specks of louse dung are noted on the scalp, and secondary impetigo is common. Lice may be identified, especially when combing the hair. Nits may be present throughout the scalp, but are most common in the retroauricu- lar region. Generally, only those ova close to the scalp are viable, and nits noted along the distal hair shaft are empty egg cases. In very humid climates, however, viable ova may be present along the entire length of the hair shaft. Peripilar keratin (hair) casts are remnants of the inner root sheath that encircle hair shafts. They may be mistaken for nits. While nits are firmly cemented to the hair, casts move freely along the hair shaft. Headlice readily survive immersion in water, but remain fixed to scalp hairs. There is no evidence that swimming pools contribute to the spread of head lice. Effective therapeutic agents must kill or remove both lice and ova. Ulesfia (containing benzyl alcohol) is the first non- neurotoxic FDA-approved treatment for lice and represents a significant advancement. Permethrin is the most widely used pediculicide in the US. It is available as an over-the-counter 1% cream rinse (Nix) and a 5% prescription cream (Elimite) that is marketed for the treatment of scabies. The 1% cream rinse must be applied after shampooing and drying the hair completely. Applying to dry hair lessens dilution of the medication. Product labeling states the medication should be applied for 10 min, then rinsed off, but longer applications may be required. Shampooing should not take place for 24 h afterward. Permethrin has a favorable safety profile, although congenital leukemia has been reported, as noted above, and the use of insecticidal shampoos is statistically associated with leukemia. Other reported side effects have included acute onset of stuttering in a toddler. Pyrethrins, combined with piperonyl butoxide (RID, A-200, R+C shampoo), are sold over the counter. Malathion 0.5% lotion (Ovide) is marketed as a prescription product in the US. The efficacy is partly dependent upon the vehicle, and the product is flammable and can be irritating to the eyes. As it has not been widely used in the US, resistance has not emerged. Lindane is also marketed as a prescription product. The efficacy is somewhat lower, and the product has potential neurotoxicity if abused and is not available in all areas. Carbaryl

is used in many parts of the world, but not in the US. Because of the potential toxicity associated with chemical pediculicides, the future belongs to asphyxiating agents such as those that contain benzyl alcohol or dimeticone. Cure rates with dimeticone are significantly higher than those with permethrin in some studies. Other agents that asphyxiate or desiccate contain isopropyl myristate 50%.

Nit combing is an important adjunct to treatment, but is impractical as a primary method of therapy. Metal combs are more effective than plastic combs. Acidic cream rinses make the hair easier to comb but do not dissolve nit cement, which is similar in composition to amyloid. Various "natural" remedies are marketed that contain coconut oil, anise oil, and ylang ylang oil, but these agents are potential contact allergens, and there are few data regarding their safety and efficacy. Some data support the efficacy of tea tree oil, which is more potent than lavender or lemon oil. Some published data also support combination lotions containing 5% lavender, peppermint, and eucalyptus oils, or 10% eucalyptus and peppermint oils in various combinations of water and alcohol. The addition of 10% 1-dodecanol improves efficacy.

Aliphatic alcohols show promise as pediculicides, and crotamiton (Eurax), an antiscabietic agent, has some efficacy in the treatment of pediculosis. As no treatment is reliably ovicidal, retreatment in a week is reasonable for all patients. Resistance to pediculicides is an emerging problem in many parts of the world. The emergence of resistance to an agent is related to the frequency with which that agent is used. Knockdown resistance (KDR) is a common mechanism of resistance that manifests as lack of immobilization of the lice. Responsible gene mutations (T929I and L932F) have been identified and can be used to screen for KDR. In countries like the US, where permethrin is used commonly, permethrin- resistant lice have emerged. Cross-resistance among pyre- throids is typical. In the UK, resistance to malathion has been reported and multidrug-resistant lice have been identified. KDR results in slower killing of lice, but may be overcome to some degree by longer applications. Monooxygenase-based resistance to pyrethrins may be

overcome by synergism with piperonyl butoxide. Sequential use of pediculicides may be useful in overcoming resistance, and systemic agents may play some role. Trimethoprim-sulfamethoxazole has been used as an off-label oral agent, although more recent data suggest it is ineffective. Shaving the head will cure head lice, but has poor patient acceptance in most cultures. Simple public health measures are also of value when epidemics of louse infestation occur in schools. Hats, scarves, and jackets should be stored separately under each child's desk. Louse education and inspections by the school nurse facilitate targeted treatment of infested individuals.

Pediculosis corporis

Pediculosis corporis (pediculosis vestimenti, "vagabond's disease") is caused by body lice that lay their eggs in the seams of clothing (Fig. 43). The parasite obtains its nourishment by descending to the skin and taking a blood meal. Generalized itching is accompanied by erythematous, blue and copper- colored macules, wheals, and lichenification. Secondary impetigo and furunculosis are common.

Body louse infestation is differentiated from scabies by the lack of involvement of the hands and feet, although infestation by both lice and scabies is common, and a given patient may suffer from lice, scabies, and flea infestation.

Lice may live in clothing for 1 month without a blood meal. If discarding the clothing is feasible, this is best. Destruction of body lice can also be accomplished by laundering the cloth ing and bedding. Clothing placed in a dryer for 30 min at 65°C (149°F) is reliably disinfected. Pressing clothing with an iron, especially the seams, is also effective. Permethrin spray or 1% malathion powder can be used to treat clothing and reduce the risk of reinfestation. Body lice are vectors for relapsing fever, trench fever, and epidemic typhus. These diseases are most prevalent among refugee populations.

Fig. 43 Body lice in seams of clothing.

The trench fever organism is also an important cause of endocarditis among the homeless.

Pediculosis pubis (crabs)

Phthirus pubis, the crab louse, is found in the pubic region, as well as hairy areas of the legs, abdomen, chest, axillae, and arms. Pubic lice may also infest the eyelashes and scalp. The lice spread through close physical contact, and are commonly transmitted sexually. A diagnosis of pediculosis pubis should initiate a search for other STDs, including HIV. Contaminated bedding is also a source of infestation. Pubic louse nits are attached to the hairs at an acute angle. Other than the presence of lice and nits in the hair, the signs and symptoms are similar to those of body louse infestation.

Occasionally, blue or slate-colored macules occur in association with pediculosis pubis. These macules, called maculae ceruleae, are located chiefly on the sides of the trunk and on the inner aspects of the thighs. They are probably caused by altered blood pigments.

