Aspects of tropical ulcerating diseases
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Citation for published version (APA):

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Chapter 1

Introduction and aims of the thesis
Cutaneous ulcers in and from the tropics

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Accepted in short version for publication in: American Journal of Clinical Dermatology
Introduction

Skin ulcers are a regular reason for consultations at the departments for tropical diseases in the Western World. It is likely that the incidence of imported ulcers will rise because of frequent travel to and from tropical countries. This is most evidently illustrated by the rising incidence of imported cutaneous leishmaniasis.

Ulcers, encountered in people living in the tropics and those returning from the tropics are often referred to as “tropical ulcers”. However, the term “tropical ulcer” is misleading because it suggests a single causative factor for ulcers originating from the tropics. By some authors the term “tropical ulcer” is used for a specific clinical entity with well defined clinical features and synergistic bacterial aetiology. In fact, ulcers originating from the tropics show a large variety. Besides clinical examination, histopathological, microbiological or molecular biological investigations may be necessary to arrive at a final diagnosis.

The list of ulcers originating in the tropics is extensive. The most common causes of tropical ulcers in travellers encountered at an outpatient clinic in the Western World are shown in Figure 1. In this overview we focus on the epidemiology, the clinical aspects, the diagnostic procedures and the treatment of the most common ulcers which are encountered as an imported disease in outpatient clinic in the Western World.

![Figure 1. Most common tropical ulcerative conditions in travellers from the Tropics encountered at an outpatient clinic in the western world.](image-url)
Bacterial infections

Pyoderma

Introduction
Pyoderma includes several clinically distinct types of skin lesions that are caused by Staphylococcus aureus and/or β-haemolytic streptococci group A. It is a common cause of (purulent) ulcerative skin lesions in the tropics. At the departments for tropical and imported skin diseases, severe (ulcerating) pyodermas, especially in the lower legs, are regularly encountered in travellers. As far as we are aware, the incidence of these pyodermas remains unknown. It is also not known whether the prevalence and the virulence of streptococci and staphylococci that cause these pyodermas are higher in the tropics than that in the Western World.

Epidemiology
Although ulcerating pyoderma is encountered all over the world, it seems to be more prevalent in the tropics. Environmental conditions such as temperature and humidity may also contribute. However, there are only a few published studies on the prevalence or the incidence of pyoderma in tropical countries.

Clinical aspects
Staphylococcus aureus and β-haemolytic streptococcus group A are the two main micro-organisms that are responsible for the ulcerating skin infections. Superficial skin infection may extend more deeply into the dermis and produce shallow ulcers known as ecthyma. It usually starts as a vesicle or vesiculopustule on an erythematous base, which later ulcerates. The ulcer is covered with a dark-brown, bloody crust. A tender punched-out ulcer remains once the crust is removed. It is usually found on the dorsal feet, shins and thighs, but less often on the upper part of the body. There are usually few lesions, but new lesions may develop without adequate treatment. Pyoderma in travellers is most commonly encountered as a secondary infection in skin lesions caused by environmental insults, such as insect bites, abrasions and atopic dermatitis.
Diagnosis

The diagnosis is often based on the clinical picture of persistent painful ulceration especially in the lower legs. One should perform a bacterial culture if facilities are available. Ideally, tissue obtained by biopsy or needle aspiration should be cultured.26 In daily practice this is often not routinely performed because it is more time-consuming and inconvenient for the patient. However, adequate culture results were obtained using the swab technique.27-29 Susceptibility tests in vitro are preferable. Methicillin-resistant \textit{Staphylococcus aureus} and tetracycline-resistant streptococci and staphylococci are frequently encountered in many areas of the tropics.30,31

Treatment

Treatment of ulcerative pyoderma is initially based on the clinical assessment. Gram-stained smears of the exudate may be helpful in starting empirical antimicrobial treatment. However, antibiotic treatment should be preferably based on culture outcome. If culture result is not yet available and the clinical condition requires antibiotic treatment one may start, in case of a community acquired ulcerative pyoderma, with flucloxacillin orally for at least 10 days as the drug of first choice. The antibacterial activity of flucloxacillin is evident on Gram-positive bacteria and above all on penicillinase-producing staphylococci.32-36 With the global spreading of macrolide-resistant \textit{Staphylococcus aureus} and \beta-haemolytic streptococci, these antibiotics should be prescribed with caution. Clindamycin is recommended in penicillin-allergic patients.37 As an alternative vancomycin may be used, although the first vancomycin-resistant \textit{Staphylococcus aureus} (VRSA) have been reported.38 Besides antimicrobial treatment, appropriate wound dressings are important, but often neglected. It is generally accepted that ulcers heal more rapidly under occlusive (moist) dressings than under dry circumstances.31,39 Special attention should be paid to ulceration in the lower legs where (sub) clinical oedema is often present. This oedema may delay or even complicate healing. Oedema may be eliminated by adequate compression therapy with elastic or non-elastic bandages or stockings.

Mycobacteria

Mycobacterial infections comprise infections that are caused by the different species of the genus \textit{Mycobacterium}. Most mycobacteria cause localized and often harmless infections of the skin.40 Cutaneous disease may be due to inoculation, by trauma or iatrogenic; may be
contiguous with underlying osteomyelitis or lymphadenitis or may be a part of disseminated disease.

In immune competent patients the disease is in generally localized, although lymphatic spread, the so-called nodular lymphangitis, is well known in for instance *M. marinum* infections.

As mycobacteria are intracellular micro-organisms, the immunological response of the host is a cell-mediated immune reaction resulting in a granulomatous tissue reaction. Infections with non-tuberculous mycobacteria in immune compromised patients may lead to severe disease.

After tuberculosis and leprosy, *M. ulcerans* is the most common mycobacterial disease and the most important cause of cutaneous ulceration. The list of mycobacteria which are potential pathogens and may cause ulceration include *M. scrofulaceum, M. fortuitum, M. chelona-abscessus, and M. avium complex*. More rare infections are caused by *M. szulgai, M. kansasii* and *M. haemophilum*. These mycobacteria are only rarely seen as causing ulceration in the skin and will therefore not be discussed further. Besides *M. ulcerans* and *M. tuberculosis, M. marinum* may cause skin ulceration and will therefore be discussed. *M. leprae* will not be discussed because the ulceration is the consequence of neuropathy which may develop as nerve damage occurs during leprosy reactions. Infection with *M. leprae* itself does not lead to ulcerating conditions.

**Mycobacterium ulcerans**

**Introduction**

Buruli ulcer is a chronic ulcerating disease of the skin, subcutaneous tissue and bone caused by *M. ulcerans*. It was named after the Buruli district in Uganda where the prevalence was high. *M. ulcerans* has been cultured from several species in areas endemic for Buruli ulcer and is believed to be an environmental mycobacterium. Trauma by vegetation seems to be essential for the introduction of *M. ulcerans* into the skin. Insects may play a role in the transmission of the infection. HIV infection seems not to be a risk factor for Buruli ulcer and it does not appear to influence the treatment outcome of Buruli ulcer.

