# Skin Disorders in Migrants

Aldo Morrone
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# Preface

Skin diseases are among the commonest of medical conditions affecting all populations and societies. Their prevalence and nature are often subject to local variations, such as social and environmental conditions. For instance, living conditions that involve severe household overcrowding and limited access to water and washing facilities favor the development of skin infections. Among migrants and mobile populations skin conditions are prevalent challenges to health. This is, in part, due to the immediate effects of travel and low-quality accommodation, but many other factors contribute to the picture. These include exposure to varying and extreme environmental conditions including severe sun exposure. Skin diseases endemic in their place of origin may also present in a new country or environment, causing both clinical confusion and the risk of wrong diagnosis. Skin problems also contribute massively to the loss of self-esteem, so often experienced by migrants and this may be compounded if there is also discrimination and prejudice directed against them in their new environment, on account of a visible skin abnormality. Overcrowding may also foster the spread of some infections, such as scabies, simply due to close contact.

Addressing these issues is an important challenge for dermatologists in all countries, as there are few parts of the world that are exempt from population mobility often with the movement of large numbers in desperate circumstances. The purpose of this book is to relate the problem, to highlight the risk of stigma and discrimination, and to bring the potential treatment solutions to the attention of a wider audience. We would like to thank all the contributors who have helped to make this work a comprehensive account of skin health among migrants for the ultimate benefit of mobile populations as our patients.

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# 1 What Does It Mean to Be a Migrant, Asylum Seeker, or Refugee: Current Global Situation

Aldo Morrone

## 1.1 The Human Rights Paradigm

Human rights are legally guaranteed protections for individuals and groups against actions that interfere with fundamental freedoms and human dignity [1]. These rights encompass a full range of civil, cultural, economic, political, and social rights and apply universally.

The international human rights framework provides an ideological construct as well as clearly articulated and widely accepted legal notions for legislative and practical responses in the realm of health and its determinants.

Respect for the basic human rights of all persons in society offers an essential and equitable basis for addressing and resolving the tensions that arise when groups with different interests interact.

International human rights instruments explicitly recognize that human rights, including specific health-related rights, apply to all persons—migrants, refugees, and other nonnationals.

Many provisions are recognized as applicable to all migrants, regardless of legal status. The denial of these rights carries a high risk that nonnationals will be socially excluded and unable to benefit from health services, with potentially severe consequences both for themselves and for their host and home communities.

In short, a human rights approach to the complex issues around migration requires that the human rights implications of any migration policy, program, or legislation be addressed.

More proactively, it requires that a human rights framework be used to consider legislative, policy, and program options. In other words, human rights would be an integral dimension of the design, implementation, monitoring, and evaluation of migration policies and programs.

## 1.2 Migration: Magnitude and Terminology

The term "international migration" encompasses a wide range of population movement, the reasons for that movement and the legal status of migrants, which determines how long they can stay in a host country and under what conditions.

Approximately 175 million people, or 2.9% of the world's population, currently live temporarily or permanently outside their countries of origin [2]. This figure includes migrant workers, permanent immigrants, refugees, and asylum seekers, but it does not account for the growing irregular or undocumented movement that is coming to characterize migration everywhere.

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Twenty million African workers live and work outside of their countries of origin, and by 2015 one out of ten African workers will be living and working outside his or her country [2].

A distinction is made between *regular* and *irregular* (*documented* and *undocumented*) *migrants*. Regular or documented migrants are those people whose entry, residence, and, where relevant, employment in a host or transit country have been recognized and authorized by official State authorities. Irregular or undocumented migrants (sometimes referred to in appropriately as "illegal" migrants/immigrants) are people who have entered a host country without legal authorization and/or overstay authorized entry as, for example, visitors, tourists, foreign students, or temporary contract workers.

There is also a distinction made between "voluntary" and "forced" migrants. Voluntary migrants are people who have decided to migrate of their own accord (although there may also be strong economic and other pressures on them to move). These include labor migrants, family members being reunified with relatives, and foreign students. Forced migration refers to "movements of refugees and internally displaced people (those displaced by conflicts) as well as people displaced by natural or environmental disasters, chemical or nuclear disasters, famine, or development projects" [3].

## 1.3 Why People Migrate: "Forced" and "Voluntary" Migrants

People have been forced to abandon their homes to escape persecution, political violence, and armed conflict throughout history [4]. What is different today, however, is the nature and health impact of armed conflict. Warfare is less about confrontations between professional armies. Rather it is about grinding struggles between military and civilians in the same country or between hostile groups of armed civilians. Increasingly wars are low-intensity internal conflicts, and they are lasting longer [5].

They are fought from apartment windows and in the lanes of villages and suburbs, where distinctions between combatant and noncombatant quickly blur [4]. As a result, civilian fatalities in wartime climbed from 5% at the turn of the century to 15% during World War I, to 65% by the end of World War II, and to more than 90% in the wars of the1990s [6]. Concomitantly, the global caseload of refugees from armed conflict worldwide has dramatically increased from 2.4 million in 1974 to over 27.4 million today [7]. The number of internally displaced persons in war-ridden countries is estimated at 30 million [8]. Growing poverty (both real and relative) is pushing people to move in search of work. Images of a better life in other parts of the world are being heralded through mass media that now reaches the most remote areas and communities. The widening disparities in wealth between North and South, and the growing need for young and relatively cheap labor in the North, suggest this migration trend will continue. The economic, demographic, technological, and labor changes taking place in many Northern countries require people to be able to move in much the same way as materials and goods are moved freely and at short notice [9, 10]. Despite these pressing factors, labor migrants are not generally considered to fall within the category of forced migrants. There is growing debate, however, as to the extent to which the lack of fulfillment of economic, social, and cultural rights also forces people to abandon their homes to seek possibilities of survival and sustenance elsewhere. In short, it is increasingly difficult to distinguish clearly between "forced" and "voluntary" migrants.

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# 2 Medical, Social, and Civic Needs of Displaced Persons

Bernard Naafs, Roderick Hay, and Aldo Morrone

The number of persons displaced from their homes, because of natural disasters as well as political unrest and war, is increasing. In addition, people are constantly looking for a better life for economic reasons, particularly where, in their home country, the opportunities to live even under the lowest of standards are scarce. According to the International Organization for Migration (IOM), 241 million people are living away from their domicile, a staggering figure that represents about 3% of the world population [1, 2]. Frequently, they are motivated by the recognition that the future of their whole family, most of whom have either remained at home or been displaced within the region, depends on them and their ability to support them through sending them money, earned elsewhere, as their core means of assistance. This burden is increased by an often misleading vision that they and their families have of the conditions and opportunities in a favored destination, Western countries (Europe and North America), countries in which they are frequently unwelcome for a variety of reasons. They travel using either their own money or money borrowed from their families and friends and, notwithstanding the difficult and hazardous journey, are often subject to robbery, abuse, and exploitation at the hands of people traffickers; this often continues in the destination countries. They are witness to the misery of fellow travellers through death, abuse, and confusion. Unsurprisingly, all this has a profound influence on their mental state [3].

When they finally reach the "West," they often don't feel welcome [3]. They fear being sent back or referred to a refugee camp or center and that, when they do receive permission to stay, they cannot find the jobs appropriate to their training. They may not realize or discover too late that their previous education was not of a standard required for a similar job in their destination country. This may be difficult for them to accept. This in turn reenforces their sense of exclusion from society, and as a result, they start to live in a social subdivision determined by religion, ethnicity, family, and country of origin. The customs, attitudes, language, and behaviors of their new society may be foreign to them. Unfamiliarity with the new social mores means that they do not know how to act and are at risk of loss of self-respect and further alienation from the society of the country of arrival. Coming from countries

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where representatives of authority cannot be trusted, they do not trust those in the new countries either. The overall experience of the refugee, of the migrant, is often one of loss of self-respect and social exclusion leading to discontent, despair, and assimilation into a subculture where poverty, ill health, addiction, and crime are major risks. Their experiences during the journey and those after arrival will define the way they cope with ill health and express their needs.

At the end of 2016, 65.6 million people were displaced from their homes due to conflict, persecution, or human rights violations (UNHCR) [4]. This vulnerable population group bears a disproportionate burden of disease, particularly skin diseases ranging from STDs, scabies, pyoderma, and keloids to leprosy, leishmaniasis, and genetic and autoimmune diseases. Poverty, lack of rudimentary sanitation, stress, overcrowding, and poor nutrition all contribute. The sheer extent of human displacement has turned migrant health into a global priority for public health intervention, an issue rendered more complex by the diversity of the populations involved that range from people in search of work or education to more vulnerable groups including asylum seekers and refugees [2].

It is not that in the Western societies the majority of the population do not sympathize with the displaced, but to many, their behavior and customs are alien and unfamiliar and the sheer numbers alarming. They also have little knowledge of the nature of the migrants' needs and experiences and do not understand and, often, do not accept their behavior.

In the Netherlands, for example, migrant health has been the subject of sustained and systematic attention since 2000, while Italy has been setting migrant-related health policy targets since the 1990s. The UK has long been a destination for migrants, and although difficulties in accessing appropriate care continue to be experienced by new entrants, it is a matter of record that migrants and their children have made significant contributions as employees to the UK National Health Service and many other professions and occupations. This is not the experience of all migrant groups, and some have remained in relatively isolated subcultures. Spain has begun to include migrant health and health-care issues in national and regional plans for the integration of immigrants from 2007 [2]. Other countries still have to start or are in the process of developing policies and programs for migrant health.

Is migrant health care, general and specialized, a major priority? From a host country perspective, it is. Many need care and in addition a few bring infectious diseases into their new country. Do migrants also feel like the same? Do they want the care that we think they need?

While there is no absolute definition of "need" versus "want," we must recognize what is essential. Abraham Maslow's description of a "hierarchy of needs" provides a different way to think about categories that are fundamental [5]. Absolute priorities include the physiological need of food, water, shelter, and physical safety. Other recognized needs are additive and secondary, such as self-esteem, self-actualization, and the feeling of being healthy, including having a healthy skin.

Economic survival is the major issue for the migrant, and this imperative cannot be thought of simply in terms of survival due to external support. Self-support, through their own efforts, is key to restoration of dignity. However, this self-sustainment may be difficult to achieve due to three main reasons. Firstly, migrants and refugees may be subject to illegal treatment including enslavement or receive pay below minimum national levels since their professional qualifications are not accepted by regulatory bodies or they remain out of sight of national agencies because they have evaded immigration controls. They become a huge labor pool which can be exploited, in particular when they are "illegal" entrants. Secondly, they may be subject to discrimination based on race, ethnic origin, language, religion, and accent that prevents them from getting jobs that match their qualifications or from being paid the appropriate wage. Thirdly, there is the cultural and language barrier for those who don't speak the local language adequately

and who do not behave as the locals. They are outsiders and in recognition set themselves apart [6, 7].

What does this mean for us as dermatologists. As human beings, we have a duty of care to the distressed, a duty also explicit in medical ethics. How best can we contribute? In general their medical needs are apparent soon enough. But restricting care to their medical needs alone is seldom sufficient. Treating the whole person and meeting their needs and expectations, although usually not great, are sometimes beyond our medical and even social abilities. There is not only the patient to consider but their support networks of family or friends too, again often an unrealistic demand on the dermatologist's position and skills. The refugee may be accompanied by a helper who is either a professional or lay person who may have his own reasons for accompanying the patient, and these individuals may also have their own agenda. The patient is caught between the two and will react the way he or she thinks is expected of him or her. The job of the dermatovenereologist is to help and mediate.

Solving all this is not simple. The ideal approach is a holistic one which requires translators, sociologists, anthropologists, psychiatrists, and experts in migrant problems and attitudes. When one is the only doctor attending the patient, it is good to realize one's limitations, despite a sound knowledge of dermatology and/or venereology. So be empathic, be aware of your limitations, whenever possible make use of a translator, and try to contact experts who may be better placed to understand the other needs of this human being who has sought your help.

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# Viral Dermatoses

3

Stefano Veraldi, Luisa Angileri, and Luisa Carlotta Rossi

## 3.1 Herpes Simplex Virus Infections

Only one epidemiological study on herpes simplex virus 1 (HSV-1) infections in migrants has been carried out [1]. In 2004, 152 Albanian migrants to Apulia (Southern Italy) responded to a questionnaire based on the European Community Respiratory Health Survey (ECRHS), and 59 out of 61 (96.7%) migrants had anti-HSV-1IgG [1].

Epidemiological studies on herpes simplex virus 2 (HSV-2) infections in migrants have been conducted in Malawi [2], China [3], Zambia [4], India [5], and Tanzania [6].

HSV-2 prevalence trends in the Karonga district (Malawi) were assessed in 1988–1990, 1998–2001, and 2002–2005.HSV-2 prevalence in these periods increased sharply with age and was higher in women than in men [2].

In 2009, in Shanghai (China), the overall HSV-2 seroprevalence was 5.5% in male rural migrants working in construction sites, markets, and factories, 5.4% in subjects reporting having had sexual intercourses, and 5.8% in subjects reporting no sexual intercourses [3].

Male farm workers were recruited from a sugar estate in Zambia to attend a prospective cohort study. Questionnaire data were collected via interview, and tests were carried out for HSV-2 at baseline and follow-up between May 2006 and September 2007. Among 1062 workers enrolled, positive HSV-2 tests were 95% [4].

Dave et al. [5] carried out in 2012 a survey on migrant men aged 18–49 years working in the diamond and textile industries in Surat (India). Laboratory tests included anti-HSV-2 antibodies. The response rate was 77% (845/1.099). Among 841 participants, "any sexually transmitted infections (STIs)"prevalence was 9.5%: 38.9% of these STIs were likely to have been recently acquired. STIs were diagnosed in some self-reported virgins. HIV and STI prevalence were lower than expected. The results of this study showed that migrants are not always at higher risk of HIV compared to the general population in their migration destination [5].

Little is known about men's experience with physical intimate partner violence (IPV), particularly in sub-Saharan Africa. In Tanzanian male migrant plantation residents, the prevalence of, and associations among, experience and enactment of physical IPV and prevalent STIs/HIV were studied. Data from 158 male plantation residents were analyzed to estimate prevalence of physical IPV experience and enactment. The

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authors assessed associations between IPV and sexual risk behaviors and HSV-2. Overall, 30% of men had experienced and/or enacted physical IPV with their main sexual partners: 19% of men had ever experienced physical IPV with their main sexual partners; 22% had enacted physical IPV with their main sexual partners. Considering overlaps in these groups, 11% of all participants reported reciprocal (both experienced and enacted) physical IPV. In addition, 51% of men were HSV-2 positive. Men's physical IPV experience and enactment were therefore common in these migrants. Physical IPV can be considered as an important risk factor for STI/HIV transmission [6].

## 3.2 Human Papilloma Virus Infections

Human papilloma virus (HPV) infections have been studied in migrants who reached in the last years' Spain [7, 8] and Italy [9–12].

A study on migrant female sex workers attending an STI clinic in Madrid was carried out in 2002 [7]. Data on sociodemographic characteristics, reproductive and sexual health, smoking, time in commercial sex work, history of STIs, hepatitis B and C, HIV, syphilis, and genitourinary infections were collected. HPV infections were recorded by Digene HPV Test and Hybrid Capture II. A total of 734 women were studied. STI prevalence was 11% and was not related to age or geographical origins. Overall HPV prevalence was 39%: 61% in Eastern Europeans, 42% in Ecuadorians, 39% in Colombians, 29% in sub-Saharan Africans, and 24% in Caribbean. HPV prevalence showed a decreasing trend by age: 49% <20 years, 35% in 21–25 years, and 14% >36 years. Area of origin, hormonal contraception in women not using condoms, smoking, age, and an interaction between these last two variables had statistically significant associations with HPV prevalence [7].

An additional Spanish study was performed in order to evaluate prevalence and determinants of high-risk HPV by countries of origin in women attending a family planning center in Alicante from May 2003 to January 2004. High-risk HPV infections were recorded by Digene HPV Test, Hybrid Capture II, and PCR. High-risk HPV prevalence in 1011 women was 10%. Compared to Spanish women (prevalence 8.2%), high-risk HPV prevalence in Colombians was 27.5%, 23.1% in Ecuadoreans, and 22.73% in women from other South American countries. Women with more than three lifetime sexual partners had an increased risk of high-risk HPV infections. The most common HPV types in women with normal cervical smears were HPV-18 (20%), HPV-16 (14%), and HPV-33 (11%) [8].

The aim of the first Italian study was to evaluate the spectrum of HPV genotypes and prevalence of cervical abnormalities in foreign women who emigrated to Southern Italy. The study included 233 migrant and 98 Italian-born women who self-referred to two gynecological outpatient clinics in the Campania region. Cervical specimens were subjected to cytological examinations and viral tests by PCR. The prevalence rates of HPV infections were 57.9% and 94.1% in migrants and 19.4% and 88.5% in Italian women with normal and abnormal cytology, respectively. HPV infections were detected in 56.1% of Southern and Eastern European, 62.5% of Central and South American, 55.5% of West African, and 73.3% of Southern Asian women with normal cervix. In the 140 HPV-positive migrants, a total of 28 HPV genotypes were identified, of which 11 types (HPV-16, HPV-18, HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-51, HPV-52, HPV-56, and HPV-58) accounted for 73.4% of all infections. HPV-16 was the most common type in all groups with frequency rates ranging from 12.5% in African to 30.1% in Eastern and Southern European women [9].

All studies are concordant on the high rate of HPV infections in migrants to Italy, which is four times higher than that observed in age-matched Italian women. The HPV prevalence in migrants and characterization of viral variants showed that the high prevalence of HPV reflects either indi-

vidual lifestyle or high prevalence of HPV in the country of origin. The high burden of HPV infections correlates with the high incidence of cervical cancer in migrant women. During the years 2000–2004, the cervical cancer incidence in women from Central and Eastern Europe and living in Central Italy was 38.3 per 100,000, which is statistically higher than that of native Italian women (6 per 100,000). In this study, the authors pooled together the results of three independent studies originally designed to assess the distribution and prevalence of HPV genotypes in 499 immigrant women living in Southern Italy. A total of 39 HPV genotypes were identified. The 12 genotypes (HPV-16, HPV-18, HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-51, HPV-52, HPV-56, HPV-58, and HPV-59) accounted for >80% of all infections. HPV-16 was the most common viral type in all groups with frequency rates ranging from 15.4% in African to 51.1% in Eastern and Southern European HPV-positive women [10].

HPV type-specific distribution was evaluated in genital samples collected from 151 women from West and East Africa, living in the Asylum Seeker Center in Bari. HPV-DNA was studied by Linear Array HPV genotyping test. HPV DNA was detected in 39.1% of women, 42.5% of whom had multiple infections and 69.5% had high-risk HPV infections. Age-prevalence rates showed a peak of HPV infections in women ≤20 years of age (53.1%). HPV-53 and HPV-16 were the most common types (13.5% and 12%, respectively). Abnormal Pap test results were found in 4.4% of women [11].

A single-center, prospective, observational study was conducted in migrant women who attended an outpatient clinic in Messina, between January 2003 and December 2013. Participants underwent gynecological examinations and cervical smear tests. Patients who showed cytological abnormalities underwent HPV typing by PCR and allele-specific hybridization. A total of 724 women were enrolled, of whom 320 (44.2%) were pregnant. The mean age was 33.1 ± 9.8 years. Cytological abnormalities were recorded in 76 (10.5%) women. Among 46 women who attended a follow-up, 32 (69.6%) were positive for HPV serotypes [12].

## 3.3 Pityriasis Rosea

Pityriasis rosea is common in sub-Saharan Africa [13–15]. In Nigeria, the incidence ranges from 2.4 to 4.8 per 100 patients with skin diseases [13–15]. At the Dermatology Unit of the University of Milan, we have had the opportunity to visit several migrants with pigmented skin, the majority of them coming from sub-Saharan Africa, affected by pityriasis rosea. Although the herald patch is similar to that which may be observed on Caucasian skin (Fig. 3.1), the rash that follows is characterized by gray, brown, or even black lesions [16]. Furthermore, it is not rare the location of post-herald patch lesions on the forehead and retro-auricular folds [13–17]. After the skin lesions resolve, hypopigmented macules can persist for several months [16] (Fig. 3.2). Oropharyngeal lesions (asymptomatic erythematous, macular, papular, vesicular, and petechial lesions) are likely more common in patients with pigmented skin [13–18].

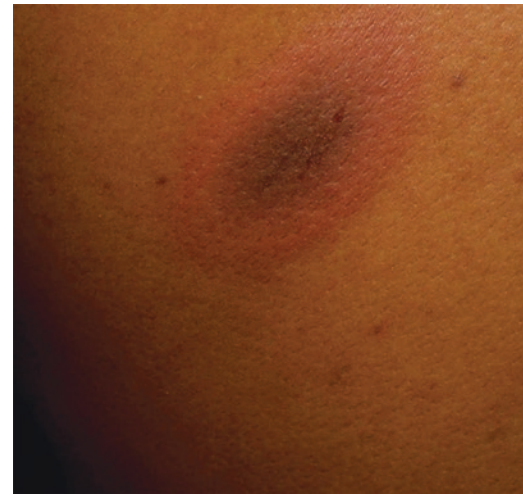

**Fig. 3.1** Lesion of pityriasis rosea in active phase

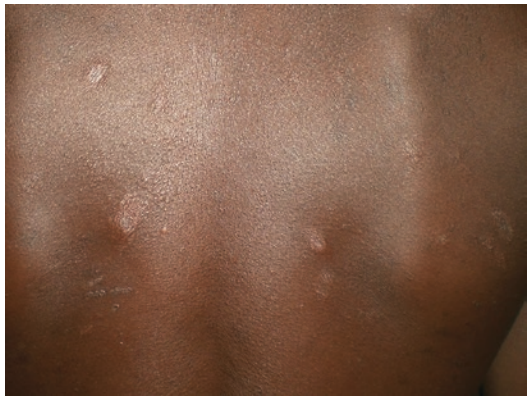

**Fig. 3.2** Pityriasis rosea after resolution step

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# Bacterial Dermatoses

4

Bernard Naafs, Federica Dassoni, and Aldo Morrone

## 4.1 Introduction

Migrating is a challenge to health. This may seem a bold statement, but it is not.

The migrant may leave "home" being healthy, or he may already harbor acquired infections. He or she may be also infected during the travel via insect bites, small scrapes, sexual activity, or simply by being exposed. The genetics together with the immune system will determine his or her condition and whether a clinical disease will develop.

Bacterial skin infections are often seen among migrants arriving from Africa and the Middle East, living in refugee camps or under poor conditions in Western countries [1–5]. Superficial pyodermas, including impetigo, and impetiginization of dermatoses such as eczema, scabies and insect bites, folliculitis, furuncles, carbuncles, and suppurative paronychia are regularly encountered. Common are also erythrasma, involving the upper epidermis, and erysipelas, involving the deep dermis and the hypodermis.

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*Staphylococcus aureus* (*S. aureus*) is the main pathogen, but group A beta-hemolytic *Streptococcus* (*S. pyogenes*) is a good second. *S. aureus* is not a permanent part of the skin flora, but it may colonize moist and inflamed skin. *S. aureus* may produce exfoliative toxins responsible for blistering, as seen, for example, in bullous impetigo and staphylococcal scalded skin syndrome (SSSS), by cleaving the cell adhesion cadherin desmoglein 1 [1, 6].

The risk that the migrant brings with him a resistant staphylococcus is high, as bacterial resistance to antibiotics is frequent in most countries migrants are coming from. Since the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA), these clones have spread all over, particularly in the developing countries. Other bacteria such as Proteus, *Pseudomonas*, and Coli are frequently resistant too and may contaminate the skin and mucosae and lead to infections [7].

Group A beta-hemolytic streptococci (*S. pyogenes* A, C, G) are present in the oral cavity, in 10% of the population on the perioral area too [1]. In hot climate and travelling or living under poor conditions, the skin is easily contaminated and infected, particularly via insect bites and small abrasions. Skin carriage in healthy individuals under normal conditions is rare. M proteins, pyrogenic and erythrogenic exotoxins (SPE), and streptolysin are the main virulence factors of these streptococci [8].



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## 4.2 Clinical Features

### 4.2.1 Impetigo

It is a contagious infection of the skin, involving the stratum corneum, usually caused by *S. aureus* or less frequently *S. pyogenes* or both. It is particularly common in children under disadvantaged conditions, such as on the move. Self-inoculation and small family or community outbreaks are frequent [1]. The diagnosis is primarily based on clinical examination. Early lesions are isolated or confluent vesicles and blisters, followed by erosions and yellowish ("honey-colored") or brownish crusts [1]. A typical location in children is around the mouth (Fig. 4.1), but all areas of the skin may be affected. There are usually no systemic symptoms such as fever, although there may be an involvement of the draining lymph nodes (Fig. 4.2). Two types are described: (1) crusted impetigo due to *S. aureus* or *S. pyogenes* (Fig. 4.1) and (2) bullous impetigo (Fig. 4.3), due to the cleavage of very superficial epidermal layers by a staphylococcal toxins; this can either result in disseminated bullae (SSSS) (Fig. 4.4) or stay more limited. Both bacteria should however be considered when prescribing treatment [1].

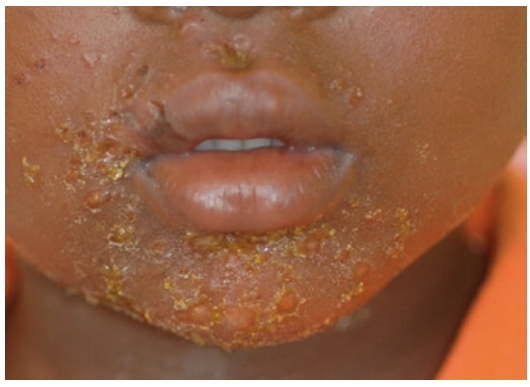

**Fig. 4.1** Around mouth honey crust impetigo

**Fig. 4.2** Lymphnodes in impetigo

### 4.2.2 Ecthyma

It is frequent among migrants with poor hygiene. It is a necrotic complication of impetiginization, particularly due to streptococci, and is clinically characterized by deep dermal ulcerations covered by roundish dark crusts (Fig. 4.5).

### 4.2.3 Folliculitis and Furuncles

Folliculitis and furuncles are acute hair follicle infections due to *S. aureus*. They are characterized by scattered or extensive follicular pustules, surrounded by erythema (Fig. 4.6). It is an infection of the ostium in superficial folliculitis and infection of the entire hair follicle in furuncles. In superficial folliculitis, other strains of staphylococcus or other microorganisms such as *Candida albicans* or *Pityriosporum* may be involved (Fig. 4.7). Apart from factors such as humidity and heat, folliculitis and furunculosis are more frequent in patients with immunosuppression,

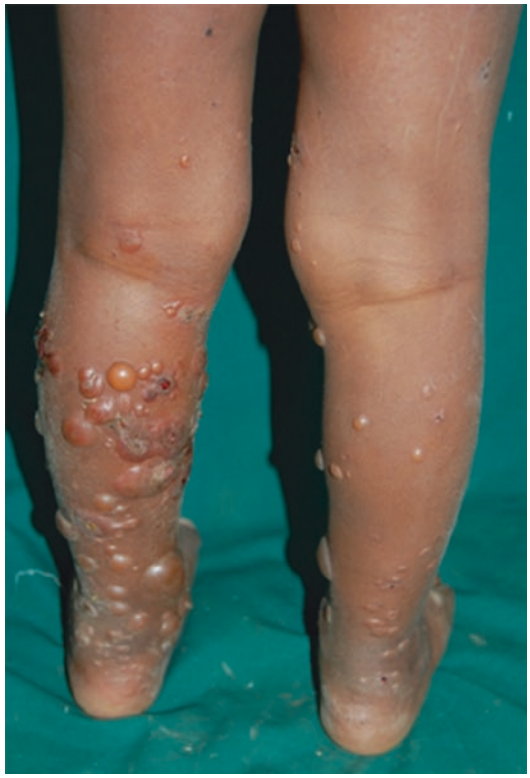

**Fig. 4.3** Bullous impetigo

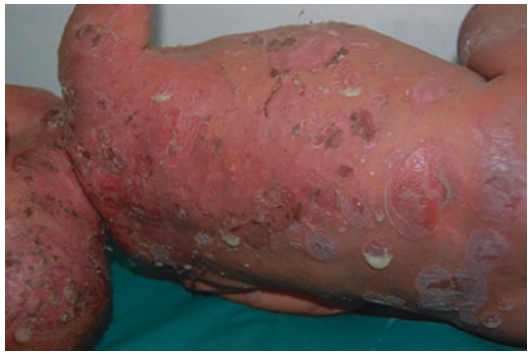

**Fig. 4.4** SSSS

diabetes mellitus, long-term antibiotic use, being on the move, obesity, wearing occlusive clothes, or frequent shaving practice, especially in pubic area. The latter two are prevalent among the migrants and even obesity in some elderly from the Middle East. A furuncle (boil) may be caused by PVL (Panton-Valentine leukocidin)-positive staphylococci. PVL is one of the β-pore-forming

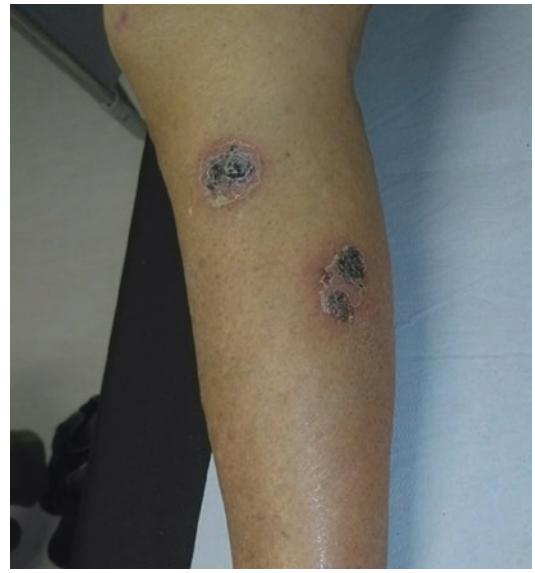

**Fig. 4.5** Ecthyma

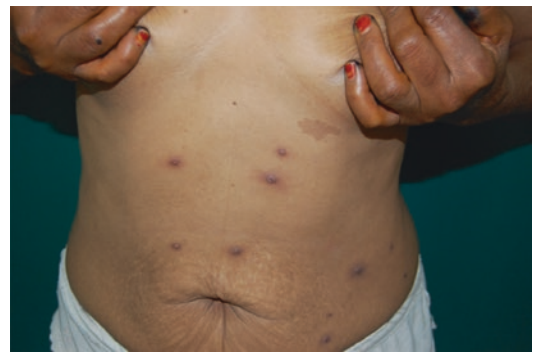

**Fig. 4.6** Furuncles

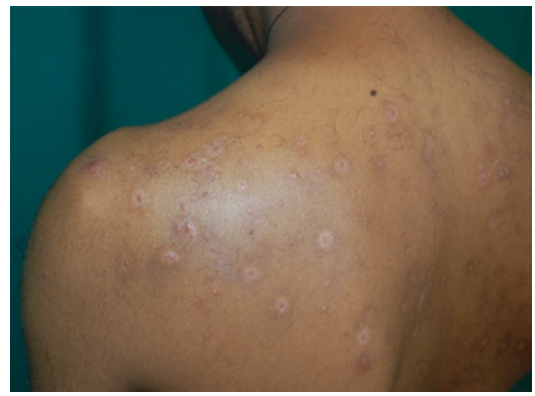

**Fig. 4.7** Superficial folliculitis

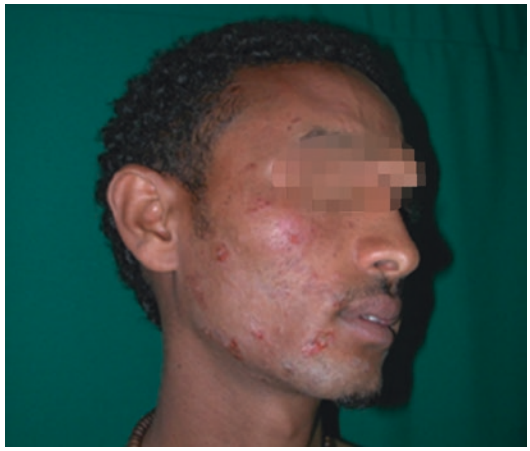

**Fig. 4.8** Papule evolving in follicular necrotic core

toxins. The presence of PVL is associated with increased virulence. It is present in the majority of community-associated methicillin-resistant *S. aureus* [9, 10]. Chronic furunculosis is frequently associated with nasal carriage of *S. aureus* [1].

The staphylococcal infection of the entire hair follicle (furuncle) starts as an inflammatory papule and then a painful nodule with a central follicular pustule leading to spontaneous necrosis and suppuration with discharge of the necrotic core (Fig. 4.8). After healing, it leaves a permanent scar. Lesions may be single or multiple, involving the face, buttocks, arms, thighs, and anogenital area. There may be occasionally fever, but systemic complications are rare [1]. The presence of furuncles on places of friction in migrants is not unusual. Chronic furunculosis is the recurrence of furuncles over a number of months and is favored by migrating under extreme circumstances, obesity, diabetes mellitus, immunodepression, iron deficiency, alcoholism, and malnutrition [1]. Staphylococcal nasal carriage and exposure to an infected travel or family member are however the main risk factors. Antiseptic decontamination is most important in order to avoid recurrences.

In (acne) patients in whom treatment with tetracyclines has not shown an improvement after 3–6 months, a Gram-negative infection should be considered [1]. An important differential diagnosis is pseudo-folliculitis (pili incarnati), which

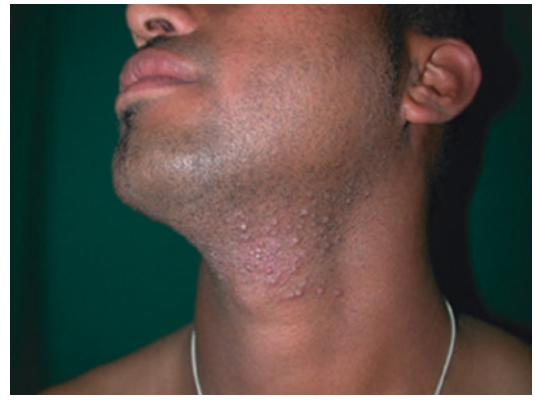

**Fig. 4.9** Pseudo-folliculitis

results from the penetration into the skin of the shaved, newly growing hairs. This condition commonly affects people with curly hair. Papules and pustules may lead to scars and post-inflammatory hyperpigmentation especially in Africans (Fig. 4.9). A similar condition, acne keloidalis nuchae, may occur on the scalp and lead to keloidal lesions; this is discussed in a different chapter.

### 4.2.4 Carbuncles

Carbuncles are aggregations of furuncles which form broad, swollen, painful, and often fluctuant nodules and deep masses with spontaneous multiple pus draining tracts. Patients are often febrile and unwell [1].

### 4.2.5 Abscess

An abscess is a collection of pus. The abscess starts as a painful inflammatory nodule or erythematous plaque. After a few days, palpation shows fluctuation indicating a purulent collection (Fig. 4.10). Fever is rare, but lymphangitis and satellite lymph nodes could be found. The majority of spontaneous abscesses are caused by *S. aureus* producing PVL. Secondary abscesses (due to accidental inoculation) are most often also, but not exclusively, due to *S. aureus* [11, 12].

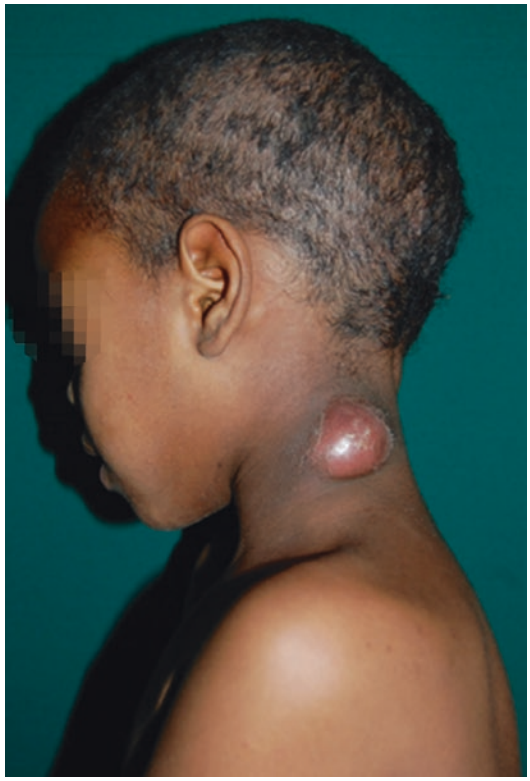

**Fig. 4.10** Abscess

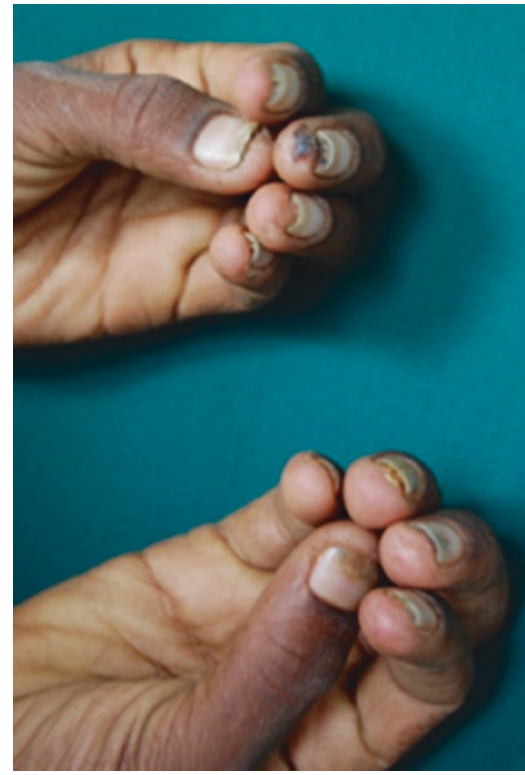

**Fig. 4.11** Paronychia

### 4.2.6 Suppurative Paronychia

Suppurative Paronychiais a superficial infection or abscess of the perionychium. Nail biting, finger sucking, aggressive manicuring, and other trauma to the nail are the most frequent causes for a portal of entry of the bacteria. *S. aureus* is the most frequent causative agent, followed by *Streptococcus*, *Pseudomonas*, anaerobes, and other microorganisms such as *C. albicans* and *Herpes simplex*. Acute paronychia must be differentiated from chronic paronychia, which is usually nonsuppurative and due to multiple physical external causes (wetness) and/or *Candida albicans* (Fig. 4.11) [1]. The patient complains of pain and tenderness of the perionychium that appears swollen, purulent, or even fluctuant. The nail may be altered. Differential diagnosis includes acrodermatitis continua of Hallopeau.

### 4.2.7 Erythrasma

Erythrasma is a superficial infection usually localized in the large folds, especially axillae and groins (Fig. 4.12), due to coryneform bacteria (*Corynebacterium minutissimum*), which belong to the normal skin flora. Travel in warm and humid climate, age, and diabetes mellitus are predisposing factors. Lesions are large, red, brown, or hyperpigmented patches, sharply demarcated. They may be either asymptomatic or are pruritic and consequently complicated by lichenification. Coral-red fluorescence with Wood's light, due to coproporphyrin III, suggests the diagnosis, although it does not necessarily indicate active infection [1, 13]. The many differential diagnoses include pityriasis versicolor, fungal intertriginous infections (dermatophytosis, candidiasis), eczema, and psoriasis. Thus, mycological (KOH) and bacteriological scraping (stain with Diff-Quik or a similar stain) may be

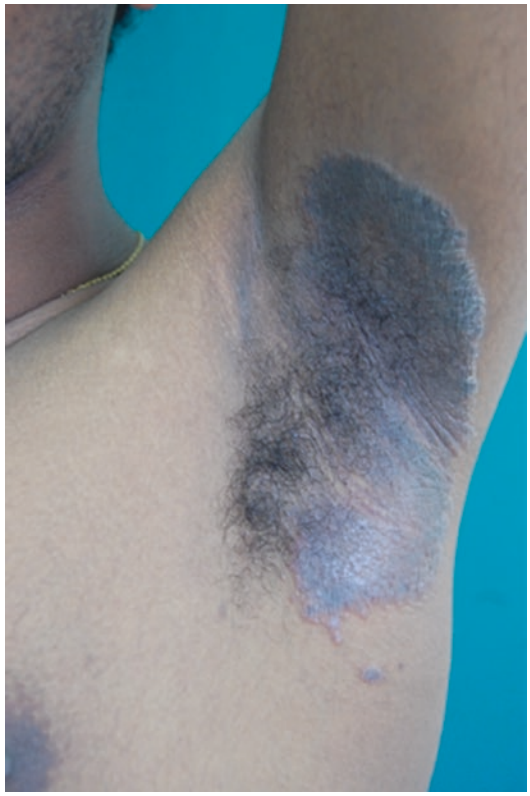

**Fig. 4.12** Erythrasma

useful. A skin biopsy may be required if there is any doubt, but usually clinical and Wood's light features are typical enough to make the diagnosis.

### 4.2.8 Pitted Keratolysis

Corynebacteria may also cause pitted keratolysis, characterized by crater-form pitting (1–5 mm in size) that primarily affects the pressure-bearing aspects of the plantar surface of the feet (Fig. 4.13). The use of boots or closed shoes may predispose. It occurs particularly under hot, wet, and unhygienic circumstances which the migrant may encounter [13]. Also other bacteria may be involved such as *Micrococcus (kytococcus) sedentarius, Dermatophilus congolensis*, and *Actinomyces*. These microorganisms produce under favorable situations (hot, moist) enzymes that attack the stratum corneum. The skin may look whitish or

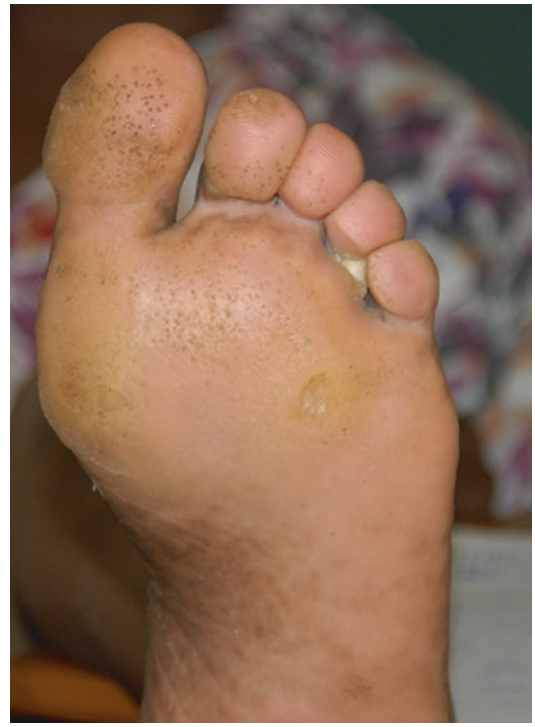

**Fig. 4.13** Pitted keratolyses

brownish and is smelly (sweaty feet); there is maceration. Sometimes it may also occur on the hands and shows a superficial collarette scaling [1]. Differential diagnosis includes dyshidrosis lamellosa sicca and tinea manuum. It may be associated with erythrasma and trichomycosis axillaris (also *Corynebacterium* infections) (Fig. 4.14).

### 4.2.9 Erysipelas

Erysipelas is an acute superficial well-demarcated dermal infection that to date usually affects the lower leg and is caused by streptococci (Fig. 4.15). It is extremely painful and the patient has fever and is ill. In contrast with the life-threatening condition necrotizing fasciitis (Figs. 4.16 and 4.17), erysipelas does not involve deep fascia and muscles. However, there is often confusion between erysipelas and cellulitis [1]. The latter is an inflammation of cutaneous and the subcutaneous tissue. It is particularly present in elderly people on the move. Whereas necrotiz-

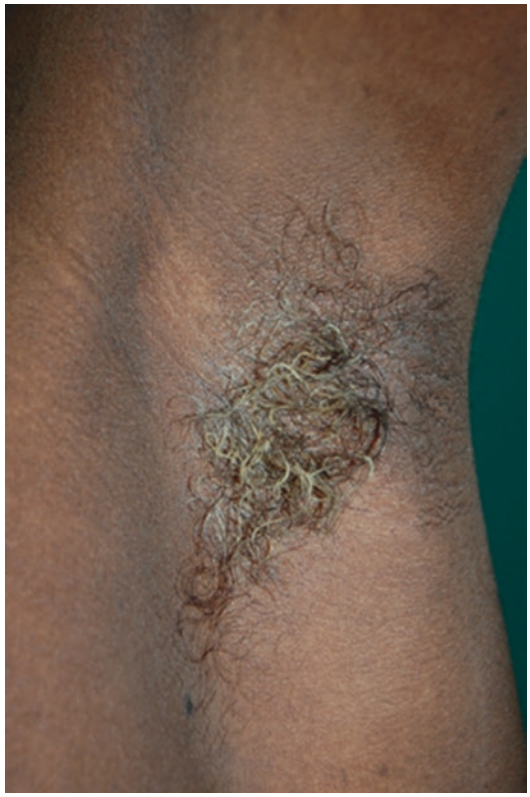

**Fig. 4.14** Trichomycosis axillaris

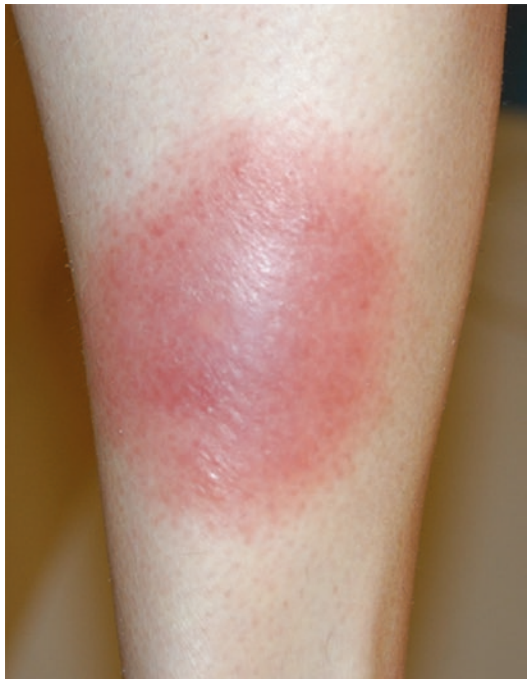

**Fig. 4.15** Erysipelas

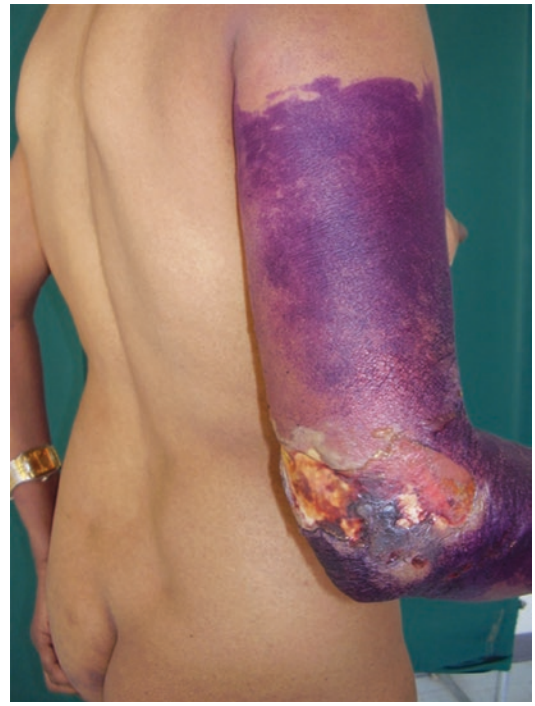

**Fig. 4.16** Necrotizing fasciitis

ing fasciitis often has a multi-bacterial origin, almost all erysipelas are due to streptococcus group A (the most frequent), C, and G. However, streptococcus B may be involved in perianal cellulitis particularly in postpartum women or in infections of the newborn. Legs are the main site involved, particularly in women, followed by the face and the upper limb. A portal of entry should be present, e.g., an ulcer, a small wound, or toe-web intertrigo. This toe-web intertrigo is the most important port of entry for particular streptococcus infections and leads via repeated episodes of erysipelas to lymphostatic edema.