Treatment of pediculosis pubis is similar to that for head lice. The affected person's sexual contacts should be treated simultaneously. For eyelash involvement, a thick coating of petrolatum can be applied twice daily for 8 days, followed by mechanical removal of any remaining nits. Fluorescein and 4% pilocarpine gel are also effective. Clothing and fomites should be washed and dried by machine, or laundered and ironed.

Order Diptera

Order Diptera includes the two-winged biting flies and mosquitoes. Adult dipterids bite and spread disease, while larvae parasitize humans in the form of myiasis. Medically important families of flies include the Tabanidae (horsefly, deerfly, gadfly), which inflict extremely painful bites, and the Muscidae (housefly, stablefly, and tsetse fly). Tsetse fly bites transmit African trypanosomiasis. Simulidae include the black fly (buffalo gnat, turkey gnat), the vector of onchocerciasis. These flies are dark-colored and "hunchbacked." They may produce extremely painful bites that may be associated with fever, chills, and lymphadenitis. Black flies are seasonal annoyances in the northern US and Canada.

Psychodidae sandflies (Diptera: Phlebotominae) are small, hairy-winged flies that transmit leishmaniasis, sandfly fever, and verruga peruana. Sandfly fever viruses are a problem in Africa, the Mediterranean basin, and Central Asia, and are carried by Phlebotomus flies. Lutzomyia flies are common in Latin America and south Texas.

Culicidae, or mosquitoes, are vectors of many important diseases, such as filariasis, malaria, dengue, and yellow fever. Their bites may cause severe urticarial reactions. Ceratopogonidae, the biting midges or gnats, fly in swarms and produce erythematous, edematous lesions at the site of their bite.

Mosquito bites

Moisture, warmth, CO2, estrogens, and lactic acid in sweat attract mosquitoes. Drinking alcohol also stimulates mosquito attraction. Mosquito bites are a common cause of papular urticaria. More severe local reactions are seen in young children, individuals with immunodeficiency, and those with new exposure to indigenous mosquitoes.

Both necrotizing fasciitis and the hemophagocytic syndrome have been reported following mosquito bites, and exaggerated hypersensitivity reactions to mosquito bites are noted in a wide variety of Epstein-Barr

virus (EBV)-associated lymphoproliferative disorders, especially natural killer (NK) cell proliferations. Mosquito bites may play a key role in reactivation of latent EBV infection. Effective repellents are mostly DEET- or picaridinbased. Effective mosquito traps are available, but electronic mosquito repellents appear to be of no value.

Ked itch

The sheep ked (Melophagus ovinus) feeds by thrusting its sharp mouth parts into the skin and sucking blood. Occasionally, it attacks woolsorters and sheepherders, causing pruritic, often hemorrhagic papules, nearly always with a central punctum. Deer keds attack humans in a similar way. The papules are very persistent and may last for up to 12 months. Favorite locations are the hips and the abdomen.

Myiasis

Myiasis is the infestation of human tissue by fly larvae. Forms of infestation include wound myiasis, furuncular myiasis, plaque myiasis, creeping dermal myiasis, and body cavity myiasis. Wound myiasis occurs when flies lay their eggs in an open wound. Furuncular myiasis often involves a mosquito vector that carries the fly egg. Plaque myiasis typically involves many maggots and occurs after flies lay their eggs on clothing. Creeping myiasis develops when the larvae of the Gasterophilus fly wander intradermally. The most common species are Gasterophilus nasalis and Gasterophilus intestinalis. An itching pink papule develops, followed by a tortuous line that extends by 1-30 cm a day. Body cavity myiasis may involve the orbit, nasal cavity, gastrointestinal tract, or urogenital system.

The human botfly, Dermatobia hominis, is a common cause of furuncular myiasis (Fig. 44) in the neotropical regions of the New World.

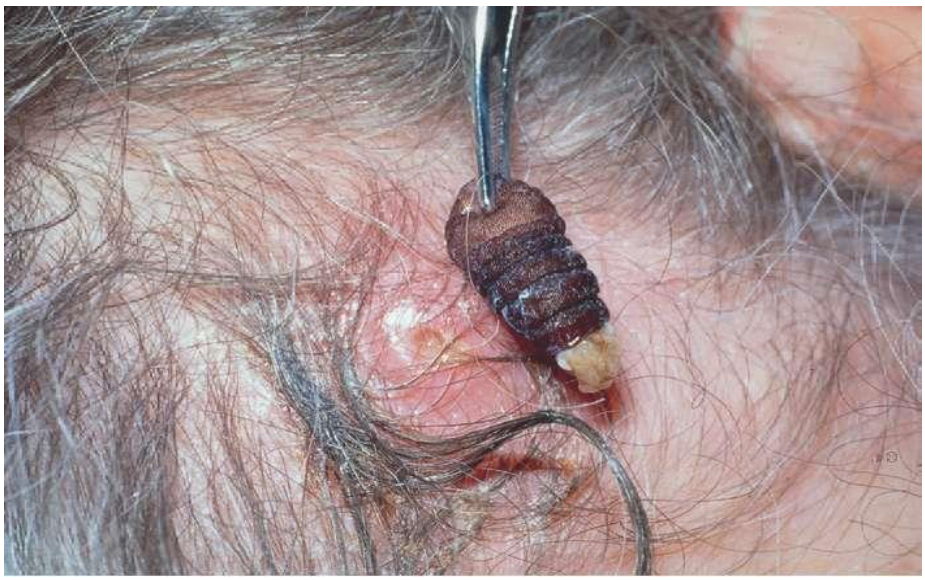

Fig. 44 Myiasis.

The female glues its eggs to the body of a mosquito, stablefly, or tick. When the unwitting vector punctures the skin by biting, the larva emerges from the egg and enters the skin through the puncture wound. Over a period of several days, a painful furuncle develops in which the larva is present. Other larvae that frequently cause furuncular lesions in North America are the common cattle grub (Hypoderma lineatum), rabbit botfly (Cuterebra cuniculi), and Wohlfahrtia vigil. This last fly can penetrate infant skin, but not adult skin. Thus, nearly all reported cases have occurred in infants. The New World screw worm, Cochliomyia hominivorax, often involves the head and neck region. Larvae of Calliphoridae flies, especially Phaenicia sericata, the green blowfly, cause wound myiasis. Other blowflies, flesh flies (Sarcophagidae), and humpbacked flies (Phoridae) are less common causes of wound myiasis. In tropical Africa the Tumbu fly (Cordylobia anthropophaga) deposits her eggs on the ground or on clothing. The young maggots penetrate the skin and often form a plaque with many furuncular-appearing lesions. Cordylobia ruandae and Cordylobia rodhaini are less frequent causes of plaque myiasis.