**Epidemiology**

The largest number of patients is found in Africa. Before 1980, reports came mainly from the Democratic Republic of the Congo and Uganda. After 1980, new foci emerged in West Africa particularly in distinct regions of Benin, Ivory coast and
Ghana.\textsuperscript{49-52} It has been reported in Asia, South America and the Western World. The majority of the cases are children younger than 15 years, with lesions mostly located on the extremities (legs more than arms). Buruli ulcer has been described as an imported disease in the Western World.\textsuperscript{53-55} The major endemic foci are located in wet lands, especially those with slow-flowing or stagnant water in tropical and sub-tropical countries. It appears that natural or man-made changes in water management influence the outbreak of Buruli ulcer.\textsuperscript{49;52;56;57}

**Clinical aspects**

Whether the disease develops after exposure to \textit{M. ulcerans} depends largely on the host defences. In most cases \textit{M. ulcerans} will probably be cleared, disease may develop or it may lead to sub-clinical or asymptomatic infection.\textsuperscript{58} A Buruli ulcer is characterised by a painless nodule, papule, plaque or oedema, evolving into a painless ulcer with undermined edges, often leading to invalidating sequelae.\textsuperscript{57}

**Diagnosis**

Diagnosis is established on the basis of clinical picture which is associated with non-specific features, especially in the pre-ulcerative stage. Therefore, every nodule and ulcer in an endemic area is suspected to be \textit{M. ulcerans} disease.\textsuperscript{57} The histopathological picture of an early lesion is characterised by circumscribed necrosis in the deep dermis with little or acute inflammatory reaction. This is followed by a septal panniculitis with ulceration of the subcutaneous tissue. Besides an acute also a chronic or granulomatous reaction can be observed. Acid-fast bacilli are especially found extracellularly in the necrotic areas.\textsuperscript{59} \textit{M. ulcerans} can be cultured from clinical specimens, although care should be taken to collect the material from sites where bacilli are normally present e.g. the necrotic base of the lesion or the undermined edges of the ulcer.\textsuperscript{60;61} Primary cultures may take between 6 and 8 weeks.

Polymerase chain reaction (PCR) has been developed as a diagnostic technique for the identification of the micro-organism.\textsuperscript{62-64} This enables rapid diagnosis, which is important because at present the standard treatment is by excision of the lesion. Confirmation with PCR is helpful also in circumstances where \textit{M. ulcerans} disease is a part of a differential diagnosis. PCR can be performed using (biopsy) tissue, from swabs taken from under the undermined edge of the ulcer and from environmental samples.
Treatment
Surgical excision followed by skin grafting is the therapeutic measure of choice. However, a combination of rifampicin and streptomycin may be effective against early forms of Buruli ulcer. A combination of amikacin and rifampicin was shown to be effective in a Buruli ulcer model in mice.

*Mycobacterium marinum* (Swimming pool granuloma)

Introduction
Swimming pool granuloma is caused *M. marinum*, a mycobacterium belonging to the non-tuberculous mycobacteria, which causes disease in fresh- and salt water fish, and occasionally in humans. It is the most common cause of non-tuberculous mycobacterial infections.

Epidemiology
As initial reports of cutaneous disease by *M. marinum* were associated with swimming pools it was called swimming pool granuloma. Infection in swimming pools nowadays is rare due to proper chlorination. The distribution is World Wide, occurring in fresh-brackish as well as salt water, and is prevalent in heated water (for instance in tropical aquaria) in temperate climates, and in pools and the sea in more tropical climates. In principle any water-related activity carries a potential risk for infection. Generally infection occurs through superficially traumatised skin.

Clinical aspects
The initial lesions starts as an inflammatory papule after a relatively long incubation period of 2 to 6 weeks. As infection is preceded by trauma majority of the lesions are located on the back of the fingers or the hand or around the knee. The papule then gradually enlarges into a bluish-red inflammatory nodule or plaque, which may ulcerate or show a warty surface. There is generally a delay of months to even years before a doctor’s opinion is sought because the lesions are painless and enlarge slowly. The lesions may heal spontaneously. However, this may take months to years. Less often deep infections such as tenosynovitis, osteomyelitis, arthritis and bursitis may occur. *M. marinum* infections are one of the causes of nodular lymphangitis (also called sporotrichoid extensions after the lymphatic spread of sporotrichosis). Clinically, there are nodules and/or ulcerating lesions resulting from spread along the lymphatic vessels. Deep infections and nodular lymphangitis do not heal spontaneously.
Diagnosis

The clinical picture, the preferential location combined with a history of aquatic activity with a skin trauma should provide high index of suspicion. The clinical diagnosis should be confirmed by diagnostic tests. At present PCR techniques using biopsy material provide a diagnosis within days. Histopathological examination of a skin biopsy can be non-specific in the early stage of the disease. A granulomatous reaction develops after 6 months. The presence of acid-fast bacilli by special staining techniques is reported in varying percentage. Absence does not rule out *M. marinum* infection. Cultures can be performed using aspirates or biopsies. The optimal growth is at 30 to 32°C, and cultures should be maintained for 6 weeks.

Treatment

Several treatment options exist. Treatment regimens consist of combinations containing clarithromycin, rifampicin or ethambutol. More recently the new macrolides such as clarithromycin are proposed as a single drug therapy. However, no randomised studies have been performed. Response to treatment is slow and is continued till clinical cure.

Mycobacterium tuberculosis

Introduction

Cutaneous tuberculosis has today become a rare disease in inhabitants of the Western World. Therefore, the majority of cutaneous tuberculosis cases are diagnosed in immigrants.

Epidemiology

Cutaneous tuberculosis was diagnosed in 2 to 4% of the out-patients at dermatological clinics in Great Britain at the beginning of the 20th century. The same figures have been reported in studies from Asia in the middle of the last century, but appear to be decreasing.

Clinical aspects

Ulcerated lesions may be encountered in primary tuberculosis, but may also be a manifestation of secondary tuberculosis. Only cutaneous tuberculosis with clinical manifestation of ulceration are discussed.
Primary infection

Primary infection accounts for only 2% of all cases of cutaneous tuberculosis. It is caused by exogenous inoculation of *M. tuberculosis*. The lesion starts 2 to 4 weeks after inoculation as a smooth papule or nodule, which enlarges during the course of several weeks to a plaque, which ulcerates forming a so-called ‘tuberculoid chancre’. The ulcer shows undermined edges and is painless. After 3 to 8 weeks non-tender regional lymphadenopathy develops, which may suppurate to form a “cold” abscess, which then may spontaneously drain with sinus tract formation. This process in general heals spontaneously with atrophic scarring in 3 to 12 months. Primary lesions are mainly located on the face and the extremities in children, but inoculation by injections and surgical procedures is also possible.