The onset of the disease is in general sudden with chills, fever, and malaise. Locally, erysipelas is characterized by a large erythematous, mildly infiltrated, well-demarcated lesion. Regional adenopathy is frequent. Superficial blistering secondary to edema, sometimes with superficial hemorrhage, may be observed [1]. The following local and/or general signs are suggestive of necrotizing fasciitis and must not be ignored because of the risk of a rapid deterioration:

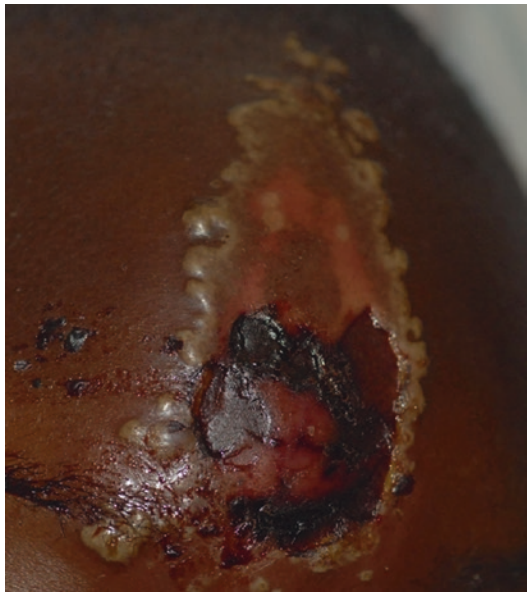

**Fig. 4.17** Necrotizing fasciitis (courtesy RDTC)

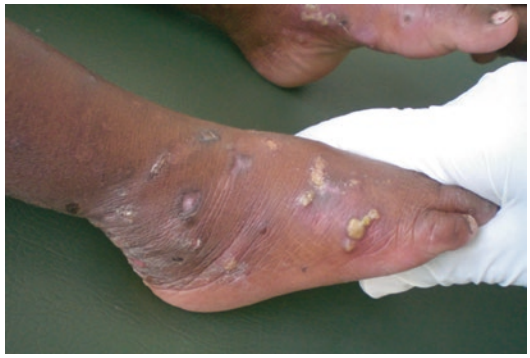

**Fig. 4.18** Dermal deep blisters

a. Hemodynamic instability, intensive pain, or, in contrast, local anesthesia.
b. Muscular pain or functional impairment.
c. Deep dermal blisters with no bleeding after incision (Fig. 4.18).
d. Livedo or extensive ecchymosis.
e. Necrosis.
f. Crepitation.
g. Gas effusion (cave: *Clostridium perfringens*) [1, 14].

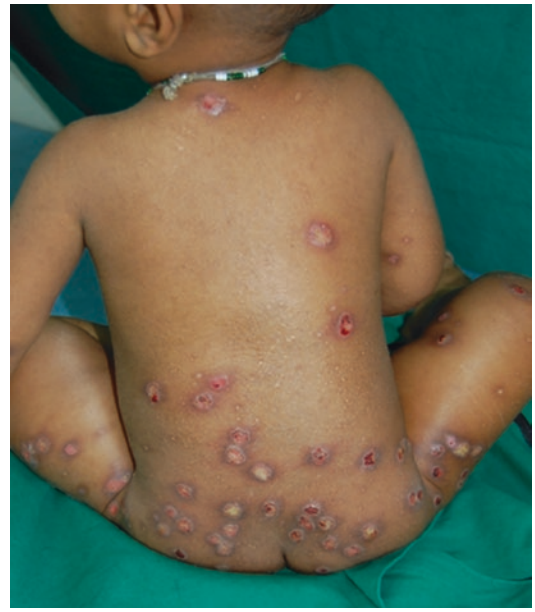

**Fig. 4.19** Postinfectious glomerulonephritis

In practice, intermediate presentations between classical erysipelas and necrotizing fasciitis may occur, requiring close clinical monitoring [1]. No laboratory test is warranted in uncomplicated cases. Bacteriological cultures are usually negative in erysipelas. The pathology shows vascular ectasia.

### 4.2.10 Systemic Complications

Without treatment, crusted impetigo usually resolves without sequelae within 2 weeks. Although systemic complications of impetigo in children are rare in developed countries, infectious or postinfectious glomerulonephritis may occur after extensive, chronic, neglected streptococcal or staphylococcal pyodermas in patients with risk factors such as being child, being on the move, or living under adverse conditions. Glomerulonephritis is a major complication of scabies-related streptococcal impetigo (Fig. 4.19) [15]. Other complications may include sepsis, osteomyelitis, arthritis, endocarditis, lymphangitis, erysipelas, guttate psoriasis, and SSSS.

## 4.3 Management

Treatment of *impetigo* not due to streptococci includes improvement of the hygiene with daily washing particularly the hands, cleaning nails, and frequent changing of clothes. These measures are helpful but mostly impossible when you are traveling. Washing lesions with water and soap or topical antiseptics (povidone-iodine, chlorhexidine, potassium permanganate) or applying gentian violet is usually sufficient for limited lesions. However, topical antibiotics are considered by some the treatment of choice [1]. Topical fusidic acid and mupirocin seem to have a comparable effectiveness and are as effective as oral flucloxacillin [16]. However fusidic acid is not that effective against streptococci and induces early resistance. Moisturizing ointments are useful to remove crusts and enhance healing [1]. When a streptococcal infection is suspected or when painful erythema or a nonhemolytic streptococcus occurs together with itch, a systemic antibiotic should be used. Similarly, when lesions are extensive, systemic antibiotics against both *S. aureus* and *S. pyogenes* are required, such as cloxacillin, amoxicillin-clavulanic acid, first- or second-generation cephalosporin, and/or fusidic acid. Because of the emerging resistance of *S. aureus*, macrolides (azithromycin) may be used as second-line drugs or where there is intolerance or allergy to the beta-lactams [1]. Erythromycin should be given with caution, since QTc interval prolongation and torsade de pointes (TdP) arrhythmia have been described as side effect [1, 17]. The current increasing resistance of *S. pyogenes* to macrolides must be taken in account in migrants from developing countries. Luckily there is hardly resistance to penicillin, and clindamycin remains a good alternative in case of allergy to penicillin.

When superficial *folliculitis* occurs, any external cause should be removed or controlled, if possible. Cleaning with water and soap (Betadine shampoo) and/or antiseptics (chlorhexidine, potassium permanganate, and benzoyl peroxide) with a broad antimicrobial activity is effective in most cases. Topical antibiotics such as mupirocin or fusidic acid are usually effective twice a day for 5–7 days [18]. Systemic antistaphylococcal antibiotics are only recommended in severe cases.

In the acute phase of *pseudo-folliculitis*, shaving should be stopped for several weeks until improvement. Topical treatments such as erythromycin, clindamycin or fusidic acid, antiseptics, or tretinoin can be useful. Shaving must subsequently be performed only superficially, leaving hair 0.5–1 mm long. Hair removal with chemical depilatories may be effective, and laser, if available and affordable, provides long-term remission, especially for beard folliculitis in patients with dark skin [1].

Lesions of Gram-negative folliculitis usually cure either spontaneously or with antiseptics such as acetic acid, chlorhexidine, povidone, and potassium permanganate within a few days. Silver sulfadiazine cream may be useful, but other topical anti-Gram-negative antibiotics are disappointing [1]. The treatment of tetracycline-induced Gram-negative folliculitis occurring during the treatment of acne is isotretinoin [19].

For *furuncles* and *carbuncles*, after incision and drainage, systemic antistaphylococcal antibiotics such as oxacillin, cloxacillin, or flucloxacillin could be prescribed for 5–7 days. This may be associated with topical antibiotics applied on the lesions and the surrounding skin. Tight clothes rubbing the skin must be avoided. Hygiene measures as far as possible should be enforced: clean clothes, handwashing, and cleaning of the nails. Washing with soap and/or antiseptics should be done regularly. In case of recurrences, an underlying condition must be sought for: staphylococcal nasal and extra nasal carriage in the patient or his household and travel members. But also diabetes and immunodepression should be considered and treated [1]. Nasal carriage is found in up to 80% of the patients with recurrent furunculosis [19]. Carbuncles require the same antibiotics approach as furuncles associated with surgical excision or incision.

Due to the risk of spreading in his close environment, the staphylococcal carriage [20] must be treated in the patient and if possible in his family, his travel, and household contacts. Recolonization is frequent. Prevention of bacte-

rial spread is based on hygiene, not sharing of personal clothes, regular handwashing, and decent housing. Decontamination procedures, based on antiseptics as chlorhexidine baths or showers associated with prolonged and intermittent topical antibiotics as mupirocin or fusidic acid, remain unproven [1]. Regular gentian violet, however cosmetically difficult to accept, in all orifices may be of use.

The first treatment for *abscess* is surgery, incision, and drainage. Benefit of antibiotic therapy is not proven. However when the patient is on the move it may be indicated. The Infectious Diseases Society of America (IDSA) recommends systemic antibiotics only in "critical" location (face, etc.), immunosuppression, large volume of the abscess (>5 cm), failure of drainage, extreme age, and the presence of systemic symptoms [1, 20, 21].

Treatment of *suppurative paronychia* includes, if there are no abscesses, tepid potassium permanganate, soda or soapy water soaks three times a day, and oral antistaphylococcal antibiotics such as amoxicillin-clavulanic acid or clindamycin, which are also effective against anaerobes. In case of an abscess, surgical drainage is necessary. Superinfection with *Candida* is frequent, particularly when moisture is involved, and the use of an azole or gentian violet paint is then indicated.

There is no agreement on the best treatment for *pitted keratolysis*. Both topical (fusidic acid, erythromycin lotion) and systemic antibiotics (erythromycin for 14 days, clarithromycin at single dose) are effective without significant difference. Azole creams are sometimes effective. For migrants, single-dose clarithromycin may be the solution. However in order to prevent reoccurrences, antiperspiration measures and hygiene are needed and if possible clean socks and shoes supplied.

The first treatment in classical *erysipelas* is antistreptococcal antibiotics (standard intravenous, thereafter oral penicillin). Because of better gastrointestinal tolerance, amoxicillin is preferred to date. Hospitalization is necessary if there are severe local or general signs. Some patients with underlying problems such as bad social circumstances (people on the move or living in poor housing conditions or abusing alcohol or other drugs) and having diabetes mellitus, old age, and immunosuppression and having not the possibility of medical reevaluation within 48 h are in need for admission in a care center. The best treatment is difficult to define. In hospitalized patients, beside cooling of the affected area and measures against the edema, intramuscular or intravenous antibiotics are preferred, whereas oral medication remains possible in less severe cases. In hospitalized patients, even if intravenous penicillin G was previously recommended as treatment, the currently recommended choice is intravenous amoxicillin 50 mg/kg/day, followed by oral administration after improvement of the local signs and disappearance of fever. In case of abscess formation, penicillin M or amoxicillin-clavulanic acid is indicated. In cases of allergy to penicillin, pristinamycin (if available), clindamycin, first-generation cephalosporin, or macrolides excluding erythromycin are good choices. The classical recommended duration of the treatment is 10–20 days. A surgical treatment may become necessary, especially in case of secondary abscess formation. There is no indication for anticoagulant therapy for erysipelas. Prophylaxis of deep venous thrombosis should be considered only when the patient has other risk factors [22]. Venous compression is recommended during the acute phase and the following weeks to reduce the risk of lymphedematous sequelae, which is a main risk factor of recurrence. The portal of entry must be treated as appropriately.

Patients who experience two or more erysipelas episodes should receive secondary prevention of recurrences. Although prevention by penicillin has shown efficacy, strong data concerning the best therapeutic scheme are lacking, and recurrences may occur despite the prophylaxis [1]. Intramuscular benzathine-penicillin G 2.4 MU at 14–28-day intervals is a good choice, particularly for people on the move, but oral penicillin V (250 mg twice a day) or amoxicillin (500–1000 mg a day) is also possible. In cases of allergy, macrolides have been suggested. The optimal duration of preventive treatment is unknown [1]. However, some patients need prolonged prophylaxis. Treatment and secondary prevention of portals of entry such as chronic toe-web maceration, fungal intertrigo, and other exacerbating factors, such as

lymphedema or venous insufficiency, are of key importance. For people on the move, gentian violet paint may be handy and cheap.

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# Non-Venereal Treponematoses

5

Bernard Naafs

## 5.1 Introduction

Non-venereal also called endemic treponematoses are a group of diseases caused by *Treponema* species that are morphologically identical (Gram-negative, spiral-shaped bacteria) and are serologically not to be differentiated from *Treponema pallidum*, subspecies *Pallidum*, the cause of venereal syphilis (Fig. 5.1). All human treponematoses share remarkable similarities in pathogenesis and clinical manifestations, consistent with the high genetic and antigenic relatedness of their etiological agents [1].

In humans, the pathogenic treponemes include *Treponema (T.) pallidum pallidum* (venereal syphilis) and non-venereal *T. pallidum pertenue* (yaws), *Treponema pallidum endemicum* (endemic syphilis or bejel), and *Treponema carateum* (pinta). Although serology remains the most common diagnostic method for treponemal infection, none of the available serological tests are able to differentiate between the infective agents of these diseases. This ability is currently limited to molecular methods that target genetic signatures thought to be specific to each subspecies [1].

In pregnant women with syphilis, *T. pallidum pallidum* readily crosses the placenta to infect the fetus, causing spontaneous abortion, stillbirth, or congenital infection of the new born, while congenital infection has been stated not to occur in non-venereal treponematoses. Furthermore, despite recognition of cardiovascular, neurological, and ophthalmological manifestations during syphilis infection, these manifestations are rarely or not reported for the non-venereal treponematoses. The treponematoses differ in their primary clinical manifestations, though the definite diagnosis may be difficult [2, 3].

*Treponema* species associated with non-venereal disease are generally transmitted among children living under poor, low economic and unhygienic conditions in tropical, subtropical, or warm arid climates. The transmission is mainly by direct contact, but indirect transmission by fomites is possible. Although the bacillus does not seem to survive outside the human body, there still may be a theoretical spread via the environment, but proof of this is lacking. There is increasing evidence that there may be an animal reservoir of treponemata [4].

*Treponema* usually invade the traumatized skin or mucosa that comes in contact with an infected discharging lesion of the index patient. Then a primary cutaneous lesion appears at the site of inoculation after an incubation period of a few weeks. *Treponema* may spread from this site either directly by scratching or *via* the lymphatics and the blood vessels. The lesions usually heal spontaneously. The infection as in syphilis can remain latent or it may recur.

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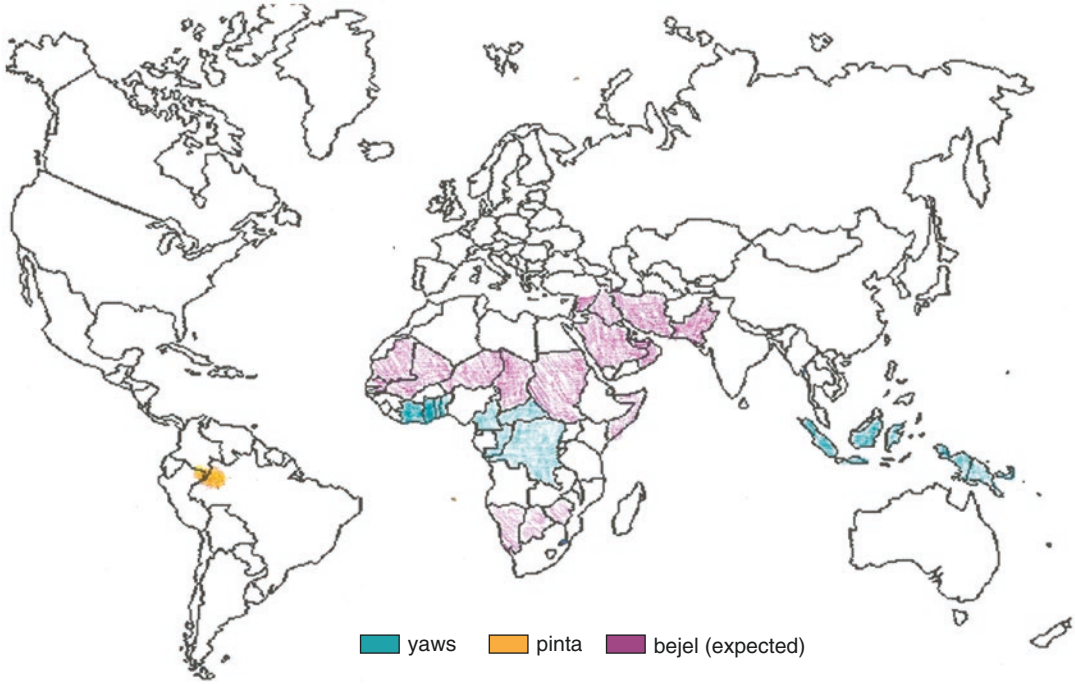


**Fig. 5.1** World wide distribution of endemic treponematoses. Based on WHO and own observation

A secondary stage of these diseases follows the dissemination of the *Treponema*. It may begin while the primary lesion is still present or after a latent period. This may also resolve spontaneously. The long-term effects may consist out of multiple skin lesions and destruction of bones or cartilage.

## 5.2 Yaws

Yaws is the most well-known infection and caused by *T. pallidum pertenue*. In the colonial times due to mass campaigns, it was nearly under control, but thereafter the disease became neglected. However, it is on the rise again often due to the political and economic disruption in the previously endemic countries. The disease presents in three stages. The first and second are easily treated. The third, however, may involve changes to the bones in many parts of the body. After an incubation time of about 3 weeks, the first stage is characterized by the appearance of small, painless bumps on the skin that group together and grow until they resemble a strawberry, called mother yaw (Fig. 5.2).

**Fig. 5.2** Mother yaw

The skin may break open, forming an ulcer (Fig. 5.3). For each case of yaws detected, there may be 5–10 subclinical cases, seropositive patients without clinical manifestations [5]. The second stage, starting in non-immunocompromised patients several weeks or

months after the first lesions, presents with an extensive moist confluent yellowish papular rash that may cover the arms, legs, buttocks, and face. The individual lesion may look like extensive primary yaws and sometimes may be confused with secondary syphilis (Fig. 5.4). There may be a painful tender osteoperiostitis affecting the fingers (polydactilitis). If the plantar surface of the feet is involved, walking is extremely painful and this symptom is known as "crab yaws." The third stage involves widespread bone, joint, and soft tissue involvement, which may include extensive destruction of the bone (sabre tibia: sharp-bowed frontside of the tibia) and cartilage of the nose (rhinopharyngitis mutilans or "gangosa") [6]. The first and second stage of yaws are at present again not uncommon in tropical areas and may be seen occasionally in migrants. However, a positive syphilis serology is common. Due to extensive antibiotic use and the high sensitivity of *Treponema*, the third phase is very rarely seen.

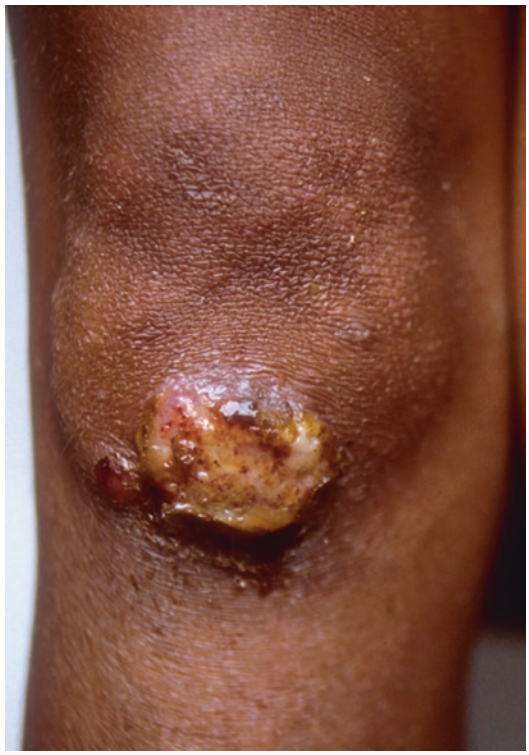

**Fig. 5.3** Ulcerating mother yaw

## 5.3 Bejel

Bejel, an endemic syphilis, is a rare infectious disease caused by *T. pallidum endemicum*. In contrast to the other treponematoses, bejel's primary lesion is often unobserved; when around the mouth, it is mistaken for impetigo. When seen, however, it appears as a small and painless mucous papule or ulcer that develops in the oral cavity or nasopharynx. Children may have in these first-stage patchy, slimy, lesions often ulcerations, particularly in or near the mouth. They infect each other by kissing and even by the use of shared fomites [7]. Later, secondary blisters and sores may appear on the back and the arms and legs, leaving hypo- and later hyperpigmented lesions. Further tertiary disease progression is indicated by infections of the bones, especially those of the legs. In these later stages,

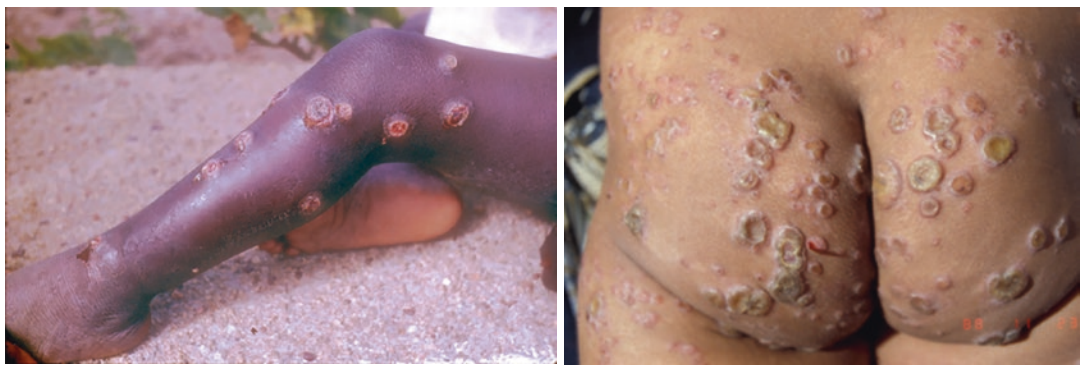

**Fig. 5.4** Secondary yaws

soft, gummy lumps (gummas) may appear on the roof of the mouth and in the nasal passages. Gangosa may be seen like in yaws. Other symptoms may include swollen glands or lymph nodes (lymphadenopathy) and/or skin ulcerations under the arms or around the rectum and groin [1, 8].

## 5.4 Pinta

Pinta**,** even more rare, is caused by the bacterium *T. pallidum carateum*, which is transmitted by direct, nonsexual contact. It is nearly extinct but occurs still in people living upstream the Amazon River in the Andes and nearby environments. Pinta again like the other spirochaetal diseases progresses through three distinct stages, which are characterized by various skin lesions and discoloration (Fig. 5.5). Other organ systems are not affected. Exposed areas of the skin such as the face and extremities are most often affected [9]. However, the chances that it might be seen in migrants are exceptionally low.

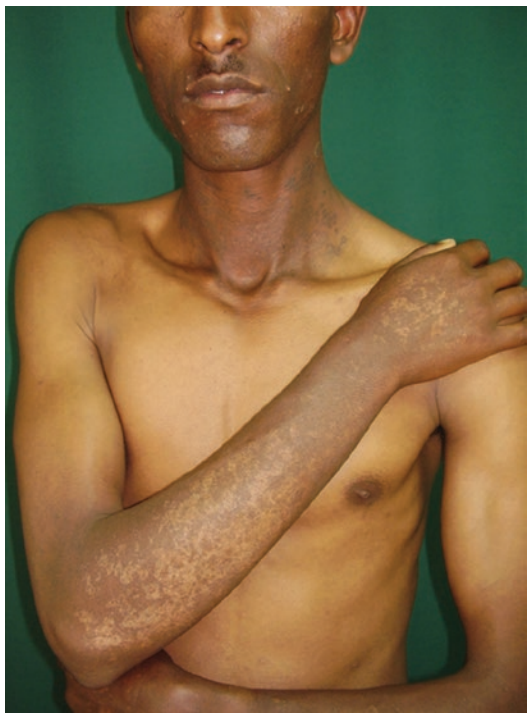

**Fig. 5.5** Pinta

In contrast to syphilis, none of the other treponematoses express noticeable vascular, cardiac, or neurological symptoms. But they all have a positive syphilis serology. With migrants, the problem lies here. Positive serology is mostly interpreted as venereal disease, and the patient is treated as a syphilis patient which can disrupt marriages and may give wrong accusations of child abuse. On the contrary, it may be used as proof of being raped when children or women want to get help and admission into the receiving country. Important for a doctor is: a positive syphilis serology does not always have to be syphilis. Since it is extremely difficult to make the difference, treatment should be instigated particularly during pregnancies. However, contrary to syphilis, the non-venereal treponematoses are not harmful for the fetus. It is important to be aware of the consequences of sharing the possible diagnosis of syphilis with the patient and the family.

A positive syphilis test should always be treated in a migrant except when it has shown to be an adequately treated syphilis.

The WHO revised the policies for treating yaws in 2012. One oral dose of azithromycin (30 mg/kg, not to exceed 2 g) is now recommended as equivalent to benzathine benzylpenicillin. Because of the ease of administration and low cost, a single dose of azithromycin by the mouth is to date the preferred treatment [10, 11].

Yaws, pinta, and endemic syphilis may still be treated with benzathine penicillin G. Children younger than 10 years should receive 600,000 U intramuscularly, and children older than 10 years should receive 1.2 million U intramuscularly.

Alternatives are appropriate only if azithromycin or benzathine penicillins cannot be used. Tetracycline (25 mg/kg/day for 10–14 days) and chloramphenicol (25 mg/kg/day for 10–14 days) have been used successfully, as has a 10-day course of doxycycline. Other penicillins, cephalosporins, and macrolides are probably active against the treponemes; however, quinolones, aminoglycosides, and sulfa antibiotics are ineffective. Treatment failures with penicillin have been reported, but reinfection could not be ruled out.

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# Fungal Infections

6

Roderick Hay

## 6.1 Superficial Mycoses

Superficial infections caused by fungi are common in all environments and, particularly in tropical areas, can spread in overcrowded and cramped conditions. Factors such as climate and pH or humidity of the skin surface may all affect their expression. The common superficial infections are dermatophytosis or ringworm, superficial candidosis, and pityriasis (tinea) versicolor. However, other conditions such as foot and nail infections caused by *Neoscytalidium* species as well as the hair shaft infections, white and black piedra, are also seen rarely.

### 6.1.1 Dermatophytosis

The dermatophyte or ringworm fungi are common causes of superficial infections. The organisms invade the epidermis but remain confined to the stratum corneum as well as allied structures such as hair and nails. They normally cause exogenous infections originating from outside the human host. There are three main sources: humans, animals, and soil, known, respectively, as anthropophilic, zoophilic, or geophilic [1–7].

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Dermatophytoses are common in warm climates where the main types of infection are tinea corporis, tinea cruris, and tinea capitis [8]. They are therefore seen in displaced populations and in overcrowded living conditions; scalp ringworm, in particular, can spread among children. Tinea pedis is also common in those sharing communal bathing facilities or wearing footwear for long periods. The microbiome of the feet, particularly the interdigital spaces, may vary from time to time, and one organism may replace another to cause infection; the term "dermatophytosis complex" has been coined to describe this phenomenon where Gram-negative bacteria replace dermatophytes. This can occur in people walking and wearing boots that get wet over long periods without removing them or drying the feet.

Patients with underlying HIV infection, although not apparently showing an increased incidence of infection, may have clinically atypical and extensive dermatophyte infections.

#### 6.1.1.1 Clinical Features and Treatment

Tinea corporis presents with a scaly and itchy rash affecting the trunk or proximal limbs. The typical lesion is a circular scaling patch with some central clearance. However, in many lesions, the main abnormalities, such as scaling or papule/pustule formation, are seen at the edge where an intact or broken rim can just be made out. Tinea corporis lesions may be very large and affect large areas on the back and chestor limbs



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(Fig. 6.1). They can also change in appearance if mistreated with potent topical corticosteroids often becoming more prominent and extensive or showing follicular accentuation (Fig. 6.2). Recently in patients from India there has been an outbreak of widespread and difficult-to treat tinea corporis.

Localized tinea corporis responds to one of the azole antifungals such as clotrimazole or econazole or topical terbinafine. Whitfield's ointment is also effective but slower. Oral therapy is generally needed for extensive disease; the main choices are terbinafine, itraconazole, or griseofulvin.

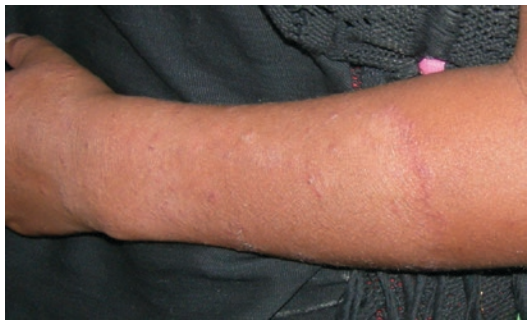

**Fig. 6.1** Tinea corporis due to *Trichophyton rubrum*

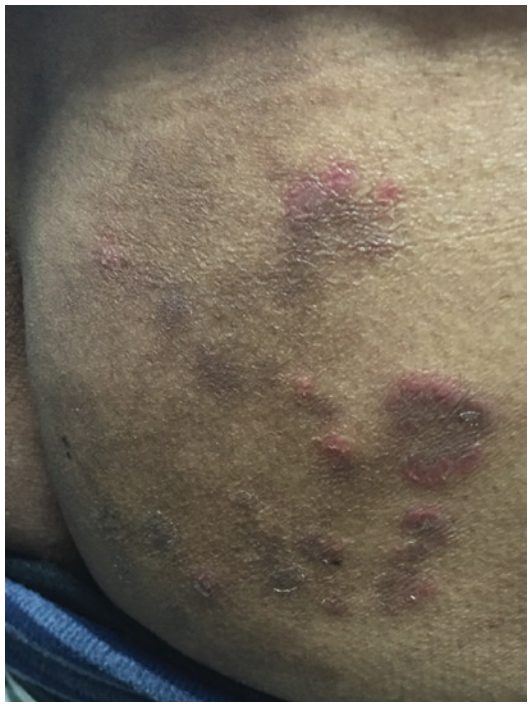

**Fig. 6.2** Corticosteroid-treated tinea corporis

Tinea capitis or scalp ringworm is endemic in many warm countries, particularly in sub-Saharan Africa [9, 10]. It can be caused by either anthropophilic or zoophilic fungi. But in overcrowded conditions, anthropophilic organisms predominate. Tinea capitis in migrant children can be common, and it has led to changes in the spectrum of disease in some northern countries following transmission to local populations.

Tinea capitis is an infection generally confined to prepubertal children. Most anthropophilic infections present insidiously with diffuse or localized areas of hair loss. Scaling is variable but on close inspection the hairs may be broken at scalp level, leaving a swollen black dot in the hair follicle. More scaly types resemble seborrhoeic dermatitis (Fig. 6.3), but highly inflammatory lesions (kerion) are occasionally seen. The course of disease is indolent but lesions normally clear at puberty. The zoophilic organisms are generally more likely to produce inflammatory lesions, and scaling with hair loss is obvious. Lesions are often quite itchy and inflammatory crusts cover the lesions. Because it is often not obvious and is without gross symptoms, tinea capitis can spread easily in households and school classes.

The diagnosis of this infection can be confirmed by examining scrapings from the patient's scalp and by culture or molecular testing.

The only effective treatments for tinea capitis are oral antifungals [11]; topically applied drugs

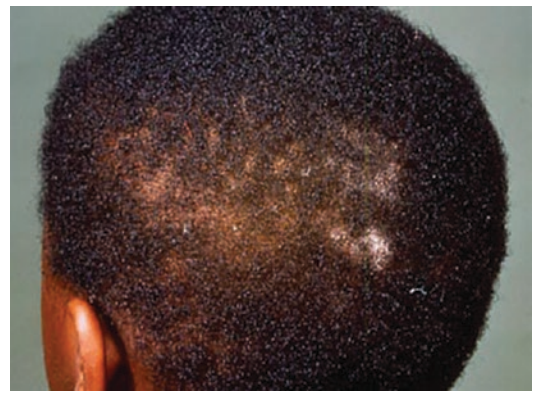

**Fig. 6.3** Tinea capitis due to *T. tonsurans*

are seldom effective on their own. Terbinafine and itraconazole are effective, the latter showing particular activity against tinea capitis due to *Trichophyton* species. Griseofulvin in a dose of 10–25 mg/kg daily is an alternative. The normal duration of therapy is 6–8 weeks.

Tinea cruris, affecting the groin, is common in most tropical countries. It is almost always caused by anthropophilic species of dermatophytes, mainly *Trichophyton rubrum* and *Epidermophyton floccosum*. Sometimes these infections become common in certain groups such as soldiers or prisoners. It presents as an itchy rash with a raised border extending from the groin down to the upper thigh and on occasions into the anal cleft. In women it may extend around the waist area. Treatment is with topically applied antifungal creams such as clotrimazole or miconazole or terbinafine. Oral treatment with terbinafine or itraconazole is also effective.

Tinea pedis is very common and affects the interdigital spaces or the soles. The main symptoms are itching and, occasionally, pain. If there are severe erosive changes, particularly if there is greenish discoloration of the area, Gram-negative bacteria such as *Pseudomonas* species may be implicated [12].

The usual treatment is a topical antifungal [13]. Good results can be obtained with a range of compounds including azoles, such as clotrimazole or miconazole, or topical terbinafine. For infections of the sole, oral therapy with griseofulvin, terbinafine, or itraconazole is preferable. *Neoscytalidium* infections, which can present with interdigital or plantar scaling, respond poorly to current antifungals.

### 6.1.2 Onychomycosis

Nail plate invasion caused by dermatophytes is common in temperate countries, where it may affect up to 15% of the population, but the incidence is lower in tropical areas. It may occur in migrant communities and is usually accompanied by sole or web space infections; it is most common in the toe nails. The usual causes are anthropophilic fungi such as *Trichophyton rubrum*. The affected nails become thickened and opaque; distal erosion of the nail plate occurs in long-standing cases.

Therapy is difficult, with few nail infections responding to topical antifungals, although in the early stages some will clear with ciclopirox or amorolfine nail lacquers. Oral drugs, terbinafine (250 mg daily) or itraconazole (400 mg daily for 1 week per month ×3), produce higher recovery rates in shorter periods (3 months), but even so there are treatment failures [14–17].

### 6.1.3 Superficial Candidosis

Superficial infections due to *Candida* species are common in those coming from a tropical environment and include oral and vaginal as well as skin infections. The principal cause is *Candida albicans*, although other species such as *C. tropicalis*, *C. parapsilosis*, *C. krusei*, and *C. glabrata* may also cause human infections. The disease is seen worldwide, although some clinical varieties such as interdigital candidosis are more common in warm climates.

*Candida albicans* is a normal commensal of the mouth, gastrointestinal tract, and vagina. Carriage rates vary but 15–35% of normal individuals have commensal carriage in the mouth. Superficial candidosis is seen in association with diabetes mellitus (groins, vagina), obesity (interdigital), and HIV/AIDS (oropharyngeal) [18–26].

Depression of either T lymphocyte or neutrophil-mediated immunity allows the organisms to grow and invade following inhibition of normal control mechanisms. So untreated HIV may be an underlying factor in persistent oral *Candida* infection. The main exception is vaginal candidosis, where most women with this common infection have no detectable predisposition.

#### 6.1.3.1 Clinical Features and Treatment

The main clinical forms are oropharyngeal, vaginal, and cutaneous candidosis.

Oral infection is seen in all countries, particularly in infants, elderly, and immunocompromised

patients. It occurs in breastfed and bottle-fed infants and may be a complication of malnutrition, in which it can affect the reintroduction of feeding because of soreness of the mouth. As a complication of human immunodeficiency virus (HIV) infection, oropharyngeal candidosis is a common and early manifestation of the development of AIDS [27].

Acute pseudomembranous candidosis presents with white plaques on the epithelium that are inflamed and easily detached, "thrush." This may present as an acute infection in infants, the elderly, or in patients who are immunocompromised, such as those with HIV infections. In the last group, the condition is often persistent and refractory to therapy. In some the mucosal surface appears red and sore. Any of the above changes can be accompanied by cracking at the corners of the mouth (angular cheilitis), which in these cases may be due to *Candida* infection; in other cases, it may signal eczema or staphylococcal infection.

Vaginal Candida infection is normally caused by *C. albicans*, although increasingly other *Candida* species such as *C. glabrata* or *C. tropicalis* have been implicated. There is usually no underlying abnormality to be found. Severely immunocompromised women do not usually show a higher frequency of persistent vaginal infections. The main clinical forms of vaginal candidosis are similar to those seen in the oral mucosa with plaques or erythema. The symptoms vary from a creamy discharge to itching and soreness. Treatment is with oral fluconazole or topical applications or pessaries (azoles). Recurrent infections are common. *Candida glabrata* is usually resistant to fluconazole.

The skin may be affected in flexural sites (*Candida* intertrigo), and a common feature is a prominent red rash. For instance in the groin and on the upper surface of the thighs it may appear together with satellite pustules and papules. This can also occur in other sites such as beneath the breasts, where it is often accompanied by bacteria.

Infection of the finger or toeweb spaces (**interdigital candidosis**) by *Candida* is more common in hot climates. Lesions are white with soggy-looking macerated skin which is superficially eroded. A relationship between repeated washing and cooking has been suggested.

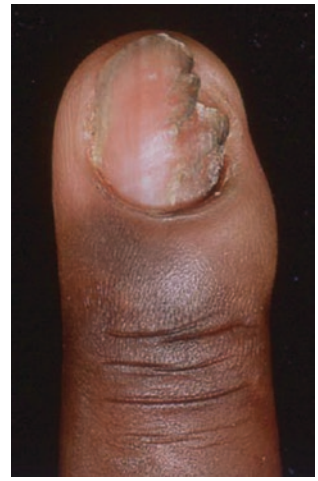

**Fig. 6.4** Chronic *Candida* paronychium

*Paronychia* are acute or chronic infections of the nail folds caused by *Candida* species such as *C. albicans* or *C. parapsilosis*. They occur in patients who are likely to immerse their hands frequently in water or whose occupations involve cooking. In addition to swelling of the nail fold, pain, and intermittent discharge of pus, the lateral border of the nail may be affected with lateral onycholysis (Fig. 6.4). In many chronically affected patients, this disease is complicated by irritant dermatitis, and eradication of the organisms alone will not affect recovery.

Candida infections respond well to a range of antifungals available in cream, vaginal tablet, or oral pastille forms. These include the polyene antifungals such as amphotericin B or nystatin and azole drugs (econazole, clotrimazole, ketoconazole, miconazole). Patients with AIDS may respond poorly to topical therapy, and orally absorbed antifungals, such as fluconazole (100–200 mg daily) or itraconazole (100–200 mg daily), given intermittently are used. Patients with infections due to *C. glabrata* and *C. krusei* are usually resistant to fluconazole.

### 6.1.3.2 Laboratory Diagnosis

The diagnosis of superficial candidosis, as well as of dermatophytosis, can be confirmed by direct microscopy of skin scrapings or swabs. Both

yeasts and hyphae can be seen. *Candida* species can be distinguished on culture or with molecular diagnostic tools.

### 6.1.4 Superficial *Malassezia* Infection

The *Malassezia* (lipophilic) yeasts are skinsurface commensals which cause pityriasis versicolor and *Malassezia* folliculitis and have also been associated with seborrhoeic dermatitis and dandruff [28]. There are a number of *Malassezia* species which are oval or round yeasts, and their distribution on the skin surface differs. The formation of short stubby hyphae and round yeasts on the skin surface is a feature of the development of most cases of pityriasis versicolor.

Pityriasis versicolor is a common disease in otherwise healthy patients. Generally this disease is associated with warm climates and sun exposure. The typical rash consists of multiple hypo- or hyperpigmented, occasionally red, powdery, scaly macules which are distributed across the upper trunk and back; with time, these coalesce. The lesions are asymptomatic. The hypopigmented lesions may be confused with vitiligo, but in the latter, there is complete loss of pigmentation and without scaling.

Scrapings from the lesions in 10% potassium hydroxide-treated mounts will show the characteristic organisms, which consist of clusters of round yeasts closely associated with short hyphae. This infection is usually caused by *Malassezia globosa*.

A second condition associated with *Malassezia* yeasts is an itchy folliculitis on the back and upper trunk which often appears after sun exposure usually in teenagers or young adult males. Lesions are itchy papules and pustules which are often widely scattered on the shoulders and back.

Seborrhoeic dermatitis is also associated with *Malassezia*. The main clinical feature is the appearance of erythema, together with greasy scales in the scalp, eyebrows and eye lashes, the nasolabial folds, behind the ears, and over the chest. The condition has been associated with a heightened immune response to antigenic products of *Malassezia*.

Treatment of *Malassezia* infections can usually be accomplished using topical azole antifungals such as clotrimazole (cream) or ketoconazole (cream or shampoo). Oral therapy with itraconazole or fluconazole is also a possibility. Alternatives include selenium sulfide (1–2%) or zinc pyrithione.

## 6.2 Deep Mycoses

The deep fungal infections or deep mycoses include a group of infections, which are largely tropical and affect the subcutaneous tissue, remaining generally confined to this site even though they may cause considerable disability. There is a second group of infections, the systemic infections, which can spread to other sites throughout the body, including the skin, usually by bloodstream dissemination. These are often confined to patients who are seriously ill with an underlying illness such as leukemia or HIV when they are often called opportunistic systemic mycoses. Others, which usually have well-defined endemic regions, may occur in otherwise healthy individuals although even here any underlying illness including HIV or treatments such as the use of antitumor necrosis factor (TNF) and biological therapies may trigger these infections. These are the endemic systemic mycoses. A detailed travel history is important in helping the doctor recognize suspected cases. Generally systemic mycoses are rare in migrants but worth considering as part of the differential diagnosis, particularly if they have an underlying illness. Likewise, it is also important to bear the origins of a patient in mind when considering any treatment including biologic agents that may disturb their immunity.

### 6.2.1 Subcutaneous Mycoses

Subcutaneous fungal infections are mainly confined to the tropics and subtropics. While they are seldom common, their diagnosis and management are difficult, and it is important to establish the correct diagnosis. They are very uncommon in

refugees but may be found in residential camps or in longer-term migrants. These infections are generally caused by traumatic implantation of organisms through the skin into the dermis or subcutaneous tissues from the environment. They generally remain confined to their site of introduction and only spread locally.

#### 6.2.1.1 Clinical Features and Treatment

Mycetoma (Madura foot) is a chronic subcutaneous infection caused by filamentous bacteria or actinomycetes or fungi in which the organisms form into aggregates (called grains), surrounded by an inflammatory infiltrate, leading to the development of draining sinuses communicating with the overlying skin and/or underlying bone to cause osteomyelitis [29–40].

Mycetoma occurs in the tropics or subtropics. It is more often seen in semidesert or desert areas. The main regions for this infection are Mexico; Central and northern South America; Africa, particularly the drier regions of Sudan, Somalia, and West and East Africa and India. The mycetoma is generally classified according to etiological organisms, namely, fungi (eumycetoma) or actinomycetes (actinomycetoma), and by grain color—black, red, or pale. Mycetoma is more common in males than females and generally affects adults. The majority of patients appear to have no predisposing illness.

The earliest sign of a mycetoma is a small dermal or subcutaneous swelling. It may take several years before the first sign of disease is seen. With time, this slowly enlarges and sinuses appear on the surface of the nodule. It is usually painless although pain may occur prior to appearance of sinuses on the skin surface. Chronically discharging sinuses are formed in well-established lesions, and there is hard swelling affecting the area, accompanied by deformity where the bones are involved. The main areas affected are those subject to trauma such as the feet, lower legs, and hands, but the trunk and abdomen and back may be involved (Fig. 6.5).

Radiological changes include cortical thinning or hypertrophy, periosteal proliferation, and lytic lesions. Magnetic resonance imaging (MRI) is the most accurate method of delineating the extent of lesions, although ultrasound scans are also useful.

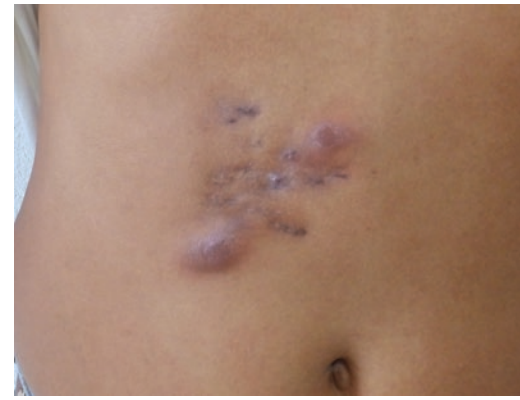

**Fig. 6.5** Actinomycetoma due to *Nocardia* spp. on the abdomen of a farm worker

The laboratory diagnosis of mycetoma depends on the demonstration of grains of the organisms. These are generally obtained by opening a sinus where there is a small amount of pus beneath the skin surface, using a sterile needle. Grains are placed in 5–10% potassium and examined directly or seen with a deep biopsy. The organisms can also be cultured. A main aim of laboratory diagnosis is to separate fungal and actinomycete causes because the treatment of each is different.

The actinomycetes respond to a variety of antibiotics such as sulfonamides and sulfones or co-trimoxazole with a second drug such as rifampicin. Alternatives include amikacin, moxifloxacin, and imipenem for difficult cases. Most of these infections will respond to therapy.

Treatment of eumycetomas is more difficult. About 40–50% of infections due to *Madurella mycetomatis* respond to an azole such as itraconazole (200–400 mg daily) or voriconazole (400 mg daily) although surgery remains an option after treatment with antifungals. However, there are few surgeons with wide expertise in the management of mycetomas. The alternative is amputation. Generally, mycetomas are only slowly progressive and are seldom life threatening.

*Chromoblastomycosis* is a fungal infection caused by pigmented fungi. Generally these organisms contain visible melanin. The production of melanin is of importance as it allows these

fungi to withstand environmental changes such as drought, heat, or cold. It is very rare in migrant populations.

Chromoblastomycosis is a chronic infection caused by pigmented fungi which form specialized cells, muriform cells, or sclerotic bodies, in tissue [41]. It involves the dermis and epidermis leading to pseudoepitheliomatous hyperplasia to granuloma formation. The organisms which cause this infection are found in the natural environment in plant debris or forest detritus. The main range of chromoblastomycosis involves the tropics and subtropics, and the incidence of infection is highest in countries with a high rainfall. The disease is mainly seen in countries of central and northern South America, parts of Africa particularly the east coast of Southern Africa, the Far East, Japan, and the West Pacific.

The most common sign of chromoblastomycosis is wartlike proliferation on the skin. The early lesions are small nodules or papules which slowly enlarge. They become raised and verrucose, and adjacent nodules amalgamate to form a complex of warty growth. Other lesions are flatter and plaque-like and extend slowly, sometimes healing with central scarring. Long-standing lesions can cause considerable local swelling and rarely squamous carcinomas can develop. The main sites affected are those on peripheral locations such as the hands, feet, and lower legs.

Direct microscopy of skin scrapings taken from the surface of lesions will show the pigmented cells with transverse septa. The histopathology of chromoblastomycosis is diagnostic. The epidermis shows pseudoepitheliomatous hyperplasia with some transepidermal elimination of fungi. The latter can also be seen as pigmented cells in granulomas or neutrophil abscess. Although the organisms grow well on conventional mycological media, they are difficult to identify because of the close resemblance of many of their specific features, such as sporulation.

The commonly used drugs are itraconazole (100–400 mg daily) and terbinafine (250 mg daily). A combination of terbinafine and itraconazole or flucytosine is probably most successful in late and extensive cases. Antifungals are often used together with cryotherapy. A further approach to therapy is the use of local heat applied from heat-retaining gels.

Sporotrichosis is an infection caused by the dimorphic fungi of the species *Sporothrix* which is widely distributed throughout the tropical world [42]. But it is rare in migrants. The main foci of infection are in Mexico, Central and South America, Africa, and Japan. Scattered cases are seen in the Far East and Australia. The genus *Sporothrix* is divided into different species, *S. brasiliensis*, *S. globosa*, *S. luriei, S. mexicana*, and *S. schenckii*, on the basis of molecular characteristics; but the clinical implication of this comparatively new classification has not been assessed, although *S. brasiliensis*, for instance, is associated with infections in humans spread from cats (see below). Exposure to infection is usually sporadic, although outbreaks of infection have been described in certain groups, such as florists, packers, plant workers, fishermen, and armadillo hunters. In Brazil (Rio de Janeiro state), there has been a recent large outbreak of infection in cats and humans.

Some patients develop fixed lesions which are usually solitary ulcerated granulomas on exposed sites, including the face. This has to be distinguished from other granulomas such as leishmaniasis. A second form of cutaneous sporotrichosis is called lymphangitic because the infection spreads from a primary lesion to form nodules or ulcers along the course of local lymphatics (Fig. 6.6). The term sporotrichoid spread is used to describe this, but in migrants other

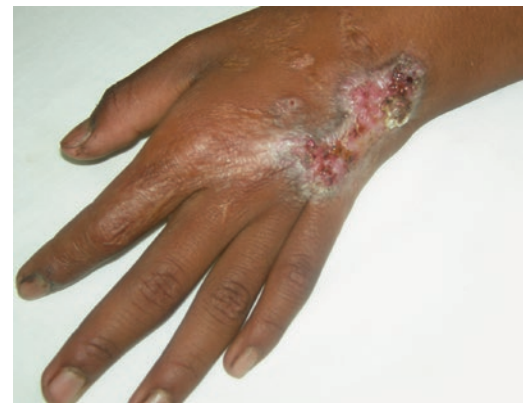

**Fig. 6.6** Sporotrichosis

causes such as the atypical mycobacterium infection caused by *M. marinum* or leishmaniasis are more likely to be seen. Disseminated deep lesions of sporotrichosis may affect other body sites such as the joints, lungs, and meninges.

Sporotrichosis differs from the other subcutaneous mycoses in that culture is the most reliable mode of diagnosis because there are few organisms present in lesions and these may be difficult to find.