Removal of the maggots of furuncular myiasis can be accomplished by injection of a local anesthetic into the skin, which causes the larva to bulge outward. The opening of the furuncle can also be occluded with hair

gel, surgical lubricant, lard, petrolatum, or bacon, causing the larva to migrate outward Successful treatment with ivermectin has also been reported.

ORDER COLEOPTERA

Blister beetle dermatitis

Blister beetle (Fig. 45) dermatitis occurs after contact with several groups of beetle. The Meloidae and Oedemeridae families produce injury to the skin by releasing a vesicating agent, cantharidin. Members of the family Staphylinidae (genus Paederus) contain a different vesicant, pederin. None of the beetles bites or stings; rather, they exude their blistering fluid if they are brushed against, pressed, or crushed on the skin. Many blister beetles are attracted at night by fluorescent lighting.

Slight burning and tingling of the skin occur within minutes, followed by the formation of bullae, often arranged in a linear fashion. "Kissing lesions" are observed when the blister beetle's excretion is deposited in the flexures of the elbows or other folds. Ingestion of beetles or cantharidin results in poisoning, presenting with hematuria and abdominal pain. In many tropical and subtropical habitats, rove beetles (genus Paederus) produce a patchy or linear erythematous vesicular eruption (Fig. 46). In parts of South America, it is known as podo. It occurs frequently during the rainy season and appears predominantly on the neck and exposed parts.

Fig. 45. Blister beetle.

Lymphadenopathy and fever are common. In the American southwest, outbreaks of rove beetle dermatitis have followed unusually rainy periods. In southeastern Australia, corneal erosions are caused by small Corylophidae beetles. Treatment consists of drainage of the bullae and application of cold wet compresses and topical antibiotic preparations. Early cleansing with acetone, ether, soap, or alcohol may be helpful to remove cantharidin.

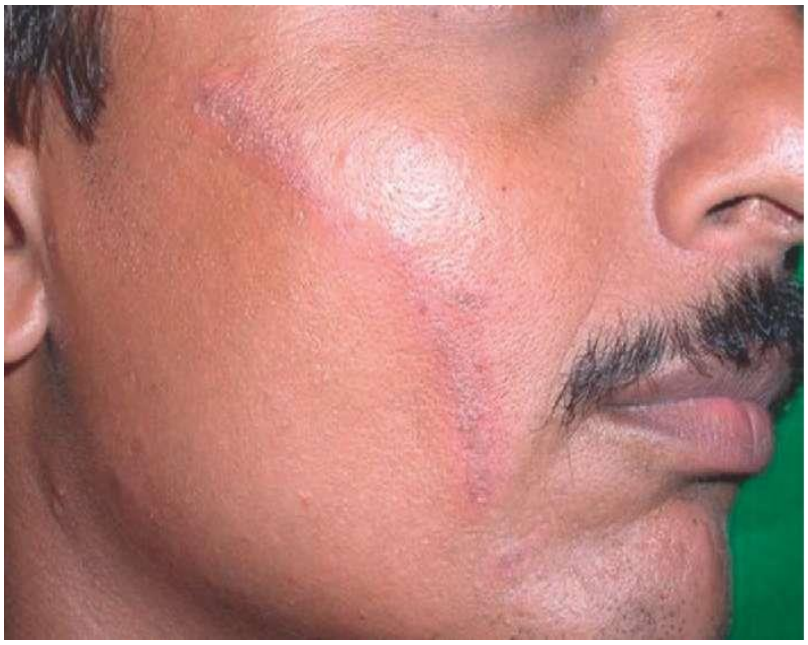

Fig. 46 Paederus dermatitis.

Other beetles

Papulovesicular and urticarial dermatitis is caused by the common carpet beetle (Dermestidae: Anthrenus scrophulariae). The eruption involves the chest, neck, and forearms. The larvae inhabit warm houses throughout the winter months. They are reddish brown, fusiform, about 6 mm long, and covered by hairs. A generalized pruritic eruption has been attributed to the larvae of the carpet beetle, Anthrenus verbasci. Bombardier beetles of the family Carabidae (subfamily Brachininae) can cause skin burns with a deep yellow-brown color. Chemicals released when these beetles are crushed include acids, phenols, hydrocarbons, and quinines. When the beetle is threatened, chemical reactions produce an explosive spray of boiling hot benzoquinones from the tip of the abdomen. Dermestidae (skin beetles) and Cleridae (bone beetles) infest exposed human remains and are useful in estimating the postmortem interval. Rare cases of allergic angioedema have been reported after exposure to ladybugs.

Order Hymenoptera

Hymenopterids include bees, wasps, hornets, and ants. Stings by any of these may manifest the characteristic clinical and histologic features of eosinophilic cellulitis (Wells syndrome), complete with flame figures.

Bees and wasps

Yellowjackets are the principal cause of allergic reaction to insect stings, because they nest in the ground or in walls and are disturbed by outdoor activity, such as gardening or lawn mowing. Bees are generally docile and sting only when provoked, although Africanized bees display aggressive behavior. The allergens in vespid venom are phospholipase, hyaluronidase, and a protein known as antigen 5. Bee venom contains histamine, mellitin, hyaluronidase, a high molecular weight substance with acid phosphatase activity, and phos- pholipase A. The barbed ovipositor of the honeybee is torn out of the bee and remains in the skin after stinging. The bumble bee, wasp, and hornet are able to withdraw their stinger.

The reaction to these stings ranges from pain and mild local edema to exaggerated reactions that may last for days. Serum sickness, characterized by fever, urticaria, and joint pain, may occur 7-10 days after the sting. Severe anaphylactic shock and death may occur within minutes of the sting. Most hypersen- sitivity reactions have been shown to be mediated by specific IgE antibodies. Anaphylaxis to vespids may also be the presenting symptom of mastocytosis, with no demonstrable specific IgE against wasp venom. Granuloma annulare and subcutaneous granulomatous reactions have been reported. Contact allergy to propolis is common among beekeepers.

Treatment of local reactions consists of immediate application of ice packs or topical anesthetics. Chronic reaction sites may be injected with triamcinolone suspension diluted to 5 mg/mL with 2% lidocaine. Oral prednisone may be required for severe local reactions.