Secondary infection

Scrofuloderma

Due to contiguous spread from a deeper localised infection such as lymph node or in some cases bone. Initially there is an indurated inflammatory area overlying the deeper infection. Due to suppuration fluctuating nodules develop, which ulcerate with formation of sinus tracks. In the course of time cordlike scars or keloids develop. The lesions are mostly localised over the lymph glands in the neck.

Lupus vulgaris

Lupus vulgaris was the most common manifestation of cutaneous tuberculosis in Europe before World War II. Today it is common in developing countries. It is caused by re-activation of the disease in patients with a high degree of cell-mediated immunity after earlier haematogenous dissemination. The lesions start as brown-red papules, which in the classical form extend into plaques with peripheral activity with an irregular border and central healing with atrophic scar formation and depigmentation. The clinical picture may be variable. Besides the plaque form, there is a hypertrophic form with nodules, which may form a hyperkeratotic mass. The ulcerative form is the most destructive variant. It may erode cartilage and bone, and result in extensive scarring and even deformities. Lesions may become chronic and may persist for decades with gradual extension with progressive scarring and deformity and function loss. The most common location is the face, with the nose, the checks, the mouth and the earlobes as preferential sites. Lesions on the legs and the buttocks are common in Asia and Africa.
Tuberculous gumma

Tuberculous gumma or metastatic tuberculous ulcer is caused by haematogenous dissemination from a primary focus during periods of lowered resistance in bacillaemia. The lesion starts as a subcutaneous nodule or a fluctuant swelling. The overlying skin breaks, resulting in an undermined ulcer with sinus formation. Then it resembles scrofuloderma.

Diagnosis

The clinical picture and epidemiological history of the patient are important. The acid-fast mycobacteria are observed by microscopic investigation of the tissue, especially of early lesions. Culture may be performed using Löwestein-Jenssen medium. PCR is performed in many laboratories and provides reliable, rapid and accurate results for the diagnosis of different types of cutaneous tuberculosis.73,74

Treatment

Treatment of cutaneous tuberculosis is commonly with a multiple drug regimen consisting of isoniazid, ethambutol, pyrazinamide and rifampicin.

General comments

A high index of suspicion is warranted because the clinical picture of mycobacterial infection of the skin can be non-specific. Investigation for mycobacteria is indicated in cases of persistent infiltrative lesions or non-healing ulcers.

Diphtheria

Introduction

Cutaneous diphtheria is an infectious bacterial disease caused by Corynebacterium diphtheriae or more rarely, Corynebacterium ulcerans.75,76 It is transmitted by direct contact with cutaneous carriers and to a lesser extent via vomit. The species of C. diphtheriae produces a toxin which is responsible for the disease diphtheria. The micro-organism (both toxigenic and non-toxigenic strains) may be harboured in the nasopharynx, skin and other sites of asymptomatic carriers. C. diphtheriae is often found secondarily in pre-existing ulcers like echtyma or as superinfection in eczema.77 In immunized individuals systemic toxic complications such as myocarditis and neuritis are rare. The skin lesions may be an important reservoir of infection. Contacts should
be investigated and treated if necessary because there is a potential for secondary transmission.\textsuperscript{78}

**Epidemiology**

Cutaneous diphtheria is still endemic in many tropical countries. It is currently rare in the developed World because of the routine active immunization, but is generally travel-related.\textsuperscript{75,79,80} The incidence of cutaneous diphtheria is not known.

**Clinical aspects**

The characteristic of a primary lesion ranges from a tender pustule to a chronic, non-healing ulcer with a punched-out appearance and an adherent membrane with a slightly undermined margin. In the first 2 weeks it is painful, later the lesion becomes painless and after (spontaneous) removal of the adhering membrane, the haemorrhagic base appears. In many cases lesions are less distinctive. Secondary infection in any pre-existing wound and superinfection of eczematous skin lesions is common and often overlooked. Cutaneous diphtheria may persist for 6 to 12 weeks. A high awareness in clinicians and microbiologists is necessary because cutaneous diphtheria ulcers are non-specific.\textsuperscript{80}

**Diagnosis**

The initial diagnosis is clinical. The definitive diagnosis is made by isolating and identifying \textit{C. diphtheriae} from the ulcer and demonstrating its toxigenicity. The physician must inform the laboratory in advance of the clinical suspicion because \textit{C. diphtheriae} is not isolated by routine culturing.

**Treatment**

\textit{Corynebacterium diphtheriae} is susceptible to a variety of antibiotics. Erythromycin and penicillin are both effective. If the diagnosis is suspected anti-toxin should be administered intramuscularly. However, isolates from chronic skin lesions are often not toxigenic or produce only little toxin, so that the role of anti-diphtheria serum is doubtful in such cases.\textsuperscript{77}
Anthrax

Introduction
Anthrax is caused by the gram-positive, spore-forming *Bacillus anthracis*. It is primarily a disease of animals that is occasionally transmitted to humans. Its incidence has dramatically decreased during the last century, probably because of the control of animal anthrax, immunization and improved hygiene. The cutaneous form is the most common, but it can be fatal in cases of systemic infection.

Patients often have a history of occupational contact with animals or animal discharges or products. Anthrax has been occasionally reported in travellers and may be related to physical contact with dead animals in nature. The endospores can survive in the soil for decades under favourable conditions; they are resistant to drying, heat, gamma radiation and disinfectants. The microbe secretes several plasmid-mediated exo-toxins that are responsible for the oedema and necrosis, which occur during infection.

Epidemiology
Anthrax infections are still endemic in parts of Africa, Asia, the Middle East, Central and South America and the Caribbean. Patients often have a history of occupational contact with animals or animal products in the endemic areas. It is encountered infrequently in travellers.

Clinical aspects
Cutaneous anthrax usually begins 3-5 days after inoculation of endospores of *Bacillus anthracis*. The cutaneous form accounts for 95% of the cases and primarily affects the exposed parts of the body, usually the forearm or the hand. There is usually a single lesion, but multiple lesions are also possible. The lesion starts as a painless papule at the inoculation site. The papule evolves into a haemorrhagic blister within 24-36 hours. The blister dries centrally and forms a haemorrhagic crust, the so-called malignant pustule. The involved area is rarely painful. The crust sloughs within a couple of weeks, leaving behind a shallow ulcer that heals by granulation.

Diagnosis
If there is clinical suspicion of anthrax, a gram stain and culture should be performed on material from the blister or wound fluid from the ulcer base. However, the rate of positive culture does not exceed 60-65%, even before the use of antibiotics. A
biopsy should be taken for histological examination. Serologic testing is useful only retrospectively.85

Treatment
Cutaneous anthrax may be self-limiting. However, treatment is recommended to prevent life-threatening complications. Penicillin and doxycycline are used. In case of systemic involvement intravenous administration of penicillin G should be started as soon as possible. Therapy should be continued for at least 14 days after symptoms abate.82 Asymptomatic carriers may be treated with a six-week course of doxycycline or ciprofloxacin.