The treatment for sporotrichosis is itraconazole in doses of 100–200 mg daily or terbinafine 250–500 mg daily. An alternative is potassium iodide made up in a saturated solution.

### 6.2.2 Systemic Mycoses

Systemic mycoses are fungal infections that involve deep organs. While some, often referred to as the endemic mycoses, affect healthy individuals, others are opportunistic infections which occur in patients with some underlying predisposition [43–46]. Generally, detailed consideration of these infections is beyond the scope of this book.

Systemic mycoses are rare in migrant populations but may occur when

1. There is underlying HIV.
2. The patient is receiving biological therapies or is severely immunosuppressed.
3. The patient is elderly, years after they have arrived at their new home.

The patients are usually sick and systemically unwell. The skin lesions may be widespread papules or soft-centered nodules like lesions of molluscum contagiosum. It is always important to obtain sufficient information on the patient's journey and origin, and if a systemic mycosis is suspected, liaison with the local microbiology or infectious disease teams is strongly advised. However, often a skin biopsy will help to establish the diagnosis.

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# Protozoan Dermatoses

7

Colette van Hees

## 7.1 Introduction

The most important cutaneous protozoan infection seen in refugees/immigrants in Europe is leishmaniasis. Leishmaniasis presents as visceral (VL), mucocutaneous (MCL), or cutaneous (CL) disease. There are 1.5–2 million new infections each year, of which about two-thirds are cutaneous leishmaniasis (CL). CL is endemic in the "Old World" and the "New World" (Fig. 7.1) [1]. CL is the most common imported infectious disease in refugees from Syria [2]. In 2016, more than 25% of the asylum seekers in the European Union were of Syrian origin [2]. CL is endemic in Syria. It was described in the Middle East as early as the ninth century [3]. In 1756, the British physician Alexander Russell described the disease as Aleppo boil or Aleppo Evil [4]. Up to 1960 it was endemic only in Aleppo and Damascus regions. The National CL Control program of Syria comprised passive and active case detection through primary healthcare centers and schools, with treatment provided free of charge. Vector control was attempted through insecticide spraying twice a year [5]. The number of cases reported annually to the WHO has risen since the war, which has led to disruption of CL control programs [6] (Table 7.1). The true current incidence is unknown and is estimated to be three to five times higher than the reported numbers in 2004–2008 [6]. Underreporting is likely to have increased in the ensuing years of war with the decline of the healthcare system. CL is also endemic in Iraq, Afghanistan, and Iran and around the Mediterranean basin (Table 7.1). CL incidence has increased in Turkey in areas which border Syria and in refugee camps [7, 8]. In Lebanon, CL has emerged as well [9].

Global warming has contributed to extending the resident area of the sandfly vector in Southern Europe and its spread further up north into France and Germany. Endemicity of leishmaniasis and the spread of its vectors as a result of climate change are also increasingly recognized in the USA [10].

## 7.2 Transmission

The protozoan parasite *Leishmania* is transmitted by female sandflies of the species *Phlebotomus* in Europe, the Middle East, and Africa and *Lutzomyia* in the Americas. The sandfly becomes infected when it ingests amastigotes during blood meals on infected hosts (Fig. 7.2). Ingested amastigotes transform into infective promastigotes in the sandfly's midgut and these migrate to its pharynx. When the next blood meal is taken by the sandfly, promastigotes enter the skin. They then actively invade macrophages where they

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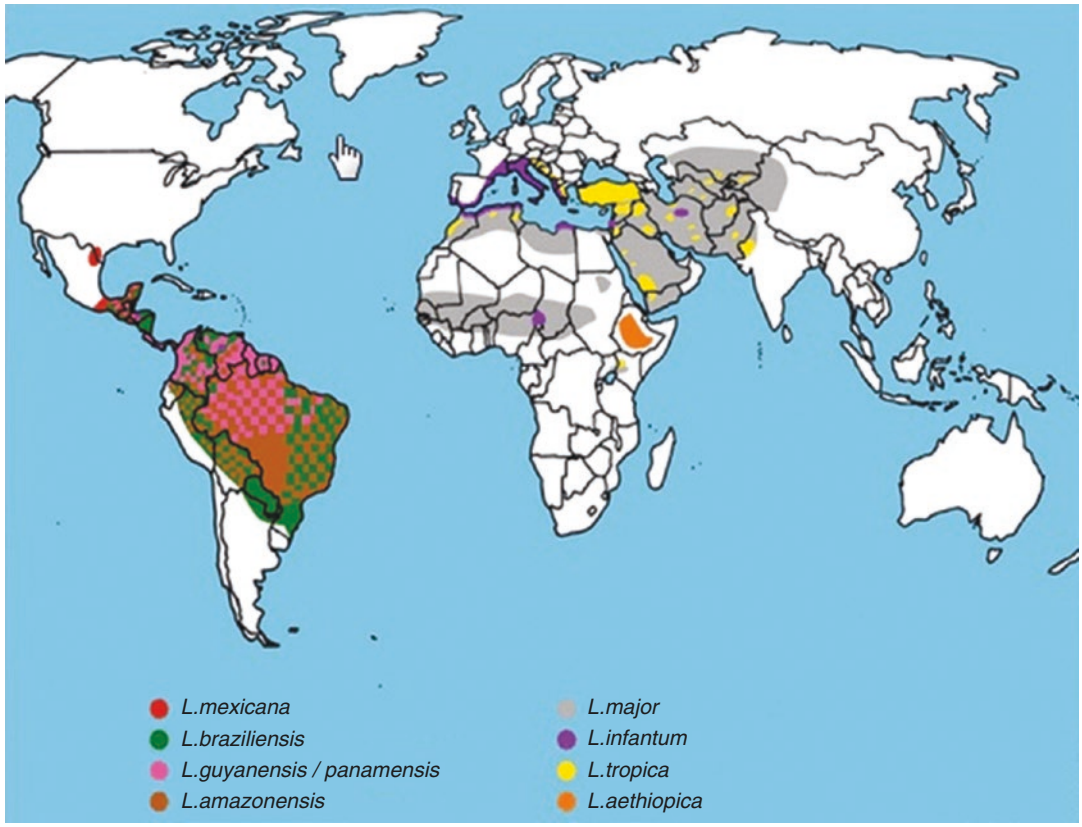


**Fig. 7.1** The main causative species of CL and their approximate global distribution (reprinted with permission from A. Magill [1])

**Table 7.1** Annual number of cases of cutaneous leishmaniasis reported by country*

| | Number of cases of cutaneous leishmaniasis reported | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2016 | 2015 | 2014 | 2013 | 2012 | 2011 | 2010 | 2009 | 2008 | 2007 | 2006 | 2005 |
| Afghanistan | 35,184 | 29,392 | 19,065 | 23,621 | 33,894 | 31,293 | 32,145 | 32,937 | 24,585 | 30,319 | 19,689 | 12,752 |
| Iran (Islamic Republic of) | No data | 18,607 | 16,024 | 16,054 | 20,947 | 19,426 | 22,921 | 24,586 | 26,824 | 26,493 | 24,517 | 21,419 |
| Iraq | No data | 18,884 | 2691 | 1648 | 2486 | 2978 | 3113 | 2086 | 1250 | 655 | 1339 | 2435 |
| Syrian Arab Republic | 47,377 | 50,972 | 53,876 | 71,996 | 55,894 | 58,156 | 42,172 | 46,348 | 29,140 | 17,709 | 18,732 | 21,951 |

*http://apps.who.int/gho/data/node.main.NTDLEISHCNUM?lang=en

transform into amastigotes and multiply by simple division. The host reservoir is usually zoonotic, varying from rock hyrax and other small rodents to domestic dogs. Humans become infected with these species as passersby. Humans can be the reservoir too, particularly in *L. donovani* and *L. tropica* infections (Table 7.2) [11].

## 7.3 Clinical Features of CL

The clinical manifestation of leishmaniasis varies according to leishmania species (Table 7.2) and host immune response. Weeks to months after infection, a papule or nodule develops at the site of the sandfly bite. Painless ulceration occurs in

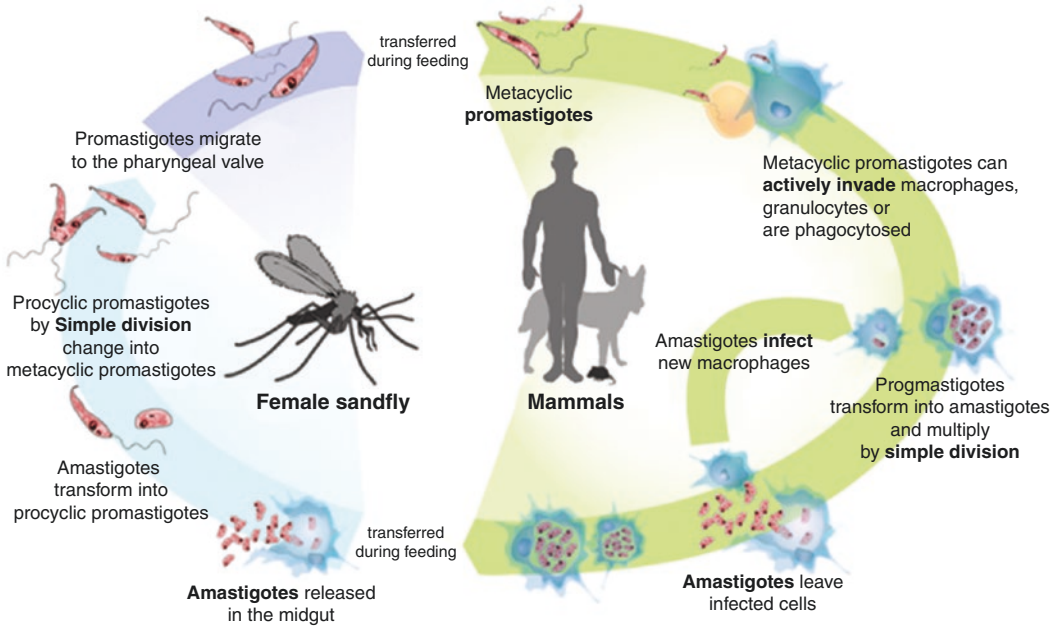


**Fig. 7.2** Life cycle of leishmania (Figure under Public Domain, Wikimedia Commons contributors, Wikimedia Commons, the free media repository, https://commons.wikimedia.org/w/index.php)

**Table 7.2** Leishmania species, geographic distribution, clinical presentation and main host

| Main leishmania species | Geographic distribution | Clinical form | Main host |
|---|---|---|---|
| *L. major* | Central/West Asia, North Africa, Sahel, Central/West Africa | CL ("wet") | Gerbil, fat sand rat |
| *L. tropica* | Middle East, Central/West/North Africa, Mediterranean basin | CL, LR ("dry"), ML, viscerotropic L | Human, rock hyrax |
| *L. infantum* | Mediterranean basin, Central/West Africa | CL, VL | Domestic dog |
| *L. donovani* | Indian subcontinent, East Africa | VL, PKDL | Human |
| *L. aethiopica* | Ethiopia, Kenya | CL, ADCL, LR | Rock hyrax |
| *L. infantum (chagasi)* | Central/South America | CL, VL | Domestic dog, fox |
| *L. mexicana* | Central America | CL | Forest rodents |
| *L. amazonensis* | South America | CL, ADCL | Forest rodents |
| *L. (V.) braziliensis* | Central/South America | CL, MCL | Forest rodents |
| *L. (V.) guyanensis* | South America | CL | Sloth, anteater |
| *L. (V.) panamensis* | Central America | CL | Sloth |

(Adapted from Bates [11], distributed under the Creative Commons CC-BY, Elsevier, 2017)
*Abbreviations: L* Leishmania, *V* Vianna, *CL* Cutaneous leishmaniasis, *VL* Visceral leishmaniasis, *MCL* Mucocutaneous leishmaniasis, *ADCL* Anergic diffuse cutaneous leishmaniasis, *LR* Leishmania recidivans, *PKDL* Post-kala-azar dermal leishmaniasis

the course of weeks to months, and a crust, which can come off and recur regularly, develops. If the ulcer is painful, this usually signifies bacterial superinfection. Spontaneous healing over months to years generally leaves an atrophic scar. Because infection occurs on the unprotected skin, the face and the extremities are often affected. CL facial scars may cause social stigmatization which leads to anxiety, depression, and decreased quality of life for patients [12]. Women, adolescents, and children harboring facial scarring are particularly susceptible to social stigmatization [13].

In the *Old World*, CL is caused by *L. tropica*, *L. infantum*, *L. major*, and *L. aethiopica*. VL is caused by *L. infantum* and *L. donovani*.

***L. tropica*** infections, which are the most common type found in Syrian immigrants, typically present as single or multiple painless, dry, erythematous papules, plaques, or nodules which develop ulceration with crusting on the exposed skin, especially on the face and extremities (Fig. 7.3). Untreated, lesions slowly lead to scarring in one to several years. *L. tropica* may cause mucosal leishmaniasis (ML) by continuous spread from cutaneous lesions or directly by an infected sandfly bite. A special form of CL which occurs in *L. tropica* infections is leishmania recidivans (LR), where healing is followed by reactivation at the edges of lesions over a period of many years. Syrian immigrants with LR often have a history of repeated treatment with partial or temporary effect. LR can lead to large areas of scarring (Fig. 7.4). Rarely, *L. tropica* may cause viscerotropic leishmaniasis, a clinical variant of VL in which the nonspecific clinical manifestations fever, anemia, weight loss, and anorexia are caused by the spread of *L. tropica* to the reticuloendothelial system.

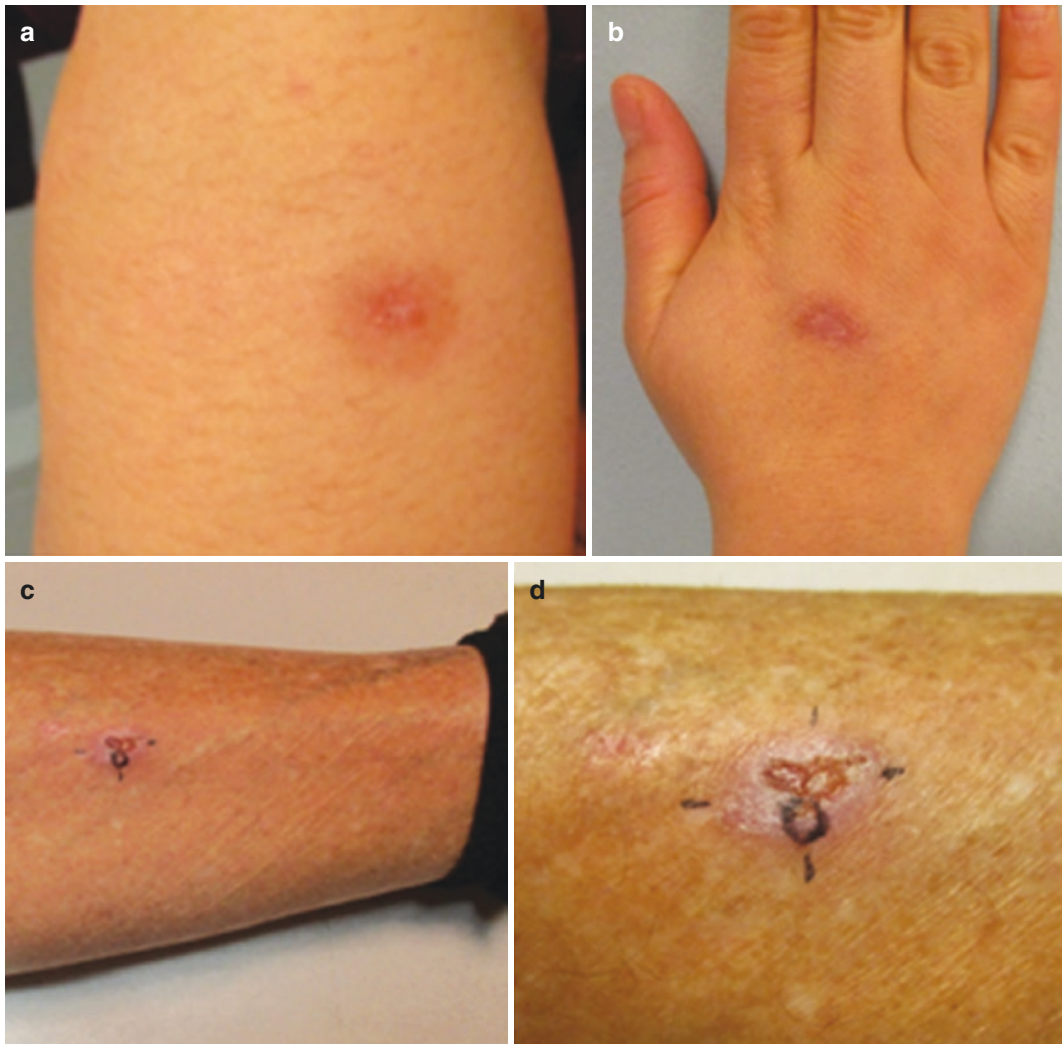


**Fig. 7.3** Syrian refugee with five CL lesions on the (**a**) arm, (**b**) right hand, and (**c**) lower leg, where (**d**) markers for biopsy for PCR are indicated. PCR analysis showed *L. tropica*

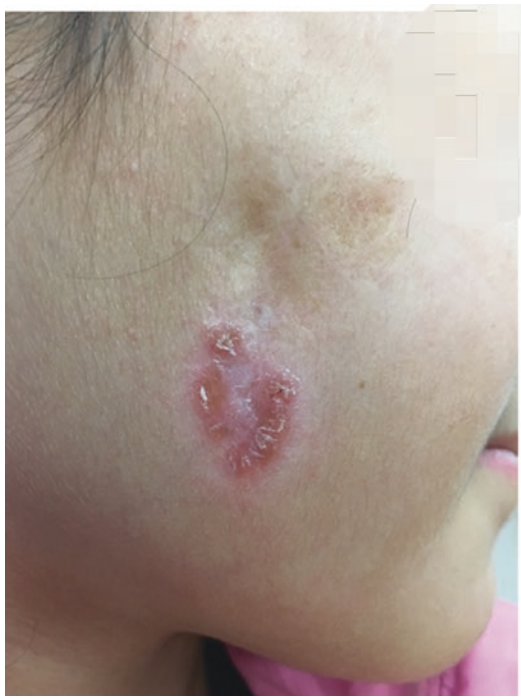

**Fig. 7.4** A 7-year-old girl from Syria with leishmaniasis recidivans. Active CL on the right cheek, proximal of which atrophic scars of CL starting 5 years previously

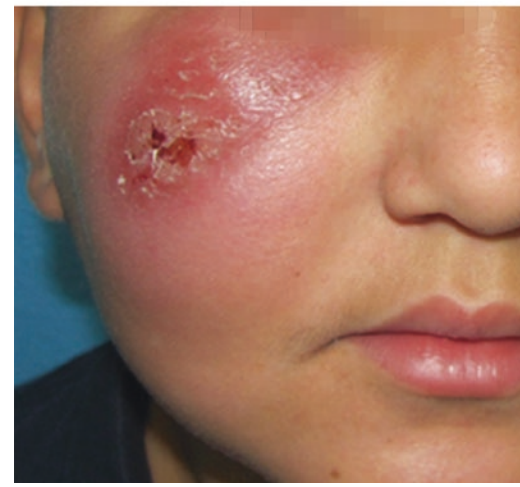

**Fig. 7.5** CL by *L. infantum* in a young boy travelling from north Morocco. Large inflammatory plaque 1 year after infection

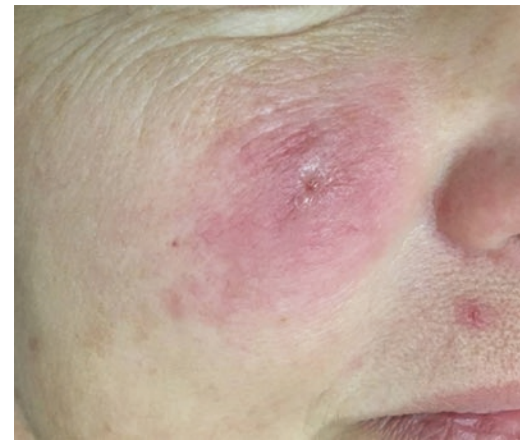

**Fig. 7.6** CL by *L. infantum*

Viscerotropic leishmaniasis was first described in American servicemen returning from the Persian Gulf War in 1991 [14].

*L. infantum* infections occur mostly around the Mediterranean basin and are endemic in Southern Europe. *L. infantum* causes CL or VL, the latter being seen in immunosuppression, particularly in HIV coinfected patients. The presentation of CL by *L. infantum* is variable, ranging from inflammatory papules or plaques which may or may not ulcerate to non-inflammatory, scarcely indurated lesions (Figs. 7.5 and 7.6). Untreated, these may persist for years. Eventually healing occurs, usually with scarring. VL symptoms include fever, weakness, weight loss, hepatosplenomegaly, pancytopenia, and hypergammaglobulinemia [1–3].

*L. major* infection occurs in the Middle East, Asia, and Africa. Papules, nodules, or plaques manifest "wet" ulceration, which heals spontaneously in the course of weeks up to 6 months.

*L. aethiopica* infection may lead to cutaneous, mucosal (by continuous spread) or anergic diffuse cutaneous leishmaniasis. It is found in Ethiopia, Kenya, and Eastern Sudan.

In the *New World*, CL is caused by *L. infantum (chagasi)*, which is avariant of *L. infantum* in the Old World, *L. mexicana*, and *L. amazonensis* as well as the *Vianna subtypes L. (V.) braziliensis*, *L. (V.) guyanensis* (Fig. 7.7), and *L. (V.) panamensis*. ADCL may occur in *L. amazonensis.* MCL is a specific syndrome in which nose, palate, oropharynx, and trachea are involved and may be severely mutilated. This occurs in a minority of patients many years after spontaneous healing of

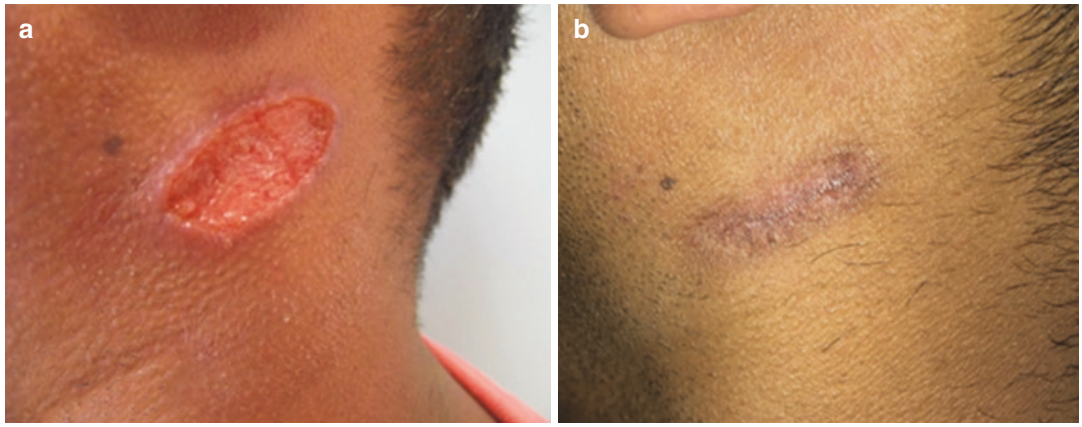


**Fig. 7.7** A 38-year-old man from Surinam with CL by *l. guyanensis*. (**a**) Before and (**b**) after 3 months of treatment with intralesional SSG

a persistent cutaneous infection (approx. one-third of patients have no history of a previous infection). Especially *L. braziliensis* may cause mucocutaneous disease.

## 7.4 Diagnosis

Leishmania parasites found in invaded tissues confirm the diagnosis. They can be detected in a skin smear. Material is obtained for microscopy by (1) making a small bloodless cut in the edge of the lesion which is scraped and transferred to the slide, (2) injecting some physiological salt into the edge of the lesion and aspirating this again, or (3) rolling and dipping a skin biopsy onto a slide before sending it in for pathology or PCR. The material on the slide is stained with Hemacolor, Giemsa, Wright, or Leishman stains (Fig. 7.8). Light microscopy shows the amastigotes as blue oval organisms with a dark nucleus and a small pinpoint kinetoplast in the cytoplasm.

Histopathology generally shows a diffuse dermal infiltrate of histiocytes, lymphocytes, plasma cells, and neutrophils. Parasites are not always detected. Epithelioid cell granulomas may be found with very few parasites in active cell-mediated immunity. In more widespread lesions with less cell-mediated response, vacuolated macrophages filled with amastigotes may be found. Finding the parasites confirms the diagnosis (Fig. 7.9).

PCR techniques performed on skin biopsy or smear are highly sensitive and allow for species identification.

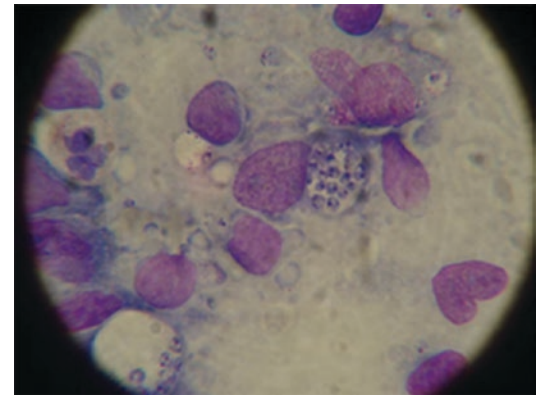

**Fig. 7.8** Skin smear and stains for leishmania

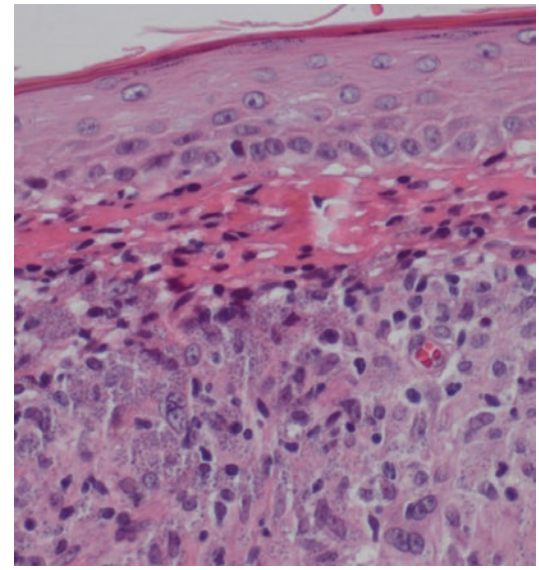

**Fig. 7.9** Amastigotes visible in skin biopsy (HE-stain). Courtesy of Dr J. Damman, pathologist, Erasmus Medical Center, Rotterdam, the Netherlands

## 7.5 Treatment

Treatment may be local (topical, intralesional) or systemic. The choice of treatment has become more individualized and is based on species identification in settings where this is standard of care [15–18]. It further depends on several factors on the basis of which lesions can be classified as "simple" or "complex" [19].

*Simple CL* is caused by a leishmania species which is not likely to cause mucosal involvement and has few lesions, small-sized lesions, a favorable location for local treatment, an immunocompetent, host and spontaneous healing lesions.

Simple CL can be treated locally. Intralesional pentavalent antimony combined with cryotherapy has shown highest cure rates [15, 19]. Usually two to eight treatments are given, once or twice weekly. Each lesion (up to 5) is injected with 0.5–2 cc of 100 mg/mL sodium stibogluconate. Care should be taken to inject into the dermis and to infiltrate the complete lesion. Alternatively, intralesional pentavalent antimony (cure rates 44–75%) or cryotherapy (cure rates 57–68%) may be used as monotherapy, as each is effective, although the combination has a synergistic effect (cure rates 89–91%) in two comparative studies [20, 21].

A "wait and see" approach applying just local wound care when applicable.

*Complex CL* is caused by a leishmania species that may cause mucosal involvement (MCL by lymphatic or mainly South American species) and is associated with lymphadenopathy, large number of lesions, large size lesions, location not favorable for local treatment, immunosuppressed host, failure to local treatment, and specific forms of CL (leishmaniasis recidivans, diffuse CL, disseminated CL).

Complex CL warrants systemic treatment, the choice of which is individualized and should be made by an experienced physician. Miltefosine is the first oral preparation for use in several types of CL and VL. It has relatively few side effects when dosed <200 mg/day and is increasingly used to treat leishmaniasis. Optimal dosing schedules still have to be developed. Gastrointestinal side effects are common. Pentamidine im or iv is the favoured drug for several subtypes of complex CL, e.g. L. aethiopica.

Intravenous treatment with the pentavalent antimonial compounds sodium stibogluconate (SSb) (Pentostam) and meglumine antimonate (Glucantime) has long been the mainstay treatment for complex CL and VL. Use may be limited by toxicity, duration, cost of treatment, and increasing reports of resistance, especially in India [22]. Liposomal amphotericin B is the favoured alternative for many cases of complex CL and VL where available.

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# Helminthic Dermatoses

8

Claire Fuller and Roderick Hay

## 8.1 Nematodes

Nematodes are common and more than 60 species are known to parasitize humans. They are round worms with a worldwide distribution but particularly common in the tropics and subtropics [1]. Although common in the gut in many environments, skin disease is seldom seen with some important exceptions.

Nematodes (roundworms)infestations include:

- Cutaneous larva migrans
- Dracunculiasis (scheduled for global eradication)
- Lymphatic Filariasis
- Gnathostomiasis
- Loiasis
- Onchocerciasis
- Strongyloidiasis

### 8.1.1 Cutaneous Larva Migrans (CLM)

It is caused by the passage of animal hookworm larvae through the skin. Common species include *Ancylostoma braziliense, A. ceylanicum*, and *A. caninum*.

These are picked up from contact with sand or soil contaminated with the feces of dogs and cats.

CLM presents with itchy red serpiginous lesions in the skin, which move between 1 mm and 3 cm each day. These lesions represent the host response to the presence of the hookworm larva within the skin. As humans are not the intended host, the larvae eventually die in the skin and do not progress the life cycle; however, until they do succumb, itching is intense.

Secondary bacterial infection of the skin or impetigo, as well as folliculitis, can complicate the scratching. Blistering lesions have also been reported, as has erythema multiforme [2].

#### 8.1.1.1 Global Distribution

Hookworms responsible for CLM are found all over the world, but infection is more frequently reported in tropical and subtropical areas, such as Southeast Asia, South America, Caribbean, and Africa. Although less common, it has also been reported in Europe, North America, and New Zealand.

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A. Morrone et al. (eds.), *Skin Disorders in Migrants*, https://doi.org/10.1007/978-3-030-37476-1_8

#### 8.1.1.2 Diagnosis

Diagnosis can safely be made clinically, although eosinophilia and raised IgE levels may be found.

#### 8.1.1.3 Differential Diagnosis

Any dermatoses that can produce serpiginous lesion, such as lichenoid eruptions, photodermatoses, jellyfish stings, herpes zoster, and larva currens (see below). These can typically be ruled out clinically.

#### 8.1.1.4 Treatment

Although the condition is self-limiting, as the larvae will die in the skin, ivermectin 0.15–0.2 mg/kg for 1–2 days will relieve symptoms and prevent impetigo and is the most effective treatment. Other treatments include albendazole 400 mg daily, and in some countries, topical cream/ointment formulations of albendazole, ivermectin, and thiabendazole are available.

### 8.1.2 Lymphatic Filariasis

This tropical lymphoedema is caused by the following nematodes: *Wuchereria bancrofti* (90%), *Brugia malayi*, and *Brugia timori* (10%).

These are transmitted to humans via the bite of an infected mosquito. Once the larvae have been deposited in the skin, they migrate to the lymphatics where they mature into adult worms. The presence of the adults within the lymphatics leads to lymphoedema.

Intermittent acute episodes of incapacitating fever, pain, and inflammation of the lymph nodes and swelling of the associated limb or genital area are the most debilitating aspect of the condition. They may occur several times per year and can occur with any lymphoedema whatever the cause.

#### 8.1.2.1 Global Distribution

Following the success of the Global Programme to Eliminate Lymphatic Filariasis (GPELF) over the last 15 years, the worldwide distribution has fallen to 73 countries across Africa, South America, and Asia (from 83 in 2000).

#### 8.1.2.2 Diagnosis

Filariasis can be confirmed by the immunochromatographic test (ICT) that detects circulating antigens. In the absence of this inexpensive, convenient investigation, night blood smears (taken between 10 p.m. and 2 a.m.) can be examined for the presence of microfilaria (MF). Bloods have to be examined at night as the microfilariae demonstrate nocturnal periodicity, so they only appear within the circulating blood at night. This test is only useful before the lymphoedema has developed.

High IgE often >10% is also seen.

#### 8.1.2.3 Differential Diagnosis

Podoconiosis (a nonfilarial noninfectious tropical lymphoedema) should be considered for those with negative ICT who have been working barefoot in the appropriate area: tropical volcanic highlands with high annual rainfall such as Ethiopia, Cameroon, and Uganda.

In practice in migrant populations, filariasis is very infrequent, but this diagnosis should be born in mind in patients presenting with unilateral or bilateral lymphoedema.

#### 8.1.2.4 Treatment

If the patient has microfilaria identified on midnight bloods or positive ICT, they should receive an antifilarial regimen to eliminate the microfilariae and adult worms. The options are as follows:

1. Diethylcarbamazine (DEC) 6 mg/kg daily for 12 days
2. Single dose of a combination of DEC 6 mg/kg and albendazole 400 mg
3. Single dose of combination of albendazole 400 mg with ivermectin 1.5–0.2 mg/kg

Additionally doxycycline 200 mg daily for 6–8 weeks kills the *Wolbachia* sp., a bacterium present in the gut of the worm that appears to be necessary for nematode reproduction; so this is a useful adjuvant therapeutic option.

If the patient has lymphoedema, simple intervention including daily washing of the feet and limb with water fit for drinking, daily emollient/

moisturizer as either glycerine added to the wash water or white soft paraffin applied after washing, and the wearing of socks or bandages to achieve some compression together with shoes to prevent damage to the swollen foot can produce significant benefit for the lymphoedema and prevent the intermittent acute episodes and cellulitis, for which breathing exercise, massage, and adequate shoes can be suggested. If hydrocele occurs, surgical correction is required.

### 8.1.3 Gnathostomiasis

This is a foodborne parasitic zoonotic disease with humans as an accidental host. The patients typically present with intermittent migratory swellings and nodules, eosinophilia, and a history of travel to endemic areas (see below).

This is associated with general malaise, fever, urticaria, and nausea as well as right upper quadrant abdominal discomfort.

The migratory swellings are usually 5–15 cm round or oval infiltrated red itchy plaques that can also be painful. Deep-seated indurated nodules can additionally form along the pathway of the larval migration. These can last up to 2 weeks and leave behind classical subcutaneous hemorrhages within its wake, which is a helpful sign to distinguish from other migrating cutaneous infiltrations.

The lesions tend to occur within about 4 weeks of ingestion of larvae.

#### 8.1.3.1 Global Distribution

Asia, Japan, Central and South America, and Africa

#### 8.1.3.2 Diagnosis

It is challenging and unusual to be able to identify the find the worm, but histology of a plaque will show a dense perivascular and interstitial infiltration with eosinophils and flame figures.

#### 8.1.3.3 Treatment

Albendazole 400–800 mg daily for 21 days or ivermectin 0.2 mg/kg two doses 48 h apart

### 8.1.4 Loiasis

This is caused by *Loa loa*, transmitted by the deerfly (also known as the mango fly) from the genus *Chrysops* usually during the rainy season.

Those infested by the worm are usually asymptomatic. However presentations can include subcutaneous large localized swellings known as Calabar swellings. These are typically on the limbs near the joints. They are itchy, painless, and migratory. Alternatively a recurrent focal angioedema on, for example, the face can occur. Finally, the adult worm can migrate across the conjunctiva accounting for the more common name of "African eye worm."

An additional key aspect of identifying loiasis infection is in those patients who also have onchocerciasis and lymphatic filariasis. *Loa loa*-infected individuals are at risk of severe adverse reactions including fatal encephalopathy should they received ivermectin for another diagnosis such as onchocerciasis or lymphatic filariasis.

#### 8.1.4.1 Global Distribution

West and Central Africa. Patients have usually lived in rain forest areas although transmission is usually highest where there are clearings. Infection is less likely but may still occur in those passing through an endemic area, risk of infection being higher in those staying for longer periods.

#### 8.1.4.2 Diagnosis

Typical presentation with Calabar swellings, ocular symptoms (i.e., the eye worm noted), and unexplained peripheral eosinophilia

The adult worm can be removed from the subcutaneous or conjunctival tissue. Microfilaria can be seen on daytime peripheral blood smear.

A polymerase chain reaction assay has been developed for accurate diagnosis [3].

#### 8.1.4.3 Treatment

Diethylcarbamazine 200 mg daily for 21 days

Albendazole 200 mg twice daily for 21 days

### 8.1.5 Onchocerciasis

Also known as river blindness caused by *Onchocerca volvulus*, a filarial nematode, it is transmitted by the female blackfly of the *Simulium* genus.

The cutaneous presentations are several and have been well categorized.

Acute popular onchodermatitis and eruption of the extremities comprising tiny 1–3 mm itchy papules with vesicles and pustules on a background of redness and local swelling

Chronic popular onchodermatitis: flat-topped, hyperpigmented, 3–9 mm itchy papules on the buttocks, waist, and shoulders. Itching is severe.

Lichenified onchodermatitis: typically localized plaque of hyperpigmentation, often associated with lymphadenopathy. Itching is intense and continuous.

Atrophy: typically around the waist, thighs, and buttocks with loss of elasticity and wrinkling, decreased sweating and hair growth. But the skin is not itchy.

Depigmentation: typically mottled and over the shins and also known as "leopard skin"

Onchocercomas: firm painless subcutaneous mobile nodules over bony prominences, e.g., the hip [4].

People with onchocerciasis may also have normal-appearing skin, a feature of the disease in West and some parts of Central Africa.

#### 8.1.5.1 Global Distribution

Sub-Saharan Africa (30 countries) and limited areas of the Americas and Yemen in the Middle East. Due to a large program of elimination of the disease using mass treatment in endemic populations using oral ivermectin, the endemic areas are changing with declared elimination in some Latin American countries. For information on the current distribution of the disease, a useful source of information is the WHO web site (http://www.who.int/onchocerciasis/distribution/en/).

#### 8.1.5.2 Treatment

Primary treatment is ivermectin 0.15–0.2 mg/kg as a single dose repeated 3–12 months, as it is only effective against the microfilaria and not the adult worms. Coinfection with *Loa loa* must be excluded before treatment to avoid triggering potentially fatal encephalopathic reactions.

Additionally doxycycline 200 mg daily for 6–8 weeks kills the *Wolbachia* sp., a bacterium necessary for nematode reproduction, so this is a useful adjuvant therapeutic option.

### 8.1.6 Strongyloidiasis

Although predominantly a gastrointestinal disorder, the larvae may migrate in the patient's skin producing a migrating, sometimes serpiginous, urticarial line moving through the skin much faster than CLM at a rate of 5–15 cm per hour. This is called larva currens and is caused by *Strongyloides stercoralis*, a human parasite.

#### 8.1.6.1 Global Distribution

Strongyloidiasis is found worldwide but more common in tropical and subtropical regions. It is more likely to present in migrant populations with gastrointestinal symptoms although the acute disseminated form (see below) has been described following the use of immunosuppression many years after an individual settles in a new country. In an immunocompetent host, skin invasion is uncommon, and the symptoms are generally mild but catastrophic, and severe life-threatening situations arise in the immunosuppressed with hyperinfection leading to edema, septic shock, asthma and hemoptysis, urticaria, and sometimes meningitis. There is a poor prognosis. Patients with HTLV-1 and HIV are more susceptible to the disseminated form.

#### 8.1.6.2 Diagnosis

Microscopic stool examination will identify the presence of larvae but this may to be repeated. Serum IgE is generally raised, and there is often a peripheral blood eosinophilia.

An enzyme-linked immunosorbent assay for anti-strongyloid IgG antibodies can be used as a screening investigation.

#### 8.1.6.3 Treatment

Ivermectin 0.2 mg/kg is given daily for 2 days. Albendazole 400 mg twice daily for 7 days is an alternative. Follow-up stool samples 4–6 weeks after treatment will confirm clearance of the infestation.

## 8.2 Trematodes and Cestodes

The common Trematodes (flukes) infestations are:

- Schistosomiasis
- Paragonimiasis
- Fascioliasis

The most frequent infestation by Cestodes (tapeworms) is:

Cysticercosis

### 8.2.1 Schistosomiasis

Also known as bilharzia, this represents a common trematode infestation caused when the free-swimming larvae or cercariae of *Schistosoma* sp. released by freshwater snails directly penetrate the skin. Where they end up depends on the species. *Schistosoma mansoni* and *Schistosoma japonicum* head for the mesenteric venules, whereas *Schistosoma haematobium* ends up in the retrovesical plexus.

Infestation occurs either following contact with freshwater containing the cercariae or drinking infected water.

Cutaneous manifestations include the following:

*Cercarial or swimmer's itch:* a nonspecific urticarial eruption a few hours after the larvae penetrate the skin.

*Katayama fever:* hypersensitivity reaction about 2–8 weeks after infestation more commonly in those exposed to the parasite for the first time. Fever, malaise, headache, and diarrhea are accompanied by urticaria, purpura, and generalized edema. Although possible in migrants the first of these skin manifestations is usually seen soon after exposure to contaminated water.

*Bilharziasis cutanea tarda:* papular, granulomatous, or verrucous lesions at the site of egg deposition in the dermis in those with chronic visceral schistosomiasis. The lesions are typically very itchy and emerge in crops. These are often genital in distribution but are fortunately uncommon.

#### 8.2.1.1 Global Distribution

Sub-Saharan Africa (see WHO Schistosomiasis Atlas), Middle East, Caribbean, South America, Southeast Asia [5]

#### 8.2.1.2 Diagnosis

Microscopic analysis of feces and/or urine will identify parasite eggs.

ELISA looking for antischistosomal immunoglobulin is available and useful to distinguish between acute and chronic infection.

ESR and eosinophil counts may well be raised.

Skin biopsy of cercarial dermatitis will show spongiosis and mixed inflammatory infiltrate.

Genital or perianal lesions may show ova in the dermis associated with a granulomatous reaction.

Antibody detection with the Falcon assay screening test (FAST) is reported to be highly specific [6, 7].

#### 8.2.1.3 Treatment

In cercarial dermatitis, topical steroids and antihistamines are used as symptomatic treatment.

However, if the diagnosis of acute schistosomiasis is established, the treatment is oral praziquantel 20 mg/kg twice daily for 3 days adding prednisolone 40 mg daily for 3 days for the Katayama fever.

In chronic schistosomiasis, praziquantel 60mg/kg is given in two to three doses 3 h apart.

### 8.2.2 Cysticercosis

This is the most common human cestode infestation caused by larval cysts of the tapeworm *Taenia solium*. The cutaneous manifestations of

this are usually gastrointestinal disorder being subcutaneous nodules which may be asymptomatic and multiple. These are rare.

They are typically round and firm, painless, and like a lipoma or epidermoid cyst.

The patient may have more generalized symptoms of the gastrointestinal infection such as abdominal discomfort, weight loss, and anorexia. Neurological invasion may present with seizures.

The disease is seen in Asia, sub-Saharan Africa, and Latin America. There is an immunoassay (serological) although cysts can be seen using CT or MRI scans.

#### 8.2.2.1 Treatment

The treatment is praziquantel. But skin lesions do not usually require therapy.

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# Dermatoses Caused by Arthropods

9

Claire Fuller

Skin lesions resulting from arthropod exposure may arise via various pathologic pathways, such as direct damage to tissue, hypersensitivity reactions to venom or saliva, or infectious disease transmitted by the arthropod.

Arthropods are invertebrates with jointed limbs, a segmented body, and an exoskeleton made of chitin. The group includes the crustaceans, insects, arachnids, and centipedes.

The aim of this chapter is to cover cutaneous disorders caused by arthropods that might affect patients who are migrants.

It will cover those conditions caused by the arthropod and not those conditions where the arthropod acts as their vector.

## 9.1 Bites and Stings

Nairobi fly of the *Paederus* sp. are found in East Africa and are examples of beetles that produce a corrosive substance pedarin when disturbed as a defense mechanism. This leads to blistering of the skin where it comes into contact, producing so-called dermatitis linearis.

The local remedy is to apply toothpaste to the blister, but topical steroids would probably work just as well.

## 9.2 Insect Bites

This general term is given to reactions, where salivary products are injected into the skin when the insect is feeding or venom is injected when the insect stings.

The reactions can be immediate, with a wheal and flare within minutes of the episode or delayed with swelling and induration coming up 48 hours later, and lasting some days. In addition, there is a rare hypersensitivity reaction that can follow mosquito bites in some patients leading to local blistering, general malaise, fever, and even lymphadenopathy. This unusual reaction is said to be more common in association with underlying Epstein–Barr virus.

Treatment for localized bites, if required, can include topical steroids. Antibiotics to cover *Staphylococcus aureus* may be required if secondary infection is suspected.

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## 9.3 Infestations

### 9.3.1 Scabies

The mite *Sarcoptes scabiei* is a common human pathogen which is easily transmitted by close physical contact between infested individuals. The mite burrows into the upper layers of the epidermis, where it lays its eggs. Symptoms start within 2–6 weeks in individuals not previously exposed to scabies and within 1–4 days in those who have had a past scabies infection. Reaction to the presence of the mite causes intense itching, as well as a nonspecific papular type rash. Additionally, the burrows may be visualized around wrists, ankles, and between the fingers. In infants, the palms and soles may feature vesicles, as well as burrows. Pruritic nodules may also form on the breasts of women and genitalia of both sexes. The itching can be dramatic and frequently lead to impetigo from vigorous scratching. *Staphylococcus* and *Streptococcal* infections commonly follow. It is likely that the majority of *Streptococcal pyodermas* globally are triggered by scabies [1]. They also cause significant impact on life quality due to the downstream effects of the secondary bacterial infections. It is estimated that 50% of acute post-*Streptococcal* glomerulonephritis is associated with scabies [1].

Common scabies infestations typically feature about 12 mites per person, but in some patients who do not react immunologically to the mite, **crusted scabies** may occur, and these patients will host millions of mites. The appearance is of widespread scaling and crusting, and microscopy of a crust will reveal several mites. These patients are highly infectious to others.

Migrants are especially vulnerable to diseases because of overcrowding, and outbreaks of scabies epidemics in refugee camps are well reported.

Management of individual cases should involve topical scabicides [2]:

If the patient is >2 months old, 5% permethrin cream is applied all over the body from head to toe, and under the nails and genitalia, but avoiding eyes and mouth. The cream should be left on overnight and washed off in the morning. The process should be repeated after 1–2 weeks.

In infants <2 months of age, crotamiton 10% cream (Eurax) is applied daily for 3 days, left on for 24 h at a time (permethrin is not recommended in children under 2 months of age).

Oral ivermectin is a more convenient alternative in patients >5 year of age or > 15 kg in weight, it is especially encouraged when topical therapy has failed.

As ivermectin is not active against scabies eggs, a second treatment maybe required after a week.

All household members should be treated at the same time, even those who are not symptomatic, as they too will host the mite but not be reacting.

Laundering clothes and sheets at >40 °C and drying in the sun, if possible, will reduce the risk of fomite transfer. If this is not possible, putting the clothes in a plastic bag in the sun for 3 days will ensure that any mites on the clothes perish and can no longer transmit infection.

Managing skin sores, associated with scabies, with antibiotic therapy against *Staphylococcus* and *Streptococcus* is recommended.

A strategy for managing crusted scabies has been published for the Northern Territories of Australia and recommends oral ivermectin between 3 and 7 doses on day 0, 1, and 7, and then at intervals thereafter depending on the severity of the crusted scabies.

In addition, this practical group advocates the use of topical approaches:

- 25% benzyl benzoate lotion to the whole body on alternate days after bathing, for the first week, and then 2–3 times per week till it is cured.
- Daily use of topical urea 10% and lactic acid 5% in cream (Clamurid®) to soften the hyperkeratosis and assist shedding of the crust which facilitates penetration of the topical scabicide.
- Careful attention to nail beds is recommended as these harbor mites.

Scabies has a worldwide distribution, but epidemics have recently been reported in the Western Pacific and Africa, particularly, Ethiopia.

### 9.3.2 Myiasis

Myiasis is the parasitic infestation of the larvae of a fly that burrows into and feeds on the host tissue. In man, this is typically *Dermatobia hominis*. The larvae burrow into the skin triggering the development of a tender motile nodule in the host tissue as they grow. Surgical removal of the larva is generally recommended, although eventually a larva will mutate and hatch into an adult fly leaving the host. An alternative strategy is to occlude the punctum overlying the nodule with grease, vaseline or even animal fat, to suffocate the larva which will then detach and emerge.

Tetanus prevention and management of secondary infection is also recommended.

### 9.3.3 Tungaiasis

Tungiasis (sand flea disease) is a tropical affliction characterized by the female sand fleas *Tunga penetrans* embedding themselves in the skin of the host. This sets up a local inflammatory response. It is common in sub-Saharan Africa and South America. It has recently been classified as a neglected tropical disease by the World Health Organisation (WHO). It is a condition associated with poverty and is more common in those who do not wear shoes. It produces significant discomfort, secondary infection, and impairment in life quality.