For severe systemic reactions, 0.3 mL of epinephrine (1:1000 aqueous solution) is injected intramuscularly. This may need to be repeated after 10 min. Susceptible persons should carry a source of injectable epinephrine. Corticosteroids and epi- nephrine may be required for several days following severe reactions. Hyposensitization by means of venom immunotherapy can reduce the risk of anaphylaxis in people at risk. Those at risk should be evaluated by an allergist. Rush desen- sitization regimens exist and ultra-rush sublingual immuno- therapy looks promising.

Ants

The sting of most ants is painful, but that of the fire ants (Solenopsis invicta, Solenopsis geminata, or Solenopsis richteri) is especially painful. Fire ants are vicious and will produce many burning, painful stings within seconds if their mound is disturbed. The sting causes intense pain and whealing. Later, an intensely pruritic sterile pustule develops at the site. Anaphylaxis, seizures, and mononeuropathy have been reported. The sting of harvester ants and soldier ants may produce similar reactions. Treatment options are similar to those for vespid stings.

Order Siphonaptera

Fleas are wingless, with highly developed legs for jumping. They are blood-sucking parasites, infesting most warmblooded animals. Fleas are important vectors of plague, endemic typhus, brucellosis, melioidosis, and erysipeloid.

Pulicosis (flea bites).

The species of flea that most commonly attack humans are the cat flea (Ctenocephalides felis), human flea (Pulex irritans), dog flea (Ctenocephalides canis), and oriental rat flea (Xenopsylla cheopis) (Fig. 47). The stick-tight flea (Echidnophaga gallinacea), mouse flea (Leptopsylla segnis), and chicken flea (Ceratophyllus gallinae) are sometimes implicated.

Fleas are small, brown insects about 2.5 mm long, flat from side to side, with long hind legs. They slip into clothing or jump actively when disturbed. They bite about the legs and waist and may be troublesome in houses where there are dogs or cats. The lesions are often grouped and may be arranged in zigzag lines. Hypersensitivity reactions may appear as papular urticaria, nodules, or bullae. Camphor and menthol preparations, topical corticosteroids, and topical anesthetics can be of benefit.

Fig. 47 Cat flea.

Vectors of disease

Xenopsylla cheopis and Xenopsylla braziliensis are vectors of plague and endemic typhus. The cat flea (Ctenocephalides felis) is the vector for Rickettsia felis (a cause of endemic typhus). Plague and tularemia are transmitted by the squirrel flea, Diamanus montanus. Several species of flea are intermediate hosts of the dog tapeworm and rat tapeworm, which may be an incidental parasite of humans.

Tungiasis

Tunga penetrans is also known as nigua, the chigoe, sand flea, or jigger. It is a reddish-brown flea about 1 mm long. It resides in the Caribbean, equatorial Africa, Central and South America, India, and Pakistan. It was first reported in crewmen who sailed with Christopher Columbus.

The impregnated female chigoe burrows into the skin, often adjacent to a toenail, where she may be seen with the aid of dermoscopy. The eggs develop and drop to the ground. These eggs develop into larvae, which form cocoons from which the insects emerge in about 10 days. Skin lesions are pruritic swellings the size of a small pea. These may occur on the ankles, feet, and soles, as well as the anogenital areas. The lesions become extremely painful and secondarily infected. Wearing open shoes and the presence of pigs in the area are risk factors for disease.

Curettage or excision of the burrows is recommended. Topical ivermectin, metrifonate, or thiabendazole can be used, and oral thiabendazole, 25 mg/kg/day, has been effective in heavily infested patients. Antibiotics should be used for the secondary infection and tetanus prophylaxis should be given. These lesions can be prevented by the wearing of shoes. Infested ground and buildings may be disinfected by the use of insecticides and growth inhibitors.

Order Acarina

Several varieties of the family Ixodidae (hard ticks) and Argasidae (soft ticks) will attack human skin, but only hard ticks remain attached. In

the US, Ornithodoros hermsi, Ornithodoros turicata, and Ornithodoros parkeri transmit tick- borne relapsing fever. The wood tick (Dermacentor andersoni) is an important disease vector in western states. It carries Rocky Mountain spotted fever, tularemia, ehrlichiosis, and Colorado tick fever. The dog tick (Dermacentor variabilis) is prevalent in the eastern states, and is the most common vector of Rocky Mountain spotted fever. It also carries tularemia. Dermacentor marginatus transmits tick-borne lymphadenopathy in Spain. The brown dog tick (Rhipicephalus sanguineus) is a vector of Rocky Mountain spotted fever, tularemia, and boutonneuse fever. The lone star tick (Amblyomma americanum) carries Rocky Mountain spotted fever, tularemia, and human monocytic ehrlichiosis. Ixodes ricinus in Europe and Ixodes scapularis and Ixodes pacificus in the US transmit Borrelia burgdorferi, the cause of Lyme disease. Ixodes ticks also transmit human granulocytic ehrlich- iosis and babesiosis. The risk of disease transmission increases with the duration of tick attachment. Unfortunately, ticks commonly attach in areas where they are not noticed, allowing them to engorge and transmit disease.

The female hard tick attaches itself to the skin by sticking its proboscis into the flesh to suck blood from the superficial vessels. The insertion of the hypostome is generally unnoticed by the subject. The attached tick may be mistaken by the patient for a new mole. The parasite slowly becomes engorged and then falls off. During this time, which may last for 7-12 days, the patient may suffer from fever, chills, headache, abdominal pain, and vomiting. This is called tick bite pyrexia. Removal of the engorged tick causes a subsidence of the general symptoms in 12-36 h.

The bites may be followed by small, severely pruritic, fibrous nodules (tick bite granulomas) that persist for months, or by pruritic circinate and arciform localized erythemas that may continue for months. Tick bite-induced alopecia has been reported.

Histologically, bite reactions demonstrate wedge-shaped necrosis with a neutrophilic infiltrate and vascular thrombosis or hemorrhage. Chronic bite reactions often have atypical CD30+ lymphocytes and eosinophils. Pseudolymphomas and immunocytomas may occur.

Tick paralysis

Tick paralysis most commonly affects children, and carries a mortality rate of about 10%. Flaccid paralysis begins in the legs, then the arms, and finally the neck, resembling Landry- Guillain-Barre syndrome. Bulbar paralysis, dysarthria, dys- phagia, and death from respiratory failure may occur. Prompt recovery occurs if the tick is found and removed before the terminal stage. Dermacentor ticks in North America and Ixodes ticks in Australia are the most important causes of tick paralysis. As Dermacentor ticks commonly attach to the scalp, they may go unnoticed.