Leishmaniasis

Introduction
Cutaneous leishmaniases (CL) is one of the most important causes of chronic ulcers in some parts of the tropical World.86-89 It is caused by protozoan parasites belonging to the genus Leishmania, which are divided into two subgenera, L. (Viannia) spp. and L. (Leishmania) spp. Further classification is based on a variety of biochemical, immunological, and molecular criteria.90-92

In the New World CL is caused by at least eight different species, primarily of the L. (V.) braziliensis and L. (L.) mexicana complexes. Old World CL is caused by four species; L. major, L. tropica, L. aethiopica and L. infantum.93-96

The parasites are transmitted to humans via the bite of the female phlebotomine sand fly which has fed on an infected mammal. Of the sub-family Phlebotominae, the genera Phlebotomus in the Old World and Lutzomyia in the New World are known vectors.97,98

Epidemiology
The disease occurs throughout the tropical and the subtropical regions and is endemic in 88 countries. Old World CL is found in the Mediterranean, Northern Africa, the Sub-Saharan, the Middle East, and South-West Asia. New World CL extends from Southern Texas to the highlands of Northern Argentina; with 90% of cases of CL in Afghanistan, Algeria, Brazil, Iran, Peru, Saudi Arabia and Syria.

In the past decades, there is a definite increase in the incidence of CL. This is because of several factors such as rural to urban migration as seen in Kabul, Afghanistan, development of new agro-industrial projects, re-locating non-immune community in endemic areas, movement of army troops into endemic regions and the termination
of insecticide spraying. Emerging of the disease in travellers is caused by the increase in eco-tourism to especially jungle areas in South and Middle America, with hotspots as Manu National Park in Peru, Madidi National Park the Tuichi river in Bolivia, and several areas in Costa Rica. HIV infection does not seem to increase the risk of CL infection, but may influence treatment response. It is estimated that 1 to 1.5 million cases of CL occur annually. It is one of the 10 most frequent (skin) diseases encountered in travellers returning from tropical countries with an increased incidence.

Clinical aspects

The clinical picture of CL varies with the endemic region and depends on the species involved, the immune status of the host, genetics and probably on the transmitting sand fly. A lesion may start as a papule or a nodule, which develops into an ulcer with or without a scab. At this stage most patients consult a physician. The lesions are usually painless; if painful there is generally a secondary infection present. Lesions caused by *L. major* are often nodular, nodulo-ulcerative and ulcerative. The lesions develop slowly over months and generally resolve in 6 months. Lesions caused by *L. tropica* may persist as an erythematous papule for more than a year. Presentation is often as nodulo-ulcerative plaques with a necrotic base and indurated margin that are frequently covered by a firm adherent crust. The time period for spontaneous resolution is not well known. It has been reported that leishmaniasis caused by *L. tropica* may affect the nose or the mouth as is seen in mucocutaneous leishmaniasis from the New World. However, this is probably because of direct extension from skin lesions rather than from the dissemination of the parasite. Skin lesions of the New World CL caused by species of the subgenus *Leishmania* will generally resolve even without treatment in 6 months, whereas lesions caused by the subgenus *Viannia* often do not resolve spontaneously. First a nodule develops, which then enlarges and eventually ulcerates. A nodular lymphangitis may be present. Mucocutaneous leishmaniasis, although uncommon, may develop in approximately 3-5% of the patients as a complication of New World CL caused by *Leishmania (V.) braziliensis*, but also occurs in infections with *Leishmania (V.) panamensis*. Disseminated leishmaniasis has been reported as an emerging form of leishmaniasis in North-Eastern Brazil. It shows multiple pleomorphic lesions ranging from acneiform, papular, nodular and ulcerating lesions.
Diagnosis

The initial diagnosis is based on the clinical picture and on the visit of the patient to an endemic area.\textsuperscript{117,118} Laboratory tests include histopathological examination of the biopsies taken from the ulcer border, direct smears from the ulcer border stained with Giemsa, culture of the material obtained by needle aspiration or by biopsy. If facilities are available, amplification of DNA using PCR may be used. None of the laboratory methods has a 100\% sensitivity.\textsuperscript{119-121} Best results have been obtained by a combination of laboratory tests.\textsuperscript{122,123}

Histopathological picture may range from a mixed inflammatory cell infiltrate with a large number of macrophages containing the \textit{Leishmania} parasite, to a highly organized and predominantly epitheloid cell granuloma with very few demonstrable parasites.\textsuperscript{122,124} Identification of the parasite by PCR is important in areas where more than one species are present, especially in case of possible infection with \textit{L. vianna braziliensis}. The choice and the duration of the treatment may depend on isolation of the specific species.

Treatment

The most common treatment options are shown in Figure 2. For the Americas, pentavalent antimony (Sb) is still the drug of choice in case of infection with \textit{L. braziliensis}.\textsuperscript{125} In 1984, the WHO recommended for CL a dose of 10-20 mg of Sb/(kg.d), which should be given until the lesion is healed and for some days longer, for a minimum total period of 3 weeks.\textsuperscript{126} It is not clear which treatment regimen

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\caption{Treatment options for cutaneous Leishmaniasis}
\end{figure}
should be used. In some areas very low cure rate was found with this recommended
drug regime. In some endemic areas, a lower dose of 10 mg of Sb/(kg.d) or for a
shorter period may be sufficient. In areas where mucocutaneous Leishmaniasis is
rare and when there are no clinical signs of dissemination of the disease, intralesional
therapy with Sb without or in combination with cryotherapy has proven to be an
effective and safe treatment in the New world cutaneous leishmaniasis. Pentamidine is the drug of first choice in case of infection with L.(V.) guyanensis. As the risk of mucosal leishmaniasis is very low in the Old World cutaneous
leishmaniasis, topical treatment is often used. Paromomycin ointment has shown to
be effective in the treatment of cutaneous leishmaniasis caused by L. major. Different studies reported good results with intralesional therapy with antimonials
(sodium stibogluconate and meglumine antimonate). It was shown that
intralesional therapy was more effectively combined with cryotherapy. Fluconazole
200 mg daily for 6 weeks showed good response in Iran caused by L. major. Ketoconazole was reported to be effective against L. major in Israel. No randomized,
placebo-controlled clinical studies have been reported for L. tropica and L. infantum.
Therapy was found to be effective in a randomized, controlled trial to treat
cutaneous leishmaniasis caused by L. tropica in Afghanistan. Miltefosine is an alkyl-phosphocholine compound that is the first oral drug for
treatment of visceral leishmaniasis. The drug may be promising in the treatment
of severe cutaneous infection as well as in areas where mucosal leishmaniasis is
prevalent.

Subcutaneous mycoses

Subcutaneous mycoses are characterized by a heterogeneous group of infections that
often result from direct penetration of the fungus into the dermis and subcutaneous
tissue through traumatic injury. This group of micro-organism is discussed in this
chapter because it may cause ulceration of the skin.