Management: There is no proven intervention for the treatment of tungiasis. However some studies are emerging using low viscosity dimeticone (NYDA®) with promising results [3]. The practice of using nonsterile needles, safety pins, etc., to remove the fleas has been associated with secondary infections such as *Staphylococcus*, *Streptococus*, and even hepatitis B. Patients with tungiasis are also at risk of tetanus.

### 9.3.4 Lice (Pediculosis and Pthiriasis)

Pediculosis is caused by *Pediculus humanus* and can infest the scalp (*P. humanus capitis*) or body (*P. humaus corporis*). *Pthirus pubis* causes pubic lice and is a slight smaller organism.

Body lice tend to live on the clothes, whereas head and pubic lice live on the hair baring areas of the host.

Symptoms of itching and irritation can occur, and in heavy infestations, anemia may be associated.

The additional significant health risk is the transmission of louse-borne infectious diseases such as epidemic typhus, relapsing, and trench fever caused by *Rickesttsia prowazeki, Borrelia recurrentis*, and *Bartonella quintana*, respectively. Management of lice infestations is thus critical in overcrowded situations such as refugee camps.

Previously, topical insecticides and physical techniques of removal, boiling clothes, and shaving heads have done little to reduce the cases, and indeed resistance has increased. Recently, promise has emerged in the use of doxycycline (acting on the bacterial symbiont) and ivermectin [4].

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# Eczema and Dermatitis

# 10

Aldo Morrone

## 10.1 Atopic Dermatitis

### 10.1.1 Pathogenesis

Atopic dermatitis (AD) is an inflammatory skin disease which is characterized by pruritus and eczematous lesions with typical distribution and morphology, usually following a chronically relapsing course (Fig. 10.1) [1]. The aetiology of AD is still only partially understood, although much progress in unraveling the pathogenetic mechanisms has been achieved. Genetic factors are very important, as suggested by the high frequency (70%) of association with a familial history of atopic disorders (AD, asthma, rhinitis, or seasonal conjunctivitis). In many populations, patients with atopic dermatitis may show mutations in the filaggrin gene which is important for maintaining the integrity of the epidermis and skin barrier. Other associated genes include some related to T-cell activation such as Th2 signaling pathways. It is likely, therefore, that the clinical expression of atopic dermatitis is based on mutations/polymorphisms in a number of different genes. There is no clear association with HLA molecules; but susceptibility to atopic diseases has been associated with a slow acetylation genotype. Against this background of genetic predisposition, a great variety of environmental factors contribute to the development and the course of dermatitis. In many cases, there are seasonal changes in the severity, with deterioration or exacerbation in autumn, winter, or spring and improvement during summer. However, this is not an absolute rule, and the course can differ from one patient to another and in different geographical areas and climates. AD skin is typically dry and susceptible to various irritant substances due to abnormal barrier function, related to an impaired content of ceramides as well as filaggrin defects, and this can be confirmed physiologically by increased transepidermal water loss. Other factors which have been implicated in

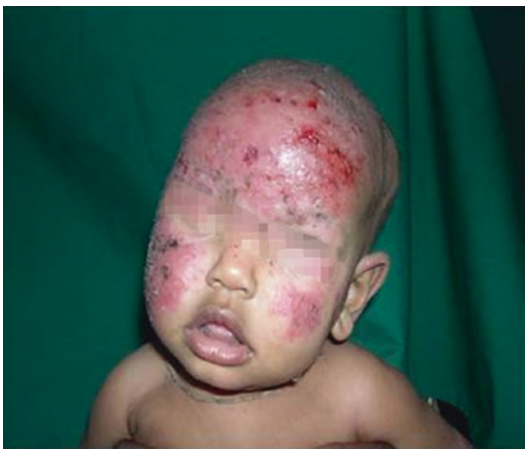

**Fig. 10.1** Atopic dermatitis

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exacerbation of AD include exposure to inhalants, foods, infections (e.g., *Staphylococcus aureus*), and contact allergens as well as emotional factors.

Immunological mechanisms play a crucial role in the pathogenesis of AD. Atopy has been associated with the functional imbalance of activation of the Th1 and Th2 lymphocytes. This imbalance may account for some AD-related features: increased IgE levels, skin prick test type I reactivity, susceptibility to cutaneous infections, and altered responsiveness to microbial antigens. Abnormal cytokine regulation is related to a preferential stimulation of Th2 cells but does not mean that the delayed-type hypersensitivity response is completely abrogated in atopic subjects. In fact, AD patients can develop allergic contact dermatitis (see below), which is in turn facilitated in part by the skin barrier defect and frequent use of topical sensitizers, and, when patch-tested with nickel, for instance, sensitive atopics release the same cytokines as nonatopic individuals. The potential for proliferation of activated T-cell clones in AD is triggered by an enhanced antigen-presenting activity; in particular IgE-mediated presentation and superantigen exposure, such as those produced by *Staph. aureus*. These play an important role in T-cell activation and, consequently, in the release of pro-inflammatory mediators.

### 10.1.2 Epidemiological and Clinical Aspects

The diagnosis of AD is primarily based on clinical features and history since there is no specific investigation. The introduction of diagnostic criteria by Hanifin and Rajka provided a means for a greater uniformity of diagnosis; later a further set of criteria were introduced by a UK working party in order to provide valid disease definitions that could be used for epidemiological purposes, even when large populations were evaluated, and that were not dependent on age or ethnicity.

AD is a common disease which usually first presents in childhood; it accounts for up to 10–20% of consultations in a dermatologists' practice in developed countries; reported prevalence is 5–18% in subjects up to 7 years and 2–10% in adults [2, 3]. Both sexes are affected. However, these numbers give only an approximate estimation due to heterogeneous diagnostic methods, as well as ethnic and social differences.

AD is present in all ethnic groups and countries. In 1986, Rajka summarized the results obtained from a questionnaire sent to physicians in different countries excluding Europe and North America. The incidence of AD appeared to be high in the majority of countries, with very high rates in New Zealand, Hong Kong, and Uruguay and low in Thailand. Caucasians were the most affected group; sometimes, Chinese, Polynesians, and Ethiopians were reported to be frequently affected. In the last decades, the prevalence of atopy and AD has showed a progressive increase, which has been attributed not only to the refinement of diagnostic approaches and to the greater demand for medical services but also, possibly, to changes in social and environmental conditions. AD is more common in wealthier families; there is a link with small family size as cross infection in large families may have a protective role in the expression of atopic disease. It has been suggested that an increased risk of atopic eczema may be also a consequence of improvement in hygienic conditions and reduction of childhood infestations and infections: an inverse relationship between helminthic infestation and allergic diseases has been pointed out in Gambia and South Africa. Studies of migrant populations in Hawaii, the UK, and New Zealand have shown notable increases in disease prevalence compared with similar groups in a migrants' country of origin, supporting the role of socioeconomic, behavioral, and environmental changes such as those associated with industrialization (greater exposure to indoor and outdoor pollution, house dust mites, dietary allergens, staphylococci and irritants). Another possible reason for this apparent increased prevalence may be also related to the access to, and availability of, medical care. However, in the last few years, the incidence of AD in some resource-poor countries has also increased.

There is also evidence of differences in the expression of AD in settled migrant communities. A study conducted by the Leicester Royal Infirmary showed that AD was 3.3 times more

common among Asian than non-Asian patients, but a subsequent cohort study did not confirm any ethnic difference. A survey performed with about 25,000 consecutive referrals in India from 1989 to 1993 showed a low prevalence rate of AD (1.6%). In another study, the 12-month cumulative incidence of AD was assessed in Caucasian, Chinese, and Vietnamese infants born in Australia. AD developed in 21% of Caucasians, 44% of Chinese, and 17% of Vietnamese babies. Parents of the Chinese and Caucasian infants had similar socioeconomic and housing conditions compared with the parents of the Vietnamese infants, who tended to be living under lower socioeconomic conditions. The authors of this research concluded that the high incidence of AD in Chinese compared with Caucasian infants tends to reflect genetic differences between the two populations, whereas the difference in incidence between the Chinese and Vietnamese infants possibly reflects the environmental contribution to disease expression. Another report from the UK found a higher prevalence of AD in London-born black Caribbean children (16.3%) compared to white children (8.7%).

Itching is the most common symptom in all lesions. In early childhood, the lesions have an acute eczematous morphology. They appear red, often edematous, at times blistering or exudative, with well-defined margins. They are preferentially located in infancy on the cheek region of the face, with the nose being spared, and in the perioral region. Subsequently xerosis (Fig. 10.2) is often present. When the eruption becomes chronic, or when it starts after the second year of age, the lesions assume the appearance of very itchy, but often lichenified, eczematous patches and are often localized in the antecubital and popliteal fossae (Fig. 10.3). In adults, it is possible to observe persistence of lichenified lesions, on top of which papules of various sizes may develop. These may become infiltrated, with a hard consistency, and when they are repeatedly excoriated, they become persistent prurigo papules or nodules.

As for any inflammatory skin disorder, erythema is generally difficult to detect in darkly pigmented subjects. In African skin, there is a tendency toward the development of follicular lesions and marked perifollicular accentuation;

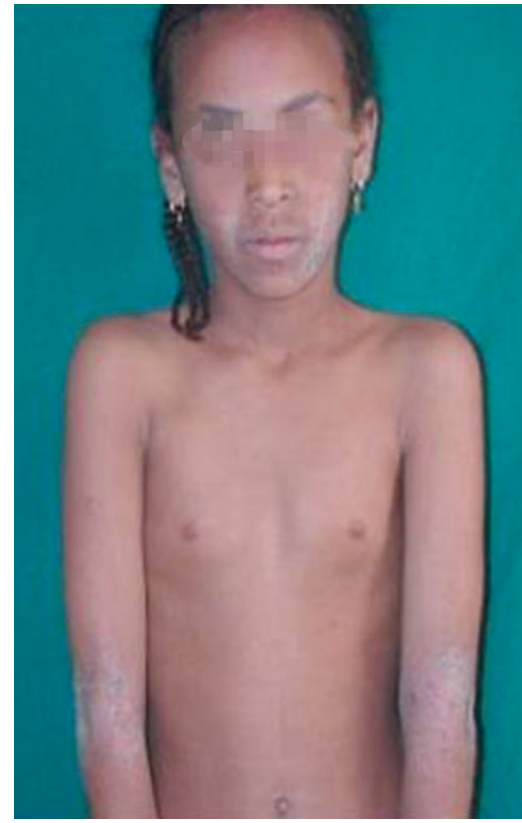

**Fig. 10.2** Atopic dermatitis with xerosis and scratching lesions

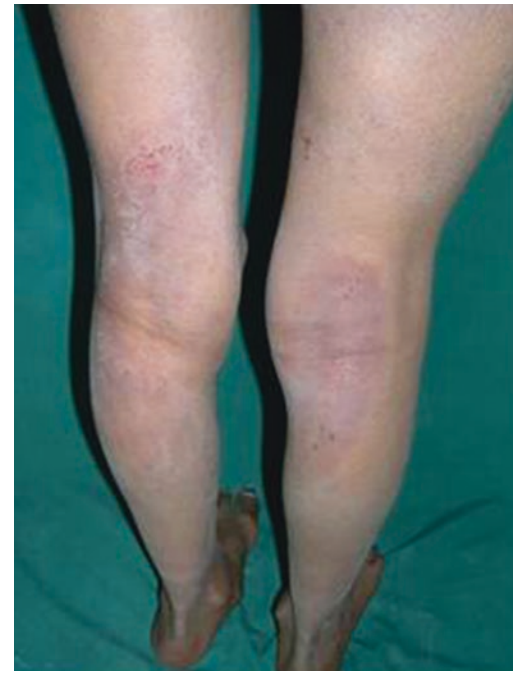

**Fig. 10.3** Atopic dermatitis in flexural area

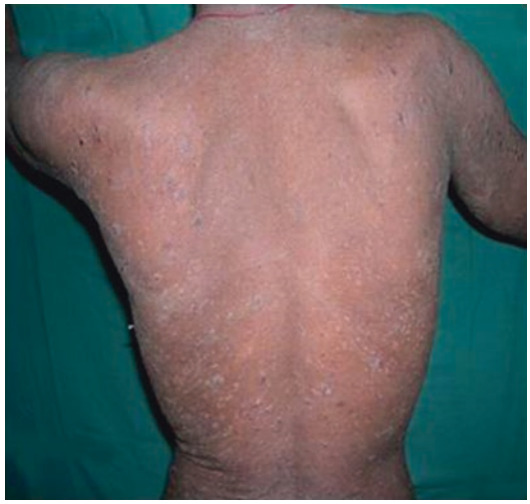

**Fig. 10.4** Eczema and lichenification of the skin

frequently, fine papules can be noted with the typical distribution of AD (posterior aspect of the neck, antecubital and popliteal fossae). In some children, follicular accentuation with scattered papules, associated, or not, with flexural involvement, may be the sole presenting feature of the disease. This micropapular form of lichenification must be differentiated from conditions such as lichen nitidus (Fig. 10.4).

Pityriasis alba is a hypopigmented condition which is frequently observed in atopics and is thought to be more common in black and mixed ethnic skin types. It may create a lot of concern for both patients and parents. Post-inflammatory hyperpigmentation is also a problem in black skin and a common sequela of excoriated lesions. Patients should be helped to stop scratching which increases hyperpigmentation. Pigmentary changes tend to improve with time; hypopigmentation clears over months, whereas hyperpigmentation requires more time to fade. Bleaching creams are of no value and can cause hypopigmentation in the surrounding unaffected areas.

### 10.1.3 Differential Diagnosis

Other types of eczema, seborrhoeic dermatitis, onchocerciasis, scabies, and other forms of allergic dermatitis, e.g. urticaria

### 10.1.4 Histopathology

The histological pattern does not show specific characters. But there is usually moderate spongiosis and vesiculation with ortho- and parakeratosis and an inflammatory pericapillary reaction in the eczema patches.

### 10.1.5 Treatment

The main stay of treatment is the use of specific anti-eczema therapies [4–6].

#### 10.1.5.1 Topical Therapies

1. Topical steroids (recommended use is once daily) in combination with at least a once-daily application of emollients. Tacrolimus and pimecrolimus are inflammatory cytokine inhibitors, with a mechanism of action similar to cyclosporin, and are helpful in some patients. Topical antihistamines and nonsteroidal anti-inflammatory drugs (NSAIDs) are not recommended because they tend to sensitize and result in allergic contact dermatitis.
2. Wet wraps (use for short periods during acute exacerbations) can be used in very extensive eczema.

Therapeutic strategies should be tailored to specific circumstances, such as severity of itch and extent of skin involvement, age of the patient, psychosocial implications, and the impact of AD on quality of life. It is important to relieve itch as scratching worsens skin lesions leading to more itching, thereby creating a vicious circle. Emollients applied directly to the skin or in bath or shower formulations are very useful and may reduce dependence on steroids. Patients vary in their preference for moisturizers of different consistencies, and it is often helpful to advise a selection of different products from which the patient can choose.

#### 10.1.5.2 Systemic Therapies

Sedating antihistamines are more effective than nonsedating antihistamines. Oral antibiotics (flucloxacillin or a macrolide such as erythromycin

for 1 week) are also of benefit in moderate to severe eczema even when there is no clear impetiginization, probably by reducing the bacterial load of the skin. Systemic use of cyclosporin (CsA) MTX and azathioprine has been proven to be effective, but its use is restricted to severe cases only. The use of a short course of oral prednisolone, for example, in a dose of 20 mg twice daily (adult dose), is occasionally needed to control difficult cases.

#### 10.1.5.3 Phototherapy and Photochemotherapy

UVA, PUVA, and UVB or UVA1 (wavelength 340–400 nm) have also been used as alternative treatments for extensive atopic dermatitis.

#### 10.1.5.4 Other Strategies

Management of AD may also involve preventive measures directed against the avoidance of trigger factors such as irritants as well as the use of emollients against dryness and drug therapies. The most relevant trigger antigens in atopic dermatitis are thought to be aeroallergens such as house dust mite or animal hair, but their role in exacerbating eczema is often unclear although elimination in addition to specific therapy may help in some patients. Contact with these allergens is prevented by using dust mite-proof covers for mattresses and pillows, wet-mopping floors, and avoiding rugs (especially in bedrooms). Some investigators have suggested that food allergens such as egg or shellfish may exacerbate atopic dermatitis and note improvement after a diet of progressive elimination. However, this is only occasionally of practical value in individual cases.

Irritants like wool, soaps, perfumes, makeup, prolonged hot showers, high temperatures, and low humidity can all contribute to the severity of atopic dermatitis and should be avoided or minimized. Stress and anxiety can be trigger factors, as well as depression, which may reduce the threshold for pruritus. Reducing repeated and persistent scratching with the help of behavioral therapy may be useful.

## 10.2 Contact Dermatitis

Contact dermatitis occurs where the clinical lesions of eczema are triggered by contact with either irritant or allergenic substances. Generally irritant reactions arise from direct damage to the epidermis which results in inflammation, whereas allergic contact dermatitis is mediated through activation of the immune system.

### 10.2.1 Pathogenesis

Allergic contact dermatitis (ACD) is an inflammatory skin disease which follows the exposure of the skin to an allergenic substance in sensitized individuals [7]. It is a very common form of eczema after both occupational and nonoccupational exposure; the estimated prevalence in the general population varies from country to country and with different exposure rates to sensitizers. The susceptibility to ACD depends partially on constitutional factors, local skin conditions (damaged skin, occlusion, pH modifications, irritant contact dermatitis which can increase percutaneous absorption), and the sensitizing potential of chemicals [8]. Exposure to high concentrations of allergens for prolonged periods increases the risk of ACD, as confirmed by the greater frequency of contact allergy in high-risk occupations. The compounds most frequently implicated in causing contact allergy include metals (nickel, chromate, cobalt), resins (acrylates, epoxy, and formaldehyde resins), rubber (accelerators, antioxidants, and other chemicals), textile dyes, medicaments (topical antihistamines, neomycin, NSAIDs, topical steroids), vehicles contained in medicaments or cosmetic preparations (lanolin, cetyl or cetostearyl alcohol, fragrances, preservatives such as the isothiazolinones), and plants (*Primula obconica*, *Rhus*, *Chrysanthemum*, tulip bulbs, garlic, onion, and others). From a pathogenetic point of view, ACD is a delayed hypersensitivity response which is linked to the antigen-dependent activation of CD4 helper T cells. Substances which

can induce contact sensitization are lipophilic and electrophilic haptens of low molecular weight (<500–1000 Da) which penetrate into the skin through intercellular spaces and skin appendages. In some cases, the skin's metabolic detoxificating processes can convert molecules without immunogenic properties (prohaptens) into true haptens; in others, haptens are derived from the transformation of prohaptens by the action of UV irradiation (photoallergens); plant allergens often work through such mechanisms. Following exposure in a susceptible patient 1–3 weeks elapse before the induction of sensitization, in sensitized individuals, the elicitation phase develops after about 48 h from reexposure to antigen; hyposensitization is of no value in management.

Some forms of contact dermatitis are provoked by skin irritants that cause damage to the skin barrier [8, 9] without the intervention of immune sensitization. Irritant contact dermatitis is probably more common than the allergic form, but it depends on the nature and intensity of exposure. Common skin irritants include lanolin, detergents, cleaning fluids, antiseptics, and acids. Exposure can occur in the home during normal household duties such as dishwashing or painting. Occupational exposure to irritants is also seen.

### 10.2.2 Epidemiological and Clinical Aspects

Contact dermatitis is clinically characterized by variable itching and scaly skin lesions localized to the site of contact with the sensitizing compound; secondary dissemination of these lesions to other areas can take place. The overall morphology of lesions is dependent on the duration of the dermatitis, with predominance of erythema, swelling, and vesicles in the acute phase; of crusting and fine desquamation in the subacute phase; and of lichenification and fissuring in chronic forms. The irritant forms of contact dermatitis are very similar in clinical appearance to the allergic variety and, again, occur at the site of exposure.

Particular clinical forms include micropapular dermatitis (frequently caused by nickel), nummular/discoid forms, pompholyx-type eczema, as well as others. Atypical non-eczematous reactions can also develop, e.g., bullous, purpuric, erythema multiforme-like, lichenoid, papular, granulomatous, pigmented, or depigmented lesions. Pigmented cosmetic dermatitis is described due to exposure to fragrances and pigments (e.g., Red 31 and DNC Yellow 11) contained in cosmetics and soaps. Oral ingestion of allergenic flavorings, such as cinnamon, can cause a focal flare in sensitized patients (systemic ACD).

Black and darkly pigmented subjects tend to present more commonly with lichenification, infiltration, and hyperpigmentary changes (Figs. 10.5, 10.6, and 10.7). The clinical picture also depends on the site of the dermatitis and on the causative agent; the severity of symptoms is influenced by the level of sensitivity and the intensity of exposure. Use of depigmenting agents by women for cosmetic purposes is a long-standing and widespread practice in some countries. Many depigmenting agents contain topical steroids and hydroquinone and can cause contact eczema along with multiple adverse effects. ACD and contact leukoderma may follow the use of "bindi," a pigment applied as a powder or paste to the central forehead by Indian women for religious and social reasons.

Generally the prevalence of contact dermatitis does not seem to vary very much with ethnicity.

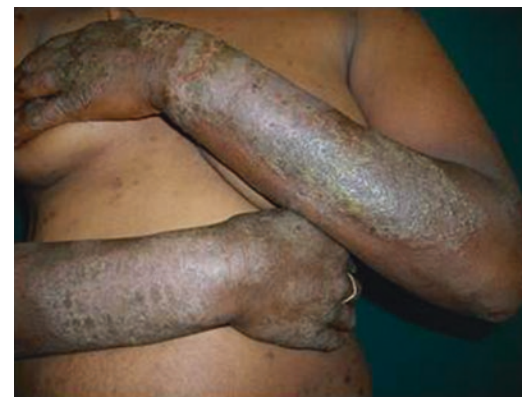

**Fig. 10.5** Lichenification of the lesions

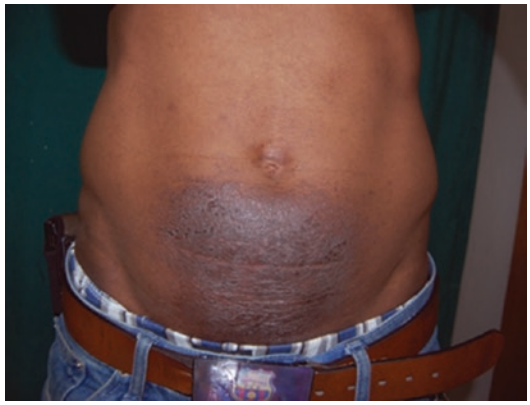

**Fig. 10.6** Contact dermatitis with hyperpigmentation

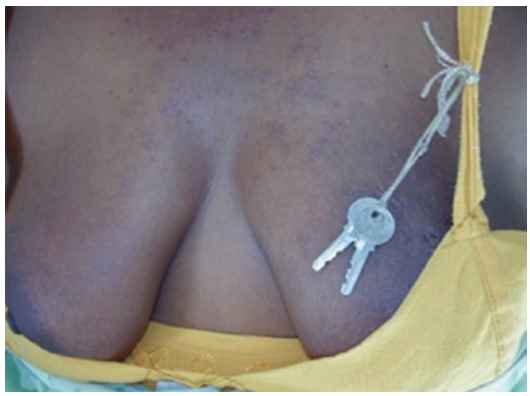

**Fig. 10.7** Contact dermatitis

The incidence and pattern of sensitivity may be variable from country to country depending on the degree and nature of exposure rather than any ethnic or genetic susceptibility. The pattern of contact allergy of migrants compared with people of the country of origin may be different due to differences in socioeconomic status, lifestyle, occupation, and access to dermatology services.

The Patch testing procedure is now well standardized, thanks to the guidelines of the International Contact Dermatitis Research Group (ICDRG) and those of local groups. Communication between dermatologist and patient is key to identify potential sensitizers, to define the clinical relevance of positive test results, and to identify and adopt correct preventive measures. Taking a careful history will also help to identify patients with irritant contact dermatitis. Patch tests are negative in these patients although short-lived areas of erythema may develop at patch sites exposed to a potential irritant such as lanolin, and interpretation of patch tests requires skills and training [10, 11]. Knowledge of traditions, customs, and social background of certain ethnic groups may be important in identifying the involvement of specific agents. For example, in Hong Kong, it has been found that the most common causes of contact dermatitis were soaps or detergents (22.0%) and traditional Chinese medicine (17.3%); the latter was a more common cause of contact dermatitis than Western medicine (9.0%) or metals (13.4%).

### 10.2.3 Differential Diagnosis

Atopic dermatitis and other forms of eczema, scabies, pediculosis, onchocerciasis, and drug-induced erythemas

### 10.2.4 Treatment

The management of ACD includes treatments which can relieve symptoms, with topical corticosteroids being the mainstay, but preventive measures aimed at avoiding or limiting the contact with the allergens are also critical. The role of a suspected allergen is confirmed by patch testing. Positive results must be correlated with history and clinical features in order to be judged as relevant.

## 10.3 Seborrhoeic Dermatitis

### 10.3.1 Pathogenesis, Epidemiological and Clinical Aspects

Seborrhoeic dermatitis (SD) is a common inflammatory skin disease in developed countries, where 1–3% of the general population is thought to be affected, with the highest frequency in young males. However, the estimated prevalence is much higher if dandruff is included as a clinical expression of SD limited to scalp skin. A significant increase in prevalence (20–83% depending

on the study population) is found in human immunodeficiency virus (HIV)-infected patients, in whom SD often produces more severe and recalcitrant symptoms. The association between SD and HIV infection suggests that immunological disturbances may be involved in the pathogenesis of the dermatitis. However, SD frequently develops in the early phase of the infection, before the occurrence of the typical immune defects and signs of full-blown AIDS. It seems that the natural course of SD is not influenced by the initial count of $CD4^+$T lymphocytes or antiretroviral treatments. The pathogenesis of SD has been under discussion with different potential triggers being put forward from the composition of sebum to variations in the skin microbiome. But there is now good scientific support for a key role of an inflammatory response to the commensal yeast *Malassezia* in SD. The course of SD is also influenced by climatic factors: in temperate climates, there is usually a relative improvement during summer with sun exposure, although aggravated symptoms during hot summer months have been also reported, especially in Northern European countries.

In the majority of cases, the diagnosis of SD is simple because of the characteristic morphology (red well-marginated scaly lesions with fine or greasy, yellow scales) and distribution (scalp, eyebrows, nasolabial folds, chest, interscapular area, and, less frequently, axillae and groin). Scalp scaling or dandruff is the most common clinical sign of SD. Some cases present with unusual clinical features particularly when SD occurs in association with atopy or psoriasis. SD is most common in adult life, and cases in infancy, previously classified as SD, are now thought to be forms of atopic dermatitis (Figs. 10.8 and 10.9) [12–14].

SD is often less common in resource-poor settings. But its prevalence in African HIV-infected persons is high in sub-Saharan areas. For this reason, the value of SD as a predictive sign for HIV infection is high in Africans, and SD may be inflammatory or non-inflammatory in black skin with the typical distribution on seborrhoeic areas. Inflammatory lesions present as follicular-

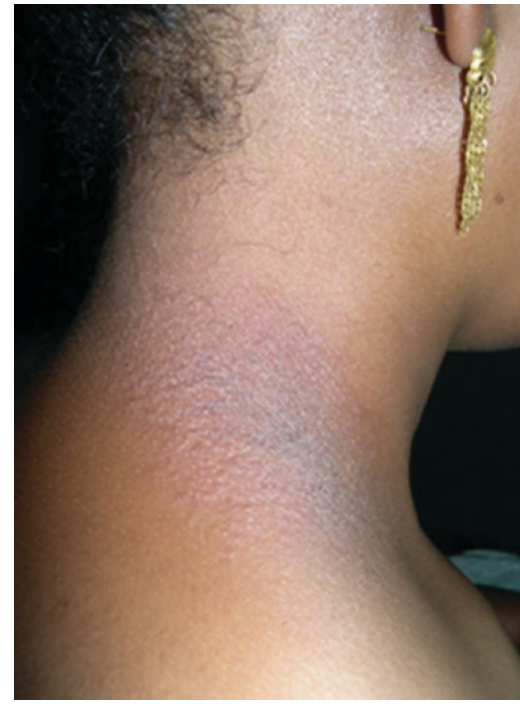

**Fig. 10.8** Seborrhoeic dermatitis

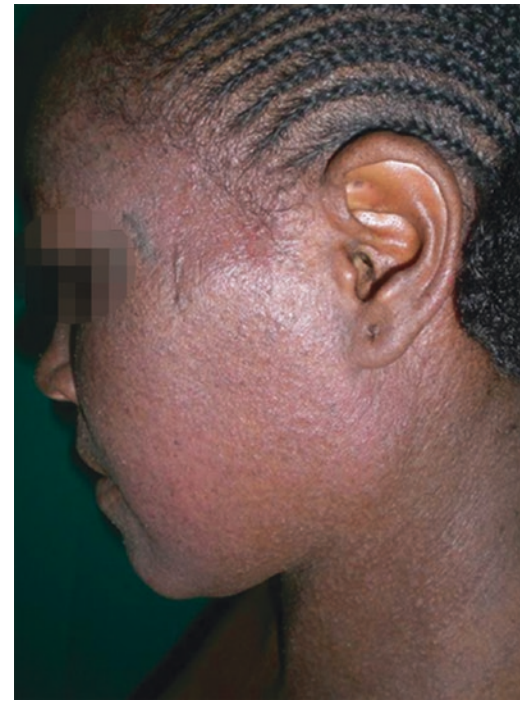

**Fig. 10.9** Seborrhoeic dermatitis

papular lesions on a diffuse mildly eczematous background and may be accompanied by mild pruritus. The non-inflammatory type comprises hypopigmented patches with indistinct margins and fawn-colored oily scales. Lesions of SD often have an annular morphology in people of African descent. Post-inflammatory hypopigmentation is frequent. Diffuse scaling of the scalp is observed and should be distinguished from that of AD, psoriasis, and tinea capitis. Frequent shampooing is not well tolerated and tends to make the hair shafts more brittle. Topical scalp preparations should be used as ointments or creams in black people (Figs. 10.10, 10.11, 10.12, 10.13, 10.14, 10.15, 10.16, and 10.17).

### 10.3.2 Differential Diagnosis

Differential diagnosis must be made with contact dermatitis, psoriasis, lichen simplex, pityriasis rosea, pityriasis versicolor, rosacea, erythrasma, and drug-related eruptions.

### 10.3.3 Histopathology

Histopathology of SD is not specific and includes changes that can be seen in both psoriasis and chronic eczema. $CD4^+$T cells close to activated

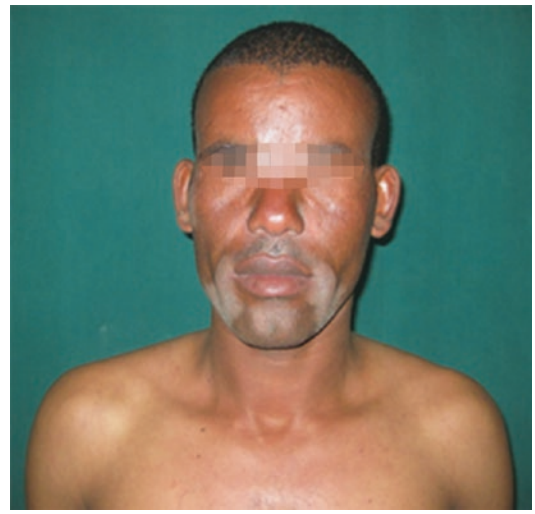

**Fig. 10.11** Eczema associated with hypopigmentation

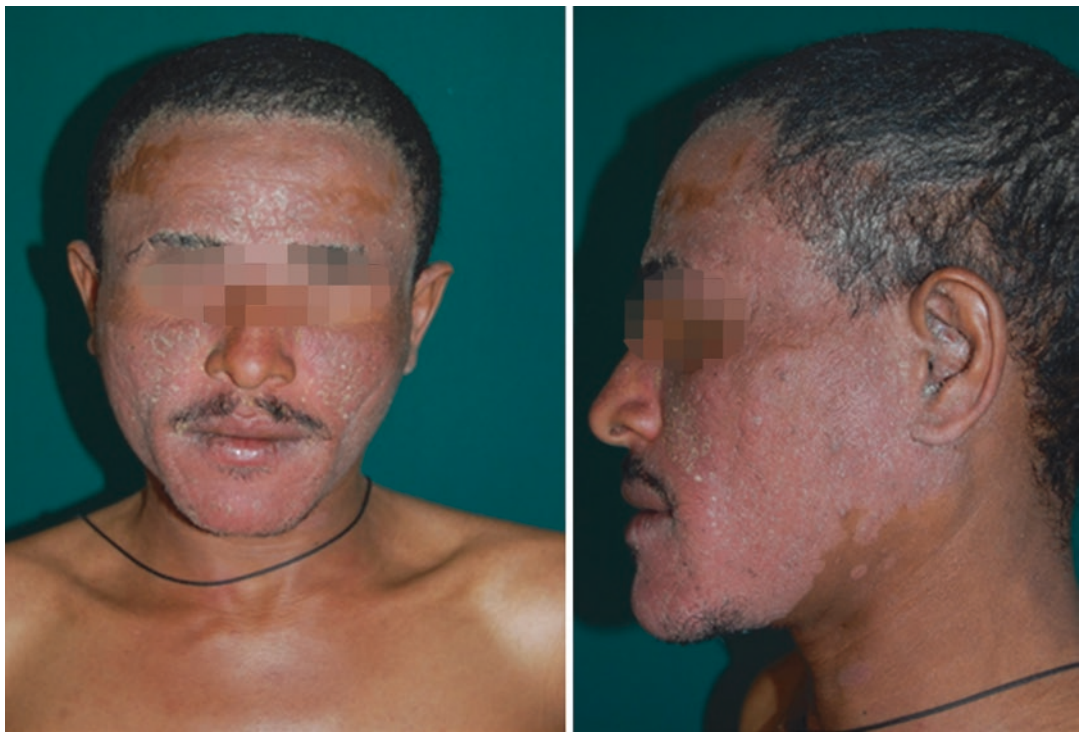

**Fig. 10.10** Seborrheic eczema associated with scales

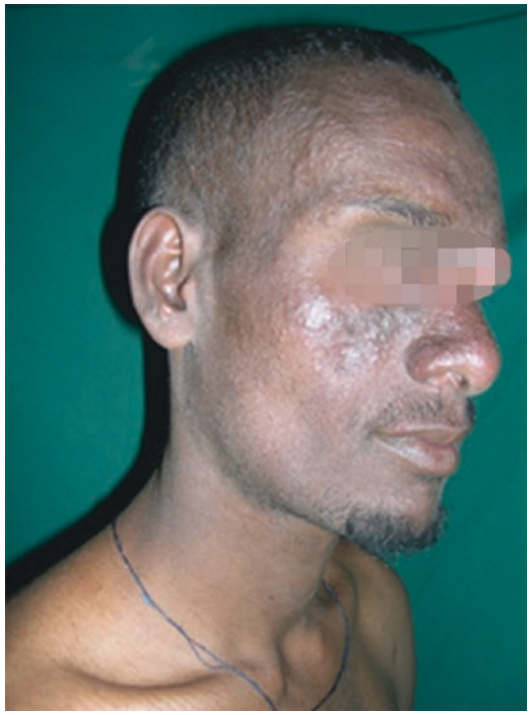

**Fig. 10.12** Eczema associated with vesicles and papules

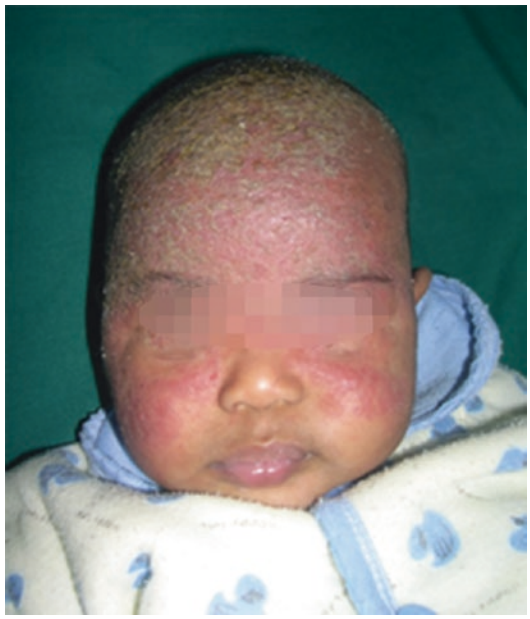

**Fig. 10.13** Seborrheic dermatitis in infant

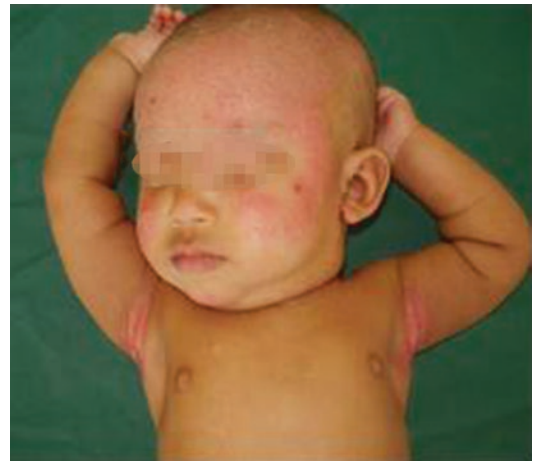

**Fig. 10.14** Seborrheic eczema on the face and axillary folds

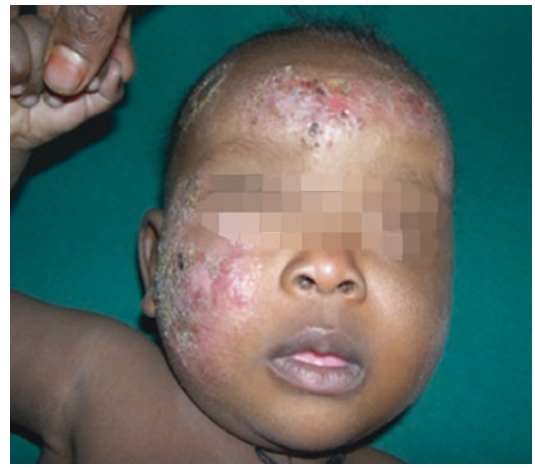

**Fig. 10.15** Eczema on the face associated with impetigo

antigen-presenting cells have been demonstrated in the upper dermis.

### 10.3.4 Treatment

Shampoos containing tar, selenium sulfide, zinc pyrithione, and ketoconazole (all antifungal agents) are usually effective for dandruff; 1% terbinafine solution may also be helpful. Severe dandruff can also be treated with salicylic acid and urea. Acute inflammatory lesions of SD elsewhere on the skin surface may be controlled by

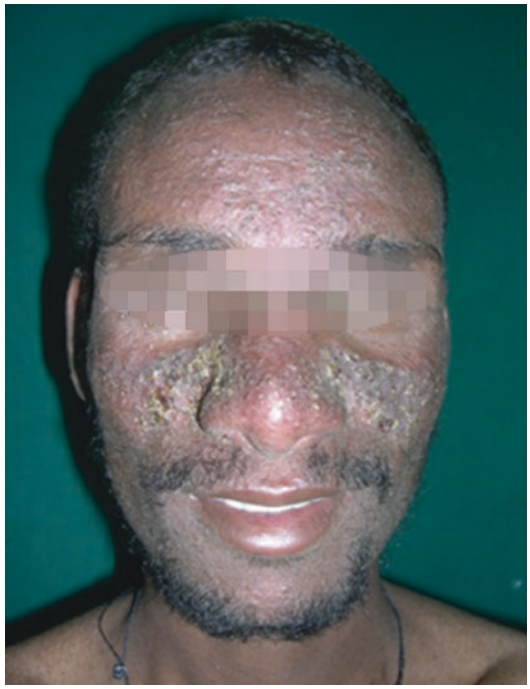

**Fig. 10.16** Eczema on the face in adult associated with impetigo

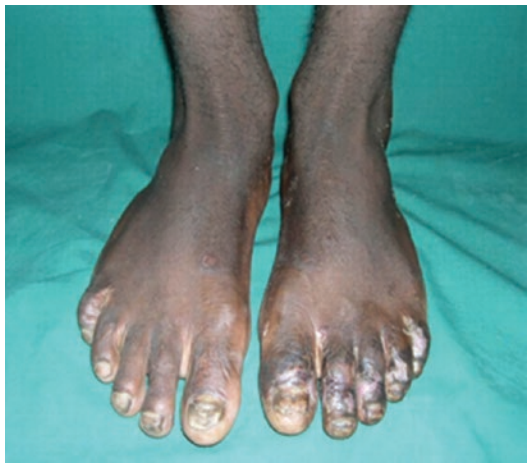

**Fig. 10.17** Contact dermatitis on the feet

antifungals, such as topical ketoconazole or clotrimazole with or without hydrocortisone. Short courses of topical corticosteroids or tacrolimus may also be helpful. More severe and diffuse forms of SD may require oral medications, including itraconazole, which has proved safe and effective in some open studies. Oral isotretinoin is also helpful in cases resistant to standard therapy, at dosages lower that those used for the treatment of acne vulgaris. Relapse is frequent and intermittent use of a topical antifungal is a simple way of controlling this [15, 16].

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# 11 Maculo-Papulo-Squamous Dermatoses

Stefano Veraldi, Luisa Angileri, and Luisa Carlotta Rossi

## 11.1 Lichen Planus

No data are available in the literature about LP in migrants.

The incidence of LP ranges between 0.22% and 1% worldwide [1]. Patients with LP represented 1.2% of all new patients with skin diseases in London and Turin (Italy), 0.9% in Copenhagen, and 0.38% in India [1, 2].

The clinical presentation of LP in patients with pigmented skin is similar to that observed on Caucasian skin; however, the color of the lesions is different: purple, brown, or black are typical colors of LP on dark skin (Fig. 11.1). Furthermore, Wickham's striae are often difficult to observe. Annular lesions may be seen on the skin (Fig. 11.2), the penis, and the oral cavity. Koebner phenomenon may be marked. The presence of violet-brown-black nodules and plaques with a smooth or verrucous surface, in particular on the legs, is due to chronic scratching because of severe pruritus (Fig. 11.3). On dark skin, LP is sometimes similar to psoriasis [3].

In children from South East Nigeria, the limbs were the most common sites of LP [4]. Classical LP was the most common clinical variety, followed by hypertrophic, linear, and eruptive generalized LP. Koebner phenomenon, nail dystrophy, and oral involvement were also observed, whereas scalp and palmoplantar involvement was not recorded. Despite the endemicity of hepatitis B, this study revealed that liver function tests were not significantly different between children with LP and hepatitis B surface antigen and those who were negative for this antigen. Anti-hepatitis C antibodies were not recorded in any of these children [4]. In a study carried out in the United States on 36 children, the authors observed that 26 (72%) of these patients were African American [5].

Persistent post-inflammatory hyperpigmentation is a characteristic feature of LP in individuals with dark skin.

Oral LP is more frequent in Indians, with a prevalence of 1.5% in the villages of Kerala, possibly related to chewing tobacco [6]. Oral LP ranges between 0.5% and 2.2% in other epidemiological studies [7, 8].

Actinic LP occurs mainly in children and young adults with dark skin, living in tropical countries. It is located on light-exposed areas (in particular the face). The incidence of actinic LP is estimated at 1 case/1.000.000/year. According to a study carried out in Tunisia, actinic LP occurs more frequently in females [9]. The annular variety predominates [9]. However, some cases of melasma-like (pigmented) actinic LP have been

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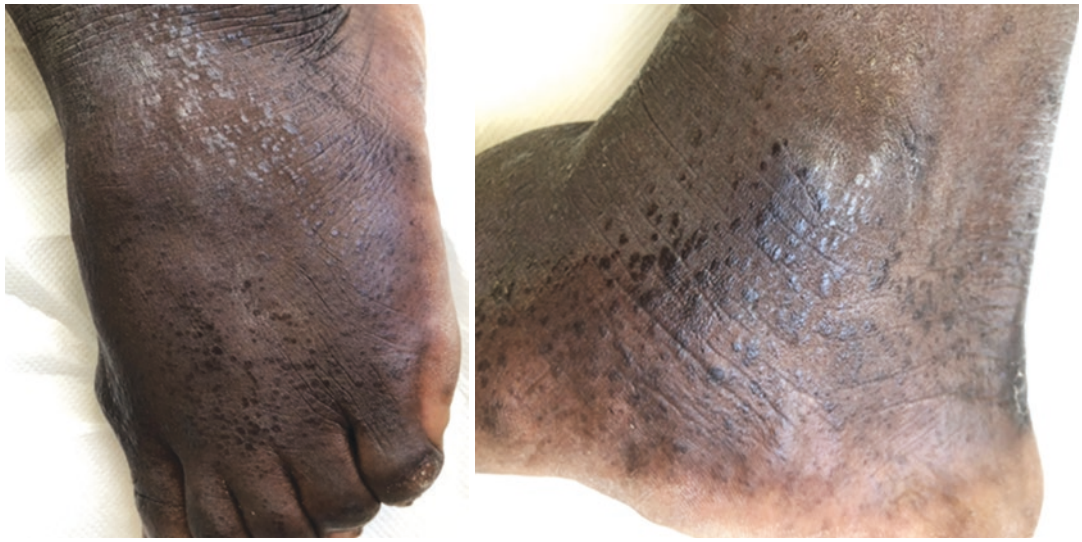

**Fig. 11.1** Lichen planus. Brown-black papules on the dorsum of the feet and ankle

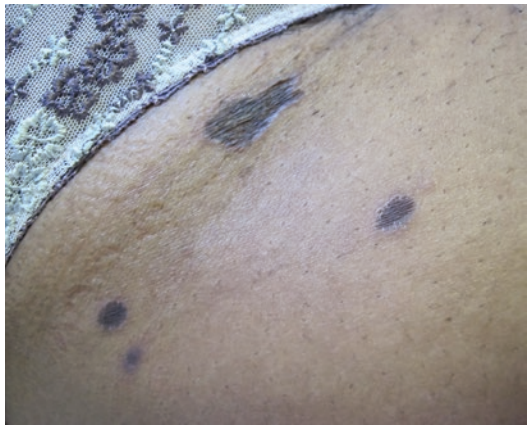

**Fig. 11.2** Lichen planus. Annular lesions on the thigh

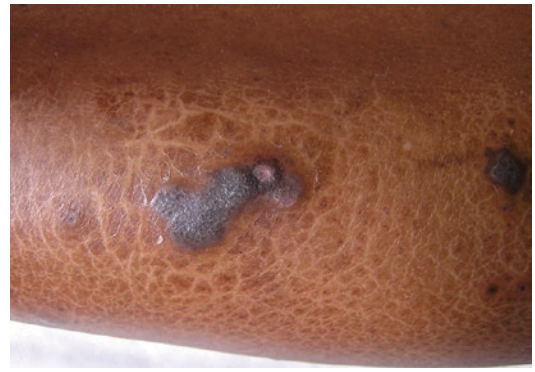

**Fig. 11.3** Lichen planus. Nodules and plaques on the leg

described [10]. The involvement of the face is typical as well as the worsening of the disease in spring and summer time [10]. Rare cases of actinic LP located exclusively on the lower lip and associated with sunlight exposure have also been reported [11].

LP pigmentosus is more common in middle-aged subjects with dark skin. It is characterized by hyperpigmented, gray-brown to brown macules in sun-exposed areas, typically on the face, neck, and upper limbs. Palmoplantar region and nails are never affected. The oral cavity may be rarely involved [12–15]. LP pigmentosus rarely presents with a linear or segmental or zosteriform distribution, also along the lines of Blaschko [15, 16]. An additional rare variety, LP pigmentosus inversus, has similar clinical and histopathological findings. However, this variant occurs mainly in Caucasians on the folds, such as axillae and groins, while sun-exposed areas are usually spared [14, 15]. LP pigmentosus may be associated with hepatitis C and autoimmune diseases [15]. Some Indian studies reported the association of LP pigmentosus with topical application of mustard and amla oils [12]. These oils are used for body massage, hair dressing, and the preparation of traditional Indian drugs. These oils contain allyl thiocyanate, which is a potential photosensitizer [12].

Lichen nitidus occurs as frequently in white as in black people, but it is recognized more easily in black people in whom it is usually characterized by hypopigmented lesions [17].

## 11.2 Psoriasis

No data are available in the literature about psoriasis in migrants.

Differences about genetic predisposition, epidemiology, clinical features, and treatment have been reported in patients with different ethnic groups. Prevalence rates of psoriasis range from 0.05% to 3.7%, depending on geographic locations. Epidemiological data on psoriasis in non-Caucasian populations are limited; however, they suggest a lower rate in non-Caucasian ethnic groups compared to Caucasians. In an epidemiological study carried out in the United States, it was observed that prevalence of psoriasis was higher in Caucasians in comparison with African Americans and Hispanics (3.6% versus 1.9% versus 1.3%, respectively) [18].