SCABIES

Sarcoptes scabiei, the itch mite, is an oval, ventrally flattened mite with dorsal spines. The fertilized female burrows into the stratum corneum and deposits her eggs. Scabies is characterized by pruritic papular lesions, excoriations, and burrows. Sites of predilection include the finger webs (Fig. 48), wrists, axillae (Fig. 49), areolae, umbilicus, lower abdomen, genitals, and buttocks. An imaginary circle intersecting the main sites of involvement-axillae, elbow flexures, wrists and hands, and crotch-has long been called the circle of Hebra. In adults, the scalp and face are usually spared, but in infants lesions are commonly present over the entire cutaneous surface. The burrows appear as slightly elevated, grayish, tortuous lines in the skin. A vesicle or pustule containing the mite may be

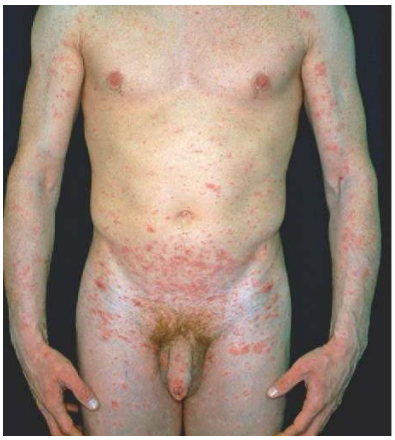

Fig. 48 Scabies.

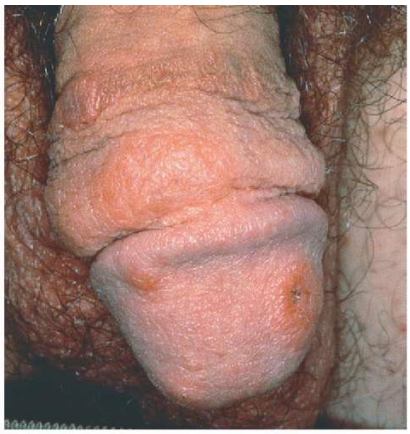

Fig. 49 Scabies mite, ova, and feces.

noted at the end of the burrow, especially in infants and children. To identify burrows quickly, a drop of India ink or gentian violet can be applied to the infested area, then removed with alcohol. Thin threadlike burrows retain the ink.

The eruption varies considerably, depending on the length of infestation, previous sensitization, and previous treatment. It also varies with climate and the host's immunologic status. Lichenification, impetigo, and furunculosis may be present. Bullous lesions may contain many eosinophils, resembling bullous pemphigoid. Positive immunofluorescent findings may also be noted. Scabies may also resemble Langerhans cell histiocytosis clinically and histologically. Misdiagnosis has led to systemic treatment with toxic agents.

Dull red nodules may appear during active scabies; these are 3-5 mm in diameter, may or may not itch, and persist on the scrotum penis, and vulva. Intralesional steroids, tar, or excision are methods of treatment for this troublesome condition, termed nodular scabies. Histologically, the lesions may suggest lymphoma.

Crusted scabies (Norwegian or hyperkeratotic scabies) is found in immunocompromised or debilitated patients, including those with neurologic disorders, Down syndrome, organ transplants, graft versus host disease, adult T-cell leukemia, Hansen's disease, or AIDS. In these patients, the infestation assumes a heavily scaling and crusted appearance. Crusts and scales teem with mites, and there is involvement of the face and especially the scalp. Itching may be slight. Psoriasis-like scaling is noted around and under the nails. The tips of the fingers are swollen and crusted; the nails are distorted. Severe fissuring and scaling of the genitalia and buttocks may be present. Pressure-bearing areas are the sites of predilection for the heavy keratotic lesions, in which the mites may abound.

Scabies is usually contracted by close personal contact, although it may also be transmitted by contaminated linens and clothing. Screening for other STDs is appropriate. Sensitization begins about 2-4 weeks after

onset of infection. During this time the parasites may be on the skin and may burrow into it without causing pruritus or discomfort. Severe itching begins with sensitization of the host. In reinfections, itching begins within days and the reaction may be clinically more intense. The itching is most intense at night, whereas during the daytime the pruritus is tolerable but persistent. The eruption does not involve the face or scalp in adults. In women, itching of the nipples associated with a generalized pruritic papular eruption is characteristic; in men, itchy papules on the scrotum and penis are equally typical. When more than one member of the family has pruritus, suspicion of scabies should be aroused. Whenever possible, though, it is advisable to identify the mite, as a diagnosis of scabies usually requires treatment of close physical contacts in addition to the patient. Because scabies cannot always be excluded by examination, treatment on presumption of scabies is sometimes necessary.

Positive diagnosis is made only by the demonstration of the mite under the microscope (Fig. 50). A burrow is sought and the position of the mite is determined. A surgical blade or sterile needle is used to remove the parasite. A drop of mineral or immersion oil can be placed on a lesion and gently scraped away with the epidermis beneath it. The majority of mites are found on the hands and wrists, less frequently (in decreasing order) at the elbows, genitalia, have often gathered mites and ova under the nails when scratching. A blunt curette can be used to gather material from under the nails for examination. Non-invasive techniques include dermoscopy and digital photography.

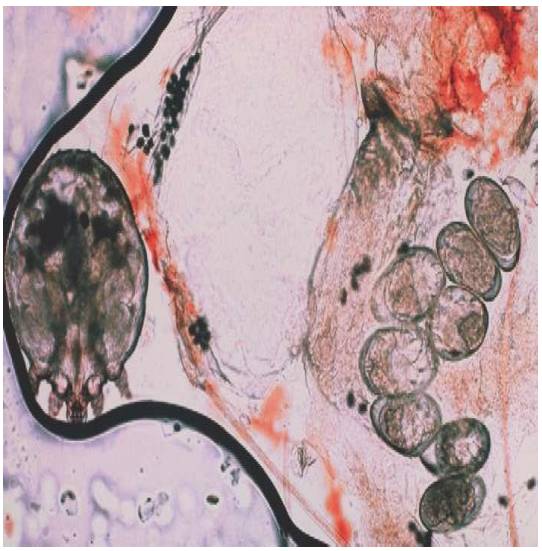

Fig. 50 Scabies mite, ova, and feces.

Permethrin 5% cream (Elimite) is the most widely used and most effective medication for scabies. It is a synthetic pyrethroid that is lethal to mites and has low toxicity for humans, although some concern has been raised about the association between topical insecticides and lymphoma.