Subcutaneous mycoses are restricted to certain regions, travellers are seldom infected.
Most cases are encountered in those living and working in an endemic area with little
availability of health resources. The most common subcutaneous mycoses, which
may show ulceration are sporotrichosis, chromo(blasto)mycosis and mycetoma. Only
sporotrichosis has a single specific aetiological agent, whereas chromoblastomycosis
and mycetoma are clinical syndromes with multiple fungal or bacterial aetiologies.
Sporotrichosis

Sporotrichosis is caused by Sporothrix schenckii, which is a dimorphic fungus that occurs in nature as a saprophyte in soil, decaying organic material and on surfaces of various plants. Infection results via traumatic inoculation of materials containing the fungus, particular wood splinters or thorns through the skin. Zoonotic transmission has been described. The organism is particularly found in warm temperate and humid tropical climates and is one of the most common subcutaneous mycoses.

Epidemiology

Individuals with activities, which expose them to the environment are at risk. Several large outbreaks of the disease have been reported. In South Africa 3000 cases were reported among gold miners from 1941 to 1944. It was believed that the fungus was inoculated through the skin via splinters of contaminated timber. Sporothrichosis has a World Wide distribution. However, most cases at present are reported in South and Central America.

Clinical aspects

The incubation period is probably a few weeks. Sporotrichosis very rarely affects internal organs. It is mostly encountered as lymphocutaneous or sporotrichoid form or less common as a localized or fixed cutaneous form. The primary cutaneous lesions may appear as papular, nodular, or pustular lesions that develop into either a superficial ulcer or a verrucous plaque. During progression, the lymphocutaneous form shows multiple subcutaneous nodules that are formed along the course of the locally draining lymphatics (sporotrichoid spread). The localized form shows no lymphatic spread and is characterized by indurated or verrucous plaques and occasional ulcers. Dissemination is rare and usually encountered in immunodeficient individuals.

Diagnosis

The initial clinical diagnosis may be confirmed by histopathological investigation and culture of the fungus. Primary lesions usually show prominent pseudoepitheliomatous hyperplasia. Fresh lesions show a non-specific inflammatory infiltrate composed of neutrophils, lymphocytes, plasma cells and histiocytes. Several types of granulomas including tuberculoid, histiocytic and supplicative granulomas are observed within the dermis of older lesions. Fungal elements may be observed after PAS or haematoxylin and eosin staining. However, they are seldom found because of their small size,
varying shape and often low numbers. The finding of asteroid bodies which are mycotic cells surrounded by radiated, eosinophilic elongations is characteristic. Definite diagnosis depends on culturing the organism from pus or tissue. The organism grows within a week on all media commonly used in medical mycology.

**Treatment**

There are no randomized, comparative trials available for evaluating the treatment of sporotrichosis. The treatment of choice for fixed cutaneous or lymphocutaneous sporotrichosis is itraconazole, which was effective at a dose of 100-200 mg a day for 3 to 6 months. However, terbinafine has showed to be effective in a dose of 1000 mg a day after 12 - 24 weeks of treatment. It is generally accepted that potassium iodide is an effective therapy. Its mechanism of action is still not understood. In adults, the orally saturated solution of potassium iodide 3 times daily 5 drops, which is increased weekly by 5 drops until 40-50 drops at the time for 2-3 months, or for 1 month after the clinical and mycological cure is achieved, is recommended. Severe infection requires treatment with amphotericin B. Immunosuppressed patients respond poorly to potassium iodide, and treatment with amphotericin B or itraconazole is required.

**Chromo(blasto)mycosis**

Chromoblastomycosis is a chronic (sub)cutaneous mycotic disease that occurs more frequently in tropical and sub-tropical areas and is caused by several dematiaceous (darkly pigmented) fungi of which *Fonsecaea pedrosoi*, *Phialophora verrucosa* and *Cladophialophora carrionii* are the main species. The disease is caused by saprophytic fungi that are found in soil and wood. It is a difficult-to-treat mycosis with low cure rates and a high rate of relapses.

**Epidemiology**

The disease is most prevalent in tropical and sub-tropical America and Africa. It has also been reported in several foci in the USA.

**Clinical aspects**

The disease occurs typically on the foot or the leg. After inoculation of the fungus through the skin slowly growing scaly wart-like nodules develop and ulceration may also occur. Clinically, it may be indistinguishable from verrucous cutaneous tuberculosis and localised sporotrichosis. It grows slowly, is painless and lymphatic spread is only seen occasionally. Moderate itching is often mentioned. It seldom involves bones.
and remains limited to the subcutaneous tissues. This may be relevant because scratching may contribute to inoculation of the fungus in adjacent areas. Scratching may also cause secondary infections, which is the most frequent complication of chromoblastomycosis. It occurs mainly in farmers and rural workers who work barefoot. 159

**Diagnosis**

Histological investigation is most important for diagnosis of chromoblastomycosis. Sclerotic bodies can be observed after haematoxylin-eosin staining of tissue biopsy or from fungal culture.158

**Treatment**

Surgery and antifungal therapy have been used in chromoblastomycosis, but results in advanced disease are disappointing.162

**Mycetoma**

Mycetoma is a chronic granulomatous infection of the skin and the subcutaneous tissue characterized by deformation and increased volume of the involved subcutaneous tissue and in the advanced stages causes the destruction of underlining bone structures.163 It is caused either by true fungi (eumycetoma) or filamentous bacteria (actinomycetoma). Nodules and openings of fistulae through which exudate containing grains, is noticed on the skin surface. The grains, also known as sclerotia, are aggregation of hyphae produced by some species of fungi or the bacterial filaments from aerobic actinomycetes.

Mycetoma has also been called “Madura foot” because of the initial descriptions of the disease in the district Madura in India. In 1860 it was called mycetoma by Vandyke Carter who demonstrated its mycotic origin.164

Actinomycetic mycetoma is caused by aerobic species of the Actinomyces group, such as *Nocordia brasiliensis*, *Nocordia asteroids* and *Nocordia caviae*, and the Streptomyces group, *Streptomyces pelletieri*, *Streptomyces somaliensis* and *Actinomadura madurae*. They are filamentous ramified bacteria that when cultured create colonies similar to fungi.165

The maduromycotic (eumycetic) mycetoma is caused by several fungi such as *Madurella mycetomatis*, *Madurella grisea*, *Pseudallescheria boydii*, etc.159

It is mainly a disease of the tropical climates and is more frequently seen in the rural areas where people work in farms under unprotected rudimentary conditions.163 Probably repeated punctures or abrasion of the skin are required for the inoculation of the organisms prior to the infection. The infection develops very slowly over the years.
Therefore, it is not likely to be encountered in travellers from tropical countries. Most cases encountered in the Western World are immigrants from endemic regions.

Epidemiology
Mycetoma is endemic in (sub)tropical regions with a low annual rainfall. These include parts of Central America, Venezuela, Brazil, Sudan, Somalia, Senegal, the Middle East, India, Pakistan and Bangladesh. Its true incidence is unknown. The disease is more frequently encountered in rural areas in where people are more exposed to contaminated soil.