Interestingly, epidemiological studies carried out in Africa found significant differences in prevalence rates: 1.9–3.5% in Eastern Africa (Kenya, Uganda, and Tanzania) and 0.025–0.9% in Western Africa (Nigeria, Mali, and Angola) [19].

Studies in Mexico and Central and South America showed a prevalence of psoriasis of 1.3–4.2%. Prevalence is lower in Asia, where it ranges from 0.05% to 0.47%. Psoriasis seems to be higher in Malay and Indian patients, followed by Chinese people [19].

Genetic susceptibility is different between ethnic groups. More than 30 psoriasis susceptibility regions are implicated in the predisposition to this disease. HLA-Cw6 is a gene located within the PSOR1 locus, encoding the major histocompatibility complex: the latter is important in the adaptive immune response, which showed higher prevalence in Africans (15.09%) compared to Caucasians (9.62%) [20]. HLA-B52 is significantly associated with Arab Omani ethnicity, while IL-10 polymorphisms or HLA-B46 are closely linked to psoriasis in Asian individuals. Therefore, genetic and environmental factors are both involved in the pathogenesis of psoriasis. Their variations throughout different geographical areas are responsible for different prevalence of psoriasis. For instance, high linoleic acid in the diet seems to be a protective factor for onset of the disease, while obesity is thought to be a risk factor [21]. This could partially explain the lower prevalence of the disease in Asian and African groups.

Plaque psoriasis is the most common presentation of the disease in all ethnicities (90% of cases), while pustular psoriasis is less common (1–3% of cases).

In patients with dark skin, psoriatic lesions usually present with thicker plaques. In addition, they have more tendency to resolve with hyper- or hypopigmentation compared to white skin [22].

Some studies conducted in different ethnic populations showed that psoriasis appears with more extensive skin involvement in African American, Asian, and Hispanic groups. The more severe of the disease in African individuals may be linked to higher diffusion of HIV infection: in HIV-positive patients, psoriasis is characterized by severe and extensive skin involvement; erythroderma seems to be not rare [23]. Indian and Chinese patients revealed an increased risk of developing psoriatic arthritis compared to Caucasian groups.

In some ethnic groups, especially in patients with pigmented skin, diagnosis of psoriasis can be a challenge and may require a biopsy for histopathological examination: sometimes it is difficult to differentiate psoriasis from lichen planus or other papulo-squamous diseases [3].

Another important aspect is the quality-of-life impact of the disease. As confirmed by some studies, in some ethnic groups—such as Hispanics, Asians, and Africans—psoriasis is associated with a bad psychosocial impacts and worse quality of life [24].

Reasons why psoriasis is associated with this different life impact can be found in several factors: post-inflammatory abnormalities of pigmentation or different perception of this disease can produce negative feeling of self-worth and embarrassment. In addition, in some geographical areas, patients

with skin diseases represent a social stigma for the local population.

Therapy is similar in all patients. Choice of specific therapy must be based on the severity of disease but also on ethnic and cultural factors as well as on skin phototype. Right choice for the right patient is very important for a good compliance. For example, for scalp psoriasis in a patient with dark skin, it is very important to choose the right vehicle, according to hair characteristics and cultural hairstyles. Phototherapy should be used carefully in patients of higher skin phototypes due to the risk of hyperpigmentation because of a more active melanogenic response to UV light. Tanning during UV exposure could not be appreciated by patients, and it could have a negative impact.

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# Bullous Diseases

12

Rudolf K. Horlings, Aaron R. Mangold, and Marcel F. Jonkman

## 12.1 Introduction

Bullous or blistering diseases are caused by a variety of traumatic, infectious, inflammatory, and autoimmune conditions. Clinically, primary lesions are characterized by fluid-filled vesicles or bullae. Lesions can affect any epidermal-derived tissue, namely, the cutaneous and mucosal surfaces. Blisters can cause significant morbidity, pain, and pruritus and can be life-threatening. This chapter provides a broad overview of common blistering diseases to allow for prompt diagnosis and proper treatment.

Specific considerations in the management of blistering diseases is the extent of disease (localized versus generalized), the cutaneous and mucosal surfaces affected (skin, eyes, mouth, anogenital area), and associated risks of complications (dissemination of primary infection, secondary infection, contagious spread, insensible water loss, and inability to eat). To appropriately treat patients, primary care providers must have some basic knowledge on which conditions can be treated by themselves and which should be referred to a (specialized) hospital.

The primary morphology of blisters are defined by size (vesicles <10 mm versus bullae 10 mm) and the depth of involvement (intraepidermal or subepidermal). Intraepidermal disease is characterized clinically as flaccid, fragile blisters that often slough off leaving superficial erosions. In contrast, subepidermal disease is characterized by tense blisters. Secondary hemorrhage (Fig. 12.1) may be seen. Purulent or pus-filled lesions are called pustules or an abscess.

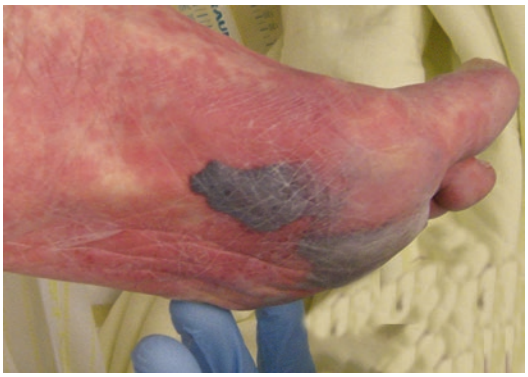

**Fig. 12.1** Hemorrhagic blister on the sole of the left foot (courtesy: UMC Groningen)

Marcel F. Jonkman is deceased at the time of publication.

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## 12.2 What Causes Skin Blisters?

Epidermal cells (keratinocytes and melanocytes) are normally attached to each other, as well as to the below dermis, by different cell adhesion proteins. In blistering diseases, the adhesive connection is disrupted. Rare inherited diseases that have absent or dysfunctional adhesion proteins are characterized by skin fragility and blister formation in areas of trauma. Similarly, trauma, infection, inflammation, and autoimmune disease can disrupt cell adhesion and result in blister formation.

One of the most common causes of skin blistering is external trauma (heat, pressure, rubbing, etc.) that damages adhesion molecules. Direct toxicity from the consumption of medications to keratinocytes can lead to necrosis or apoptosis. Finally, different infectious diseases are able to make the skin blister due to direct toxicity to keratinocytes or through the production of proteins that disrupt cell adhesion. Inflammatory diseases, such as eczema, lead to intercellular edema (spongiosis) which can tear the skin cells apart. In autoimmune mucocutaneous blistering diseases (AMBDs), proteins made by one's own body, antibodies, can disrupt the normal cell adhesion process resulting in blisters on the skin and/or mucous membranes.

## 12.3 Diagnostic Approach to Blisters

When a patient presents with blisters, there are some important historical and clinical questions to determine the underlying aetiology, including the following: What known illness(s) or comorbidities does the individual have? What sort of work do they do? What type of exposures do they have in the home or at work? When did the blistering start? Where did the blistering start? Were there symptoms prior to the onset of blisters? Were there any exposures prior to the onset of blisters? How did the disease progress? Have any close contacts had similar blisters?

On your clinical examination, carefully examine the primary lesion (vesicle, bullae, pustule, abscess) as well as secondary changes (erosion, crust, hemorrhage) and associated findings (scarring, milia, erythema, or erythroderma). Determine if the primary lesion is flaccid or tense. Then, determine the extent of the blisters (localized or generalized) and the distribution (body region, photo-exposed, trauma prone). Always check mucosal involvement (eyes, nose, mouth, and anogenital region) as this might give you a clue for diagnosis, and involvement may suggest more complex disease, requiring a higher level of care.

If localized blisters are grouped, painful vesicles on the head and neck or anogenital region, it is highly suggestive of a type of herpes simplex. A dermatomal (linear) pattern of similar appearing lesions is most likely herpes zoster. Linear lesions that lack grouping and significant pain and itch may be seen in contact dermatitis or trauma. Blisters on hands and feet are likely secondary to mechanical contact (friction or rubbing). In the absence of trauma, on should consider eczema or infection (impetigo, fungus virus). Targetoid lesions and blisters on the hand and mucosae are more common in erythema exsudativum multiforme.

Generalized rather flaccid bullae or skin sloughing and possible mucosal involvement are most commonly due to medications (Steven Johnson/TEN) or are caused by an AMBD (Pemphigus). In young children, staphylococcal scalded skin syndrome is possible. In the elderly, itchy, large, tense blisters combined with urticarial papules and plaques are suggestive of bullous pemphigoid.

Lesions in sun-exposed areas (photodistribution) are suggestive of a sun allergy (polymorphic sun eruption) or a severe sunburn.

Clinical history for contagious or environmental causes of blistering should be considered. Bullous impetigo as well as culicosis bullosa from bug bites should be considered as well as chemical exposure or a preceding burn [1].

## 12.4 Etiopathogenetic Classification

### 12.4.1 Mechanical/Physical Blisters

Mechanical and physical blisters can occur from a variety of external sources, including rubbing or friction, pressure, sucking, irritating contactants, and extreme cold or heat exposure. Migrants might have had prolonged exposure to extreme weather conditions while travelling on boats or on foot. This could, depending on the type of weather, lead to a blistering sunburn or frozen limbs (frostbite). Long walking in inappropriate footwear can result in blisters on feet through mechanical rubbing. The cornerstones of treatment include avoidance of mechanical or physical stimulus, proper wound care, and time.

Less commonly, mechanical and physical blisters may occur secondary to intentional trauma. In migrants, or any vulnerable population such as children, disabled, and elderly, primary care providers should be aware of the possibility of abuse/torture or self-mutilation (malingering). "Dermatitis artefacta" *is a term used for* self-inflicted skin lesions. Unlike other conditions such as eczema where the primary driver to scratch is the underlying skin condition, individuals with dermatitis artefacta feel an unconscious psychological (dissociation) or emotional need to scratch or traumatize the skin. Although these conditions can resemble existing skin diseases, there are clinical clues the primary care provider should recognize. These features include regular patterns, bizarre linear or rectangular shapes with sharp borders, and a non-affected surrounding (Fig. 12.2). In the case of abuse/torture, they are more commonly seen in areas covered by clothing, and in dermatitis artefacta, they are often in areas that can be reached by hand(s) (especially the dominant hand).

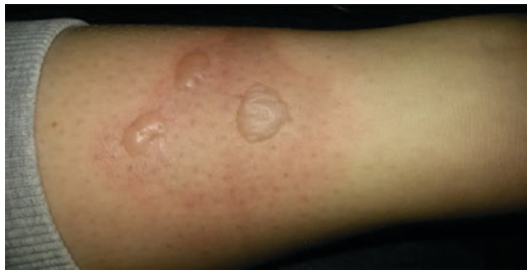

**Fig. 12.2** Grouped, sharply demarcated, tense, fluid-filled blisters in an erythematous area. There is no existing skin disease that causes this remarkable pattern. Suspect for (suction) trauma (courtesy: UMC Groningen)

Due to the underlying psychological comorbidities associated with these conditions, it can be very difficult to discuss this with the patient directly. Management of these conditions should include a team-based approach involving primary care, psychological care, social support, and, in select cases, legal authority [2].

### 12.4.2 Infectious Blistering

Viruses, fungi, and bacteria are all able to cause blistering. As most of these causes are profoundly discussed in other chapters of this book, but do form diseases in your differential diagnostic considerations, they will just shortly be addressed below.

#### 12.4.2.1 Herpes Simplex Virus

Herpes simplex virus (HSV) is a common cause of oral and genital blisters. There are two common types of HSV (HSV-1 and HSV-2). The virus is transmitted through direct contact with saliva or direct contact of an active blister. The most common locations are the lips and anogenital area. Disseminated disease may be seen in the setting of immunodeficiency (such as HIV) or in individuals with underlying skin conditions like eczema (eczema herpeticum).

The typical clinical presentation is that of grouped painful vesicles and ulcers with a clean, scalloped boarder (Fig. 12.3). The most common location is the lips, anogenital region, and the lower back and buttocks. The surrounding skin is often red and swollen and may be tender or itchy. When the mouth is involved, the gums can be swollen and bleed easily. Local lymph nodes may be enlarged and tender. The patient usually feels feverish. Healing of the lesions usually takes about 8 days and during that time individuals are contagious. After this period, the virus resides in a latent state in the sensory nerves. External stimuli like sunlight exposure, menstruation, and stress can lead to viral reactivation and recurrent HSV lesions.

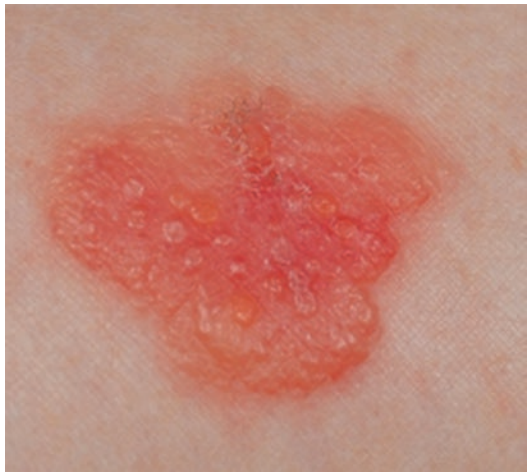

**Fig. 12.3** Grouping of coalescing vesicles on circumscribed erythematous base in HSV on the thorax (courtesy: UMC Groningen)

The painful vesicles in the mouth, genitals, or lower back are usually diagnosed clinically. Atypical cases, resolving disease that lacks intact vesicles, a secondary infection, and underlying skin disease like eczema can make the diagnosis difficult. The abrupt onset of pain and abnormal sensation can differentiate atypical cases. Additionally, HSV can be confirmed by a Tzanck smear. This is done by scraping material from the floor of a vesicle. This is then smeared on a slide and stained with Wright's stain. The diagnostic cell is the multinucleated giant cell. Alternatively, PCR can be performed, if this diagnostic test is available.

HSV is highly contagious disease; it is important to avoid spreading especially in densely populated areas like migrant camps. Topical application of zinc oxide-containing products helps to dry out the lesions. If the patients are symptomatic, have underlying skin conditions, or are immune compromised, oral antiviral treatment with valaciclovir 500 mg twice daily for 5 days or 2000 mg twice daily for 1 day in the immune competent and 1000 mg twice daily for 5 days in the immune compromised should be given.

#### 12.4.2.2 Herpes Zoster Virus

Herpes zoster virus (HZV), also known as shingles, is an infectious blistering disease secondary to HSV-3. In some countries, varicella is encountered in its primary form, chicken pox, while in other countries the varicella vaccine is the primary source.

Chicken pox is a highly contagious primary form of HZV seen most commonly in children and young adults. The clinical course starts with airborne droplet or direct exposure; a prodrome of mild fever, malaise, and muscle aches; and finally the development of a rash that starts on the face and neck and then spreads to the entire body. The primary lesion is a single vesicle on an erythematous base, "dew drop on a rose petal." The rapid evolution (12 h) can be concerning for small pox; however, the clinical lesions show various stages of healing in contrast to small pox. The disease is self-limited in healthy children but remains highly contagious 1–2 days before the skin lesions, until all skin lesions crust over. Atypical forms may be seen in the immune compromised, and congenital or neonatal disease may be seen in mothers who contract chicken pox. These cases require special attention and will not be discussed.

Shingles is caused by the reactivation of the latent VZV and is most commonly seen in adults. The onset of shingles in an individual under the age of 40 years should prompt consideration of underlying immunodeficiency. The majority of patients will have a prodrome of itching, tingling, pain, or hypersensitivity prior to the onset of lesions. The primary lesions are similar to HSV with grouped vesicles on an erythematous background. However, unlike HSV, the vesicles in HZV follow a linear or dermatomal pattern. The most common areas are the chest, neck, and forehead. Valaciclovir 1000 mg, three times daily for 7 days, as soon as HZV is suspected, should be given. In individuals with significant pain at baseline and in those who have persistent pain beyond 6 weeks (postherpetic neuralgia), tricyclic antidepressants (amitriptyline 25 mg daily) and/or gabapentins (initial dose of 300 mg daily with rapid titration by 900 mg each week up to 1200 mg three times daily if needed) should be given [3].

#### 12.4.2.3 Culicosis Bullosa

Culicos is bullosa is a hypersensitivity reaction to insect bites (mosquitos, louse, and flea). Primary lesions may display a "breakfast, lunch, and

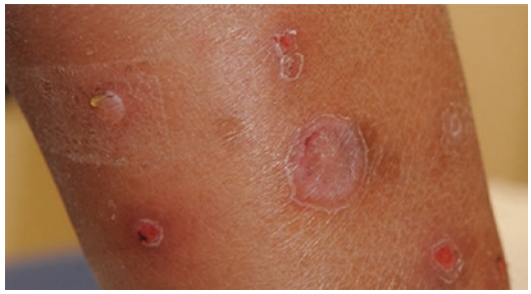

**Fig. 12.4** Clear fluid-filled blisters, dried out lesions and erosions (due to scratching) in culicosis bullosa (courtesy: UMC Groningen)

dinner sign" with red, linear papules or vesicles on a slightly erythematous base. The lesions tend to favor exposed areas of the skin. Secondary changes of hemorrhage and crust may be present (Fig. 12.4). Unlikely HSV or VZV, these lesions are not grouped and often do not display any prodromal symptoms other than itch. Additionally, other house members or close contacts may display similar lesions. Good wound care should be used to prevent secondary infection. Identification and eradication of the arthropod may be necessary. Although self-limiting, topical steroids (triamcinolone 0.1% ointment twice daily), when available, and oral antihistamines (diphenhydramine 25–50 mg twice daily) can be taken.

#### 12.4.2.4 Bullous Impetigo/ Staphylococcal Scalded Skin Syndrome

Localized skin infection with the *Staphylococcus* bacteria can lead to a crusted or bullous condition called impetigo. The lesions are characterized by abrupt onset and are highly contagious. The primary lesion is a well-marginated erythematous plaque with secondary honey-colored crusts. Certain types of *Staphylococcus* can disrupt keratinocyte adhesion and lead to the blister formation. Local treatment is with topical antibacterials (fusidic acid cream twice daily until healed) and systemic antibiotics (flucloxacillin 500 mg four times daily for 5 days) when more widespread.

A special type of staphylococcal infection is staphylococcal scalded skin syndrome (SSSS), a skin condition characterized by sepsis and the release of a toxin that disrupts normal keratinocyte function and leads to widespread, superficial skin sloughing. In contrast to impetigo, these toxins are spread through the bloodstream, and cultures of blisters or erosions will be negative. SSSS is most often to babies and children below 5 years old and in adults with compromised renal function. The kidney is required to clear the SSSS enterotoxin. SSSS can lead to extensive areas of desquamation that can resemble a toxic epidermal necrolysis or pemphigus but has a far better prognosis. Individuals with SSSS need prompt treatment with the appropriate, intravenous antibiotics (flucloxacillin, augmentin, or clindamycin), close clinical monitoring in the hospital, and aggressive wound care [4].

#### 12.4.2.5 Bullous Tinea

Tinea is caused by various types of dermatophytes or fungus. The common locations of tinea infections include the scalp (tinea capitis), body (tinea corporis), groin (tinea cruris), hands (tinea manuum), and feet (tinea pedis) (see Chap. 6). Specific species of tinea cause blistering and are most commonly seen on the hands and feet (Fig. 12.5). Bullous tinea can be diagnosed testing with potassium hydroxide (KOH) the gentle scraping of the roof of the blister or any nearby skin. When examined under the microscope, branched hyphae can be visualized. The following actions should be done to obtain a proper KOH: (1) gently scrape skin cells onto a glass slide using a surgical scalpel blade 15; (2) add

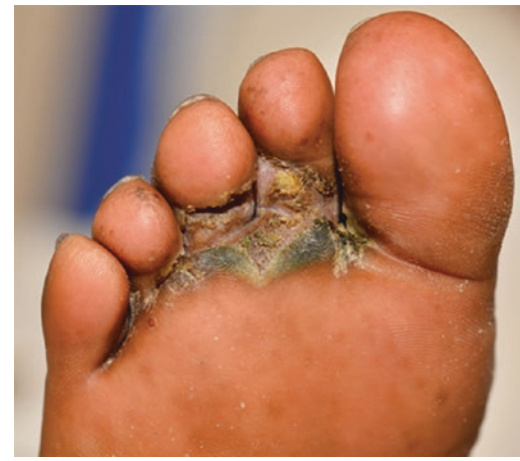

**Fig. 12.5** Softening and breaking down of the skin (maceration) around the base of the toes caused by tinea species (courtesy: UMC Groningen)

one to two drops of 20% KOH; (3) place the coverslip on the slide and remove any air bubbles; (4) allow the slide to sit for 5–15 min; (5) examine the slide. If KOH is not available, culture or empiric treatment may be used. Treatment should include topical terbinafine, miconazole, clotrimazole, or ketoconazole twice daily until 1 week after lesions heal completely [5].

#### 12.4.2.6 Contagious Ecthyma

Contagious ecthyma (Orf) is caused by the parapox virus. Orf is most commonly seen in people who are in close contact to sheep and goats. Those at highest risk are sheep farmers, slaughterhouse workers, and individuals who may slaughter sheep as part of a religious ceremony. The virus enters the body through direct inoculation after contact with an infected animal or through an existing wound or scratch. The primary lesions are most commonly seen on the fingers or the hand. Incubation time ranges from a couple of days to 1 week. The classical presentation is a 2–3 cm firm, red, or reddish-blue nodule or bullae with secondary pustule formation and hemorrhage (Fig. 12.6). Secondary bacterial infections as well as swollen joints, fever, malaise, and enlargements of the lymph glands may occur.

The lesions are generally diagnosed clinically (see Chap. 4). The virus is self-limited and should resolve within 6 weeks. No treatment is necessary; however, it is important to maintain good wound care and monitor for secondary infection [6].

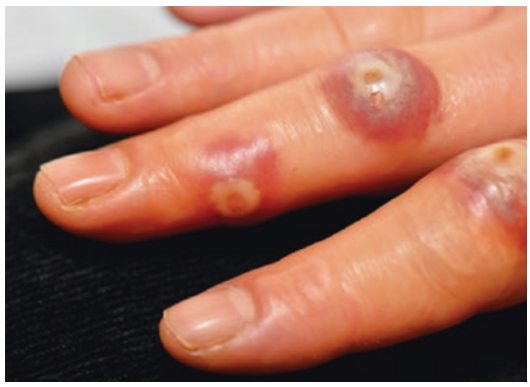

**Fig. 12.6** Red-bluish lumps (bullae) with yellowish center in a patient with Orf (courtesy: UMC Groningen)

### 12.4.3 Edema and Spongiosis

Spongiosis refers to the separation of cells in the skin secondary to swelling and fluid accumulation. Exuberant spongiosis may lead to blister formation. Spongiotic conditions may be seen as a primary feature in eczema and contact dermatitis and a secondary condition in other diseases with chronic skin inflammation with scratching. Skin blisters on the hands should prompt the clinician to consider infectious (see above), traumatic (see above), and inflammatory conditions such as hand eczema. A detailed history will determine an atopic history (asthma, allergies, hay fever, and itchy skin as a child) associated with eczema as well as contact with specific substances, prior to the onset of the blistering.

### 12.4.4 Hand-Feet Eczema

A common cause of blistering on hands and occasionally feet is (acrovesiculous) eczema (see Chap. 10). In the acute phase, patients present with small vesicles located on the sides of the digits and the central hand or foot. Lesions are associated with itch, scaling, and redness. A subtype of hand eczema (Pompholyx) presents with larger, often painful bullae. Pompholyx is seen in patients with excessive sweating or as a reaction to an untreated fungus (tinea pedis; see above) at a different body site. Long-term hand eczema can result in a dry, hyperkeratotic, thickened skin.

The most common external cause of eczema is contact with chronic irritants such as water and soap. Clinical history of frequent hand washing, work in wet environments, or contact with industrial chemical is a helpful clue. Irritant reactions are dependent upon the type of counteractant, the concentration, temperature, and time of exposure. Allergic reactions occur when the body mounts a specific immune response against some substances. They are not dose dependent, and even a brief exposure can stimulate the immune system and drive a rash for many weeks. Chronic hand dermatitis with no clear drivers is more

common in individuals with a history of atopy (constitutional eczema/asthma/hay fever).

Hand eczema can be resistant to treatment. Minimization of exacerbating and irritating factors and contact avoidance is essential. First-line treatment is gentle skin care which consists of minimizing unnecessary hand washing, avoiding drying soaps, avoiding frequent wetting and drying of the hands, and the usage of thick topical moisturizing creams or ointments one to two times daily at minimum. If refractory or highly itchy, the use of potent topical steroid creams (clobetasol) twice daily for 2–4 weeks followed by a taper down to a maintenance for 2 days per week is suggested. Large bullae of diffuse vesicles may need to be dried out with a soak and smear method (10–15 min of soaking in warm tap water followed by the application of topical corticosteroids three times daily), for 1–2 weeks [7].

### 12.4.5 Autoimmune Mucocutaneous Blistering Diseases

Autoimmune mucocutaneous blistering diseases (AMBDs) are a heterogeneous group of blistering diseases in which the body attacks the skin. All AMBDs target cell adhesion molecules. The clinical manifestations of disease are dependent upon the specific cell adhesion molecule targeted. Thankfully, AMBDs are rare. The diseases may be mild and localized requiring topical treatment only or may be generalized and life-threatening. The most common AMBDS are bullous pemphigoid (BP) and pemphigus of which there are two major types: P. vulgaris (PV) and P. foliaceus (PF).

To distinguish between the different types, complex (immuno) pathological diagnostics, only performed in specialized centers, are required. However, specific morphological features of primary lesions as well as other clinical features may aid in the diagnosis. It is critical as a primary provider to be able to recognize these diseases and understand the basic principles of management. Patients with AMBDs often need systemic medication and team-based care focused to wound care, infection prevention, and pain control. If there is concern for AMBDs, the primary care provider should refer the patients to a hospital.

#### 12.4.5.1 Bullous Pemphigoid (BP)

Classic BP is mostly seen in the elderly (those over 70 years old), does not affect the head and neck, does not result in any scar formation, and does not affect the mouth or the eyes. Individuals will often complain of itch prior to the onset of blisters. If an individual does not meet three of these four features, another diagnosis should be considered. In BP, the body produces antibodies that target keratinocytes deeper in the epidermis (at the junction of epidermis with the dermis – basal membrane zone). As a result of this relative deep process, the blisters in BP are tense with surrounding erythema (Fig. 12.7). Urticarial or hive-like papules and plaques coexist in BP. The most common locations of diseases are the lower legs and intertriginous areas. The mucosa, most commonly the mouth, may be involved in half cases. Eye involvement in classic BP is rare and can lead to severe impaired vision.

Localized forms can be treated with potent topical steroids like clobetasol ointment (one to two times daily for 1 month, daily to every other day for 1 month, two times weekly for 1 month, then one time weekly for 1 month).

Generalized cases may require systemic anti-inflammatory or immunomodulatory therapy. If there is no immediate access to a hospital, you can start with oral prednisone 0.5 mg/kg body weight per day or in less severe cases oral tetracycline antibiotics and aggressive use of topical steroids (clobetasol systemic transcutaneous or to affected areas). Note that all three methods of oral and topical steroids as well as oral tetracyclines can be used in order to minimize systemic exposure to corticosteroids.

These patients requiring long-term steroids should be placed on calcium and vitamin D (1200 mg and 1000 International Units (IU) daily) treatment. They should be regularly checked for side effects of oral corticosteroids (e.g., blood pressure and blood glucose levels). If the patient has not improved in 1 month or

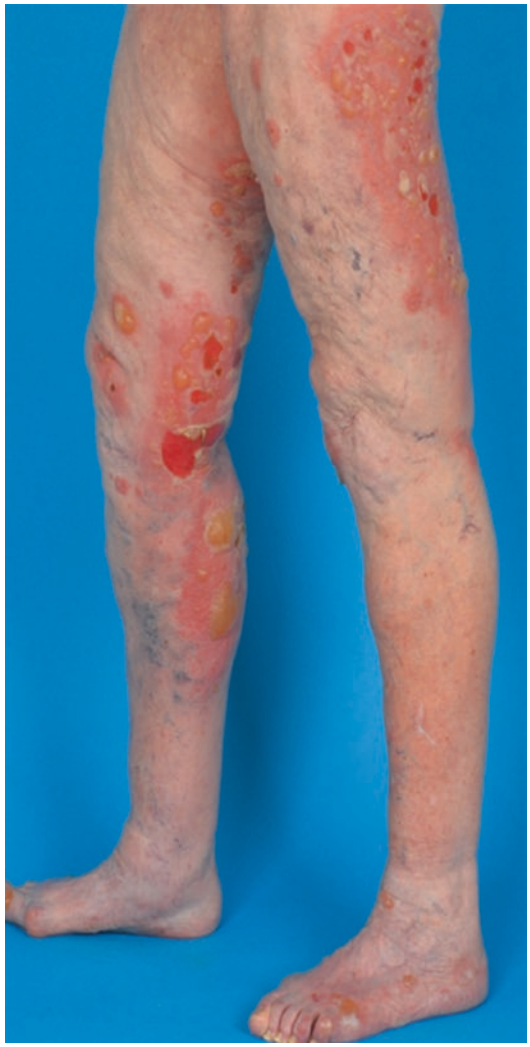

**Fig. 12.7** Tense bullae and partially sloughed of skin with erosions on an erythematous skin in a patient with bullous pemphigoid (courtesy: UMC Groningen)

cannot be tapered down in the first 3 months, an additional agent should be considered.

Methotrexate (MTX) 7.5–20 mg/week (often 12.5 mg/week) is a cheap and effective medication. Blood monitoring for cytopenia as well as elevated liver enzymes is advised. Caution should be used in individuals who drink more than two drinks of alcohol per day, as well as in those with compromised kidney function. MTX should be avoided in individuals with significantly compromised kidney function [8].

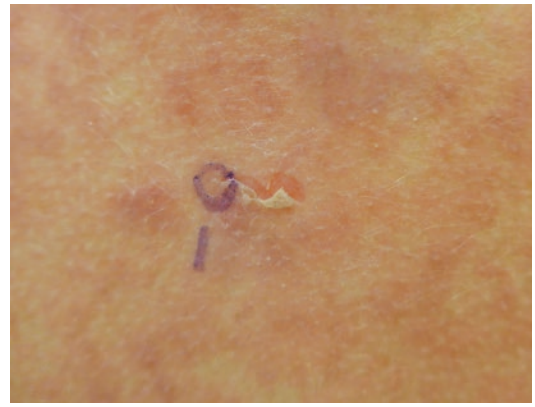

**Fig. 12.8** Nikolsky's sign (courtesy: UMC Groningen)

The Nikolsky's sign can be helpful in distinguishing BP from other blistering diseases. The sign isoften present (positive) in pemphigus and toxic epidermal necrolysis (only red skin) but usually absent in bullous pemphigoid. The test is positive if the outside pressure, with a finger or thumb, applied to the apparently normal skin in an affected individual, results in blistering or exfoliation of the outer layer (Fig. 12.8).

#### 12.4.5.2 Pemphigus Vulgaris and Pemphigus Foliaceus

Although pemphigus is a rare disease, doctors working with migrants should be aware that certain populations are at greater risk of disease: Jewish, Southeast Europe, Middle East, and inhabitants of India. In pemphigus, the body makes proteins (antibodies) that target cell adhesion proteins (called desmogleins, Dsg) above the basement membrane in the epidermis. Desmogleins normally act as glue to attach adjacent skin cells. When this function is impaired, the skin becomes fragile and blisters and erodes. Pemphigus vulgaris (PV) often involves the skin and mucous membranes, whereas pemphigus foliaceus (PF) involves the skin only. Additionally, PV patients make antibodies against cell adhesion proteins deeper in the skin than PF. Therefore, PV is characterized by significant oral and cuta-

neous erosions and PF is characterized by superficial erosions and scaling and crusting. In general PV is more severe than PF. In contrast to BP, the blisters in PV and PF are fragile and are characterized by flaccid blisters. Additionally, erosions, abrasions, and exfoliation are more common than true, fluid-filled blisters (Fig. 12.9). PF may have less severe blisters and erosions and often shows an adherent crusting and scaling.

PV often starts with mucosal ulceration and erosions followed by secondary development of skin lesions. Up to half of PV cases will only have mucosal disease. The most common areas of mucosal involvement are oral, anal, nasal, conjunctival, and genital. Eating and swallowing can be difficult with oral disease, and skin and mucosal lesions can be extremely painful.

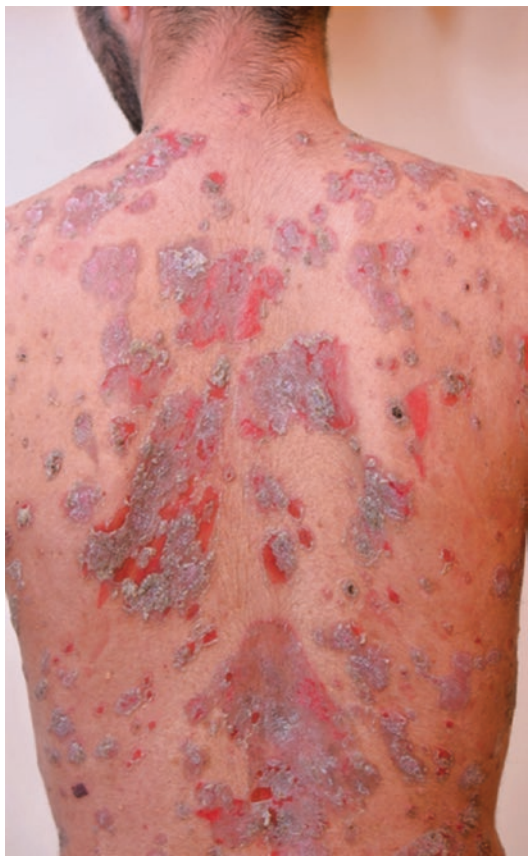

**Fig. 12.9** Flaccid blisters with a mostly detached roof leaving erosions with secondary crusts on the back of a patient with pemphigus vulgaris (courtesy: UMC Groningen)

Individuals with PV and some with PF require hospital admission for initial treatment, wound cares, monitoring for infection, and proper nutrition. Initial treatment for pemphigus is high-dose prednisone (1–1.5 mg/kg/day), with same adjuvant possibilities as described above under BP (MTX). Other treatment options include azathioprine 50–150 mg daily or mycophenolate mofetil 500–1000 mg twice daily. Monitoring labs will not be discussed for these agents.

Due to the extent of skin lesions, loss of epidermal barrier function, and the use of immunosuppressive medications, there is a high risk on opportunistic infections and associated death. Patients with pemphigus require proper wound care and close monitoring for signs of infections with prompt use of antibiotics. In addition to common bacterial infections, individuals with oral pemphigus are at a high risk of secondary herpes reactivation. Clinical symptoms of increased pain as well as signs of tense blisters with smooth, scalloped erosions should be clues. Esophageal involvement should be considered in the setting of progressive dysphagia to solids than liquids. Due to high catabolic states of pemphigus and barrier disruption, fluid balance should be monitored closely and intravenous replacement may be necessary [9].

### 12.4.6 Toxic Epidermal Reactions

Toxic epidermal reactions are secondary to a stimulus (drug or infection) that triggers an immune attack upon epidermal cells and subsequent necrosis and erosion of the skin mucous membranes. While erythema exsudativum multiforme (EEM) is more common secondary to bacterial and viral infections, Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are often secondary to medications. The body surface involved in EEM is up to 10%, up to

30% in SJS, and over 30% in TEN. Toxic epidermal reactions are serious and can belife-threatening. Urgent, team-based care is required.

#### 12.4.6.1 Erythema Exsudativum Multiforme (EEM)

EEM is often secondary to herpes simplex and mycoplasma pneumoniae. The primary lesions are often target-like and located on the dorsal and volar surfaces of the hands and feet. Target lesions are a round macules with three concentric color zones, a dark center, surrounded by a paler ring and a bright-red outermost ring (Fig. 12.10). Papules, vesicles, blisters, nodules, and purpura can be seen as well. The skin lesions are preceded by a sore throat and constitutional symptoms of malaise, fever, and joint pain. Mucous membranes may be involved, leading to erosions and ulceration in the mouth, namely, the lips and less commonly the genitals and eyes. Oral disease is more common in mycoplasma-associated EEM.

EEM is self-limiting and usually heals in a couple of weeks. Individuals with recurrent EEM secondary to herpes can be prophylaxed with low-dose valaciclovir 500 mg once daily.

#### 12.4.6.2 Stevens–Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

SJS and TEN are rare, severe drug reactions that can be fatal. SJS and TEN are thought to be secondary to the accumulation of toxic drug metabolites which, in a genetically predisposed individual, lead to immune activation and attack upon the epidermis and other epithelial tissues. Massive apoptosis results in large areas of epidermal detachment and denuded skin resembling a burn (Fig. 12.11).

Individuals with SJS and TEN should have the suspect drug stopped immediately and be managed as a burn victim with aggressive wound care, fluid and electrolyte repletion, and monitoring for signs of infection and end-organ dysfunction. Mucous surfaces are involved in the majority of cases which can lead to decreased oral intact as well as may result in visual loss and even blindness. Secondary infections with HSV or bacteria are common and should be carefully checked for and treated.

It is critical to stop the suspected drug as soon as possible. In most cases the causative drug has been added within the last 2 weeks. Common culprits include sulfonamides, antiepileptics, NSAIDS, allopurinol, and antiretroviral drug. If there is uncertainty due to polypharmacy, all medications may need to be stopped.

The cornerstone of management of SJS and TEN is wound care. However, most experts use an adjuvant agent such as high-dose steroids, prednisone 120 mg or dexamethasone 100 mg daily for three consecutive days, intravenous immunoglobulin 2 g/kg over 2–5 days, or cyclosporine 3–5 mg/kg/d until reepithelialization [10, 11].

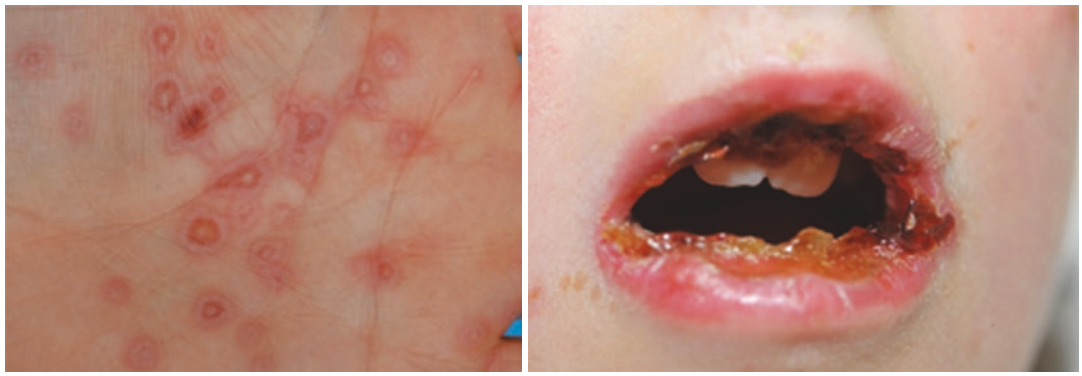

**Fig. 12.10** Target lesions on the palms and erosions on the lips in EEM due to mycoplasma pneumonia infection in a child (courtesy: UMC Groningen)

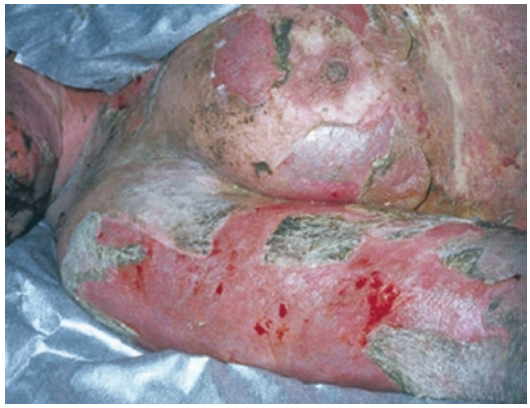

**Fig. 12.11** Widespread exfoliation in patient with TEN (courtesy: UMC Groningen)

## 12.5 Practical Tips for Blister/Wound Care

The skin has three basic functions: protection from and interaction with the external environment, sensation, and regulation of temperature. The primary function of the skin is to act as a barrier against mechanical contact, temperature changes, microorganisms, and other antigens. When the skin is damaged by blistering, the epidermal integrity and ability to perform its primary functions are compromised. Secondary infections are seen when large areas of the epidermis are damaged. Additionally, the skin loses its ability to minimize waters loss as well as regulate temperature which leads to dehydration. It is essential to treat the underlying cause of skin blistering to prevent further epidermal compromise.

Proper wound care is essential to restore the normal function of the skin. Key elements in wound care are the prevention of infection and the minimization of pain. Blisters should be left intact whenever possible. The roof of the blister acts as a protective barrier to the underlying, healing epidermis. Large, tense blisters may be emptied and drained and the overlying epidermis left intact to cover the wound. Topical barrier creams or ointments should be used to encourage wound healing and prevent desiccation of underlying tissue. The use of a silicon or nonstick gauze is recommended to prevent further skin detachment. For dry wounds, a barrier that holds in moisture should be used, and in wet, exudative wounds, an absorbent material should be used. Tubular bandages or wraps should be used to hold the bandages in place and plasters should be avoided. With widespread, exudative blisters (e.g., TEN, PV) the use of wet compresses for 5–15 min two to three times daily may help to debride secondary buildup of crust, bacteria, and skin as well as will prevent maceration [12].

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# Connective Tissue Disorders

# 13

Aldo Morrone

## 13.1 Lupus Erythematosus Chronicus Discoides

### 13.1.1 Synonyms

Other possible terms can be erythematodes, discoid lupus erythematosus, lupus erithematoso crónico fijo, and lupes érythémateux chronique.

### 13.1.2 Definition

Lupus erythematodes chronicus discoides is a chronic, relatively frequent dermatosis, characterized by erythema, hyperkeratosis, and cicatricial atrophy [1, 2].

### 13.1.3 Distribution

It is ubiquitous and common in the tropical areas. It is prevalent in women. The ultraviolet exposure is a relevant trigger factor.

### 13.1.4 Clinical Features

The skin lesions are represented by an eruption, often triggered by sun exposure, characterized by well-defined, painless patches on the face and scalp (nose and cheeks, zygomatic regions, preauricular areas, lips) but even on the dorsum of the hands and medio-sternal region. Other coexisting signs can be erythema, hyperkeratosis, and cicatricial atrophy. Erythema is pronounced at the border of the lesions. Hyperkeratosis affects the follicular orifices, and the scales produced may thicken and become adherent and stratified. Cicatricial atrophy comes rather late and affects the central area of the lesions, and its morphology is not uniform due to the presence of prominent telangiectasias and hyperpigmented macules (Figs. 13.1, 13.2, 13.3, 13.4, and 13.5).

### 13.1.5 Diagnosis

The occurrence of the three peculiar morphological elements (erythema, follicular hyperkeratosis, and cicatricial atrophy) appears fundamental. Histology and direct immunofluorescence may confirm the diagnosis. The histologic analysis shows orthokeratotic hyperkeratosis with corneous plugs of the follicular openings and epidermal atrophy with vacuolar alteration of the basal cell layer. Direct immunofluorescence test shows a band granular deposit of Ig and C at dermo-hypodermic junction.

Differential diagnosis includes lupus vulgaris, seborrhoeic dermatitis, rosacea, leishmaniosis, Hansen's disease, lichen planus, South American blastomycosis, and tineafaciei and capitis.

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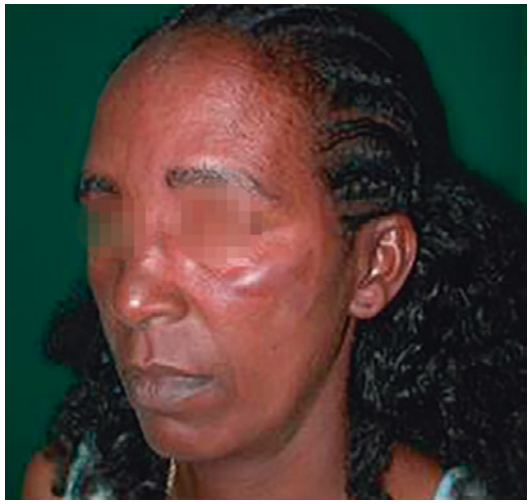

**Fig. 13.1** Dermatomyositis

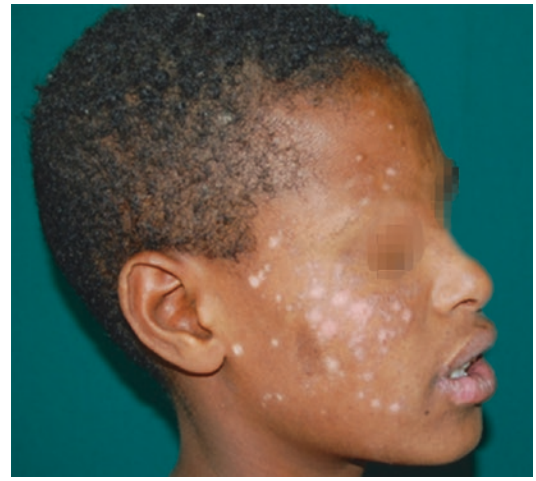

**Fig. 13.3** Discoid lupus

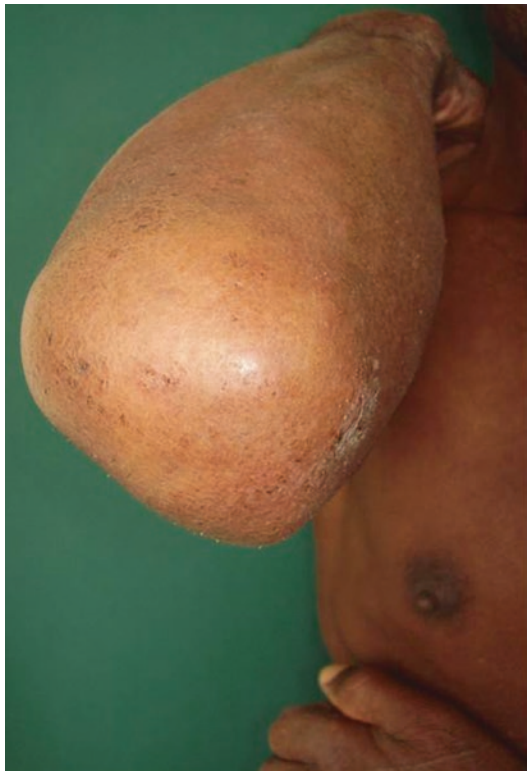

**Fig. 13.2** Dermatomyositis lesions on the arms

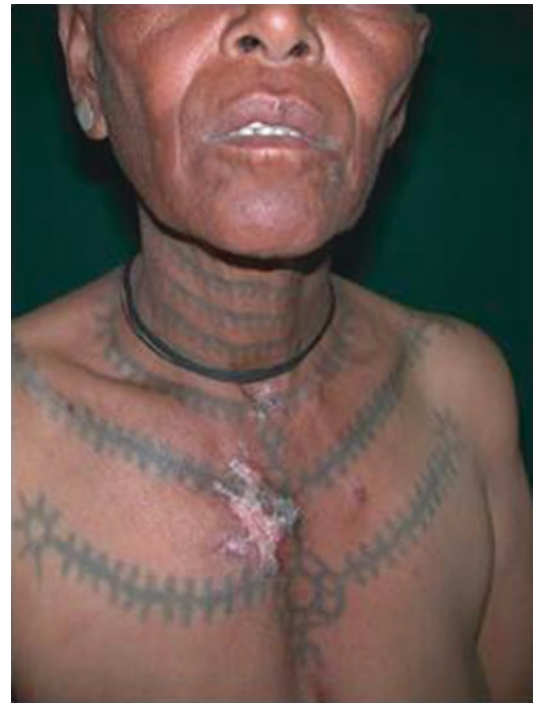

**Fig. 13.4** Discoid lupus scar

### 13.1.6 Management

Minimal dose of corticosteroids and other anti-inflammatory drugs (e.g., antimalarials, low-dose immunosuppressants) can be used for mild or severe disease. Corticosteroid dosage is usually determined by decreasing it at intervals of 10% (depending on the rate of clinical improvement). Arthralgias are usually controlled with NSAIDs. Aspirin is useful, especially in patients with the

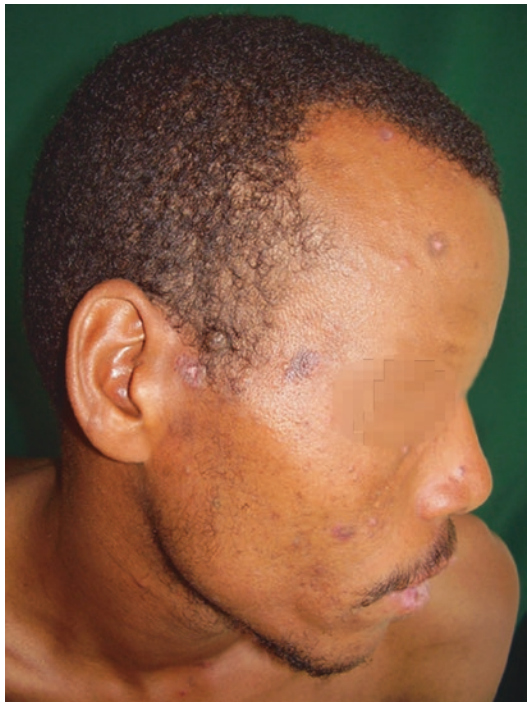

**Fig. 13.5** Discoid lupus on the face

thrombotic tendency, but high doses in SLE may cause liver toxicity. An alternative is hydroxychloroquine 200–400 mg/day, chloroquine 250 mg/day or quinacrine (mepacrine) 50–100 mg/day. Severe disease requires immediate corticosteroid therapy. Starting oral prednisone dosages (20–60 mg/day), together with oral immunosuppressive agents, is necessary. The most common immunosuppressive drug used for renal SLE is azathioprine or cyclophosphamide (both at 2.5 mg/kg/day). In CNS lupus or other critical crises, methylprednisolone 1000 mg by slow (1 h) infusion, together with cyclophosphamide on 3 successive days, often is the initial form of treatment. Sun-protective measures must be taken always.