Lindane (y-benzene hexachloride) is also effective, with a low incidence of adverse effects when used properly. Because of the availability of less toxic agents, lindane is rarely used as a first-line agent. In much of the world, benzyl benzoate and 10% precipitated sulfur in white petrolatum are used to treat scabies. The scabicide should be thoroughly rubbed into the skin from the neck to the feet, with particular attention given to the creases, perianal areas, umbilicus, and free nail edge and folds. It is washed off 8-10 h later. Clothing and bed linen are changed and laundered thoroughly. Crotamiton (Eurax) has a lower cure rate than other available agents. When used, it should be applied on five successive nights and washed off 24 h after the last use.

Ivermectin has been used to control onchocerciasis since 1987, and is marketed in the US for the treatment of strongy- loidiasis. Numerous publications attest to its efficacy in treating scabies. It is supplied as 3 and 6 mg pills, and is usually given at a dose of 200 g/kg. Although an oral treatment is very convenient, it may not be any more effective than topical therapy. In the crusted type, it should be used in conjunction with a topical

agent. It may need to be repeated two or three times at intervals of 1-2 weeks. The drug appears to have a good margin of safety, although neurotoxicity may be possible.

Individuals in close contact with the patient should be treated. Scabies in long-term healthcare institutions is an increasing problem. Delays in treating close contacts may result in large numbers requiring treatment.

Animal scabies Zoonotic scabies and scab mites may affect humans who come in close contact with the animal. The reaction resembles scabies, but typically runs a self-limited course. Burrows are usually absent.

Other mite diseases

Demodex mites Demodex folliculorum is a vermiform mite that inhabits the pilosebaceous units of the nose, forehead, chin, and scalp. The mite has a flattened head, four pairs of short, peglike legs, and an elongated abdomen. Demodex brevis is shorter, and is more commonly found on the trunk.

In dogs, the lesions of demodectic mange contain numerous mites. In humans, there are convincing reports of demodectic blepharitis, demodectic folliculitis, demodectic abscess, and demodectic alopecia that respond to eradication of the mites. Some rosacea-like lesions may also be caused by Demodex.

Treatment of the eruptions in which Demodex has been implicated consists of applying permethrin, sulfur, lindane, benzyl benzoate, or benzoyl peroxide. Oral ivermectin and metroni- dazole have also been used Cheyletiella dermatitis Cheyletiella yasguri, Cheyletiella blakei (Fig. 51), and Cheyletiella parasitovorax are three species of nonburrowing mite that are parasitic on dogs, cats, and rabbits, respectively, where they present as "walking dandruff." They may bite humans when there is close contact with the animals, producing an itchy dermatitis resembling scabies or immu- nobullous disease. The mites are similar in diameter to

S. scabiei, but are elongated and have prominent anterior hooked palps. They may be found by brushing the animal's hair over a dark piece of paper. The brushings can be placed in alcohol, where the scales and hair sink while the mites float. The pet should be treated by a qualified veterinarian.

Chigger bite The trombiculid mites are known as chiggers, mower's mites, or red bugs. In North America, Trombicula (Eutrombicula) alfreddugesi attacks humans and animals. In Europe, the harvest mite, Neotrombicula autumnalis, is a common nuisance. Attacks occur chiefly during the summer and fall, when individuals have more frequent contact with mite-infested grass and bushes. The lesions occur chiefly on the legs (Fig. 52), and at the belt line and other sites at which clothing causes constriction. Penile lesions are common in males. Lesions generally consist of severely pruritic hemor- rhagic puncta surrounded by red swellings. On the ankles, intensely pruritic, grouped, excoriated papules are noted. Several varieties of trombiculid mite in East Asia and the South Pacific are vectors of scrub typhus (tsutsugamushi fever).

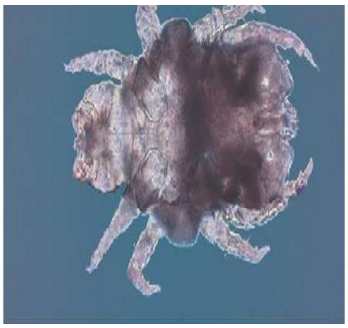

Fig 51

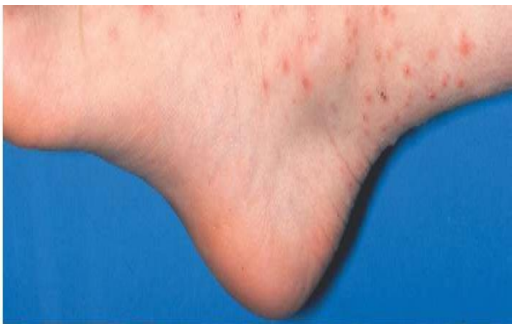

Fig 52

Gamasoidosis Persons in contact with canaries, pigeons, and poultry are prone to develop gamasoidosis. The dermato- sis occurs chiefly on the hands and arms, where the bite produces inflammatory, itchy papules. Any area on the body may be attacked and common additional sites are the groin, areolae, umbilicus, face, and scalp. The mites may wander from birds' nests as soon as the young birds begin to fly, and they may infest terrace cushions and furniture. In large metropolitan areas, especially where pigeons tend to gather, it is not unusual to see pigeons roosting on

window ledges. Through the open windows or even through air conditioners, the pigeon mites attack humans and cause urticarial and papular eruptions. The tropical fowl mite (Ornithonyssus bursa), widely prevalent in wild birds in both continental US and Hawaii, may do this as well.

Two genera of mite, Ornithonyssus and Dermanyssus, commonly infest birds. O. bursa and Ornithonyssus sylvarium are the two common species of feather mite. Dermanyssus gallinae, the red or chicken mite, is also a common parasite of birds. Dermanyssus mites may carry Erysipelothrix rhusiopathiae. D. gallinae tends to leave the bird during the day and hide in cracks and crevices, and therefore can be killed without direct treatment of the bird. Thorough spraying of the surroundings with an agent such as malathion is effective. Mites of the Ornithonyssus group require treatment of the birds themselves. In pet stores, bird mites may be transmitted to rodents with human disease related to contact with a gerbil or hamster

Grocer's itch This is a pruritic dermatitis of the forearms, with occasional inflammatory and urticarial papules on the trunk. It results from the handling of figs, dates, and prunes, when it is caused by Carpoglyphus passularum, or from exposure to the cheese mite (Glyciphagus domesticus). This must be distinguished from grocer's eczema, which is caused by sen- sitization to flour, sugar, cinnamon, chocolate, and similar items.