Clinical aspects
Mycetoma is most often seen on the lower limbs (65-70%). However, any body region may be affected after exposure to the agent. Clinically, it is characterized by a slow progressive swelling, deformity of the tissue involved, nodular lesions and fistulae exudate containing grains. The incubation period is not exactly known and may range from several weeks to months.

Diagnosis
Clinically, the diagnosis is suspected in the presence of an increased volume of the affected tissue, formation of abscesses and fistulae exudate containing grains. Histopathological investigation of the lesion is important for the diagnosis of mycetomas. The epidermis shows hyperkeratosis and hyperplasia of varying degree. There is an inflammatory infiltrate within the dermis, microabscesses with polymorphonuclear leukocytes, generally surrounded by many macrophages, plasma cells and lymphocytes. Granules are observed in the centre. Sometimes, tuberculoid granulomas are also observed. The giant cells that appear are of Langhans or foreign body type. Gram stained and potassium hydroxide preparations, may be used for direct observations. It is important to undertake cultures to identify the causal micro-organism. Secretions from fistulae and abscess or tissue biopsies can be used for culture in media to isolate the fungi or the bacteria. Identification is performed using their macroscopic and microscopic features.

Treatment
Choice of treatment depends on the micro-organism involved and the extent of tissue invasion. Eumycetoma is very difficult to treat, surgery is still the most common
treatment in most cases.\textsuperscript{165,166} There are a few reports on treatment with ketoconazole and itraconazole.\textsuperscript{166}

Actinomycetoma with \textit{Nocardia} spp are treated with a combination of dapsone plus sulfamethoxazole-trimethoprim and recently, amikacin for 2 to 3 years.\textsuperscript{165,169,170} As an alternative treatment amoxicillin-clavulanate has been reported.\textsuperscript{171}

\textbf{Summary}

Patients with infectious ulcers that are endemic to the tropics occasionally present to dermatologists in the Western World. It is likely that the incidence of imported ulcers will rise because travel to and from tropical countries is becoming more frequent. Therefore it is important that physicians be familiar with the manifestations of such infections and that they be prepared to diagnose most common imported ulcers and treat these patients.

\textbf{Non-infectious}

\textbf{Sickle cell}

Sickle cell disease is caused by an abnormality in the gene encoding the $\beta$ chain of haemoglobin. When deoxygenated, sickle cell haemoglobin interacts hydrophobically with other haemoglobin molecules, it tends to aggregate and polymerize resulting in the characteristic sickle shape. The rigidity of these deformed cells contribute to the vaso-occlusive episodes that characterizes the acute crises in the disease.\textsuperscript{172,173} Activation of both blood coagulation and platelets was reported in some studies.\textsuperscript{174} It is uncertain whether hypercoagubility is the primary or the secondary event. The pathogenesis of leg ulceration in sickle cell is not completely understood. Abnormal adherence of the sickle cell to endothelial cells has been postulated to be important in the initiation and/or progression of vaso-occlusive events leading to infarction in the skin. Oedema appears to precede the onset of ulceration, although evidence for venous insufficiency has never been found in patients who have sickle cell disease and leg ulcers.\textsuperscript{175-177} The sickle cell ulcers are commonly seen in adult males with homozygous sickle cell disease (HbSS) and are unusual in patients with sickle cell haemoglobin-C disease (HbSC) as well as those with sickle cell beta* thalassaemia.

\textbf{Epidemiology}

Ulcers are a common cause of morbidity among African American and African Caribbean patients with homozygous sickle cell (SS) disease in whom prevalence of 75\% have been reported.\textsuperscript{178} The reported incidence from Africa is much lower
and from 5%-9.6%. The reason for these differences is not known. However, age distribution of the population and genetic factors may play a role.180,181

Clinical aspects

Ulcers are more common in adult males with homozygous sickle cell disease and show more severe clinical manifestations than in those with heterozygous disease. The incidence is very low in children younger than 10 years and markedly increased for those older than 50 years.182 Ulcers persist for months to years, heal slowly and, often recur.

Most ulcers are located in the ankle area over the medial or lateral malleoli.178 The size of the ulcers varies from a few millimetres to large circumferential ulcers. Ulceration is preceded by prodromal pain and is often spontaneous or after a minor trauma. The ulcer has a punched-out appearance with raised margins and a deep base. Radiographs often show some periostal reaction, which makes it difficult to rule out osteomyelitis.182,183 Secondary infection is found very often and may delay wound healing.184 Pain is often very severe and probably the major problem. It has a great impact on the quality of life of these patients.185

Diagnosis

Diagnosis is established after clinical observation of a painful leg ulcer, mostly in the ankle area in patients with sickle cell anaemia. Pathological investigations show obstruction of vessels with intimal proliferation and neovascularization.178 Oedema is often present.177

Treatment

Leg ulcers caused by sickle cell anaemia are very recalcitrant. Many treatments have been promoted, although no controlled clinical trials are available.186 Oedema must be treated with compression bandages or elastic stockings. If unsuccessful, strict bed rest is effective. Secondary infection should be treated with systemic or topically applied antibiotics; after culture outcome when resistance pattern is known. Different wound dressings can be used. Hydrocolloid dressing can be used to initiate debridement. These dressings often relieve pain. Skin grafts using split-skin, or full-thickness punch grafts may be considered, but are not always effective.

Hyperbaric oxygen therapy was postulated to be successful in leg ulcers, but no controlled studies in patients with sickle cell leg ulcers have been published.187 Hyperbaric oxygen showed no effect on the morphology of sickle cells in vitro.188 New therapies in sickle cell anaemia that interrupt the sickling process may be helpful.189
Vascular

Vascular disease seems to be generally rare in tropical countries. In the Western World chronic venous insufficiency is responsible for about 70% of the ulcers in the lower limbs. Studies in the tropics revealed a very low or no prevalence of vascular ulcers. However, a study in Brazil in 1755 adults attending a university clinic for various reasons signs of chronic venous insufficiency were noted in 3.6%. This figure is comparable with that in the Western World.

The incidence of arterial disease is still increasing in the Western World. It is expected that arterial disease will become more prevalent in the developing countries because people are converting to Western life style. Because vascular ulcers are not specific for tropical disease it will not further be discussed.

Malignant

Most cases, which are seen are malignant transformations in chronic traumatized or inflamed skin as seen in chronic leg ulcers, particularly after burns. It has also been described in chronic plantar ulcers in patients of leprosy. Most common are squamous cell carcinoma (SCC), to a lesser extent basal cell carcinoma (BCC) and there are also some reports on sarcomas and melanomas associated with scars.