Intercurrent infection, often complicating the disease and easily mistaken for some of its manifestations, should be treated vigorously. The usual measures to combat heart failure and renal insufficiency must be taken, in addition to using suppressive drugs [3].

## 13.2 Dermatomyositis

### 13.2.1 Synonyms

It is also known as polymyositis, dermatomyosite, and Lilakrankheit.

### 13.2.2 Definition

Dermatomyositis is a connective tissue disorder, characterized by inflammatory and degenerative alterations of the skin and muscles [4].

### 13.2.3 Distribution

It is ubiquitous but relatively rare. It occurs in people aged between 10 and 50 years and is more frequent in women.

### 13.2.4 Clinical Features

The elementary cutaneous lesions include erythema, edema, hyperkeratosis, and poikiloderma. Red to violaceous erythema develops together with pityriasic scaling on the face, and it is accompanied by hard periorbital edema. Edema may extend on the whole face, leading to the so-called alabaster mask, if facial muscles are involved. In the acute phase, pseudo-paretic asthenia manifests itself with symmetrical involvement of the proximal muscles, especially of the girdles. In the chronic forms, telangiectasia may appear associated with atrophic and pigmentary pattern, thus causing poikiloderma. Muscle weakness represents a peculiar element. Myositis can also affect the mimic muscles. Articular,

myocardial, pulmonary, and digestive involvement may occur.

### 13.2.5 Diagnosis

Clinical features, determination of the values of the muscle enzymes, electromyogram (EMG), and muscle biopsy may help the diagnosis. The differential diagnosis includes systemic lupus erythematosus, scleroderma, trichinosis, Hansen's disease, African sleeping sickness, and Wernicke-Korsakoff syndrome. Cutaneous biopsy does not show specific features and may show hyperkeratosis, edema, and dermal parvicellular infiltrate. Muscle biopsy reveals myositis with edema and muscle fiber degeneration.

### 13.2.6 Therapy

During the acute phase, oral prednisone is given 40–60 mg/day. The measurement of creatine kinase provides the best guide for therapeutic effectiveness. As soon as the enzyme levels have returned to normal, the prednisone dose may be reduced slowly. In adults, maintenance with prednisone (10–15 mg/day) is sometimes necessary. Children require high initial doses of prednisone (30–60 mg/$m^2$/day). In case of apparent remission in children, it may be possible to discontinue prednisone after 1 y. Chronic corticosteroid treatment should be avoided because of the superimposed corticosteroid myopathy. The corticosteroid should be discontinued or decreased and substituted by another drug (e.g., an immunosuppressive drug) [5].

## 13.3 Scleroderma

### 13.3.1 Synonyms

Other usual terms are circumscribed scleroderma, sclerosis circumscripto, morfea, sclérodermie en plaques, morphée, and lokalisierte Sklerodermie.

### 13.3.2 Definition

Sclerodermas represent a group of chronic disorders of unknown aetiology, characterized by sclerotic induration of the skin and atrophy of the appendages, possibly involving the entire skin surface (generalized scleroderma) or a part of it (morphea). In systemic sclerodermas, all organs could be involved, in particular the alimentary tract, joints, lungs, kidneys, and heart [6, 7].

### 13.3.3 Distribution

It is ubiquitous, with predominance in women and young adults. The infection caused by *Borrelia burgdorferi* after a tick bite has been suggested as a possible trigger factor.

### 13.3.4 Clinical Features

In systemic scleroderma and in its most frequent variant (CREST), Raynaud's phenomenon usually represents the first manifestation. Later sclerodactyly occurs; it is characterized by fingers thin and permanently flexed, with the thin, atrophic skin of the finger pads attached to the bone. Acrosclerosis involves the face, the extremities, and the trunk in a variable manner, thus giving patients a peculiar look. Telangiectasias and calcinotic skin may be frequently observed. In localized scleroderma, one or more plaques, irregularly oval in shape, occur at first as lilac macules and gradually develop a waxy, ivory color and indurated consistency. A violaceous border (lilac ring) often surrounds the indurated area. The "en coup de sabre" variant usually affects the face and the scalp. Generalized morphea, atrophoderma of Pasini and Pierini, and Shulman's eosinophilic fasciitis represent other particular subtypes of localized scleroderma (Fig. 13.6).

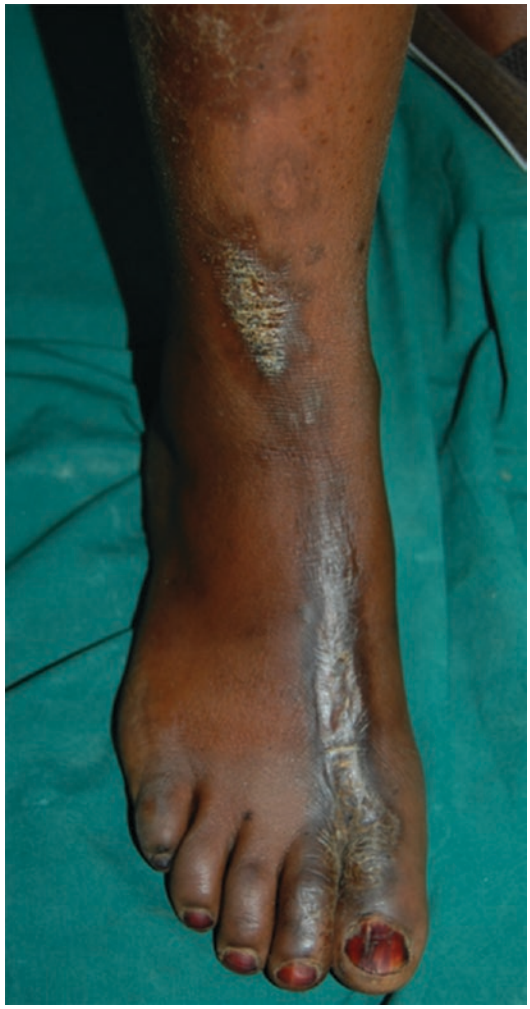

**Fig. 13.6** Sclerodermia

### 13.3.5 Diagnosis

Clinical manifestations and course suggest the diagnosis. In darker skin, it is more difficult to follow the evolution of the disease. Differential diagnosis includes Hansen's disease, pseudoscleroderma of the lower extremities in the African Bantu population, vitiligo, basalcell epitheliomas, and sclero-atrophic lichen. The histologic analysis shows in late stages collagen bundles thicker, horizontally oriented, involving the entire surface of the skin. Vessels are few and present thick walls and reduced lumen.

### 13.3.6 Therapy

There are no proven effective treatments. Arthralgia, arthritis, and tendon friction are treated with nonsteroidal anti-inflammatory drugs, Cox II inhibitors, and glucocorticosteroids. Dryness (sicca syndrome) can be improved with artificial tears and saliva substitutes. Reflux esophagitis can be successfully treated with the proton pump inhibitor omeprazole and metoclopramide, which acts as a gastroprokinetic. Ca-channel blockers are the therapy of choice in Raynaud's phenomenon. Prostacyclins can inhibit platelet aggregation and mediate vasodilatation. Angiotensin converting enzyme inhibitors, e.g., captopril® (4 × 12.5 mg/day) or enalapril® (10 mg/day), are used in hypertension; they prevent or counteract an acute renal crisis. Prednisolone is definitely the most effective drug in early inflammatory stages or episodes of the disease (with significant immunological activity): 40–80 mg/day at the onset lowered at maintenance dose (about 10 mg/day). Prednisolone can be combined with other immunosuppressants, in particular with cyclophosphamide (2 mg/kg body weight/d per os maximum) against lung fibrosis. Chlorambucil and azathioprine are less effective. The use of methotrexate has also provided good results in lung function. To prevent fibrosis, penicillin G (10 Mill IU/day intravenously within 30 min for 14 days) acts as prolyl hydroxylase inhibitor with beneficial effects. PUVA bath photochemotherapy enhances collagenase activity of fibroblasts and improves skin sclerosis, in particular in generalized morphea. Nifedipine may be useful in the treatment of Raynaud's syndrome; prednisone has been reported to be helpful in patients with myositis. In the localized form, systemically administered vitamin E and topical corticosteroids have been used [7, 8, 9].

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# Urticaria and Drug-Induced Eruptions

# 14

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## 14.1 Urticaria-Angioedema

### 14.1.1 Definition

Urticaria (from the Latin word *urtica*) is an inflammatory cutaneous reaction, due to complex mechanisms induced by the release of histamine. The wheal represents the specific element of the disease.

### 14.1.2 Synonyms

Hives, nettle rash, urticaria, Nesselsucht.

### 14.1.3 Distribution

Ubiquitous, frequent in adults of both sexes.

### 14.1.4 Clinical Features

Urticaria is a common problem with many possible causes and presentations. It can last a few days or persist for years with a very serious impact on the quality of life. The characteristic lesion of urticaria is a wheal. Angioedema swellings are deeper and often facial and may be life-threatening if they affect the throat. Wheals and angioedema may occur in the same individual but can also present as distinct conditions. According to the evolution of the disease, urticaria can be subdivided into acute urticaria and chronic relapsing urticaria. Recurrent attacks of urticaria (with or without angioedema) lasting a few weeks are defined as acute. Daily or almost daily attacks which go on for at least 6 weeks or more are chronic. Urticaria which occurs intermittently with intervals of freedom is known as episodic. In delayed pressure urticaria wheals appear after pressure on the skin surface, appear more deep seated, and often last for up to 1–2 days before subsiding [1–12].

Eruption is characterized by pruriginous, raised wheals with well-demarcated round or irregular borders; lesions are elastic, pink in color, but the center sometimes develops an opalescent white color. A single cutaneous region or multiple sites over the whole skin surface could be involved. Lesions appear suddenly, last for some minutes or hours, and then disappear without leaving a trace. Meanwhile other lesions may appear, so that eruption persists for a longer time—days to months or years. Wheals can assume a figurate form (annular, circinate, figurate urticaria), and the lesions can be either small and sparse or large (giant urticaria); a hemorrhagic component (purpuric urticaria) or

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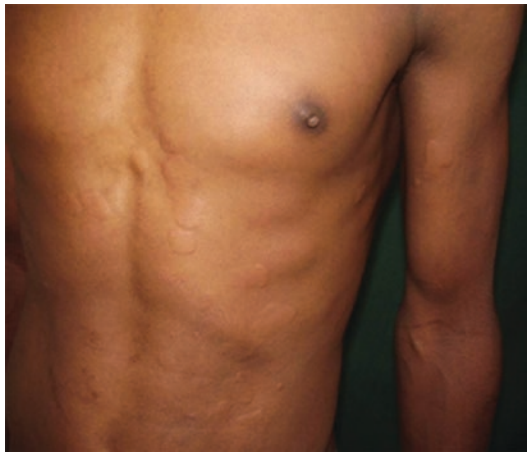

**Fig. 14.1** Urticaria with wheals

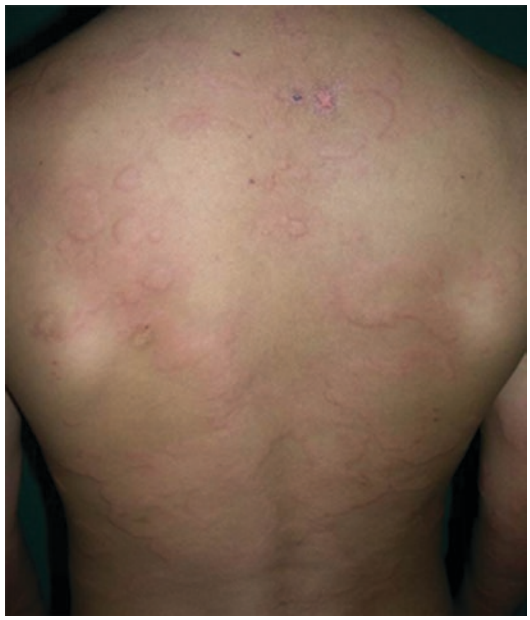

**Fig. 14.2** Urticaria large

a bullous (urticaria bullosa) component may be detected. Angioneurotic edema is a severe form of urticaria, which affects the lips, larynx, and glottis. Patients report discomfort rather than itching. In cholinergic urticaria, wheals are often grouped and small. In taking a history, it is important to ask the patient about potential triggers (Figs. 14.1, 14.2, and 14.3).

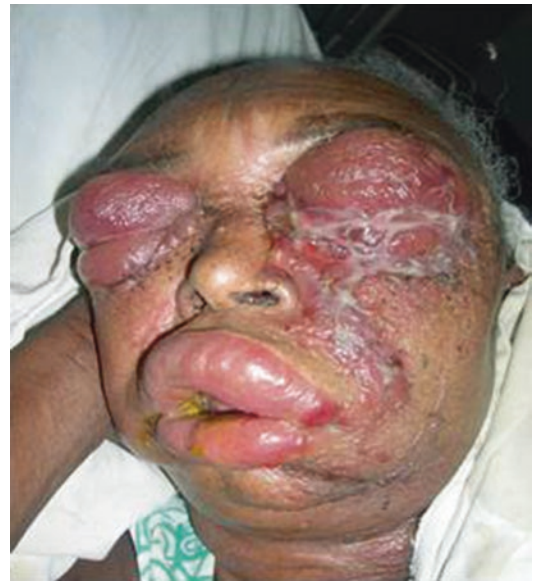

**Fig. 14.3** Angioedema

### 14.1.5 Pathogenesis

The main advancement in understanding urticaria over the last decade has been the appreciation that some cases of previously unexplained (idiopathic) urticaria have an autoimmune etiology [4]. The evidence for this is now strong. Studies have shown that 30–50% of patients with chronic idiopathic urticaria have autoantibodies in their blood which can release histamine (and other mediators) from basophils and skin mast cells. These autoantibodies are directed against the high affinity IgE receptor or IgE itself on mast cells and basophils. Their activity appears to be complement-dependent. Blockade of the C5a receptor on basophils or de-complementation of chronic urticaria sera will prevent release. The absence of the C5a receptor on lung mast cells might explain why urticaria develops in the skin but does not affect the lungs. High-affinity IgE receptor autoantibodies have also been detected by very sensitive immunoassays in other conditions including pemphigus and dermatomyositis. However, in these, the $IgG_2$ and $IgG_4$ subclasses predominate over $IgG_1$ and $IgG_3$ which are mainly present in urticaria.

Urticaria can be triggered by sunlight (solar urticaria), cold exposure (cold urticaria), exercise (cholinergic urticaria), medications including aspirin, and some exogenous allergens such as nuts and shellfish. A particularly persistent form is delayed pressure urticaria, in which wheals last longer and develop after pressure on the skin surface including walking. Exposure to water may also trigger urticaria (aqueous urticaria). In some patients, itching may appear intermittently without whealing. Such patients may show dermographism (see below), and the condition is regarded as a partially developed form of urticaria known as symptomatic dermographism.

### 14.1.6 Diagnosis

The diagnosis is based on clinical features, pruritus, and transience of lesions; laboratory studies may be helpful in detecting the possible etiology. It is important to take a detailed history of the patient, because this will determine which investigations to do. Urticaria patients show reactive skin change, wheal, and flare after drawing a line firmly on the skin with a firm instrument such as a wooden spatula. This reaction is known as dermographism or skin writing and is typical of urticaria (Figs. 14.4, 14.5, and 14.6).

Differential diagnosis: distinction should be made from insect bites, toxicodermias, acute eczema, polymorphous erythema, and annular erythema. In migrants, it is important to identify any medications or food allergies that may have triggered these reactions.

Although immunoassays are under development, it is unlikely that they will be able to distinguish between functional autoantibodies, which can release histamine from mast cells under physiological conditions, and nonfunctional autoantibodies. Basophil and mast cell histamine release assays are technically difficult and beyond the scope of most clinical laboratories. The best clinical test currently available is the autologous serum skin test, whereby a small volume of serum from the patient is reinjected intradermally. The appearance of a pink wheal at least 1.5 mm greater than an adjacent saline control injection at 30 min has reasonable sensitivity and specificity for the detection of histamine release autoantibodies by the in vitro basophil assay. The observation that patients with functional autoantibodies usually have very low or absent numbers of peripheral blood basophils may be another useful pointer to those with autoimmune disease.

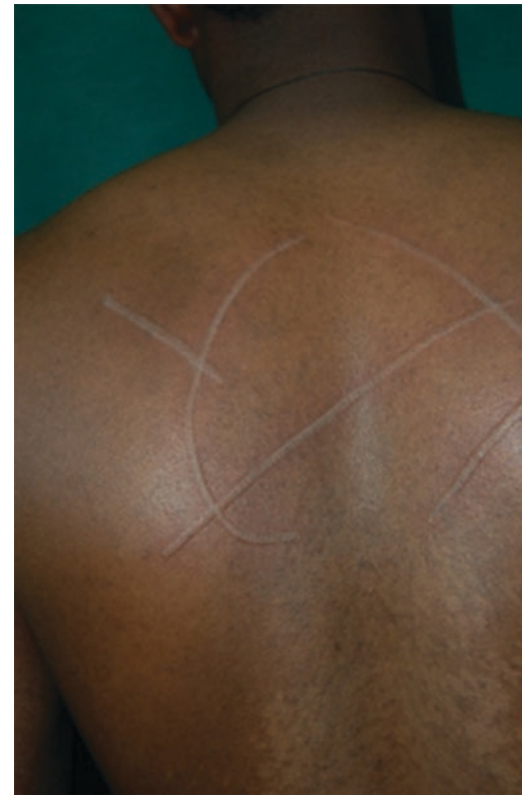

**Fig. 14.4** Dermographism

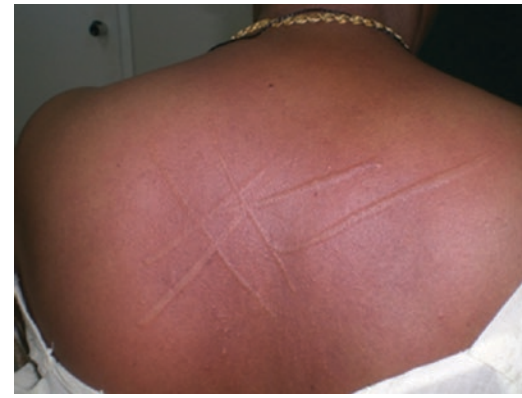

**Fig. 14.5** Wheal and angioedema

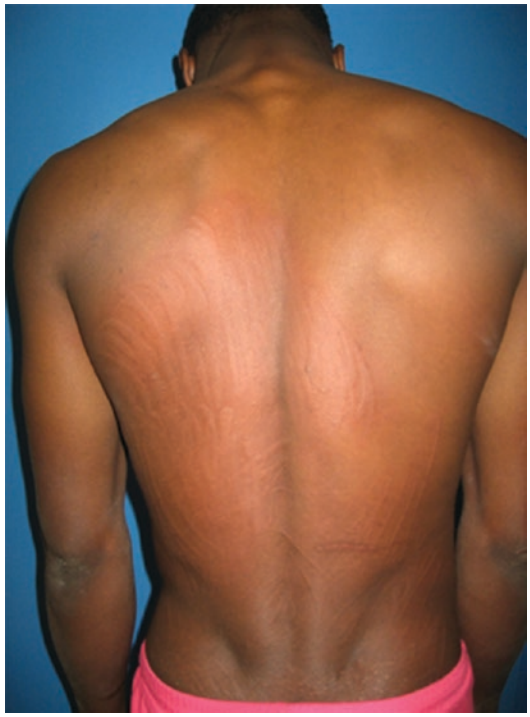

**Fig. 14.6** Angioedema on the back

Clinically, there are no specific distinguishing features between those urticaria patients with and without autoantibodies although those with autoimmune urticaria tend to have more severe disease and may have an associated autoimmune condition such as thyroiditis, vitiligo, or pernicious anemia. This lack of a clear distinction indicates that the clinical features of urticaria are determined more by mast cell degranulation than stimulation of specific receptors. It also raises the possibility that a higher proportion of patients with chronic idiopathic urticaria have an autoimmune etiology than can be currently demonstrated by existing assays.

### 14.1.7 Histopathology

Intercellular edema may be present in the epidermis and evident edema in the dermo-epidermal junction, and perivasal lymphohistiocytic infiltrate has been observed.

### 14.1.8 Therapy

Therapy should be selected after the determination of the possible cause. Second-generation antihistamines are the first-line drug treatment for urticaria. This group of drugs includes cetirizine, loratadine, acrivastine, mizolastine, and ebastine. Third-generation H1 receptor antagonists, active metabolites of the second generation, have also been used, which have fewer side effects and some antiallergenic properties (fexofenadine hydrochloride, desloratadine). If sedation might be helpful, a first-generation antihistamine could be used, especially for nighttime sedation. It should be emphasized to the patient that the antihistamine is not a cure but is best taken regularly as a prophylactic, until the urticaria is resolved. If this does not suppress symptoms, a combination of antihistamines may be effective. Particularly in dermographism, a combination of anti-H1 and anti-H2 molecules can be useful.

Systemic steroids are best avoided for the treatment of chronic urticaria except in special circumstances and for very short periods. Severe angioedema is treated with epinephrine (adrenaline) (0.5 mg–1.0 mL of 1:1000 mg/mL solution by intramuscular or subcutaneous injection) and then by hydrocortisone (100–200 mg i.m.).

A consequence of the recognition of autoimmune urticaria is that new treatments involving immunosuppressive therapies may be appropriate for selected patients with severe disease who have not responded to first-line therapy with full-dose antihistamines or alternatives. Open studies of plasmapheresis and intravenous immunoglobulin infusions in patients with chronic urticaria (who also showed a positive autologous serum skin test) have shown convincing benefits. Cyclosporin Acan be effective and safe when used at 4 mg/kg/day for 4 weeks. Two-thirds responded and 25% of these remained clear or substantially improved on an antihistamine alone 4–5 months after finishing treatment. Optimum immunotherapy protocols still need to be defined. Combinations of drugs such as steroids with azathioprine or alternative immunotherapeutic

agents, such as methotrexate, now need to be used to maximize benefit from this approach and minimize the risk of adverse effects. Good results may be obtained also with a specific biologic agent, apremilast (omalizumab), although this treatment is very costly [13–22].

## 14.2 Cutaneous Drug Reactions

### 14.2.1 Epidemiology, History, and Global Burden

Movement is a fundamental aspect of modern human life. Travelling in particular has slowly evolved from an exceptional activity to a very common and frequent event. The number of journeys worldwide per year are estimated to exceed 5000 million, on top of the movements of those in search of work and the involuntary migrations of refugees. A forecast by the World Tourism Association estimated a doubling during the first decade of this century. Europe is by far the leading destination with about 60% of the world numbers. Therefore it is essential to recognize this phenomenon, not only in specialized clinics but also in the offices of general practitioners encountering issues related to travel medicine. Beyond this, the world's attention has been drawn to the linkages between international movements and health. As a consequence of modern economic, political, and social life, both the number of people on the move and the frequency of their movement will force physicians to prepare for the health implications of the globalized world in which we now live.

Although cardiovascular mortality is the most common cause of death among tourists travelling outside their home country, adverse drug reactions (ADR) must also be taken into account as contributing to the incidence of mortality. Drugs are the most frequent cause of potentially life-threatening anaphylactic reactions, exceeding insect stings and foods.

An initially underappreciated side effect of the beneficial use of drugs is the harm caused by adverse drug reactions (ADR) of medications. Public awareness of this problem grew with an increasing number of notorious historical precedents: mercury (1948), thalidomide (1961), flecainide (1989), terfenadine (1992), calcium channel blockers (1995), fenfluramine (1997), and finally cerivastatin (2001). As spontaneous reporting of ADR identifies only about 1 in 20 such reactions, they are consequently an underestimated cause of morbidity and mortality due to underreporting. According to the Food and Drug Administration (FDA), only about 1% of adverse events are reported. Several events seem to be responsible for the difficulty in identifying ADR during product testing: (a) the size of testing groups is far too small, (b) patients with complicated medical histories as well as children and geriatric patients are often excluded from these studies, and (c) adverse events of long-term use are detected only after an appropriate time lapse. Recently ADR have been recognized as a major problem in a meta-analysis of 39 prospective studies from the USA that were set up after the thalidomide tragedy in the 1960s: an ADR is defined according to the World Health Organization as "any noxious, unintended, and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis, or therapy" and thus it excludes errors in drug administration, noncompliance, overdosage, and abuse. The above study found an extremely high incidence of serious and fatal ADR. The number of fatal ADR was estimated to be as high as 76,000 to 137,000 (mean value: 106,000) in 1 year, making ADR the fourth to sixth leading cause of death in the USA after heart disease, cancer, stroke, pulmonary disease, and accidents, even if the lower confidence limit of 76,000 was used. Beyond the heterogeneity of the studies, small biases and the fact that teaching hospitals were overrepresented in the analysis—teaching hospitals usually dealing with more seriously ill patients—ADR represent an important clinical issue. The proportion of allergic and pseudoallergic reactions was not evaluated but estimated to be 23.8%. The annual costs associated with ADR have been estimated to be as high as $1.56 to $4 billion in the USA. The use of NSAID alone has resulted in more than 70,000 hospitalizations and 7000 deaths annually in the USA. Computer-

assisted prescribing could identify even the most obscure drug interactions, avoid errors due to handwriting or similarities of medication names by printing out a prescription, and finally have an economic impact by showing comparative prices.

ADR occur in10–20% of hospitalized patients, allergic or pseudo-allergic etiologies being in up to one-third. Allergic ADR can occur in 74% and 60% of subjects with previous allergic and nonallergic ADR, respectively. In analyzing epidemiological data on ADR, reports on allergic and cutaneous drug reactions are especially sparse and imprecise, often being difficult to prove and are thus underreported. There have been some studies on the epidemiology of anaphylaxis due to drugs that accounted for 12.8% of all anaphylactic cases in one paper. For certain drugs such as penicillins, radio contrast media, or general anesthetics, the incidence of serious anaphylactic reactions is estimated to lie between 1:500 and 1:10,000. But ADR may be life-threatening not only through anaphylactic shock but also potentially lethal cutaneous drug eruptions such as Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) (with mortality rates of up to 30%), hypersensitivity syndrome or drug reactions with eosinophilia and systemic signs (DRESS), and acute generalized erythematous pustulosis (AGEP) (see Chap. 12).

An important group of drug eruptions are indeed fixed drug eruption, erythema multiforme (EM), Stevens–Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) (see Sect. 14.2.3).

As already mentioned, there are several studies concerning ADR, whereas accurate data on the incidence and prevalence of allergic and pseudo-allergic drug reactions are rare and often biased. This may be due to the multitude of clinical manifestations and pathological mechanisms and the lack of reliable diagnostic tests since data are often based mainly on unreliable histories in selected populations and very rarely are confirmed by tests, as these are seldom available or useful. Additionally there are differences in the prescribing practices of physicians in different countries, a fact further complicated by rapid changes in the production output of the pharmaceutical industry. Extrapolated data estimate 10,000 hospitalizations per year due to drug allergies in France. An often cited American study of 1986 showed a global incidence of 2.3% drug-induced cutaneous reactions in 15,438 consecutive inpatients over a 7-year period, giving detailed incidence numbers for 51 drugs. Including proven and probable allergic reactions, a more recent Swiss study found a frequency of 2.7% for cutaneous adverse reactions in 48,005 patients over a period of 20 years. Of the 1317 patients involved, 1201 reactions were classified as maculopapular exanthema, 78 as urticaria, 18 as cutaneous vasculitis, and 20 as “special exanthema” (erythema multiforme, fixed drug eruption, photosensitivity, and acneiform eruption). The most common causative drugs were penicillins followed by sulfonamides and nonsteroidal anti-inflammatory drugs. Whereas there exist estimates of the socioeconomic impact of ADR (see above), these have seldom been evaluated for allergic reactions to drugs. Costs arise not only from treatment of reactions and prolonged hospitalization but also from indirect costs such as invalidity, sick leave, and costs for alternative drugs which are often more expensive and less effective medically, for example, putting the patient and the department at risk through colonization with resistant organisms.

Increasing human mobility may lead to presentation of diseases and drug reactions that otherwise would not have been encountered. Thus, an increase in tuberculosis among immigrants will lead to an increase of drug reactions associated with antituberculosis therapy. On the other hand, with increasing tourism (see above), travelers will present with adverse reactions to medications used for prophylaxis or treatment of diseases acquired in foreign countries. Management of the returning traveler with eosinophilia includes the exclusion of drug-associated eosinophilia leading to pulmonary infiltrates (nonsteroidal anti-inflammatory drugs, nitrofurantoin, sulfonamides), hepatitis (semisynthetic penicillins, tetracyclines), vasculitis (allopurinol, phenytoin), and bronchial asthma (aspirin).

Since trade names usually differ from country to country, generic names of drugs the patient

is allergic to should be listed in the allergy record handed out to the patient. As emergency care units may be difficult to reach, the patient should carry an "emergency set" (corticoid, antihistamine, and epinephrine) with the order to be protected if reactive to a drug or some other cross-reactive agent.

### 14.2.2 Pathogenesis

ADR can be due both to allergic and pseudo-allergic mechanism. In allergic one, the reaction is caused by specific IgE and/or activated T lymphocytes that mostly follow the ingestion of even low drug doses after a specific interval, the symptoms disappearing after drug discontinuation. In the pseudo-allergic mechanism, no specific antibodies and/or activated T lymphocytes can be found [23–44].

### 14.2.3 Clinical Features

As most travelers find themselves in countries where they are exposed longer to stronger UV light, photoallergic and (mostly) phototoxic reactions due to systemic drugs are an important issue. Cutaneous reactions include eczematous, erythematous, papular, or vesiculobullous lesions predominantly in skin areas exposed to sunlight (top of the ears, nose, malar eminences, cheeks, neck, forearms, and hands), often resulting in hyper- or hypopigmentation. Dose-dependent *phototoxic reactions* present like an intensified sunburn reaction. As there is no allergic pathology, no sensitizing period is required. Onycholysis may be part of a phototoxic reaction because the lack of melanin protection makes the nail bed especially susceptible to the damage by UVlight (Figs. 14.7, 14.8, 14.9, and 14.10).

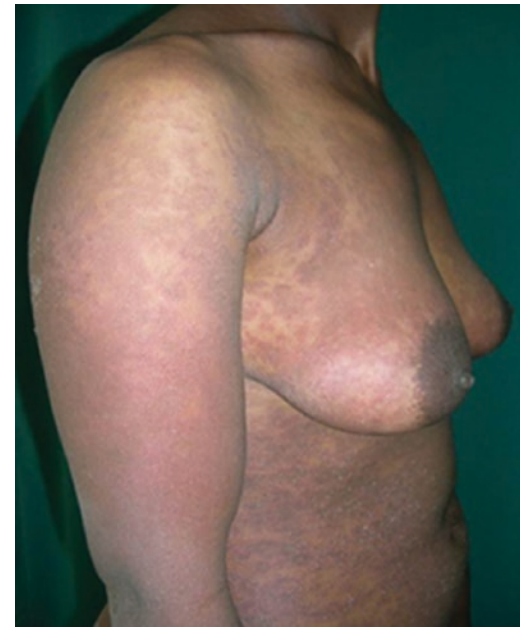

**Fig. 14.7** Adverse drug reaction

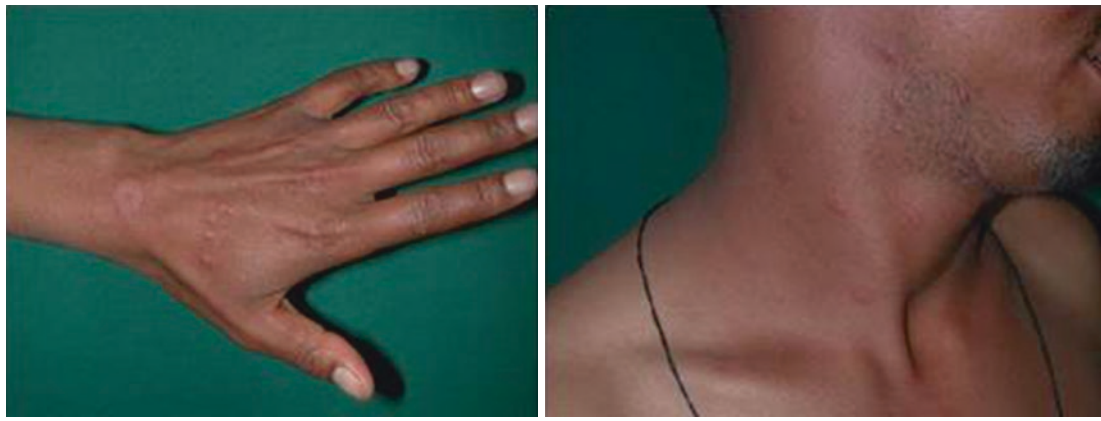

**Fig. 14.8** Adverse drug reaction on the hand and face of the same individual

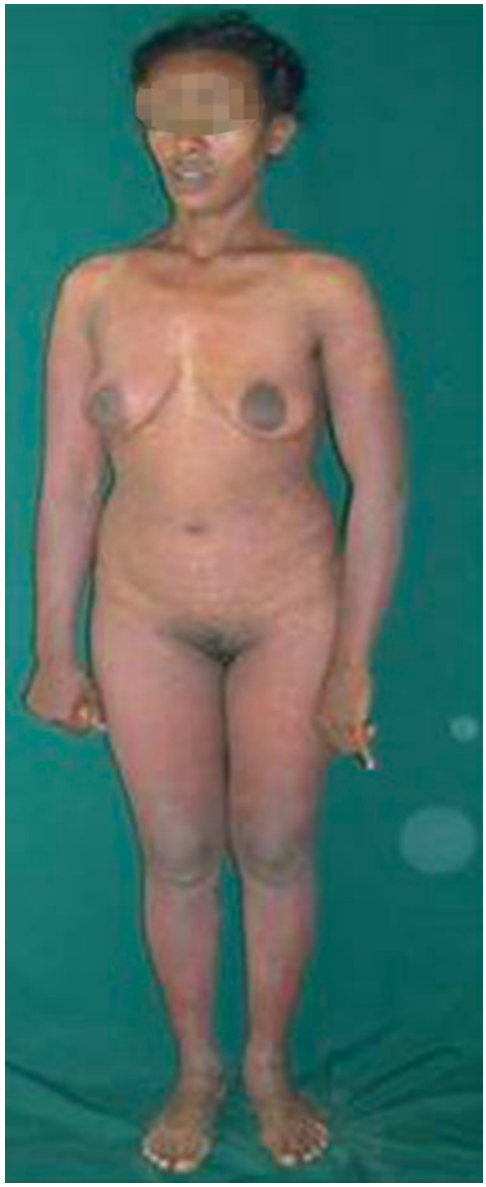

**Fig. 14.9** Diffuse adverse drug reaction

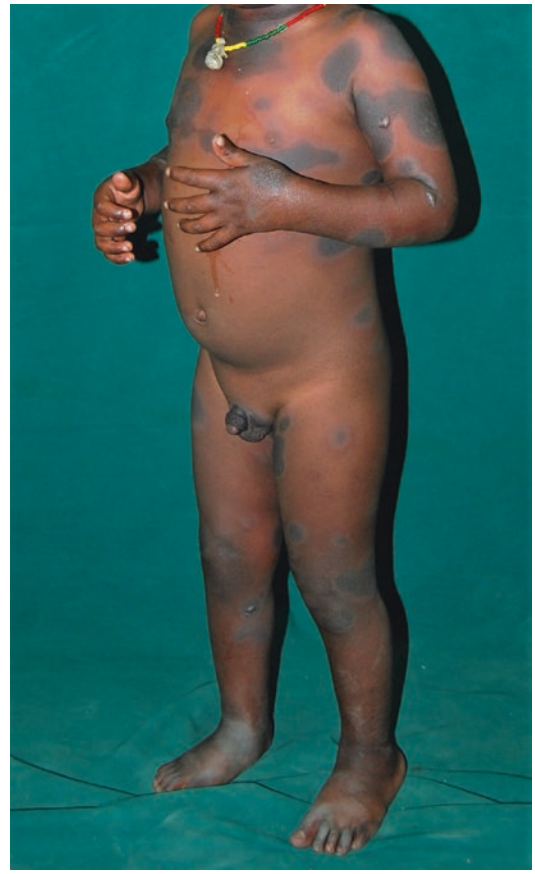

**Fig. 14.10** Adverse drug reaction with wheal

After a delay between exposure and sensitization, minimal amounts of the hapten induced by UV light are sufficient to induce *photoallergic reactions*. Clinically they range from urticarial to delayed papular or eczematous lesions that regress only slowly after discontinuation of the drug responsible. Sometimes light reactivity persists as so-called chronic actinic dermatitis even in the absence of the originally drug, probably through a delayed hypersensitivity reaction directed against skin constituents altered by shortwave UVB light. Only few systemic drugs induce photoallergic reactions, but externally applied agents include local anesthetics and antihistamines [35–44].

*Fixed drug eruption* is the development of one or more annular or oval erythematous lesions as a result of systemic exposure to a drug. In some cases, bullae may appear on top. These reactions normally resolve with hyperpigmentation and may recur at the same site with reexposure to the drug. The number of lesions may increase.

It is thought that an antigenic determinant from the drug activates cytotoxic T cells in the epidermis. These release cytokines such as interferon-γ, granzyme B, and perforin. The

cytokines, together with helper T cells and neutrophils, destroy the local skin cells (keratinocytes and melanocytes). The cytotoxic T cells then remain in the epidermis and release more cytokines when again exposed to the causative drug.

A great number of drugs may lead to fixed drug eruption, including paracetamol/phenacetin, tetracycline, doxycycline, minocycline, sulphons and sulfonamides (trimethoprim + sulfamethoxazole, sulfasalazine, fansidar), dapsone, nonsteroidal anti-inflammatories (NSAIDs) (acetylsalicylic acid and ibuprofen), sedatives(barbiturates, benzodiazepines, and chlordiazepoxide), hyoscine butylbromide (against abdominal cramps), phenolphthalein (laxative), and quinine.

*EM* is a relative frequently occurring reaction and certainly not always caused by a drug. Viral and other infections are more often the culprit, contrary to what thought in the past. But a drug eruption occurs in about 10% of the cases. In a few patients, it is idiopathic.

Many drugs have been reported to trigger erythema multiforme, including barbiturates, nonsteroidal anti-inflammatory drugs, penicillins, sulfonamides, phenothiazines, and anticonvulsants. However many claims have come from the time that the common cause herpes simplex was not recognized as such.

Skin eruption is characterized by typical target lesions. There may be mucous membrane involvement; this is often an indication of a more severe reaction. It is acute and self-limiting and usually resolving without complications if the causative drug is discontinued. There is the risk of EM major/SJS and TEN, when the drug is not interrupted.

The exact pathophysiology is not known. It is thought to be a cell-mediated immune reaction, and cytokines have been found in the blisters. This hypothesis is further supported by the finding that individuals possessing human leukocyte antigen (HLA)-B12 are three times more likely to develop this disorder. A reaction occurs 9–14 days after the initiation of the offending drug. After recurrent exposure, the reaction occurs within several hours to 1–2 days. This is also consistent with a cell-mediated reaction.

*SJS* is a blistering disorder, more severe than EM, hence the term EM major. It is characterized by mucosal erosions, small blisters, purpuric macules, and atypical target lesions on the skin with rare areas of confluence followed by detachment of 10% or less of body surface area. Fever and lesions of the respiratory and gastrointestinal tract are seen in 10%–30% of patients.

*TEN* is the most serious cutaneous drug reaction and may be fatal. It is characterized by the acute onset of skin and mucosal lesions as in SJS, but with confluent erythema, large sheets of necrotic epidermis, and total detachment of the skin over more than 30% of the body surface area. Fever, lymphadenopathy, hepatitis, nephritis, carditis, eosinophilia, and atypical lymphocytes are present in 30%–50% of patients.

An overlap of SJS-TEN has the characteristics of both SJS and TEN with the involvement of 10–30% of the body surface area, epidermal detachment, fever, and malaise. The disease may occur as a primary skin disorder or as a skin manifestation of systemic infections and malignant or chronic disease of internal organs but most often as a reaction to various drugs including those of traditional herbal medicine.

The mechanism of TEN has still to be unraveled. The toxic theory was quickly discarded. During active TEN, on the one hand, there is a paucity of inflammatory cells at the dermis, but on the other hand there are extensive apoptosis and consequent necrosis, indicating that the immune system is involved. There appears to be a cell-mediated cytotoxic reaction against keratinocytes that leads to keratinocyte apoptosis. Drug-specific cytotoxic T cells and NK cells may not be the sole effect or mechanism of the keratinocyte death, and their action may be amplified by the production of multiple cell-death mediators, altered antiapoptotic pathways, and altered or defective regulation of drug-specific immune reactions. Various cytotoxic proteins and cytokines have been implicated as mediators of the apoptosis in TEN. These include granulysin, Fas-Fas ligand interaction, tumor necrosis factor-α (TNF-α), TNF-related apoptosis-inducing ligand (TRAIL), and perforin granzyme B.

#### 14.2.3.1 Focus on Allergy to Vaccines

Immunization is one of the basic principles in preventive travel medicine. Allergy to constituents of vaccines such as preservatives, animal proteins, antibiotics, and tissue culture proteins often causes the patient and physician unexpected problems. The following section summarizes the main aspects of practical importance.

There are several components of vaccines that are able to cause adverse reactions:

1. *Antigen of the vaccine itself* usually does not cause symptoms, even if specific IgE is produced against it after adsorbate vaccinations. The quantity of circulating antigen seems to be too low.
2. *Components of the culture medium* are usually removed to a great extent except egg protein which is discussed below. Protein remnants of yeast cells may cause problems in some individuals (e.g., in hepatitis B vaccination) with preexisting severe alimentary yeast allergy. Calf serum is used in the production of some vaccines (e.g., rabies), traces of which may extremely rarely lead to adverse reactions in patients allergic to bovine serum.
3. *Ingredients used in the production/inactivation* of vaccines: antibiotics (e.g., neomycin) are used in the production of viral vaccines and removed to a great extent by preparatory steps. If they, very rarely, cause problems, only local reactions are usually observed. Traces of formaldehyde, thiocyanate, ether, succinic acid, phenolsulfonphthalein, sodium tetraborate, protamine sulfate, and phenoxyethanol are clinically not relevant because of their extremely low concentration. Beta-propiolactone is hydrolyzed; phenol (e.g., in pneumococcal or in cholera vaccine) or polysorbate (Tween 80) in contrast may lead to late-phase as well as type IV reactions especially in patients who are exposed to disinfectants or to ointments, respectively. As regards to preservative agents and stabilizers, as there have been no reports of anaphylaxis due to human albumin as yet (excluding reactions in combination with beta-propiolactone), anaphylactoid reactions—as they are dose-dependent—should not be expected. The same may be said of lactalbumin hydrolysate as, e.g., present in oral polio vaccine, since the concentrations are so low that the oral administration should not cause allergy in patients with alimentary lactoprotein allergy. Similarly, low concentrations account for no reports regarding adverse reaction against cetyltrimethylammonium bromide. Preservative agents are not used in live vaccines and have never led to fatalities. Thimerosal and benzalkonium chloride may cause local type IV reactions and may be avoided by intramuscular application even if preceding vaccinations had shown such a local reaction. Skin tests (patch tests) have no significant predictive value. Adsorbents like aluminum hydroxide or aluminum phosphate never cause allergies but may lead to foreign body reactions such as granulomas.

There are some vaccines that may require particular attention:

*Yellow fever vaccine:* the most serious allergic problem in travel vaccination concerns the attenuated yellow fever vaccine that is cultured in chick embryos. It is currently the only vaccine regulated by the World Health Organization, and proof of vaccination is required for entry into several countries. Extreme caution is necessary when the vaccine is given to a person with a history of anaphylactic reactions following ingestion of eggs. For details about vaccination in egg-allergic patients, see below.

*Tetanus toxoid vaccine:* local reactions after booster vaccinations have been reported in up to 85% with pain and tenderness and up to 30% with erythema and edema, but anaphylactic reactions are very rare (1:one million). Cutaneous manifestations also include exanthemas, urticaria, and vasculitis. In patients with vasculitis, circulating immune complexes can be detected, whereas the results of skin tests (frequent false-positive and false-negative results after prick testing, 1:1000, and intradermal test, 1:10,000) and the occurrence and role of specific IgE (many false-positive results) are controversial. The need for booster injections should be verified in aller-

gic patients by determining the anti-tetanus IgGlevel, and reactions to preservatives may be managed by the use of a formulation with a different preservative. Isolated tetanus toxoid formulations provoke fewer reactions than combination vaccines including diphtheria and pertussis. A protocol for desensitization has been developed.

*Measles vaccine:* vaccination with attenuated live measles virus (cultured on chick embryo fibroblasts) is recommended for young children travelling to measles-endemic countries. Life-threatening anaphylactic reactions occur in 71.6/million doses, mostly involving specific IgE to ovalbumin or gelatin. Diagnostic testing should include specific IgE to gelatin and egg proteins and skin tests with the vaccine and eggwhite. For details about vaccination in egg-allergic patients, see below.

*Poliomyelitis vaccine:* like most viral vaccines, the attenuated poliomyelitis vaccine contains traces of antibiotics that do not cause problems after oral application. Severe allergic reactions are extremely rare.

*Meningococcal meningitis vaccine:* this vaccination may be required for entry into Saudi Arabia during the time of the annual Hajj pilgrimage. Rarely a localized erythema may appear on the injection site for up to 2 days.

*Cholera vaccine:* local pain and swelling are experienced in about 10–20% after parenteral vaccination. Oral vaccination is recommended.

*Typhoid fever vaccine:* with the oral attenuated vaccine, cutaneous eruptions are extremely rare. Erythema and induration at the injection site are relatively uncommon (1–7%) consequences of the parenteral (Vi) vaccine. Allergic reactions with urticaria, sometimes associated with arthralgia, are rare.

*Hepatitis A vaccine:* local reactions occur in 10–20%.

*Hepatitis B vaccine:* cutaneous manifestations of intolerance include eczema, erythema multiforme (1:100,000), erythema nodosum, pruritus (1:122,500), purpura, as well as local reactions such as local urticaria and aluminum granuloma. As the vaccine is cloned in yeast cells, yeast allergy may be one cause for the few allergic reactions (including anaphylaxis) reported so far, other causes being aluminum hydroxide, thiomersal, formalin, and latex intolerance. Diagnostic measurements should include patch testing (thimerosal, aluminum chloride, formaldehyde), prick tests (vaccine: 1:10; *Saccharomyces cerevisiae*, thiomersal, aluminum chloride, latex), intracutaneous test (vaccine: 1:100), and the determination of specific IgE (*Saccharomyces cerevisiae*, latex).

*Japanese encephalitis vaccine:* relatively rare symptoms are urticaria and angioedema usually occurring minutes to up to 2 weeks (median:2 days) after vaccination (about 1:1000). Vaccinated people should be observed for at least 30 min and also be warned of the possibility of delayed reaction. When adverse reaction occurs, future boosters should be avoided. The same precautions concern individuals with hypersensitivity to mouse-derived vaccines. Other cutaneous adverse events include tender erythema and local swelling at the injection site.

*Rabies vaccine:* about 6% of vaccinated persons develop a type III hypersensitivity reaction characterized by urticaria, pruritus, and malaise after booster injections, probably caused by sensitization to human albumin structurally altered by beta-propiolactone (which therefore should not be used during preparation of the vaccine). In type I reactions, prick tests and the demonstration of specific IgE can be useful. The use of a new vaccine derived from human diploid cells seems to exclude type III reactions, as the intradermal application evidently also reduces the reaction rate. For details about vaccination in egg-allergic patients, see below.

*BCG vaccine:* cutaneous manifestations of intolerance include EEM, Sweet's syndrome, and vasculitis. Anaphylactic reactions are very uncommon, some of which are reported in neonates and infants that have been attributed to a reaction to transferred maternal dextran reactive antibodies (detected in mother's and child's blood in some instances) with a 100 kD dextran as a component of the vaccine. Therefore a vaccine without dextran or with low-molecular-weight dextran should be used. HIV-infected children may get severe adenitis.

*Tick-borne encephalitis vaccine:* common local reactions rarely are associated with regional lymphadenitis. Contraindications include a history of anaphylactic reactions to eggs.