Grain itch Grain itch is also known as straw itch, barley itch, mattress itch, and prairie itch. Causative mites include Pyemotes tritici, Pyemotes ventricosus, Cheyletus malaccensis, and Tyrophagus putrescentiae (the copra itch mite). Those chiefly affected are harvesters of wheat, hay, barley, oats, and other cereals, or farm hands and packers who have contact with straw. Grain itch has a typical lesion consisting of an urticarial papule on which there is a small vesicle. There is intense pruritus, with lesions occurring predominantly on the trunk. Frequently, there is a central hemorrhagic punctum in the beginning that rapidly turns into an ecchymosis with hemo- siderin pigmentation.

Other mite-related dermatitis Dermatophagoides pteronyssi- nus and Dermatophagoides farinae are dust mites implicated in atopic diseases. Lepidoglyphus destructor is the hay mite. There have been outbreaks of Pyemotes boylei bites in homes fumigated for termites. Although mites do not appear capable of survival when forced to share an environment with termites, they thrive in locations in which there are termite carcasses. Vanillism is a dermatitis caused by Acarus siro and occurs in workers handling vanilla pods. Copra itch occurs on persons handling copra who are subject to Tyrophagus longior mite bites. Coolie itch is found in tea plantations in India and is caused by Rhizoglyphus parasiticus. It causes sore feet. Rat mite itch, caused by Ornithonyssus bacoti, the tropical rat mite, may result in an intensely pruritic dermatitis. This papulovesicular urticarial eruption is seen in workers in stores, factories, warehouse, and stockyards. The rat mite may transmit endemic typhus, rickettsial pox, equine encephalitis, tularemia, plague, and relapsing fever. Feather pillow dermatitis is a pruritic papular dermatitis traced to the Psoroptid carpet mite, Dermatophagoides scheremetewskyi, which may infest feather pillows. Finally, the house mouse mite, Allodermanyssus (Liponyssoides) sanguineus, is the vector of Rickettsia akari, the causative organism of rickettsialpox.

Order Scorpionidae Scorpion sting

Scorpions (Fig. 53) are different from other arachnids in that they have an elongated abdomen ending in a stinger. They also have a cephalothorax, four pairs of legs, pincers, and mouth pincers. Two poison glands in the back of the abdomen empty into the stinger. Scorpions are found all over the world, especially in the tropics. They are nocturnal and hide during the daytime under table tops, and in closets, shoes, and folded blankets.

Fig. 53 Common Centruroides scorpion.

Ground scorpions may burrow into gravel and children's sandboxes. Buthid scorpions include the most venomous species of medical importance. Important scorpions include Tityus serrulatus, found in Brazil, Buthotus tamulus, found in India, Leiurus quinquestriatus and Androctonus crassi- cauda, found in North Africa and southwest Asia, and Centruroides suffusus, found in Mexico. Centruroides exilicauda and C. sculpturatus are the most toxic scorpions in the United States. Vaejovis scorpions in the southeastern United States have been reported to cause "brown recluse-like" dermo- necrotic reactions.

Scorpions sting only by accident or in self-defense. The venom causes pain, paresthesia, and variable swelling at the site of the sting. The sting of the Egyptian scorpion (L. quin- questriatus) has a mortality rate of 50% in children. The neuro- toxic venom may produce numbness at the sting site, laryngeal edema, profuse sweating and salivation, cyanosis, nausea, and paresthesia of the tongue. There is little or no visible change at the site of the sting. Death may occur from cardiac or respiratory failure, especially in children. Renal and hepatic toxicity may also occur.

Treatment depends on the species and toxic symptoms. Antiarrhythmics, antiadrenergic agents, vasodilators, and calcium channel-blockers may be required. Antivenin is available for many species of scorpion.

ORDER ARACHNIDAE

Arachnidism

Spiders are prevalent throughout the world. Most are beneficial to humans, as they trap many insects, but a few species are dangerous to humans. Many spider venoms are not well characterized, and in most cases of envenomation, the responsible spider is never identified. The Brazilian armed spider (Phoneutria nigriventer) is well characterized. Its venom contains neurotoxins that may be fatal in children. Various reactions to spider bites have been reported, including dermonecrotic reactions, systemic toxicity, and acute generalized exanthematous pustulosis.

Latrodectism

The various species of Latrodectus have similar toxins and cause similar reactions in humans. The black widow spider, Latrodectus mactans, is of chief concern in the continental US. It may also be found in the Caribbean. Black widows are web - building spiders, and are commonly found in woodpiles and under outhouse seats. Their venom may be less potent than that of related brown widow spiders, but they inject more of it. Latrodectus curacaviensis is native to South America, and Australia and New Zealand have related red-back spiders (Latrodectus mactans hasselti). Latrodectus indistinctus is found in Africa, and the brown widow, Latrodectus geometricus, is native to southern Africa and Madagascar.

Fig. 54. Back widov

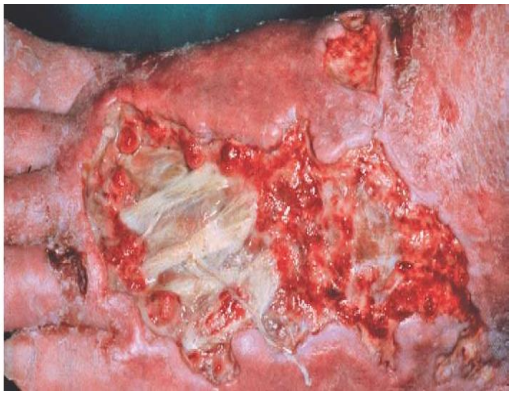

Fig. 55 Brown recluse bite

The female Latrodectus mactans (Fig. 54) spider is 13 mm long and shiny black, with a red hourglass-shaped marking on its abdomen. The legs are long, with a spread of up to 4 cm. The black widow spider is not aggressive, and bites only when disturbed. Severe pain usually develops within a few minutes and spreads throughout the extremities and trunk. Within a few hours there may be chills, vomiting, violent cramps, delirium or partial paralysis, spasms, and abdominal rigidity. The abdominal pains are frequently most severe and may be mistaken for appendicitis, colic, or food poisoning. Toxic morbil- liform erythema may occur. Myocarditis has also been reported. Antivenin is indicated for severe symptoms of envenoma- tion. Benzodiazepines reduce the associated tetany.

Loxoscelism

The brown recluse spider (Loxosceles reclusa) (Fig. 55) is the major cause of necrotic arachnidism in the US. It is most common in the lower Midwest and Southwest. This reclusive spider may be identified by a dark, violin-shaped marking over the cephalothorax and three sets of eyes, rather than the usual four. It is light brown and about 1 cm long, with a small body and long delicate legs. It is found in storage closets, basements, and cupboards, and among clothing. Outdoors it has been found in woodpiles, in grass, on rocky bluffs, and in barns. It stings in self-defense and is not an aggressive spider.