Epidemiology

No data are available of malignant ulcerations in the skin as an imported disease. There are only a few studies available on this subject from tropical countries. The development of squamous cell carcinoma in traumatic scars seems to be most important. A large study in Nigeria showed a preponderance of SCC in the leg related to neglected, poorly managed and chronic ulcers or scars from burns or injuries. Malignant melanoma was found on the feet, dermatofibrosarcoma affected the trunk and Kaposi sarcoma affected the limbs. Basal cell carcinoma comprised only 2% of all skin cancers. Albino patients had a higher frequency of both SCC and BCC mostly on the head and the neck. A study performed in Malawi showed a surprisingly large number of malignancies in skin ulcers. It was reported that the prevalence of HIV disease, which is very high in this population may be responsible. A 3 to 5 fold increased risk of developing a non-melanoma skin cancer was reported in patients with AIDS. More aggressive types of both BCC and SCC were reported. Unique examples of burn scar ulcers are the Kangri burn cancer in India and the Kairo burn cancer in Japan. Both are a result of the use of hot coals in utensils applied to
the abdomen in order to provide heat. Many users of these devices develop SCC in the abdominal wall.207

Clinical aspects
Carcinomas that arises in repeatedly traumatized or chronically inflamed skin are called Marjolin's ulcers after Jean-Nicolas Marjolin who in 1828 described malignant ulceration in burn scars. Today the term “Marjolin’s ulcer” is used to describe malignant tumours arising in many different types of cutaneous scars and chronic wounds, such as burn scars, chronic venous ulcers and pressure ulcers.208

Signs and symptoms associated with the development of the carcinoma include a change in the scar with the formation of a mass or an ulcer, possibly with increased pain, increasing discharge, foul odour and bleeding. These symptoms may be ascribed to the colonization of bacteria in these wounds. Mean latent periods with a range of between 8 and 63 years were reported.166 Burn scar cancer occurs in areas of full-thickness or deep non-grafted burns, and has a predilection for the extremities, specifically for flexion creases of the extremities, where blood supply is decreased and trauma is increased.209

Diagnosis
In all non-healing ulceration of the skin biopsy remains the most important definitive diagnostic aid. A biopsy should be obtained from any suspicious lesion or any chronic ulceration, especially those with any recent change in appearance.210

Treatment
The first choice of treatment is generally surgery, application of adjunctive measures such as radiotherapy, chemotherapy or the use of immunomodulatory drugs depend on histopathological findings, tumour site and size, level of invasion and other specific parameters. Enlarged regional nodes should be investigated first.211-213

Neuropathic
Neuropathy may be encountered in several diseases. Neuropathy caused by leprosy and diabetes mellitus is clinically most important. Leprosy is an infectious disease caused by Mycobacterium leprae, which mainly infects macrophages and Schwann cells. Nerve invasion is a unique characteristic of Mycobacterium leprae and results in nerve damage. This usually becomes chronic and results in nerve function loss. The so called reaction may occur during the course of the disease. These reactions are episodes of acute inflammation in which the skin and the nerves may be involved
resulting in further damage to nerves. It is estimated that 20-30% of the leprosy patients have foot problems due to loss of nerve function. As a result, injury to the skin and the deeper layer of especially the feet and the hands may occur. Diabetes mellitus was once considered to be a disease of the developed World. However it has become a Worldwide pandemic with two-thirds of the global diabetic population living in the developing countries. The burden of diabetes foot problems will therefore continue to increase in the coming years. However, diabetes is not a typical tropical disease and will therefore not be discussed in this chapter. This chapter will focus on one of the most common complications of neuropathy caused by leprosy, which is plantar ulcers.

**Epidemiology**

Leprosy is still endemic in Middle and South America, in Sub-Saharan Africa and in Asia from Iran to Indonesia, on some islands in the Pacific and in the Northern Territory of Australia. The most endemic countries with 85% of the leprosy patients are India, Brasil, Indonesia, Nepal, Mozambique, Madagascar, United Republic of Tanzania, Democratic Republic of the Congo and Central Africa.

**Clinical aspects**

Damage of peripheral nerves causes function loss in the sensory, the motor and the autonomic nerve fibres. Damage to the common peroneal nerve at the side where the nerve passes around the neck of the fibula results in sensory loss of the lateral side of the leg and the dorsum of the foot. Impaired innervation of the peroneal muscles and dorsiflexors of the foot results in decreased dorsiflexion. This may result in a drop foot. Sensory loss in the sole of the foot occurs when the posterior tibial nerve is damaged, usually where it passes around the medial malleolus. Besides sensory loss, damage to the nerve also gives rise to paralysis of the intrinsic muscles of the foot resulting in a hollow foot and in clawed toes. Ulcers will occur were most pressure is applied, that is on the metatarsophalangeal heads, the PIP-joints and tip of the toes. During type-I (Reversal reaction) and type-II (Erythema Nodosum Leprosum) reaction, further damage to the nerves also may occur.

**Diagnosis**

Diagnosis is based on specific skin signs and nerve function-loss. Clinical examination of the foot may reveal changes in the shape of the foot. Sensory loss may be found by testing with monofilaments or with the two point discrimination test. Motor function should be assessed. Autonomic loss results in loss of sweating with dry skin. The presence of a plantar ulcer will result in a local
increase in temperature, which can be measured by thermometry or palpation on the dorsal side of the foot.\textsuperscript{217}

**Treatment**

The basic treatment is relieving pressure on the ulcer by means of special footwear, plaster or bed rest.\textsuperscript{218} Necrotic tissue should be removed, either surgically or non-invasively if necessary. Pathogens should be ruled out by culture of tissue. Bone should be cultured if osteomyelitis is suspected. Choice of antibiotics should be based on the outcome of the culture. There are many wound dressings available. However, there is no single wound dressing which has proved to be superior to others.\textsuperscript{194}

**Aquatic**

Water sports as scuba diving are popular among travellers to tropical countries. During such recreational activities there is a risk of contact with potentially dangerous sea creatures. The skin may be mechanically traumatized by punctures, and venom may be involved.\textsuperscript{219}

**Epidemiology**

Epidemiological data are scarce. Most data are on life threatening severe envenomation.\textsuperscript{220,221}

**Clinical aspects**

Trauma to the skin may be caused by stings (hydroids, Portuguese man-of-war, shells), puncture, suction wounds (cephalopods (Octopi)), abrasion and cuts (corals, fish spines).

**Diagnosis**

Ulcers may be traumatic or caused by punctures or lacerations and, secondary infection may occur. Pain is immediate after puncture by sting rays. Systemic reactions may occur.\textsuperscript{222} Barracudas (Sphyraena spp.) and moray eels may also strike if they are disturbed.\textsuperscript{223} Sea-urchin stings may produce injurious and venomous wounds. There are hundreds of species of the sea urchin. In some species the spines that are mostly located on the upper surface have poisonous tips. Envenomation may also be caused by the seizing organs (pedicellariae) on the lower surface. Pedicullarial stings are reported to be dangerous. However, there are little clinical data. People step on sea urchins or brush
against them. Puncture wounds may be numerous, pain is immediate and intense. The broken spines remain embedded or leave the skin unbroken. A “tattooing” pattern is frequently seen. Most of the fragments are absorbed after a while or eliminated through the epidermis. Destruction and synovitis may occur if the spines enter near a joint. The development of foreign body granulomas is a regular finding after such injuries in the skin.220,224

Treatment
Treatment is symptomatic. Several therapies are recommended by local people, but their use has never been reported in studies. It is recommended to rinse the wounds thoroughly with clean water. Vinegar may be used to inactivate nematocysts and isopropylalcohol should be used to disinfect.225 Antibiotic prophylaxis may be used. Wounds are self-limiting but secondary infection is not rare.226 Topical steroids may be useful for persistent inflammatory reactions 227.