However, not all vaccines produced in different countries use the same production procedures and ingredients as well as control standards. There are reports of travellers who had been vaccinated with rabies vaccines grown on sheep, goat, or duck embryos or with Japanese B encephalitis vaccine grown on mouse brain suspension. Vaccination with these preparations may be associated with demyelinating diseases as, for example, Guillain-Barré syndrome or allergic encephalitis.

#### 14.2.3.2 Features and Management of Adverse Reaction to Vaccine or its Components

*Pronounced local reactions* (red, tender, warm swellings) represent a nonspecific pathological response to vaccinations and are thought to represent a type III allergic reaction. The incidence and severity depend on several factors: attenuated virus live vaccines very rarely induce these reactions in contrast to inactivated bacterial vaccines (in up to 30%), especially those with adsorbents. They appear after 6–48 (mean 12) hours and usually last for only 1 day. Local reactions with a diameter of more than 50 mm are suspect for hyperimmunization (especially after tetanus booster vaccinations). The titer of specific antibodies may be measured after an interval of about 3 months, which helps to identify the most appropriate date for the next boostervaccination. Dividing the dose into two injection sites may also decrease the local reaction.

*Type IV allergic reactions* at the site of injection (frequency from 1:100 to 1:1000) present as red and tender swellings at the injection site and are regularly misdiagnosed as an increased local reaction. But in contrast to the latter, they appear later (after a mean of 48 h) and last longer (up to 7 days). These reactions usually are not contraindications for future vaccinations, and the response may be attenuated by deep intramuscular injection since type IV reactions usually take place in the dermis and subcutis. Where reactions are extreme, modified vaccines containing other ingredients or without preservatives should be used after allergy testing. It is always advisable to consider contact allergy to disinfectants or ointments applied by the patient during the course of immunization as a cause of local problems especially in reactions with a distinct epidermal component.

*Immediate systemic reactions:* since symptoms do not differ, the differentiation between anaphylactic (IgE-mediated mechanism) and anaphylactoid (without proof of IgE mechanism) may pose a problem. Reactions can be classified as anaphylactic if skin tests (prick) are positive. Another significant proof for anaphylaxis is obtained by determination of the mast cell-specific tryptase level 2–6 h after the reaction (>13.5 mg/L) in comparison with the value shortly after the reaction. Clinically there often is a longer interval between exposure to the trigger and the reaction in anaphylactic reactions.

Monitoring future vaccinations of the patient is obligatory, and medications such as adrenaline for immediate therapeutic intervention should be at hand. Anaphylactoid reactions usually do not occur after the first application of the vaccine (but, e.g., may do so in egg-allergic patients as they are usually sensitized by oral consumption of eggs).

Patients with vasovagal syncope have a different symptomatology (mostly nausea and posture-induced fainting), and they often have a history of low blood pressure and previous collapses.

*Subacute reactions* (some hours to 2 days after vaccination) presenting as exanthemas (rare) or more frequently fever should trigger a search for other causes. The so-called hypotonic hyporesponsive episodes (HHE) lead to low body temperature, decreased reactions to various challenges, and hypotonia in newborns and infants several hours after vaccination.

*Late-phase reactions* (few days to 2 weeks after vaccination) are rare complications mostly attributed to immune complex-mediated reactions. The long interval between vaccination and reaction may be caused by a slow liberation of

the antigen in adsorbent vaccines or by the slowly increasing antibody responses in live vaccines. Symptoms include arthritis (rubella vaccine in adult women in up to 15%, hepatitis B vaccine in up to 1%), thrombocytopenia (rare and mainly after measles, rubella, diphtheria, and tetanus booster vaccination), and vasculitis; several other, mostly questionable complications have been reported.

The management of individuals with suspected egg white allergy is based on the following classification:

- Group 1*:* "Intolerance" of eggs, no typical allergic symptoms.
- Group 2*:* Positive skin prick test to egg white without a history of anaphylaxis.
- Group 3*:* History of anaphylaxis after consumption of a hen's egg.

Only patients of group 3 seem to have a predictable risk of anaphylaxis. Depending on the content of egg protein, the risk decreases from yellow fever vaccine (chick embryos) to influenza vaccine (allantoic fluid), measles, mumps, tick-borne encephalitis, and finally rabies vaccine (fibroblast cultures). The last four vaccines seem to be safe because egg protein is reduced to such an extent that it cannot be detected by Western blot. If there is a history of anaphylaxis after a previous vaccination, further vaccination is contraindicated [45–50].

### 14.2.4 Management of ADR

The role of corticosteroids is currently under revision. Some studies reported a lack of efficacy or increased mortality in their use, but the use of high doses early in the course of the disease may actually reduce morbidity and mortality. There is no generally accepted steroid treatment for TEN. However, it was reported in children that a high initial dose of steroids could be beneficial. Thereafter, steroids only hinder the recovery. The benefit of initial steroids in adults is still not proved. However, there are strong indications that they also may be beneficial. Intravenous immunoglobulin was previously an accepted therapeutic agent in TEN. However, its efficacy is becoming more questionable. The current European guidelines on the use of intravenous immunoglobulin in dermatology indicated that it should be used early in the disease in the absence of an alternative evidence-based therapeutic agent, given that the potential benefits of high-dose intravenous immunoglobulin outweigh the risks of the medication considering the disease's natural course. Cyclosporine appears to be an effective agent as well, although randomized controlled studies are required to demonstrate its benefit and to establish the dose, the duration of therapy, and the safety profile. The role of plasmapheresis and antitumor necrosis factor-alpha (TNF-α) biologics and the development of anti-IL-17, anti-IL-23, and N-acetylcysteine are promising, but further studies are required to elucidate their benefit. Preventive strategies such as pharmacogenetic screening need to be considered earnestly, with the provision of cost-effective assays with a rapid turnaround time.

The management of skin failure is most important: the hydration, electrolytes, protein, and temperature loss. Be careful of superinfections and bacterial resistance. The mucous membranes should be cared for: the eyes, the mouth, the trachea, the bronchi, and the genitals.

Beside dehydration with electrolyte loss and hypothermia, pneumonia and sepsis are the most life-threatening. To prevent superinfection, intravenous antibiotics may be given at the start. Antibiotics which are known to cause TEN must be avoided, as antibiotics drugs like macrolides look safe.

Woundcare: excessive touching should be avoided. A good solution to clean is potassium permanganate solution. Dressing with Vaseline gauze or better silver dressings, if available, can be used. Even honey is for some time used with reasonable results. Keep air around the patient, and let him or her be touched as little as possible, but prevent under cooling. Start with active movements as soon as possible when the risk of new lesions diminishes. Prevent urine infections and protect against insects.

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# Hair, Nails, and Sweat Glands Disorders

15

Aldo Morrone

## 15.1 Hair

### 15.1.1 Hair Care

In contrast to Caucasian hair, which is fine and silky, black African hair has a dry and frizzy consistency. The natural hairstyle mirrors in various contexts self-expression; in particular, it expresses female beauty. Dry and frizzy hair does not easily lend itself to different methods of hairstyling. Nevertheless, specialized hair salons produce hairstyles that are impressive in aesthetic terms which are poorly documented. Hair care may also be sought for scalp problems such as pruritus, dandruff, and alopecia. The types of hair care and styles available, as well as the side effects of the techniques employed, are often poorly taken into account. The plaited style masking frontal alopecia, the "kossogoni," the chignon worn by the newly married woman, and the double chignon net appeared to be the hairstyles most frequently created among the Mali women. Straightening, shampooing, oil bathing, and coloring were the hair care procedures most frequently performed.

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### 15.1.2 Physiopathology

When taking into account the health of the hair, it is relevant to note that mechanical fragility of hair increases with higher degrees of curl.

Looking for the parameters index of physiology of the hair, the hair growth should be considered. The hair growth parameters can be assessed also using the noninvasive technique of phototrichogram. This method consists of shaving hairs from a scalp area of around 1 cm taking a picture of this area and, 2 days later, taking another picture of this same area. Comparison of these two pictures enables us both to differentiate between anagen hairs, which have grown during these 2 days, and telogen hairs, which have not, and to measure the increase in the length of anagen hairs. Three parameters of hair growth (hair density, telogen percentage, and rate of growth) were recorded on three scalp regions: the vertex region (the top of the head), the temporal region (right or left; 2 cm above the ear), and the occipital region (the point of crossing of the line joining the ears and the line extending from the nose to the occipital protuberance). Hair density, which was highly variable among African, Asian, and Caucasian people, decreased significantly in each group in order of vertex, occipital, and temporal areas. Moreover, this parameter differentiated the Caucasian group from the Asian and African ones, with the last two groups having lower values for hair density. In all regions and ethnic



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groups, the percentage of hair in the telogen phase varied greatly, even if Africans tended to have higher telogen counts than Asians and Caucasians. The rates of growth varied consistently, but African hair grew more slowly than Caucasian hair, which in turn grew more slowly than Asian hair. This parameter seemed to be much less variable than the others and more related to ethnic specificity. African hair was thus characterized by both low growth and low hair density. Asian hair was characterized by low density and high growth rate, and Caucasian hair was characterized by high density.

Many theories were put forward to explain why hair crimped and curled. One such theory was based on the geometric shape of the hair shaft. It was indeed generally considered that hair shape was related to the cross section of the hair shaft. A circular cross section was assumed to give rise to straight hair, while a pronounced elliptical cross section was supposed to produce curly hair. It was well known that African hair had a large maximum diameter and a small minimum diameter, resulting in the most elliptical shaft found in any racial group.

Other theories were based on the morphology of the hair bulb, and an explanation of crimping as being a result of keratinization within a retroverted hair bulb was proposed. It had been observed that the retroverted hair bulb had a golf club-like shape which could determine the slope and direction of the emerging hair shaft. Asymmetry of keratinization was another morphological factor associated with crimping. This asymmetry was believed to result in a bilaterality of fiber formation, but this phenomenon remained unexplored. Other researchers suggested that the inner root sheath (IRS) played a major role in hair fiber molding. In all follicles, the IRS starts keratinizing at a lower level than does the hair, thus building a tube through which the hair emerges. It was postulated that the IRS was thicker on the concave side of wool fibers and that this could play a part in molding the less keratinized hair shaft into its crimped shape. Finally, it was suggested that hair slope and whorl patterns were controlled by the dermis. Only one study suggested that the shape and morphology of the hair follicle itself may play an important role in the macroscopic appearance of hair. Using 3D computer-aided reconstruction, it was indeed concluded that hair form was governed by the shape of the hair follicle and that a straight follicle even with an oval cross section might produce a straight hair shaft. Recently, it was suggested that human curly hair follicles exhibited a retrocurvature similar to that of wool hair follicles. The asymmetry of the curly hair bulb and the alteration of the various programs of differentiation were found to be very close to the morphological features of wool follicles. In addition, it was demonstrated that such characteristics were not specific to African hair type, as both curly African and Caucasian hairs revealed the same pattern. The direct comparison of straight hair and curly hair highlighted the altered differentiation programs involved in curly hair generation. When the 2-mm-long proximal part of the follicle was put into culture, thus avoiding any influence of the appending sebaceous gland, arrector pili muscle, or dermal environment, curly hair maintained its curly growth throughout the duration of the experiment. In other words, the shape of the hair shaft appeared to be intrinsically programmed by the lower half of the follicle, independent of the dermal environment. In conclusion, in vitro growth strongly suggests that curvature of curly hair is programmed from the basal area of the follicle. The phenotype of hair in Africa varies from very tightly coiled in the south to very straight in the north of the continent. Lindelof demonstrated that the shape of the follicle (curly or spiral in Africans and straight and perpendicular to the skin in Asians) is more important than the cross section. Lindelof's study showed not only that Europeans have a follicle shape that is intermediate between that of Africans and Asians but also that even a straight follicle may produce a hair shaft that has an oval cross section. The biochemical composition of hair in people from different geographic regions has been shown to be virtually identical in terms of keratins and amino acid content. This is in spite of significant morphologic differences (in compatibility, elasticity).

### 15.1.3 Hair Loss

As frequently reported, traction alopecia is present in about one-third of African women. This occurred at the temporal hair line and was caused by tension exerted on the hair from the use of tight braids. In general, hair loss occurs in all ethnic populations, but the etiology varies considerably from group to group. It can range from a bare patch to an extensive diffuse pattern of hair loss. In black women, many forms of alopecia are associated with hair care practices. The use of thermal (hot combing, hot iron curling, blow dryers) or chemical hair straightening and hair braiding or weaving are examples of styling techniques that place African-American women at high risk for various "traumatic alopecias." Chemical relaxants were consistently used, whereas some women alternated relaxation with other styles such as weave-ons and braids/plaits, or they applied hair dyes immediately after relaxation. Local concoctions for hair care management were also routinely used, with subsequent frequent pain and hair breakage. Concoctions applied to the scalp included crushed raw marijuana, cocaine, aloe vera, henna, akanwu (potash), lime, raw egg, and various pomades. The duration of hair care practices varied from 5 to 37 years, with a mean of 19.2 ± 9.3 years for permanent relaxation of the hair with chemical relaxants. Sodium and potassium hydroxide-based relaxants were commonly used, preferred to the guanine hydroxides that are more expensive and less harmful. Histological analysis indicates mainly atrophic epidermis, lymphocytic proliferation around hair follicles, destroyed hair follicles, and a densely sclerotic dermis. Traction alopecia was seen often as a primary condition but also occurred in association with other scalp disorders. Other diseases are discoid lupus erythematosus (DLE), central centrifugal cicatricial alopecia (CCCA), and alopecia areata (AA). Women with scarring alopecia were found to have used chemical relaxants for longer than those with non-scarring alopecia. Moreover, women with scarring alopecia also changed relaxants more frequently and applied local concoctions or oily pomades to stimulate hair growth and relieve scalp discomfort. Hair relaxation with chemical relaxants was found to be the first step in hairstyling. It was also found that women with scarring alopecia complained most often of local chemical burns and local contact irritation of the scalp, especially after their too frequent and prolonged use of chemical relaxants. Thus the frequent contact of the scalp and hair with lye relaxants in a bid to straighten the hair must have been the initial trigger of primary irritation, followed by inflammation and fibrosis, ultimately resulting in scarring, particularly in women with CCCA. Itchy scalp, painful scalp, ready hair breakage, scalp heaviness or irritation, and flaking scalp were common presenting complaints. Hair care practices and their duration and styling are thus relevant with respect to hair loss in black African females because of the intrinsic properties of their hair type [1–22].

## 15.2 Nail

The nails appear to be similar in black and white people, even if the pigmentary striae are more frequent in the first ones without a pathological value. Nails can frequently show lesions due to abuse or torture (see Chap. 20) [23, 24].

## 15.3 Gland

The black African people are provided with the same number (2–3 millions) of eccrine gland, even if the amount of those functional is higher than those present in black American people, probably due to adaptive mechanism to the different environment. The amount of sweat produced by a person depends on climatic condition and on the ability of the person to acclimatize, not on individual anatomical features. The amount and the distribution of the apocrine glands are characterized by high interindividual variability but independent on skin pigmentation.

Even the sebaceous glands show the same density among the black African, black American, and Caucasian people. The highest amount of

lipids extracted by the hair of black people probably is due to a different reservoir of sebum and not to a different production. However, this is still a controversial topic [25, 26, 27].

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# Benign Cutaneous Neoplasms

16

Markus Vincent Starink

## 16.1 Seborrhoeic Keratosis

Seborrhoeic keratoses (SK) are very common benign skin neoplasms, affecting almost all older individuals. They can appear all over the body. They can usually be recognized easily, but sometimes they can be difficult to distinguish from among others nevi, melanoma, actinic keratosis, and squamous cell carcinoma [1–4].

### 16.1.1 Epidemiology

The prevalence is extremely high: 80–90% of elderly patients have SK. Before the age of 20 years, they do not appear. Caucasian skin type is most often affected.

### 16.1.2 Pathophysiology

SK are a proliferation of keratinocytes, filled with a variable amount of melanin. The cause is unknown.

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### 16.1.3 Clinical Features

Seborrhoeic keratoses can have a variable appearance (Fig. 16.1). The color varies from yellow, gray, light brown to dark brown, and black, and usually there is a mixture of some of these colors. They can be flat or raised and range in size from 1 mm up to several cm in diameter. SK evolve from a macule and may progress to become papular or verrucous. Usually SK appear to stuck to the surface. They can arise everywhere on the body, with the exception of mucosal surface, palms, and soles. Some clinical variants are dermatosis papulosa nigra (1–2 mm, round, dark SK on face and neck, mainly in skin type IV–VI), stucco keratoses (white, small pap-

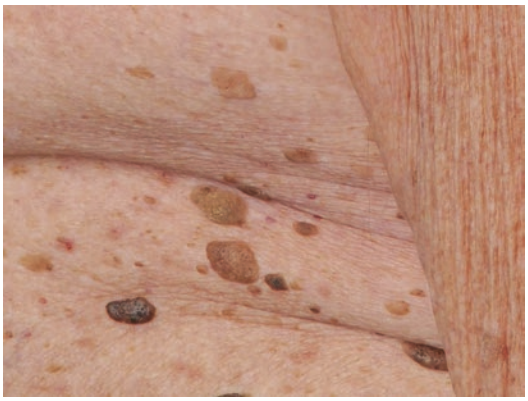

**Fig. 16.1** Typical seborrhoeic keratoses on the back



A. Morrone et al. (eds.), *Skin Disorders in Migrants*, https://doi.org/10.1007/978-3-030-37476-1_16

ules on the lower extremities), and (some) benign lichenoid keratoses (inflammatory reaction arising in a regressing solar lentigo, SK, or actinic keratosis).

### 16.1.4 Diagnosis

Usually SK can be recognized easily. Especially in very dark lesions, SK with different colors, or if there is a history of recent change or if there is inflammation, differentiation from melanoma or other malignant proliferations can be difficult. In SK one can see so called milia-like cysts (yellow or white, tiny round structures, comedo like openings, fissures and ridges, fingerprint-like structures and a yellow-brown border, where horn pseudocyst and a lack of pigment network favors the diagnosis SK.

### 16.1.5 Therapy

Not necessary. If desired curettage or cryotherapy can be performed.

## 16.2 Melanocytic Nevus

Melanocytic nevi are benign proliferations of nevomelanocytes. They can be congenital or acquired. Melanocytic nevi are very common and malignant degeneration is rare. Nevertheless, the question whether a certain nevus is benign or malignant is one of the most common reasons for patients to visit a dermatologist [1–4].

### 16.2.1 Epidemiology

Almost every human being has nevi. On average, people have 15 nevi; however, there is considerable variation. They usually start appearing at the age of 3 years and increase in number throughout puberty. At the age of 35–40 years, they stop appearing (and even tend to disappear), so new nevi in an elder person should raise suspicion. Caucasians usually have more melanocytic nevi than darker-skinned populations. However, nevi on palms, soles, conjunctivae, and nail beds are more prevalent in darker skin types.

### 16.2.2 Pathophysiology

It is thought that melanocytic nevi originate from large melanoblasts from the neural crest that migrate to the epidermis during the embryonic phase. As a consequence of sun exposure and genetic factors, they start to proliferate. It is believed that nevi start as junctional nevi, and as the cells migrate to the dermis, they become compound nevi and after that dermal nevi.

### 16.2.3 Clinical Features

Melanocytic nevi are well-circumscribed, relatively symmetrical, dome-shaped/raised or flat, pigmented or skin-colored lesions, usually 2–6 mm in diameter. The surface can be flat or verrucous and hairs can grow out. They are mainly found on sun-exposed skin. The color and whether they are flat or raised depend largely on where in the skin the proliferation of nevomelanocytes is found. Based on this, different types of nevi can be distinguished.

*Junction nevi* are darkly pigmented, flat nevi. Histopathologically, the cells are found on the dermo-epidermal junction.

*Compound nevi* are less dark, raised nevi, with a flat or somehow verrucous/papillomatous surface. The nevomelanocytes are located in the dermo-epidermal junction and in the superficial dermis.

*Dermal nevi* are skin-colored or light brown nevi. The cells can be found only in the dermis.

*Blue nevi* are usually solitary, 0.5–1 cm in diameter, dome-shaped, bluish lesions. They can be found mainly on the dorsal hands/feet, face, and scalp, more often in people of Asian origin. The blue color is the consequence of the deep location of the pigment (“Tyndall phenomenon”).

*Halo nevi* are nevi with a depigmented ring. This is the consequence of regression. They can

be present for years but can also change or disappear.

*Congenital nevi* are light brown up to almost black lesions, varying in diameter from less than 1 cm up to many decimeters. They can be flat or (partly) raised and sometimes very hairy ("Tierfell nevus"). The larger these nevi are and the more are present, the higher the chance of malignant degeneration and of neurological diseases.

*Acral nevi* are usually macular or slightly raised. They often have linear striations in the furrows of the acral skin.

*Dysplastic nevi* are usually larger nevi (>5 mm), with vague, irregular borders, asymmetry, and different colors (red, different shades of pigmentation). There is still debate how they relate to melanoma. However, in doubt the nevus should be excised.

### 16.2.4 Diagnosis

Nevi are easy to recognize, but differentiating them from melanoma can be difficult. Sudden changes are suspicious, for example, itching, growth, change in color, or loss of hair in nevi with previous hair growth. Also, a family or personal history of melanoma is suspicious. On physical examination, suspicious signs are size >5 mm, irregular surface, a red border, asymmetry, and three or more different colors. The ABCDE acronym can help in separating benign from suspicious nevi: asymmetry, border, color, diameter, and evolution.

If available and if experienced, one can use dermoscopy as an additional tool.

### 16.2.5 Therapy

Treatment is not necessary, unless there is doubt on malignant degeneration. If doubt exists, diagnostic excision with a small margin of 2 mm should be performed. If desired, for cosmetic or mechanical reasons, nevi can be excised conventionally with a minimal margin or by "shave-excision."

## 16.3 Epidermal Cyst

Cysts are defined as closed "sacs," lined by a layer of cells, containing fluid or a semisolid substance. Cysts are common cutaneous lesions. Patients can present because of cosmetic or medical concerns or because of inflammation or irritation. Cysts can be classified on histologic features of the cyst lining. In the skin, cysts are lined by stratified or non-stratified epithelium.

Epidermal cysts (synonyms: epidermoid cyst, infundibular cyst, epidermal inclusion cyst, sebaceous cyst) are the most common cysts. Other types of cysts are trichilemmal cyst (scalp), vellus hair cyst (trunk/chest), steatocystoma (trunk, axilla, groin), pilonidal cyst (sacrococcygeal), hidrocystoma, mucocele (oral mucosa), digital mucous cyst (finger, toe), and ganglion (wrist). The last three are actually pseudocysts, as they are not lined by a proper wall [1–4].

### 16.3.1 Epidemiology

Epidermal cysts are very common and can affect all age categories and gender.

### 16.3.2 Pathophysiology

Epidermal cysts form by several mechanisms. They can be the consequence of sequestration of epidermal rests during embryonic life, they can be the result of occlusion of the pilosebaceous unit, or they may be formed after traumatic or surgical implantation of epithelial elements. Keratin will build up in the dermis and subcutis, and this keratin can either be released via the central pore or it can leak in the adjacent dermis and subcutis, causing an inflammatory response.

### 16.3.3 Clinical Features

Epidermal cysts are most common on the face and upper trunk but can occur everywhere on the body. They are usually skin-colored or yellowish nodules, several millimeters to centimeters in

size. Often a punctum or pore can be seen, representing the follicle from which the cyst originates. Usually the cyst is solitary, but multiple cysts can occur in, for example, syndromes, in patients with severe acne vulgaris, or without known reasons. Multiple scrotal cysts are an example.

Epidermal cysts are asymptomatic, but they can get painful when inflamed.

### 16.3.4 Diagnosis

Epidermal cyst can be recognized easily. *Milium* is a highly prevalent variant of small (1–2 mm), superficial, disseminated epidermal cysts in the face. *Trichilemmal cysts* are clinically similar. They are less prevalent, usually presenting as solitary or often multiple, sometimes inherited swellings on the scalp. If desired, histology can distinguish epidermal cyst from trichillemmal cyst. *(Eruptive) Vellus hair cysts* are small, skin-colored to dark papules, usually multiple. They are located on the trunk. They can be seen in conjunction with *steatocystoma multiplex*—these cysts are a few millimeters to several centimeters in diameter, located on the chest, axillae, and groin, draining oily substance if punctured. *Pilonidal cysts* present as inflamed, painful swellings in the upper gluteal cleft/sacrum, usually in male who are hirsute.

### 16.3.5 Therapy

Cysts can be excised. This is usually not necessary, unless cosmetically desired or in case of frequent inflammations.

## 16.4 Fibroma

Fibromas (synonym "acrochordon," "skin tag") are small, soft tumors that can arise all over the body [1–4].

### 16.4.1 Epidemiology

Fibromas are extremely common. The incidence increases with age. Sometimes they can be seen in association with diabetes mellitus.

### 16.4.2 Pathophysiology

Fibromas are swellings of loose, collagenous stroma and thin-walled blood vessels. The etiology is unknown.

### 16.4.3 Clinical Features

Fibromas are skin-colored or light brown tumors that feel soft on palpation. They can vary in size from 1 mm up to a couple of centimeters. The smaller variants (*skin tag*) can be seen as solitary or multiple, small (1 to a couple of millimeters in size), pediculated papules in the neck, axilla, or groin. Sometimes variants of a couple of centimeters can be seen as soft, pediculated swellings, usually on the trunk but sometimes on the extremities (Fig. 16.2).

### 16.4.4 Therapy

For cosmetic or mechanical reasons, they can be cut with a scissor, or coagulation can be performed.

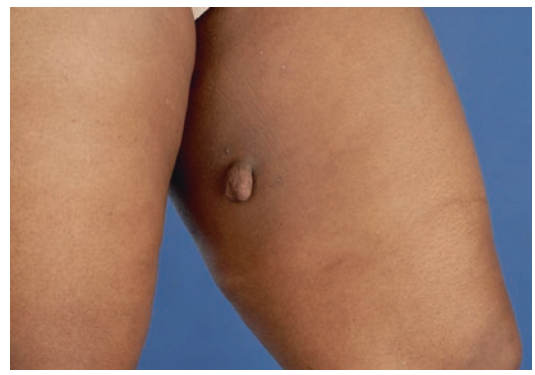

**Fig. 16.2** Large fibroma on the upper leg

## 16.5 Dermatofibroma

A dermatofibroma is a solid, subcutaneous swelling, typically seen on the lower legs. It is usually asymptomatic. Clinically it can be confused with, for example, nevi and cysts [1–4].

### 16.5.1 Epidemiology

Dermatofibroma are primarily seen in adults, more often in females. They are very common, although the exact prevalence is unknown.

### 16.5.2 Pathophysiology

The etiology is unknown, but it is thought that dermatofibroma arise at sites of insect bites or other traumas.

### 16.5.3 Clinical Features

Dermatofibromas are firm, slightly elevated, dome-shaped nodules (Fig. 16.3). In the center, they can be red, skin colored, or slightly pigmented; typically, they have a darker border. On palpation, a subcutaneous nodule is felt. When the lesion is taken between two fingers, the lesion seems to sink downward. This is called the "dimple sign." Size varies from a couple of millimeters up to 2 cm. They are commonly seen on the legs of adults but can arise on other parts of the body.

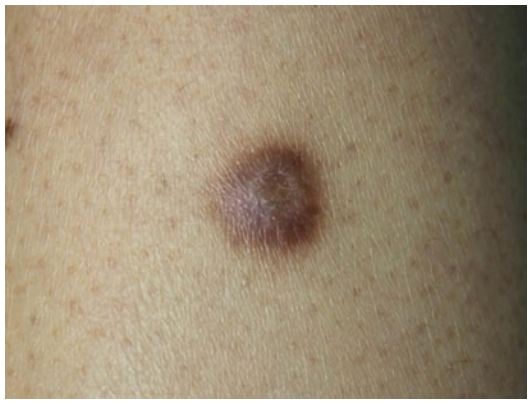

**Fig. 16.3** Pigmented dermatofibroma on the lower leg

### 16.5.4 Diagnosis

Dermatofibroma can usually be recognized clinically. The pigmented border and a positive dimple sign make the diagnosis almost sure. When dermatofibromas are larger in size (cave dermatofibrosarcoma protuberans) or when there is doubt about the diagnosis (e.g., to distinguish it from melanoma or cutaneous metastases), histological examination should be performed.

### 16.5.5 Therapy

Not necessary. If there is doubt about the diagnosis or if the patient wants removal for cosmetic reasons, excision can be performed. However, excision should be done with a relatively wide margin, as the lesion is usually smaller at the visible surface of the skin and larger deeper in the skin. This leads to a bigger scar than the initial lesion. As dermatofibromas tend to become softer and smaller over time, it might be better to discourage patients to treat it.

## 16.6 Cherry Angioma

Cherry angioma (synonym *senile angioma*) is an extremely common swelling caused by dilatation of the capillaries in the papillary dermis. They appear during adult life, and it is the most commonly acquired cutaneous vascular proliferation[1–4].

### 16.6.1 Epidemiology

Cherry angioma are extremely common, the lifetime prevalence is almost 100%. Both sexes are affected. The age of onset varies, but usually they start to appear in the third decade.

### 16.6.2 Pathophysiology

The etiology of this swelling of dilated and congested capillaries is unknown. There might be a hormonal factor contributing, as they can also appear during pregnancy and involute afterwards.

### 16.6.3 Clinical Features

Cherry angiomas are flat or slightly raised, sometimes polypoid, round to oval, cherry-red swellings, usually a couple of millimeters in diameter (Fig. 16.4). They are commonly found on the trunk, solitary in the beginning, but as age rises the number increases up to often more than 100. The hands, feet, and face are usually spared. They are asymptomatic, but sometimes they can bleed when traumatized.

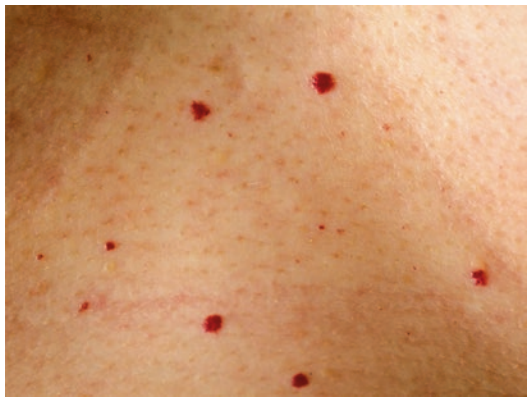

**Fig. 16.4** Cherry angiomas of different sizes on the back

### 16.6.4 Therapy

Not necessary. Electrocoagulation or laser therapy can be performed for cosmetic reasons. Thrombosed lesions that are dark or bluish are sometimes biopsied to distinguish them from melanoma.

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# Malignant Cutaneous Neoplasms

17

Marlous L. Grijsen

## 17.1 Introduction

Worldwide more than 65 million people are forcibly displaced and live outside their country of origin. Among them are 22.5 million refugees, many of whom are adolescents and young adults [1]. Health problems affecting the skin comprise one of the largest burdens of disease worldwide. They can occur during any stage of life causing significant discomfort, disfigurement, and loss in quality of life [2]. For immigrants, who often arrive from countries with limited healthcare access and a high prevalence of infectious diseases including HIV infection, the burden of skin conditions is even larger. Skin diseases often are a reflection of many contributing factors, including socioeconomic status, level of education and living conditions, cultural behaviors, the prevalence of infectious diseases in the country of origin, genetic susceptibility, and overall mental health. The latter claims an important role, since the process of immigration and settlement is incredibly stressful, not to mention the language barriers, unemployment, and financial constraints which most migrants are facing in the following years in their new country of residence.

This chapter will focus on the different malignant cutaneous neoplasms commonly seen in migrant populations. In this chapter, the term immigrant or migrant is used for asylum seekers, refugees, and economic migrants and includes a broad range of ethnicities, skin types, and geographic origins.

Skin cancer represents 20–30% of all cancers in Caucasians, 2–4% in Asians, and 1–2% in Asian Indians and people with a black skin [3]. The risk of developing skin cancer is associated with environmental and genetic factors. For most skin tumors, exposure to ultraviolet (UV) solar radiation is regarded the predominant environmental risk factor. Phenotype (Fitzpatrick skin type I–III), geographic location (e.g., equatorial latitudes and high altitudes), albinism, xeroderma pigmentosum, chronic immunosuppression, lifestyle, and exposure to other exogenous factors such as smoking, human papilloma virus (HPV), and certain chemicals (e.g., arsenic and coal tar) also play key roles in the induction of skin cancer [4, 5].

The literature on cutaneous neoplasms in migrant populations is scarce. Frequently reported conditions often concern skin infections or infestations, but very few malignant tumors. In most migrants, the occurrence of skin cancer, apart from Kaposi's sarcoma, is less common than in light-skinned Caucasians, but data are limited to draw firm conclusions. This may in part be explained by the darker skin color and the related increased

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amounts of protective melanin levels, which result in a lower susceptibility to UV damage, but also by differences in cultural behavior with regard to sun exposure. For example, in Western cultures, deliberate tanning behaviors are common since a tanned skin is perceived to be healthy and attractive, which contrasts with Africans and Asians many of whom tend to avoid sunlight exposure for cultural and/or religious purposes and desire a fair skin complexion. In addition, many immigrants are relatively young adults whom migrate for work purposes. In 2015, the median age of immigrants arriving in one of the European Union Member states was 28 years [6]. In this age group, the development of malignant skin tumors is unusual. Nevertheless, despite many misconceptions, skin cancer occurs in all races and ethnicities [7]. In fact, recent studies have shown that among Afro-Americans, skin cancer is diagnosed at a more advanced stage leading to a worse prognosis and overall survival rate as compared to other ethnic groups [3, 8, 9]. Lack of knowledge and awareness among patients and physicians, atypical clinical presentations, the taboo of (skin) cancer among many cultures, low socioeconomic status, and limited access to appropriate healthcare are several features explaining this remarkable difference. People who have limited financial resources often only seek medical care when the skin lesions are severely symptomatic, contributing to an unfavorable outcome. Worldwide, skin cancer is an emerging public health issue, which encompasses all ethnicities and socioeconomic communities.

## 17.2 Kaposi's Sarcoma

### 17.2.1 Definition and Etiology

Kaposi's sarcoma (KS) is a low-grade mesenchymal tumor involving blood and lymphatic vessels [10]. It is a multifocal systemic disease which is caused by human herpesvirus 8 (HHV8), previously called KS-associated herpesvirus. In 1872, Moritz Kaposi was the first to describe KS as a rare form of skin cancer that primarily affected elderly, Ashkenazi Jewish men. This scenario, changed with the advent of the AIDS epidemic in the 1980s when a sudden dramatic rise in HIV-associated KS was observed in young homosexual men in New York City and California [11].

### 17.2.2 Epidemiology

The seroprevalence of HHV8 varies between geographic areas and subpopulations, ranging from 4% or lower in the general population of the United States and Northern Europe to about 10–35% in the Mediterranean area and up to 87% in sub-Saharan Africa [12, 13]. Risk factors for HHV8 transmission are multiple sex partners, high-risk sexual behavior, and the presence of HIV and other sexually transmitted illnesses [14]. In endemic settings, where the seroprevalence of HHV8 in children is high and increases with age, transmission most likely occurs horizontally (e.g., from mother to child or between siblings) through extensive and repeated exposure to infected saliva. Blood transfusion and organ transplantation are also plausible routes of HHV8 transmission [15].

HHV8 is found in migrants from African countries. In a Swiss study evaluating the HHV8 seroprevalence of pregnant women in Geneva, 9 of 27 African women (33%) were HHV8 seropositive [16]. There is however a vast discrepancy between the seroprevalence of HHV8 and the development of KS, acknowledging the importance of cofactors such as the genetic profile of the host, and (iatrogenic) immunosuppression, including coinfection with HIV [17]. A population-based study from Sweden described that immigrants have a higher risk of developing KS [18]. In the United States, sub-Saharan African-born blacks had significantly higher proportional incidence ratios of KS than US-born non-Hispanic blacks [19].

### 17.2.3 Clinical Features

KS is classified into four clinical-epidemiological subtypes:

1. The classic form, typically affecting the lower limbs in elderly Mediterranean, East European, and/or Jewish men.
2. African endemic KS which mainly occurs around the equatorial belt, has a polymorphic

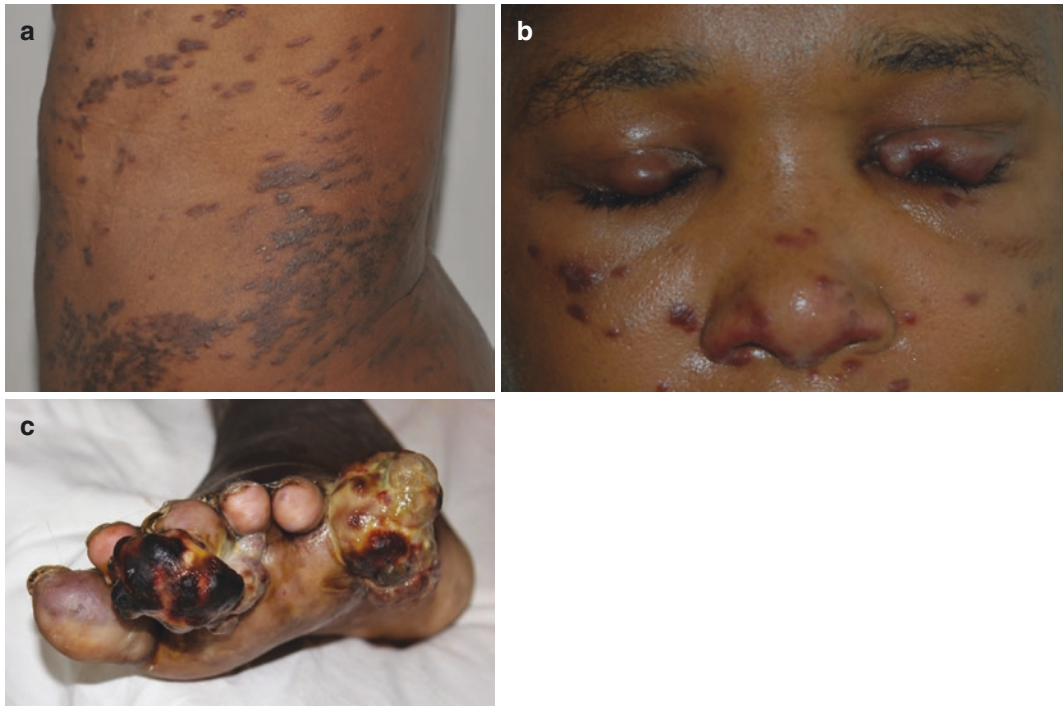


**Fig. 17.1** Different forms of Kaposi's sarcoma showing livid, brownish plaques and tumors on the trunk, face, and foot. (**a**) African endemic. Note the distribution of the lesions along the Blaschko-lines; (**b**) HIV-associated; (**c**) African endemic with exophytic lesions on the foot which clinically may resemble an acral lentiginous melanoma. (Courtesy of Regional Dermatology Training Centre (RDTC), Moshi, Tanzania)

clinical picture and presents in distinct patterns (Fig. 17.1a). It may mimic the classic form and involve nodular lesions, though it mostly affects young adults. It can also present as a more aggressive form and invade the soft tissue and bone, which is often fatal. Other presentations are florid mucocutaneous and visceral disease and a fulminant lymphadenopathic variant which primarily affects children, rapidly disseminates to lymph nodes and visceral organs, and has a poor outcome [10].

3. Iatrogenic KS which is associated with organ transplantation or immunosuppressive therapy; it is clinically similar to the classic form and may completely resolve upon discontinuation of immunotherapy.
4. Epidemic or HIV-associated KS, which is the most common malignancy in people with AIDS [10] (Fig. 17.1b, c). Traditionally, a low CD4 T-cell count during chronic HIV-1 infection is the most important factor associated with the development of KS, although most KS cases nowadays occur at higher CD4 T-cell counts [20].

In all clinical forms, the cutaneous lesions vary from pink patches to blue-red plaques, nodules, or diffuse infiltration of the skin and subcutaneous tissue depending on subtype and stage.

### 17.2.4 Management

Treatment options are diverse and must be tailored to each individual patient. Localized skin lesions may be treated by surgical excision, cryotherapy, topical alitretinoine, intralesional chemotherapy, or, in case of multifocal lesions, radiotherapy. Extensive multifocal disease will require systemic chemotherapy. In HIV-related KS, the initiation of combination antiretroviral therapy (cART) may prevent or treat KS lesions. With the global introduction of cART, the incidence of KS has decreased remarkably. Recurrence rates of KS are high.

## 17.3 Cutaneous Malignant Melanoma

### 17.3.1 Definitions and Etiology

Cutaneous malignant melanoma (CMM) is a tumor that arises from the malignant transformation of melanocytes, the pigment-producing cells in the skin which are also responsible for the color of the skin. Invasive cutaneous melanoma is a potentially fatal form of skin cancer. Mounting evidence suggests that UV radiation has a less significant role in the aetiology of CMM in the skin of color than in white populations. One study revealed that frequencies of BRAF and NRAS mutations were specifically low in CMM from black Africans [21]. Other studies found increased expression of KIT, a tyrosine kinase receptor, in acral lentiginous melanomas [22, 23]. These data suggest a different pathogenesis and specific genetic alterations of CMM in dark-skinned persons.

### 17.3.2 Epidemiology

In the United States, CMM is the fifth most commonly diagnosed cancer [24]. Over the last 10 years, incidence rates for CMM have been rising with an average of 1.4% [24, 25]. However, the global incidence and mortality of melanoma varies considerably between countries and populations. In the United States, CMM predominantly occurs in Caucasians (95%), followed by Hispanics, American Indians/Alaskan Natives, Asian/Pacific Islanders, and people with a black skin [26–28]. Although CMM is uncommon in minority populations, they often present with advanced-stage disease that are more likely to metastasize and have poorer outcomes [9, 26]. A study on melanoma incidence and survival based on registered data from the United States stated that Hispanics (odds ratio 3.6), African-Americans (OR 4.2), American Indians (OR 3.4), and Asians (OR 2.4) were more likely to present with stage IV CMM and had a worse survival than their Caucasian counterparts [27, 29]. A Swedish population-based study showed that first-generation migrants from Southern Europe had more advanced stages of CMM at diagnosis compared to Swedish-born patients, specifically among women originating from Yugoslavia, causing a lower survival rate [30]. These studies combined demonstrate that CMM has a bad prognosis in minority populations, such as immigrants, due to its late presentation due to either socioeconomic or cultural reasons (e.g., ignorance, taboo) and less accessibility to medical care.

### 17.3.3 Clinical Features

People with a pigmented skin have CMM at different anatomical sites than Caucasians, in whom it generally occurs on the sun-exposed areas of the body. However, in people of color, areas unexposed to the sun are more common with acral lentiginous melanoma (ALM) being the predominant histologic subtype. Up to 60–70% of melanomas in pigmented skin arise on the soles (Fig. 17.2a), palms, and subungual sites [3, 28, 31, 32].

Typically, CMM presents as a dark brown/black pigmented, asymmetric lesion with irregular borders (Fig. 17.2b). When the nail matrix is affected, the melanoma can present as longitudinal melanonychia, gradually becoming wider over weeks to months at the proximal end, or as a diffuse black/brown hyperpigmentation of the nailbed, extending onto the adjacent nail folds, also referred to as the Hutchinson sign. Other symptoms may be nail dystrophy, onycholysis, or infection/ulceration of the nail. However, ALM is frequently misdiagnosed and associated with a poor prognosis due to its atypical presentation and morphology (mimicking benign lesions) and higher rate of amelanosis [33, 34]. In experienced hands, dermatoscopy may assist as a supportive diagnostic tool to differentiate between benign and malignant nevomelanocytic lesions.

### 17.3.4 Management

In case of a suspected lesion, it should, preferably, be excised entirely, with a 2 mm margin, and sent for pathological examination. Regarding larger lesions or ALM, a biopsy may be considered and is preferred in case of subungual melanoma. Following the histological confirmation of the diagnosis, an extensive re-excision (depending on the Breslow thickness) of the primary site should be performed. Treatment options depend on the stage of CMM and can vary from local

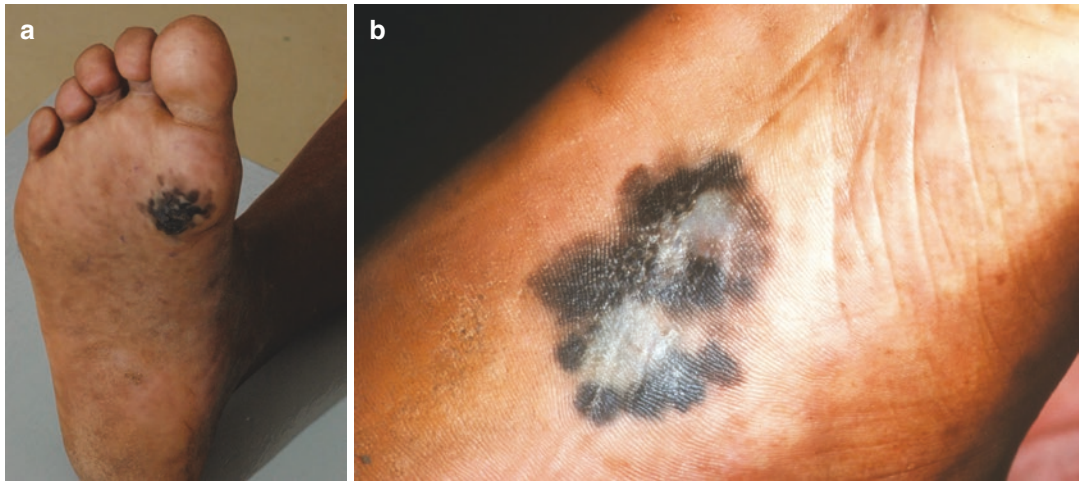


**Fig. 17.2** (**a**, **b**) Two cases of acral lentiginous melanoma on the soles of the feet. (**a**: Courtesy of Regional Dermatology Training Centre (RDTC), Moshi, Tanzania. **b**: Courtesy of Department of Dermatovenereology, Erasmus Medical Center, Rotterdam, The Netherlands)

surgery with high survival rates to chemo-and/or immunotherapy with poor survival rates.

## 17.4 Keratinocyte Cancers

### 17.4.1 Definition and Etiology

Keratinocyte cancers refer to basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), globally the two most common skin cancers. Multiple trigger factors have been considered: increased sun-seeking behavior, including exposure to tanning beds, aging populations, increased general public awareness, improved detection methodologies, and depletion of the ozone layer exposing humans to higher UVradiation levels. Additional risk factors for developing skin cancer are albinism and xeroderma pigmentosum, two genetic conditions which are not uncommon on the African continent, possibly as a result of consanguinity [35, 36]. People with albinism in sub-Saharan Africa have up to a 1000-fold higher risk of developing SCC [37].

### 17.4.2 Epidemiology

Since the 1960s, the annual incidence rates of both these malignancies have been rising by 5–8% in white populations, driven by the above multiple factors. In the United States, similar trends are seen among Asians and Hispanics. Among Asians residing in Singapore, the annual incidence rate between 1968 and 2006 increased by 2–8% [38, 39]. Chinese residents in Singapore, who have a fairer skin tone than the Malays and Indians, had three times as much BCC and SCC than their counterparts [38]. Although the mortality rate in keratinocyte cancers is very low, they have a significant impact on the quality of life, since many occur in visible areas, and cause substantial economic burden to the health system [40]. BCC is the most common cutaneous neoplasm in Caucasians, Latin Americans, Chinese, and Japanese populations. On the other hand, SCC is more often seen in Africans and Indians and represents 30–65% of cutaneous neoplasms in both of these ethnic groups as compared to 15–30% in Caucasians, Chinese Asians, and Japanese [3]. A retrospective study from Egypt, studying the clinicopathologic features of skin cancer, revealed that BCC was more prevalent, followed by SCC and CMM. This finding, however, probably reflects the lighter skin complexion of North Africans compared to sub-Saharan populations [41]. The prevalence of keratinocyte cancers in migrant populations is low. Yet, due to its atypical presentation, lack of awareness among patients and physicians, and socioeconomic barriers, they often present at a more advanced stage causing an unfavorable prog-

nosis. A case-control study performed in Western Australia revealed that immigrants had lower risks of developing SCC, but people who had migrated to Australia early in life or had lived in Australia for a long time had higher risks of developing SCC than those who had arrived more recently [42].

### 17.4.3 Clinical Features

Classically, BCC is a slowly growing, locally invasive, pink to erythematous plaque or nodule that is particularly common in the body areas exposed to the sun like the head and neck [43]. BCC has several clinical variants, e.g., the nodular, superficial, pigmented (conveying a brown/black color), and morphoeic form (Fig. 17.3a). In Asian populations, pigmented BCC is the predominant subtype, representing 60–75% in Hong Kong Chinese and Japanese patients [44]. BCC rarely metastasizes or is fatal, but it may cause disfigurement which can result in physical or emotional distress.