The incidence of brown recluse bites is grossly overestimated. Loxosceles rufescens, Loxosceles deserta, and Loxosceles arizonica cause lesser degrees of skin necrosis. Loxosceles laeta occurs throughout Latin America and produces changes similar to those of L. reclusa. The venom contains a phospholipase enzyme, sphingomyelinase D, which is the major toxin. Hyaluronidase contributes to a gravity-dependent spread of the necrotic lesions.

In the localized type of reaction, known as necrotic cutaneous loxoscelism, extensive local necrosis develops. A painful severe edematous reaction occurs within the first 8 h, with development of a bulla

with surrounding zones of erythema and ischemia. In about a week the central portion becomes dark, demarcated, and gangrenous. Systemic loxos- celism is rare, but may be associated with minor-appearing bite reactions. Systemic toxic symptoms are associated with disseminated intravascular coagulation.

Treatment

Treatment consists of rest, ice, and elevation. Tetanus toxoid should be given if the patient has not received the immunization within 10 years. Some data suggest a trend towards better outcome with injections of intralesional triamcinolone, and there are anecdotal reports of sparing of necrosis in the injected site, while the areas above and below the injection site show necrosis. Antibiotics and conservative debridement may be needed for necrotic wounds. Dapsone has been used, but some studies show that it is no better than placebo, and it may be toxic, especially in the setting of venom-induced hemolysis. Colchicine has also been disappointing in animal models, but tetracyclines show some promise and deserve further study.

Funnel web spiders

Funnel web spiders include Tegenaria agrestis (the hobo spider or aggressive house spider of the Pacific Northwest) and Atrax robustus (the Sydney funnel web spider of Australia). Australian funnel web spiders are dangerous, but antivenin is available.

Tarantulas (Lycosidae: Theraphosidae)

Tarantulas are large, hairy hunting spiders. American species have urticating hairs that produce cutaneous wheal and flare reactions and embed in the cornea, causing ophthalmia nodosa.

PHYLUM CHORDATA STINGRAY INJURY

The two stingray families (Dasyatidae and Myliobatidae) are among the most venomous fish known to humans. Attacks generally occur as a result of an unwary victim stepping on a partially buried stingray. A

puncture-type wound occurs about the ankles or feet, and later ulcerates. Sharp, shooting pain develops immediately, with edema and cyanosis. Symptoms of shock may occur.

Persons wading in shallow, muddy waters where stingrays may be found should shuffle their feet through the mud to frighten the fish away. Successful treatment is usually attained by immersing the injured part in hot water for 30-60 min. The water should be as hot as can be tolerated, since the venom is detoxified by heat. Meperidine hydrochloride administered intravenously or intramuscularly may be necessary. If the ulcer remains unhealed after 8 weeks, excision is indicated.

Snake bite

Venomous snake bites are a serious problem in some parts of the world. In the US the rattlesnake, cottonmouth moccasin, copperhead, and coral snake are the venomous snakes most frequently encountered. Patients are usually young men, with 98% of bites on the extremities, most often the hands or arms. In Europe, 39% of envenomations from exotic pets are snake bites from rattlesnakes, cobras, mambas, or other venomous snakes. Nearly 30 enzymes are found in snake venom, most of which are hydrolases. Snake venom has effects on the cardiovascular, hematologic, respiratory, and nervous systems. Severe envenomation may mimic brain death, with loss of other brainstem reflexes. Local effects at the bite site include the rapid onset of swelling, erythema, and ecchymosis. In more severe reactions, bullae and lymphangitis may appear. Fang marks are often visible and pain is common, except with Mojave rattlesnake bites. Antivenin is used in severe envenom- ation, and antitetanus measures are indicated. In the eastern United States, copperheads inflict most snake bites, followed by rattlesnakes and cottonmouths. Most of these children can be managed conservatively, although Crotalidae antivenin, antibiotics, and fasciotomy may be needed.

Lizard bite

Heloderma suspectum (the Gila monster) is found chiefly in Arizona and New Mexico. Another venomous lizard is the beaded lizard of southwestern Mexico (Heloderma horridum). Bites from these poisonous lizards may cause paralysis, dyspnea, and convulsions. Systemic toxicity usually resolves spontaneously with supportive care within 1 or 2 days. Death is rare. There is no antivenin.

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CONTENT

Sheet

ANDIJON DAVLAT TIBBIYOT INSTITUTI

GUVOHNOMA

ANDIJON – 2024

O‘QUV ADABIYOTINING NASHR RUXSATNOMASI

O‘zbekiston Respublikasi Oliy ta’lim, fan va innovatsiyalar vazirligi, Andijon davlat tibbiyot instituti rektorining 2024 yil “27” Apreldagi “01/08/972-Sh”–sonli buyrug‘iga asosan

A.Paqirdinov
(muallifning familiyasi, ismi-sharifi)

General medicine - 60910200
(ta’lim yo‘nalishi (mutaxassisligi)

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talabalari (o‘quvchilari) uchun tavsiya etilgan.

Leprae hansen's disease. Cutaneous leishmaniasis. Dermatozoonoses
nomli o‘quv qo‘llanmasi
(o‘quv adabiyotining nomi va turi: darslik, o‘quv qo‘llanma)

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O‘zbekiston Respublikasi Vazirlar Mahkamasi tomonidan litsenziya berilgan nashriyotlarda nashr etishga ruxsat berildi.

Rektor _____ M.M.Madazimov
(imzo)

O‘ZBEKISTON RESPUBLIKASI SOG‘LIQNI SAQLASH VAZIRLIGI ANDIJON DAVLAT TIBBIYOT INSTITUTI

Ro‘yxatga olish raqami:
133

NOTE

O‘QUV QO‘LLANMA

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“LEPRAE HANSEN'S DISEASE. CUTANEOUS LEISHMANIASIS. DERMATOZOONOSES."

Muharrir: Maxmudov A.
Korrektor va dizayn: Maxmudov T.

Tasdiqnoma № X-25171, 300325805, 15.06.2023.
Bosishga 2024 yil “27-aprel” ruxsat berildi.
Format 60x84/16. Garnitura Times New Roman.
Muqova uchun rasm manbasi:
OCHIQ INTERNET MANBASIDAN OLINDI
Shartli bosma tabog‘i 7.67., 140 sahifa, Adadi 10 dona, Buyurtma №55

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