Traumatic
Traumatic wounds can be defined as a cutaneous lesion resulting from an acute exposure to energy (mechanical, thermal, electrical, chemical or radiant). Road traffic injuries and intentional injuries (self-inflicted injuries, interpersonal violence and war-related injuries) are most important causes of traumatic wounds.228

Epidemiology
Injury is a significant health problem throughout the World. Annually 5,168000 (9% of the total deaths) people die of violence, accidents or suicides and several thousand more are injured 229 By far the largest part of the total burden of injury, approximately 90%, occurs in low- and middle-income countries.230 The risk factors for road accidents are increasing in some developing countries; for example, motor vehicle ownership may double within five years clogging the streets and the highways with inadequately maintained vehicles.231 The global burden of disease because of road traffic injuries is expected to move from the ninth position in 1990 to the third position by 2020.232 It is also estimated that if low-and middle-income countries do not act immediately, up to 1% of a country’s gross domestic product will be consumed by road traffic injuries.233
Clinical aspects

The clinical picture depends on the response of the damaged tissue to trauma. Secondary factors such as arterial or venous flow, nutritional status of the patient, the presence of auto-immune diseases, medication, diabetes mellitus and smoking will also affect the clinical presentation.

Diagnosis

A carefully obtained medical history is most important in revealing the origin of the ulcer. Attention must be paid to other factors, which may negatively affect the healing. If the ulcer is traumatic in origin, it should be defined in terms of high impact, low impact, repetitive, temperature-related, caustic, radiation-induced, type of bite, presence of drug abuse, and so on. In chronic ulcers, the age of the wound is important because long-standing wounds can be malignant (Marjolin’s ulcer). Previous topical therapy to the ulcer should be delineated because certain topical agents can contribute to the ulcer’s chronicity (e.g. caustic agents such as hydrogen peroxide, 10% iodine, Dakin’s solution and so on).

Treatment

In general traumatic wounds without damage to the underlying tissue should be treated conservatively. Necrotic tissue should be removed by surgery. The most important surgical step in treating any wound is to undertake adequate débridement to remove all foreign matter and unhealthy or nonviable tissue until the wound edges and base consist only of normal and healthy tissue. A chronic wound has to be converted by débridement to an acute wound, so that it can proceed through the normal healing phases. Deep tissue cultures should always be analyzed for pathogenic bacteria and to obtain sensitivities to potential therapeutic agents. In addition, the débrided tissue should be sent for pathological examination for confirming the specific diagnosis of osteomyelitis, vasculitis, or cancer.

Aims of the thesis

Many “tropical” doctors are familiar with slowly healing ulcers in travellers in or from tropical areas. No scientific studies have been published on this subject, but it is an observation by doctors working in the tropics or at outpatient clinics for tropical diseases in the western world. Various aspects of skin ulcers in patients in tropical areas or in travellers in and from such areas were investigated and are presented in this thesis.
Ulcers originating from the tropics show great variations. In the introduction an overview of the most frequently encountered wounds in travellers at an outpatient clinic in the western world is given. This overview is based on clinical experience and an extensive search of the literature. A guideline for clinicians dealing with “tropical ulcers” is also described.

At our outpatient clinic for tropical and imported skin diseases, serious (ulcerating) pyodermas, especially in the lower leg, are regularly encountered in otherwise healthy individuals who have visited a tropical country. There are several factors that may influence the healing of these ulcers.

Many of us are aware of oedema, which develops in the lower legs during travel, especially after arrival in tropics. It is well known that wound healing is delayed when oedema is present. In studies described in chapter 2, we hypothesized that in travellers to tropical areas, a change from temperate to hot humid climate may result in a subsequent change in the microcirculation of the dermal plexus. An adaptation to higher temperatures could lead to distension of dermal capillaries, which may cause oedema. In this study we determined the capillary filtration rate (CFR) as a measure for micro-oedema. Changes in tissue volume of the mid-calf caused by the CFR were calculated from changes in the diameter of the limb measured with a (mercury in rubber) strain gauge plethysmograph. The purpose of this study was to investigate whether CFR increased in travellers, who had recently arrived in the tropics from a temperate climate and thereby support the hypothesis that (micro)-oedema impairs wound healing.

In studies in chapter 3, we focussed on the bacterial colonisation, the resistance of the bacteria to anti-bacterial agents and the aetiology of wounds encountered in tropical countries.

Although chronic ulcers are an important cause of morbidity in tropical countries, in contrast to developed countries, little is known on the prevalence and the aetiology of skin ulcers. The prevalence and the aetiology of chronic skin ulcers was investigated in patients at the Queen Elizabeth Central Hospital (QECH) in Blantyre, Malawi in order to obtain further insight into this subject (chapter 4). Data on the history and physical examination were collected; on indication skin biopsies were taken for histological examination and bacterial cultures were set-up when infection was clinically suspected.

In studies pursued in chapter 5, a hydrocolloid dressing was tested under tropical conditions. Hydrocolloid dressings are widely used for treating wounds. However, little is known on their tolerability and efficacy under tropical conditions. Besides the financial factors, alleged increase in the frequency of wound infection may be an important reason that these semi-occlusive dressings are not used regularly under these conditions. Therefore, a clinical study in which the tolerability and the efficacy
of a hydrocolloid dressing in the treatment of venous leg ulcers under the humid and hot conditions of tropical Suriname was performed.

The import of skin ulcers caused by 2 emerging infectious diseases is described in chapters 6 and 7. Cutaneous leishmaniasis (CL) is seen as an imported skin disease, with a rising incidence in the last 20 years. It is highly endemic in some countries and travellers from these areas may be at risk. The clinical picture is diverse and may vary from one or more papules to ulcers with or without a scab. A previous Dutch study reported 49 patients with CL, in the period 1979-1989; Mediterranean countries were the most important source of infection. We were interested in investigating whether a change in this pattern had occurred in the subsequent years. The sensitivity of our diagnostic procedures, the mode of treatments and the results of treatment were examined. The incidence, the clinical picture, the treatment modalities and the response of patients diagnosed with CL from January 1990 to January 2000 at our hospital were retrospectively studied (chapter 6).

A patient who developed a Buruli ulcer after travelling in the Shan Dong Province in the People’s Republic of China is described in chapter 7. It is the first reported case of Buruli ulcer in People’s Republic of China and proves that M. ulcerans infection is also present in the temperate climatic zone in the Northern Hemisphere.

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