In dark-skinned Africans, SCC often presents on lower extremities (Fig. 17.3b). Marjolin ulcers, an aggressive, ulcerating type of SCC that evolves in previously traumatized or chronically inflamed areas such as burn injuries, chronic venous ulcers, or chronic illnesses like lupus erythematosus, scleroderma, and leprosy, comprise 20–40% of SCC in people with a black skin. Marjolin ulcer has 30% metastasis rate as compared to a 2–4% rate seen in the SCC caused by UV solar radiation that is commonly seen in Caucasians [31].

### 17.4.4 Management

The majority of keratinocyte cancers are treated with local surgery. In case of a superficial BCC, other modalities may be topical therapy with fluorouracil or imiquimod cream or photodynamic therapy.

## 17.5 Primary Cutaneous Lymphomas

### 17.5.1 Definition and Etiology

Primary cutaneous lymphomasare an uncommon heterogeneous group of extranodular non-Hodgkin lymphomas characterized by clonal expansion of malignant T-(65% of cases) or B-cells (25%) within the skin, with no evidence of extracutaneous diseases at the time of diagnosis [45]. The diagnosis and classification of cutaneous lymphomas are based on clinical, histopathological, molecular, and immunophenotypic criteria.

### 17.5.2 Epidemiology

Little is known on the prevalence of primary cutaneous lymphomas in low- and middle-income countries, let alone among immigrant populations. Only few reports have been published suggesting that the condition is either infrequent or underreported [46, 47]. Mycosis

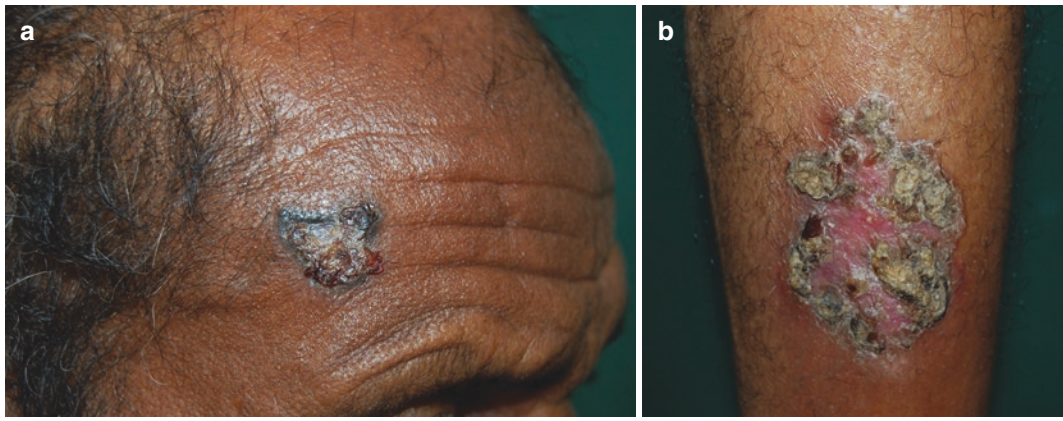


**Fig. 17.3** (**a**) Pigmented basal cell carcinoma on the forehead and (**b**) squamous cell carcinoma on the lower leg. (Courtesy of Dr. Workalemahu Alemu, Department of Dermatovenereology, Ayder Referral Hospital, Mekelle, Ethiopia)

fungoides is the most common subtype of primary cutaneous T-cell lymphomas and is thought to be more common and aggressive in African-Americans with higher mortality rates. In contrast, in Asians and Hispanic Whites, it is less common [3].

In immigrants, however, adult T-cell leukemia lymphoma (ATLL) may be of concern. ATLL is an aggressive lymphoproliferative malignancy of CD4+ cells in which the provirus of human T-cell lymphotropic virus type 1 (HTLV-1) has integrated [48]. HTLV-1 is a retrovirus transmitted by breastfeeding, sexual intercourse, blood transfusion, or needle sharing which are endemic in southern Japan, Africa, the Caribbean, and parts of South America. If acquired early in life, a minority of HTLV-1 seropositive people may develop ATLL [49, 50]. Based on this association, clinicians must be aware that immigrants from HTLV-1 endemic countries may present with ATLL.

### 17.5.3 Clinical Features

MF is characterized by an indolent clinical course and initially presents with nonspecific skin lesions that subsequently develop into the more typical erythematous patches or infiltrated plaques and tumours, which may progress to more advance stages with blood, lymph node and/or visceral involvement. Repeated skin biopsies are often necessary to confirm the diagnosis. In the darker skin complexion, MF typically presents as a hypo- or hyperpigmented variant with ill-defined, pruritic patches, plaques, and/or tumours which are distributed more centrally than acrally (Fig. 17.4). Folliculotropic mycosis fungoides (FMF) is an uncommon, yet severe subtype of MF characterized by the presence of folliculotropic infiltrates. It accounts for <10% of MF cases and preferentially involves the head, neck and upper trunk regions.

### 17.5.4 Management

The treatment of early-stage MF involves topical corticosteroids, phototherapy, topical chemotherapy or radiotherapy, whereas advanced-stage MF requires more aggressive therapies. FMF is known to be more refractory to standard treatment, and usually has a poor survival.

## 17.6 Conclusion

Malignant cutaneous neoplasms are less prevalent in people of color than in white populations but are associated with a higher morbidity and mortality owing to lack of knowledge and awareness among patients and healthcare workers and less accessibility to high-quality medical care. Apart from a few studies from the United States and Europe, little is known concerning the epidemiology of skin cancer in migrant populations. The available data are mostly from their countries of origin, enabling us to develop a general understanding on some specific characteristics of skin neoplasms in these populations. Given that migrant populations are growing on a global scale, it is of increasing importance that general practitioners and hospital specialists enhance their knowledge and understanding of the prevalence, distribution, and clinical presentation of cutaneous neoplasms in people with a pigmented skin. At the same time, education and screening programs are needed targeting uninsured, minority, immigrant populations to promote skin self-examination and stress the importance of proper UV -protection while taking into account the different cultural backgrounds.

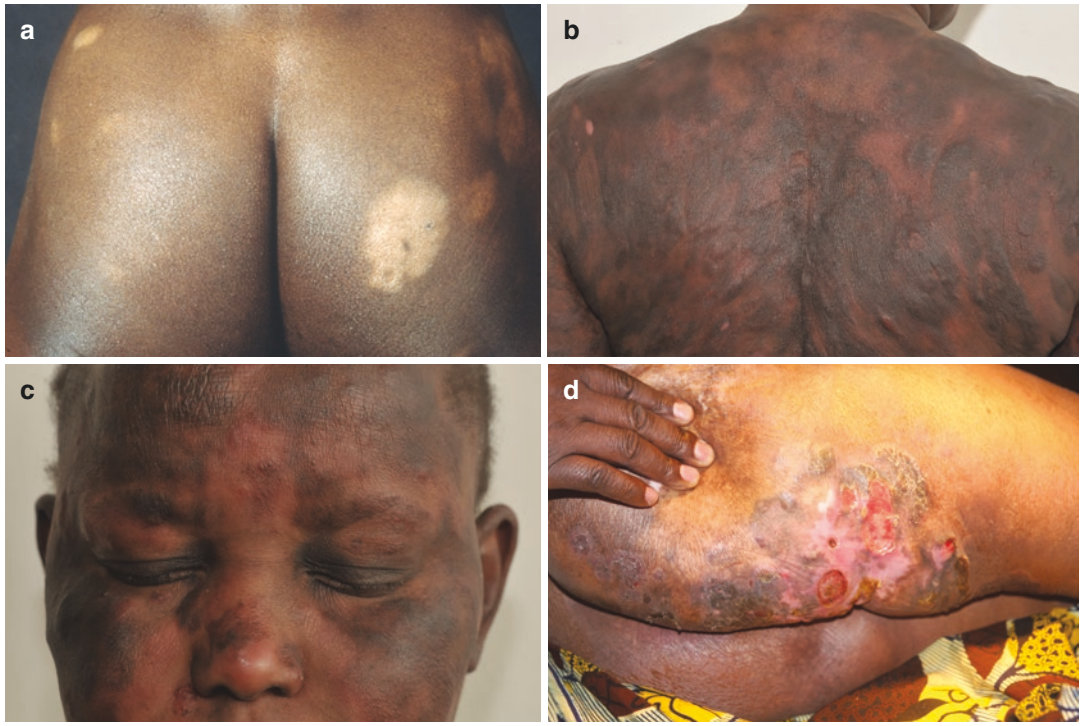


**Fig. 17.4** Primary cutaneous T-cell lymphomas: (**a**) hypopigmented lesions on the buttocks, histopathology supportive of mycosis fungoides (MF) (Courtesy of Leiden University Medical Center); (**b**, **c**) infiltrated, hyperpigmented plaques and tumors on the trunk, extremities, and face with hair loss on the scalp and lateral eyebrows. Histopathology was consistent with folliculotropic MF; (**d**) ulcerative tumor on right buttocks, histopathology compatible with tumor stage MF. (**b-d** Courtesy of Regional Dermatology Training Centre (RDTC), Moshi, Tanzania)

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# 18 Sexually Transmitted Infections and Migration

Ismael Maatouk, Antonio Cristaudo, and Aldo Morrone

## 18.1 Definitions and Scope of the Problem

According to the United Nations definition, "any person who lives temporarily or permanently in a country where he/she was not born and has acquired significant social ties to this country" is called an "international migrant" [1].

There are many categories of "migrants": regular migrants, students, migrant workers, refugees, asylum seekers, trafficked migrants, temporary migrants, and internally displaced [2].

There are four phases of migration that are defined by locations: the *pre-departure* (place of origin), the *travel* with *interception(s)* sometimes (place of transfer), the *destination* (place of destination), and the *return* (to the place of origin) [1, 2].

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According to the United Nations data, the global number of migrants increased over years [3]:

- 1980: 82 million
- 2000: 175 million
- 2015: 248 million
- 2017: 258 million

Most migrants persistently travel from developing countries to developed countries [3].

An STD (sexually transmitted disease or infection) is a disease that can occur following an unprotected sexual intercourse [4]. Globally, they are among the most common acute conditions. They can lead to severe complications and long-term sequelae, including pelvic inflammatory disease, ectopic pregnancy, infertility, chronic pelvic pain, and neurological and cardiovascular disease in adults; neonatal death, premature delivery, blindness, or severe disability in infants; and increased risk of HIV acquisition and transmission [4].

Theoretically but not universally, the word "STD" includes both HIV and non-HIV infections. In this chapter, STD will be used in that theoretical meaning.

Migration has been associated with the spread of diseases, particularly infections. This is how small pox was imported to the New World in the fifteenth century and to Australia both in 1780 and 1870 [5]. This is how syphilis devastated Europe in the fifteenth century [6]. And the list goes beyond these two infections.



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The spread of an infectious disease depends on the rate of contact between susceptible and infectious subjects. That is how migration can concur to this mechanism [7].

This model partially applies to sexually transmitted diseases (STD). Why partially? Because unlike other infections, STD varies with another major factor: sexual behavior [8].

## 18.2 Mechanisms of Correlation Between Migration and STD

The relationship between migration and STD can be schematically and childishly understood as a linear relation between "migrants" who come to a populated land and "bring" their diseases with them. However, many factors correlate to create a more complex actuality [9]:

- Migrants' socio-demographic characteristics and culture and beliefs that are usually acquired at the *pre-departure* country
- Risk from the place they migrate from that are acquired at the *pre-departure* country
- Risk and risk environment acquired at the *destination* country
- Access to care at the *destination* country
- Continued contact with the place they migrate from, which creates a *bridging effect* between the *pre-departure* and the *destination*
- Different health services in the *pre-departure* and the *destination* which creates a *bridging effect* too

Thus, the mechanisms of the correlation between the two facts belong to three locations:

- *The pre-departure effect:* including migrants' socio-demographic characteristics and culture and beliefs along with the risk from the place they migrate from
- *The destination effect:* including risk and risk environment along with the access to care at destination
- *The bridging effect:* including continued contact with the place they migrate from along with the different health services in host country and country of origin

### 18.2.1 The Pre-departure Effect

The pre-departure effect is defined by socio-demographic characteristics and culture and beliefs and risks of the migrants. They are all "acquired" before his travel. This is the oldest and the classical mechanism reported in the literature. Through HIV/AIDS first era, this mechanism has been examined in many different contexts around the world [10].

Within the last two decades, researchers have cited increasing rates of mobility as one of the most important factors leading to the rapid diffusion of HIV. The very early papers focusing on migration and HIV clearly showed a spread of HIV from urban to rural areas, with particularly in Sub-Saharan Africa a role of truck drivers [11–13] initially reported, followed by another major group: commercial sex workers [14–21].

It is generally understood that the spread of infectious diseases has been historically always associated with population movements at varying scales. Almost by definition, migration brings more people into close contact and creates a greater mixing of people at the places of destination, both of which work to provide a ready milieu for STD transmission. Migrants bring new diseases to existing residents at the place of destination. But this relationship can be reciprocal too: migrants subject themselves to the diseases that may be endemic in some locations.

Thus, migration determines the spatial distribution of an STD and the rate of its transmission in a specific location.

### 18.2.2 The Destination Effect

The destination effect is defined by risk and risk environment and access to care after reaching a "new" destination.

Besides the numerous empirical researches that documented the role migration plays in the

spread of HIV/AIDS and other STDs, theoretical work attempting to understand the social/behavioral mechanisms underlying HIV risk-taking behaviors among migrant groups has proven how complex the picture becomes. At the individual level, the transmission of HIV requires more specific and intimate personal contacts than is the case for many infectious diseases. HIV can only spread when there is intimate human contact (involving either sexual activity or needle sharing), so a first step in understanding of the impact of migration on the AIDS epidemic must be to identify and understand the underlying mechanisms by which the process of migration may lead to behavioral changes that make migrants more susceptible to particular HIV risk-taking behaviors [22]. Through these mechanisms of HIV transmission, STD transmission can be understood. This is the reason behind all new studies of sexual behavior in countries receiving new migrants and the comparison between the behavioral differences in hosting and migrants' groups.

### 18.2.3 Pre-departure and Destination Bridging's Effect

Bridging in context of migration is defined by continued contact with the place subjects migrate from and different health services in host country and country of origin.

Through the movement of infected persons, migration also provides a vehicle to spread viruses even further afield, to places where they were previously unknown, including the homes of the migrants themselves. Obviously, this sequence of events is more likely to be enacted under situations of temporary and circular migration activities, in which people move backward and forward between two or more regions.

Mobile individuals have the potential to bridge sexual networks and thus provide bidirectional paths for infectious disease transmission if they engage in concurrent sexual partnerships with partners in different places. Concurrent sexual partnerships are defined as overlapping sexual partnerships where sexual intercourse with one partner occurs between two acts of intercourse with another partner [23, 24]. Bridging can also occur when sexual acts with partners in a concurrent triad occur in different places or sexual partners in a concurrent triad live in different places. Therefore, if mobile individuals engage in high-risk concurrent partnerships, then the locations of the individuals in the concurrency triads will identify where the bridging occurs.

Since needle sharing among injecting drug users and unprotected sexual intercourse with multiple partners are the most common mechanisms of HIV transmission globally, it is not surprising that sexual networks and social relationships among injecting drug and the people who are workers and clients in the sex trades have been identified as key activities by researchers interested in understanding the spread and transmission of HIV.

Today, we know that HIV is transmitted through sexual networks with heterogeneous spatial and socio-demographic structure. Mobile individuals that periodically change their residences between urban, rural, and peri-urban areas disconnect from the local sexual network associated with the origin of their move and are likely to connect with another local sexual network associated with their destination. Even if mobile individuals continue to maintain ties with the partners they leave behind, their sexual behavioral patterns are fundamentally different from those of less mobile individuals that travel only for shorter periods of time and over shorter distances because of uprooting, losing social ties, and needing to find new social networks. Furthermore, they experience a higher likelihood of becoming a victim of violence, including sexual violence.

This behavior change is not only due to migration but to the situations people find themselves in once they have migrated like poor living and work conditions, poor access to healthcare services, and social problems. And within these unfavorable conditions, transactional sex, sex for survival, rape, and non-professional commercial sex occur.

## 18.3 Examples of Disproportionally Affected Migrants

### 18.3.1 MSM Migrants

Men who have sex with men (MSM) are a key population for HIV worldwide, contributing 42% of estimated new HIV cases in Europe in 2013 and 40% in 2016 [25, 26]. In addition, 40% of new HIV infections in Europe in 2016 were reported among MSM [26]. A recent study reports that the majority of migrants diagnosed with HIV within the last 5 years, living in Spain, the UK, Belgium, Portugal, Greece, Switzerland, the Netherlands, Italy, and Germany, probably acquired the disease in their current country of residence rather than their birth country [27]. Migrants in Europe also have a higher risk of late diagnosis of HIV than non-migrants, and this risk is due to many barriers to HIV testing [28]. This is a clear example of the pre-destination and post-destination mechanisms mentioned above.

Barriers to HIV testing among migrant MSM in the UK are reported to include fear of HIV, fear of legal consequences if living with HIV, stigma and discrimination, lack of culturally sensitive and competent services, language difficulties, lack of knowledge of health services, and low priority given to HIV [29].

Moreover, a study from San Francisco showed that MSM migrants living in San Francisco for more than 5 years have the higher post-migration HIV acquisition risk [30]. Factors associated with post-migration HIV acquisition among MSM were age at migration, length of stay in host country, and HIV diagnosis year [30]. This of course has important implications for public health policies.

### 18.3.2 Syrian Refugees

The Syrian conflict has created the worst humanitarian crisis of our time. Half the country's pre-war population—more than 11 million people—have been killed or forced to flee their homes.

According to the United Nations High Commissioner for Refugees (UNHCR), as of 2016, there were 6.5 million internally displaced persons (IDPs) and 1.3 million people hosting IDPs [25]. Additionally, neighboring countries have taken in 4.7 million Syrian refugees. In the region, 2.7 million refugees are in Turkey (as of 3 March 2016); 1.07 million in Lebanon (as of 31 January 2016); 639,704 in Jordan (as of 3 March 2016); 246,051 in Iraq (as of 29 February 2016); and 118,512 in Egypt (as of 31 January 2016). More than 1 million refugees and migrants arrived in Europe in 2015, and nearly 390,000 more in 2016, many fleeing conflict in the Middle East and North Africa [25].

It is too early to have published data about STD in Syrian migrants especially that this health issue is less prioritized compared to other more severe like polio and mental health. However, some reports are available.

Among 157 eligible female married Syrian refugees living outside of the camps in Sanliurfa City Center in Turkey, the prevalence of *Trichomonas vaginalis* in women aged between 15 and 49 years with complaints of vaginitis was 36% (mean age: 31.6 ± 8.7 years) [31]. This prevalence was higher in the female Syrian refugees compared to the hosting population (3–13%) but close to the prevalence (40%) in groups with risky behaviors (sex workers).

Another report from Germany, the largest single recipient of new asylum seekers in Europe, analyzed the rate of certain infectious diseases among asylum seekers screened at a reception center in Southern Germany [32]. Among 2602 subjects screened by a local public health authority in 2015, whose majority came from Afghanistan and Syria, 75.4% were male. A total of 78 (3.9%) individuals were infected with hepatitis B and 8 (0.4%) with HIV; 44 (1.7%) cases had scabies, and 9 (0.3%) cases had lice. No evidence was found that the overall prevalence of these infectious diseases was considerably higher than in previous migration studies.

From Italy, a report on 48 Syrian migrants who upon their arrival in Italy were accommodated at the asylum seekers center of Castelnuovo

di Porto could not document any case of HBV, HCV, or HIV infections [33].

Another report from Italy based on a cross-sectional retrospective study in a large asylum seekers center had larger number of participants [34]. Over 792 subjects (80% males, 58% from Africa), 43% underwent voluntary infectious disease screening. One patient had a positive VDRL, and 11 were HIV-infected (3.5%), all from Africa. Eleven were HCV-Ab-positives (3.4%), five from Africa (1.5%) and six from Asia (1.9%). Concerning HBV infection, 33 subjects (9.9%) were infected. Among all tested groups, West Africans showed the highest HBV prevalence (15.5%; $n = 18/116$).

Thus, the available reports lack of representability and show all the difficulties in methodologies when it comes to assessing STD in migrants. Camps are usually easier to analyze because of the concentration of the migrants with similar origins. However, in Europe, asylum seekers are difficult to analyze: they have different origins, different years of migration, different ages, and socio-demographic. These difficult methods are highly responsible for the different rates of STD in different reports. That's why, studies about "Syrian" refugees are difficult to find and to perform, especially that recent years have shown large migration movements from many countries such as Iraq, Syria, Afghanistan, and Yemen, rather than one country. However, studies years after migrants' movements should be prompted in the future to check the accuracy of the theory of the "high post-migration HIV diagnoses".

## 18.4 Global Results of STD Issues in Migration Settings

STDs are global health problems. They are multifactorial, and there are multiple sides to analyze them. Key populations by definition are heterogeneous: some of them seek sex for work; some other groups seek sex for pleasure. With the globalization, and the easiness of dating based on the multiple internet-based dating applications over cell phone, and based on other factors like frequent travels and less cultural taboo, STD has seen some emerging aspects since the 2000s. Migration under its many aspects is one added factor of emergence of STD.

Some areas of the world have seen outbreaks of pathogens through sexual route, especially among key populations (re-emergence of lymphogranuloma venereum and syphilis, outbreak of hepatitis A in 2017) [35].

Moreover, change in the molecular epidemiology of *Chlamydia trachomatis* strains was involved in an outbreak of anorectal LGV in Europe [36]. Until 2012, the L2b strain predominated, a finding that is in agreement with reports coming from other countries in Europe. Different LGV strains have spread widely in the MSM community since 2013, and prevalence of the L2 genotype has increased [37, 38].

Some other "new" STD has shown in many areas of the world: newly described role of sexual route in Zika transmission, *Neisseria meningitidis* urethritis [39, 40].

One of the major global health issues is antimicrobial resistance (AMR) in *Neisseria gonorrhea* and other organisms like *Mycoplasma genitalium*. According to the World Health Organization (WHO), gonococcal infections represent 106 million of the estimated 498 million new cases of curable STD that occur globally every year [41]. The emergence in *gonorrhea* of decreased susceptibility and resistance to the "last-line" cephalosporins, together with the longstanding high prevalence of resistance to penicillins, sulfonamides, tetracyclines, and, more recently, quinolones and macrolides (including azithromycin), is a cause for concern [41]. The combination of high sexual network connectivity and excess antibiotic usage has selected for the emergence of AMR [42, 43].

Gonorrhea has the potential to become untreatable in the current reality of limited treatment options, particularly in settings that also have a high burden of gonococcal infections. That's why the WHO has implemented a global action plan to control the spread and minimize the impact of AMR in gonorrhea [44]. The vision informing this global action plan is to enhance the global response to the prevention, diagnosis, and control of *Neisseria* gonorrhea infection, and mitigate

the health impact of AMR, through enhanced, sustained, evidence-based, and collaborative multi-sectoral action.

Concerning HIV, antiretroviral therapy is not available to all immigrants. A report from Europe clearly states that "more than 50% of European Union countries do not provide antiretroviral therapy to irregular migrants" [45]. This is a major gap in the HIV management.

## 18.5 Interventions to Reduce Influence of Migration on STD

Following the European experience in migrant health and according to a report about sexual transmission of HIV within migrant groups in the European Union, effective interventions should include [46]:

- Identifying the scope of the problem: migrants are an important part of the national HIV/STD epidemic.
- Reviewing prevention policies and programs targeted toward migrant populations. This step can be achieved by exploring and understanding pre- and post-migration patterns of sexual transmission, as well as sexual attitudes and lifestyles. It also includes new policies around combined prevention (medical, behavioral, and structural prevention strategies).
- Considering which surveillance variables should be collected and analyzed in order to better understand the degree to which sexual transmission of HIV/STD occurs among migrant populations. This intervention can be achieved by collecting variables such as "CD4 cell count," "date or year of arrival," and "country of birth." Wider implementation of these variables could allow countries to estimate probable country of infection and to better direct prevention policies. In some settings, sentinel surveillance or repeat cross-sectional surveys could play an important role in providing this necessary evidence.
- Developing an evidence-based, long-term strategic policy to reduce post-migration HIV-acquisition and transmission. This policy would ideally include a focus on increasing resources for research that aims to explore and understand post-migration patterns of sexual transmission, as well as sexual knowledge, attitudes, and behaviors. Additionally, targeted primary prevention programs delivered at sufficient scale should be considered.
- Involving migrant communities in developing and delivering migrant-sensitive HIV prevention services, with a special focus on migrant MSM.
- Improving access to HIV treatment for all infected persons, regardless of immigration status, which could positively impact on reducing incident infections both within and beyond migrant communities. This would necessitate addressing the barriers to HIV prevention, testing, and care that have already been identified for migrant communities. Failure to ensure access to HIV treatment for all persons in need could prove detrimental to efforts to ameliorate the HIV epidemic.

Many interventions can be discussed according to the geographical and social conditions. A golden rule does not exist; and if it applies for a European country, it might not be suitable for another one in Africa or in the Middle East.

## 18.6 Conclusions

Migration does not only act as a transporter of STD (*pre-departure effect)*; it sets the stage for broader social and behavioral changes that are thought to render migrant workers particularly vulnerable to behaviors that put them at risk—which in turn makes them more susceptible to STD. In the context of sexual activity and drug abuse, the decision among migrants to engage in risk-taking behaviors might be influenced by a number of activities, including their individual characteristics associated with pre-migration selectivity, their separation from a spouse or regular sexual partner, and their post-migration exposure to a new social, economic, and cultural environment in the place of destination [47]. In a

number of separate studies, migrants have been identified as a sub-population whose members are more likely than the average to engage in socially "deviant" and epidemiologically "risky" behaviors [45, 48–50].

This chapter aimed to describe how migration can influence the spread of STD, in general and in some key populations, and to analyze the results of such an increase globally. Although some key interventions were introduced at the end of the chapter, based on European experience, the overall image is much more complex. Analyzing this topic is based on available methodologies used to have data. Thus, literature depends on what human mind has decided to be a "valuable" data and a "correct" method.

However, many questions are still arising about other multiple factors that mediate the relationship between migration and STD.

First, what is the sociological burden and who is driving this burden? Social context is continuously changing. Data collected in 2015 might not be accurate in 2016 in the same society. On the other hand, data collected in Europe is different within European countries and with other parts of the world. In context of labor work, many problems were raised in Europe concerning the competitive labor work due to migration. What are the consequences of such problems on the long term in terms of funding STD diagnostic and therapeutic management? Which "part" of a population usually migrates? What "kind" of migrants does each government need? Students or workers? Is there a "function" for these migrants? Aren't these questions biasing available data?

Second, what is the economic burden of both the migration and the STD spread globally and who is paying this burden? Available answers to this question have not been analyzed yet. United Nations agencies, governments, and nongovernmental organizations depend on funds to respond to this burden. Who is driving this fund? What is the role of the pharmaceutical companies in all this burden?

Last but not the least, how will all these different actors (societies, governments, political persons, religious institutions, hospitals, pharmaceutical companies) and the unknown (yet) actors intervene to shape STD burden globally?

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# 19 Rare Diseases Including NTDs and Their Management

Bernard Naafs, Roderick Hay, and Aldo Morrone

## 19.1 Introduction

There are more than 6500 identified rare and neglected diseases [1]. Clinicians often know little about the symptoms and biology of these conditions. Most rare diseases are genetic and thus are present throughout the person's entire life, even if symptoms do not immediately appear. Many rare diseases show early in life, and about 30% of children with rare diseases will die before reaching their fifth birthday [2]. However, a disease may be considered rare in one part of the world, or in a particular group of people, but still be common in another. There is no single, widely accepted definition for rare diseases. The European Commission on Public Health defines rare diseases as "life-threatening or chronically debilitating diseases which are of such low prevalence that special combined efforts are needed to address them." The term low prevalence is later defined as generally meaning fewer than 1 in 2000 people. Diseases that are statistically rare, but not also life-threatening, chronically debilitating, or inadequately treated, are excluded from their definition.

Rare diseases are seen among migrants, but are generally not diagnosed. It is important that these diseases, such as inherited bullous diseases (see Chap. 12), ichthyotic conditions, and skin diseases with mycobacterial or deep fungal infections (see Chap. 6), when recognized are referred to experts. If there is no possibility of referral, the symptoms should be treated where appropriate, but recorded as well, because treatment may change the presentation.

However, a group that should be recognized and diagnosed are the neglected tropical diseases (NTDs), in particular because they are usually treatable and in the countries of origin of the migrants they are often not rare. NTDs consist of a diverse group of communicable diseases that prevail in tropical and subtropical conditions in about 150 countries and affect more than one billion people [3]. Populations living in poverty, without adequate sanitation, and in close contact with infectious vectors and domestic animals and livestock are those worst affected even in temperate climates, and they are potentially prevalent among migrants [3].

In 2017 the 10th meeting of the Strategic and Technical Advisory Group for Neglected Tropical Diseases declared 20 infectious NTDs

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as such registered. They are responsible for more than one and half billion affected people (including more than 500 million children) and costing the developing economies billions of dollars. Chromoblastomycosis and other deep mycoses, scabies, and other ectoparasites and snakebite envenoming were added to the list in 2017 [3]. At least half of the NTDs are diagnosed by their skin symptoms. These include Buruli ulcer, dracunculiasis, endemic treponematoses (yaws), leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis, chromoblastomycosis, and other deep mycoses, scabies, and snakebite envenoming. Most of these are included in other chapters. This chapter will cover infections due to mycobacteria: tuberculosis, leprosy, Buruli ulcer, and non-tuberculoid mycobacteria (NTM).

## 19.2 How Are Mycobacterial Infections Diagnosed?

The most important issue is to have a high index of suspicion. One must suspect the possibility of a mycobacterial infection and recognize granulomatous processes. Sometimes, however, there is only crusting, ulceration, or erythema; this is often chronic. These are "infectious" processes not reacting to normal antibiotic therapy and immunosuppression. Differential diagnoses are mycotic and leishmania infections.

## 19.3 Tuberculosis

### 19.3.1 Introduction

Tuberculosis [4] (TB) is an infectious disease caused by bacteria from the *Mycobacterium tuberculosis* complex, which are acid-fast using the Ziehl-Neelsen stain. Scrofuloderma and lupus vulgaris are the oldest forms of cutaneous tuberculosis described in the medical literature. The range of clinical manifestations of cutaneous tuberculosis provides an example of the varying immune response of the host toward infection with mycobacteria, which is also dependent on genetic susceptibility, previous exposure to other mycobacteria, and the route of infection. *M. tuberculosis*, *M. bovis*, and M. Bacille Calmette-Guérin may cause "tuberculosis" involving the skin. Cutaneous tuberculosis can be acquired exogenously or endogenously and present as a multitude of differing clinical morphologies. Cutaneous tuberculosis has become a rare disease in the western hemisphere (Table 19.1). The majority of cutaneous tuberculosis cases will be diagnosed in immigrants. However, what seems to be tuberculosis may be a NTM [5].

### 19.3.2 Clinical Features

#### 19.3.2.1 Exogenous Cutaneous Tuberculosis: Tuberculous Chancre [4]

The lesion starts 2–4 weeks after inoculation, with a smooth papule or nodule which enlarges in the course of several weeks to a plaque which subsequently ulcerates. The ulcer has undermined edges and is painless (Fig. 19.1). Non-tender lymphadenopathy may ensue producing a clinical picture of a lymphocutaneous complex. This process generally heals spontaneously with atrophic scarring in 3–12 months. Differential diagnosis includes other causes of ulceration, other mycobacteria (e.g., Buruli, NTM), and other chronic conditions like subcutaneous mycoses, cutaneous leishmaniasis, and malignancies. It includes also infections which show sporotrichoid spread, such as sporotrichosis, cat scratch disease, and tularaemia.

#### 19.3.2.2 Exogenous Cutaneous Tuberculosis: Tuberculosis Verrucosa Cutis

It is also known as Warty tuberculosis [4], the most common type of skin tuberculosis in the East, particularly in India [6]. Due to a rapid cell-mediated response, the infection remains localized. Regional lymphadenopathy is not prominent. The lesion develops from an asymptomatic reddish-brown papule into a verrucous plaque of varying shapes and sizes. The verrucous fissures may become superinfected (Fig. 19.2). The plaque may heal spontaneously

**Table 19.1** Cutaneous tuberculosis classification

| Type | Subtypes | | | | Diffusion by |
|---|---|---|---|---|---|
| Exogenous | Tuberculous chancre | Tuberculosis verrucosa cutis | | | – |
| Endogenous | Scrofuloderma | Orificial tuberculosis | Lupus vulgaris | | Contiguity/ autoinoculation |
| | Tuberculous gumma | Acute miliary tuberculosis | Lupus vulgaris | | Blood |
| Immunological reaction to *M. tuberculosis* | Papulonecrotic tuberculid | Lichen scrofulosorum | Nodular vasculitis | Erythema nodosum | – |
| Post-BCG vaccine | | | | | – |

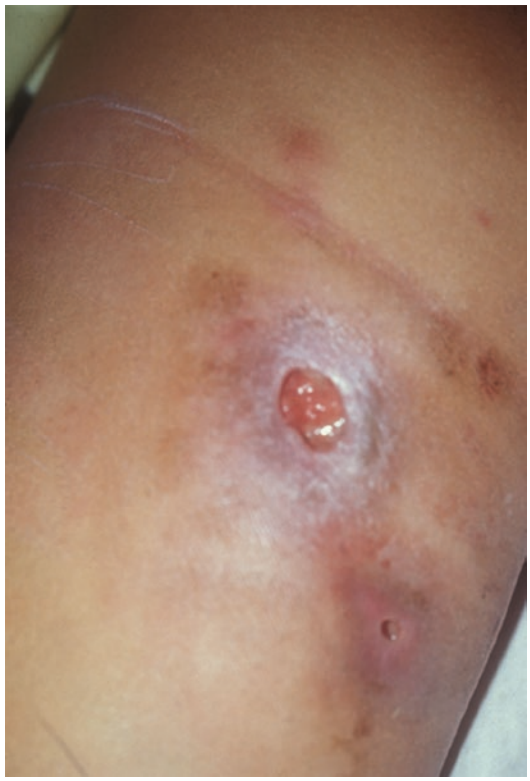

**Fig. 19.1** Tuberculosis chancre

in the course of months to years, with atrophic scarring and activity in different parts of the same lesion [7]. An identical lesion may be seen among cattle workers. Here the species involved is most commonly *M. bovis*. Differential diagnosis includes common warts during the initial stage, hypertrophic lichen planus, and verrucous lesions caused by NTM or by deep mycoses like blastomycosis, sporotrichosis, chromoblastomycosis, lobomycosis, some forms of leishmaniasis, verrucous tertiary syphilis, rupioid psoriasis, and squamous cell carcinoma.

#### 19.3.2.3 Endogenous Cutaneous Tuberculosis: Lupus Vulgaris

Lupus vulgaris [4] was a common disease in the early twentieth century. Today it is rare in Western Europe and North America, and it also occurs less frequently in the developing countries. It is due to reactivation of a mycobacterial infection in patients with a moderate to high degree of CMI, hence paucibacillary "tuberculosis." Reactivation usually stems from cervical adenitis or pulmonary tuberculosis but sometimes from an old, apparently quiescent primary complex. Rarely, it follows primary inoculation or BCG vaccination. Lupus vulgaris lesions have been described around warty tuberculosis, papulonecrotic tuberculid, and scrofuloderma.

Classic lesions start as brown-red papules which extend to plaques with active, irregular borders and central healing with atrophic, depigmented scarring. Spontaneous involution may occur and new lesions may arise within old scars (Fig. 19.3). Complete healing rarely occurs without treatment. Squamous cell carcinoma may develop in these chronic lupus vulgaris lesions. Differential diagnosis includes lupoid and recidivans variants of cutaneous leishmaniasis, subcutaneous mycoses, sarcoidosis, chronic discoid lupus erythematosus, and basal cell carcinoma.

#### 19.3.2.4 Endogenous Cutaneous Tuberculosis: Scrofuloderma

Scrofuloderma [4] or tuberculosis cutis colliquativa is the result of contiguous spread from an

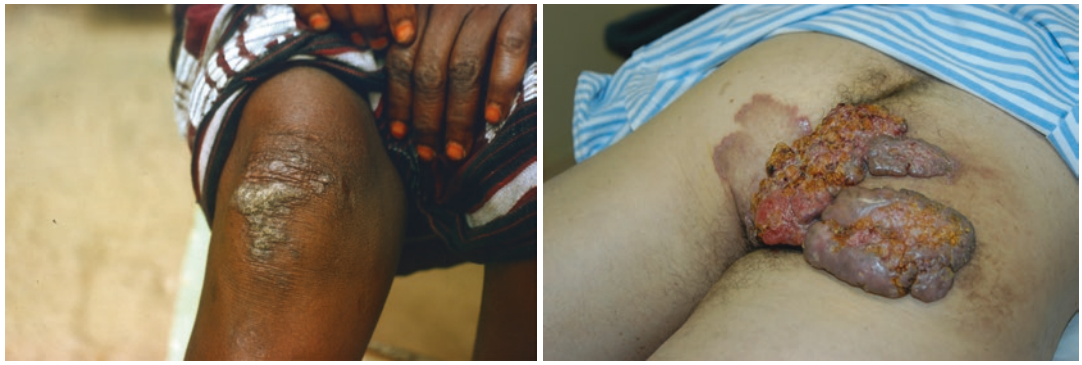

**Fig. 19.2** Tuberculosis verrucosa

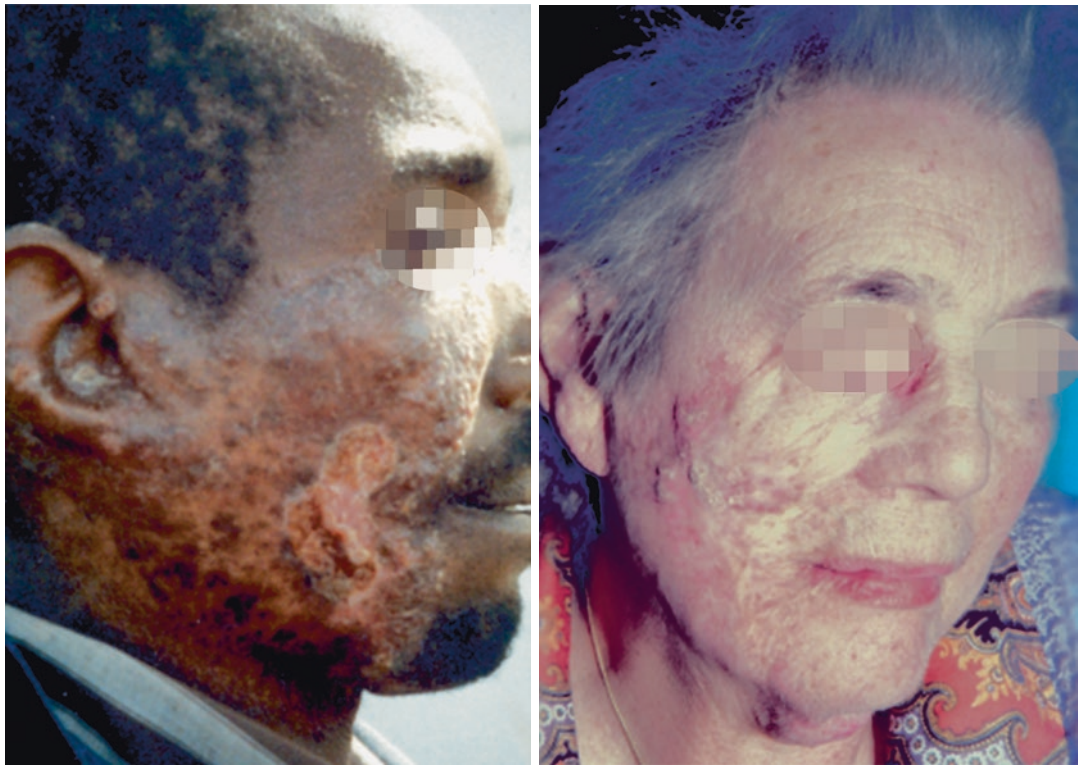

**Fig. 19.3** Lupus vulgaris

underlying mycobacterial infection, commonly in the lymph nodes or in some cases the bone. It is the most common cause of cervical lymphadenitis in children. Due to suppuration fluctuating nodules develop, which ulcerate. In the course of time, cordlike scars develop. The lesions heal over years with a characteristic pattern of fibrosis, atrophy, and scarring. Recurrence of drainage is common (Fig. 19.4). Today other mycobacteria, NTM, more often cause scrofuloderma such as *M. chelonae*, *M. scrofulaceum*, *M. haemophilum*, and *M. avium.* Differential diagnosis includes deep mycoses, such as sporotrichosis or coccidioidomycosis, but also actinomycosis, hidradenitis suppurativa (in axillary lesions), granuloma inguinale and lymphogranuloma venereum (in inguinal lesions), and chronic bacterial osteomyelitis (when localized over the bone).

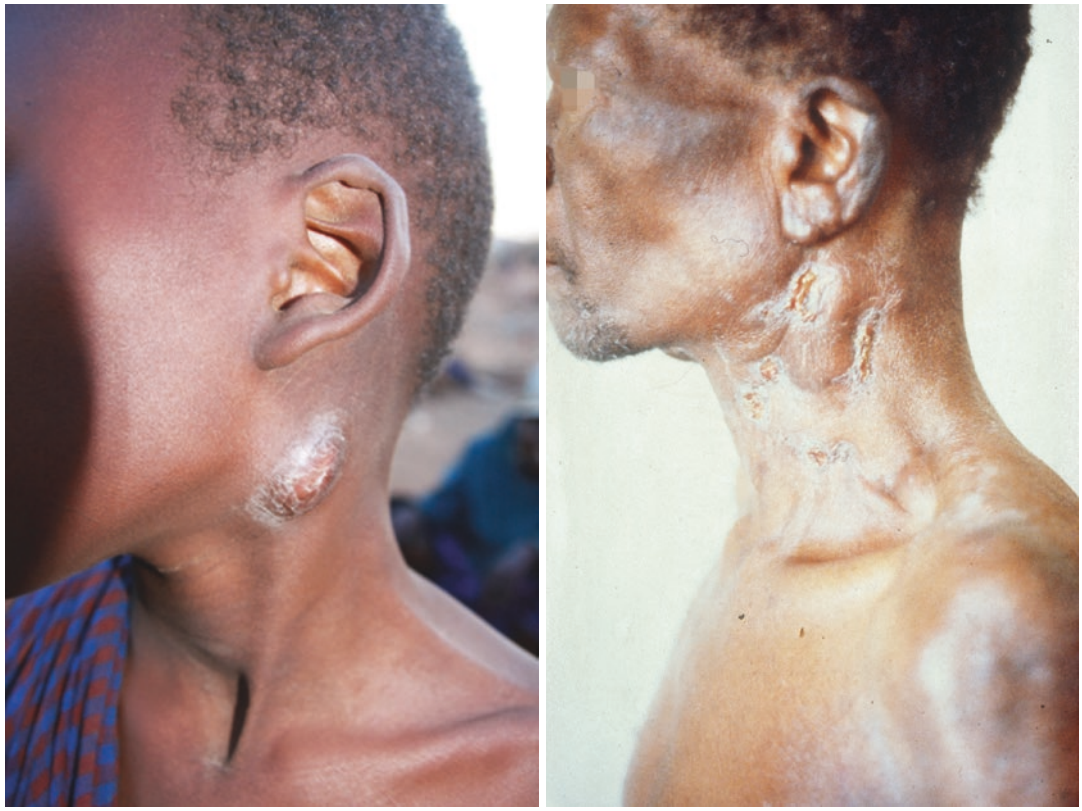

**Fig. 19.4** Scrofuloderma

#### 19.3.2.5 Endogenous Cutaneous Tuberculosis: Orificial Tuberculosis

It is also known as ulcerative tuberculosis of the mucosa [4]. This rare form of cutaneous TB starts with single or multiple nodules which become fluctuant and ulcerate showing draining sinuses. The cause is autoinoculation from active tuberculous foci affecting the mucosa or skin near the oral, genital, or anal orifices (Fig. 19.5). Pain is a cardinal feature [8]. It mainly affects middle-aged adults and seniors who present advanced form of lung, intestinal, or genitourinary tuberculosis or a severely impaired cellular immunity. The affected patient is usually in poor health with long-standing advanced tuberculosis involving multiple internal organs. Differential diagnosis includes leishmaniasis, aphthous ulcers, dental and perianal abscesses, M. Crohn, paracoccidioidomycosis, malignancies, herpes simplex lesions, or ulcerating venereal disease. Painful anal ulcerations may also be seen in cutaneous amebiasis.

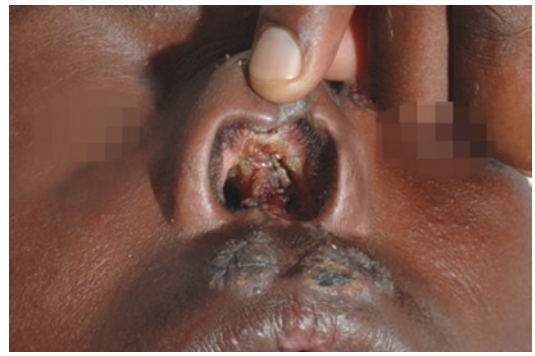

**Fig. 19.5** Orificial tuberculosis

#### 19.3.2.6 Endogenous Cutaneous Tuberculosis: Tuberculous Gumma

The gumma [4], or metastatic tuberculous ulcer, is due to hematogenous dissemination from a primary focus, during periods of decreased immunity. A subcutaneous nodule or fluctuant swelling results in an undermined ulcer with sinus formation, also known as a "metastatic tuberculous

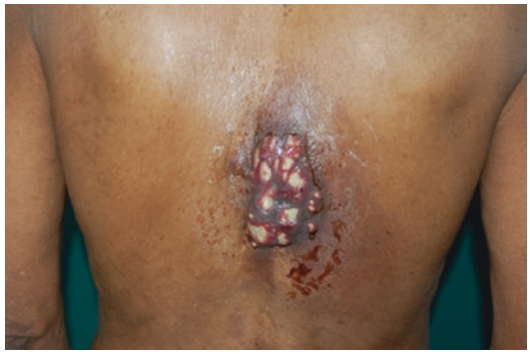

**Fig. 19.6** Gumma

abscess" or "metastatic tuberculous ulcer" which may resemble scrofuloderma (Fig. 19.6). It is histologically characterized by massive necrosis [9]. Some of these patients may have an underlying malignancy (lymphoma). Differential diagnosis includes cold abscess, scrofuloderma, tertiary syphilitic gumma, subcutaneous mycoses, and cutaneous leishmaniasis.

#### 19.3.2.7 Endogenous Cutaneous Tuberculosis: Acute Miliary Tuberculosis

Miliary tuberculosis [4], or tuberculosis cutis miliaris disseminata, is the result of hematogenous dissemination of *M. tuberculosis* to the skin and other organs in the absence of a CMI reactivity. It shows a generalized eruption of small purplish macules and papules (1–5 mm), with vesicles on top which may break, forming crusts. Due to the absence of CMI reactivity, the histopathological picture is that of a nonspecific inflammation with numerous acid-fast bacilli. A patient with miliary tuberculosis usually presents with nonspecific signs, such as low-grade fever, cough, and enlarged lymph nodes, and there may be an enlarged liver, enlarged spleen, inflammation of the pancreas, and multiple organ dysfunction with adrenal insufficiency. Differential diagnosisis large, but the patient is ill.

#### 19.3.2.8 Immunological Reactions to Tuberculosis: Papulonecrotic Tuberculids

Tuberculids [4] are generally considered to be the consequence of a CMI response to a dissemination of *M. tuberculosis* or antigenic particles to the skin. Papular necrotic tuberculids would represent the paucibacillary pole of blood-borne disseminated TB, as opposed to the multibacillary picture of acute miliary TB. But often *M. tuberculosis* cannot be detected in the skin or elsewhere in the body, because antigenic determinants of the host are similar to those of *M. tuberculosis* or because of the very low bacillary load.

Papulonecrotic tuberculid occurs as crops of symmetric, small, inflammatory papules which have a predilection for acral and dorsal surfaces. Lesions may undergo central ulceration and heal spontaneously within weeks, leaving varioliform scars. They may heal with treatment but may also resolve spontaneously with a depressed scar with a hyperpigmented border. The tuberculous etiology is suggested by a positive tuberculin skin test, the demonstration of *M. tuberculosis* DNA in the lesions, and prompt resolution of the condition on antituberculosis treatment. Differential diagnosis includes prurigo papules, folliculitis, and papular lesions of syphilis. Necrotic lesions should be differentiated from pityriasis lichenoides acuta, necrotizing vasculitis, necrotic insect bite reactions, and self-inflicted injury.

#### 19.3.2.9 Immunological Reactions to Tuberculosis: Lichen Scrofulosorum

Lichen scrofulosorum [4], also known as tuberculosis cutis lichenoides, is a rare tuberculid that presents as a lichenoid eruption of minute papules in children and adolescents. The lesions are usually asymptomatic, closely grouped, skin-colored to reddish-brown papules often perifollicular and are mainly found on the trunk and proximal parts of the limbs (Fig. 19.7). The eruption is associated with a strongly positive tuberculin reaction [10]. Differential diagnosis includes lichen planus, lichenoid drug eruptions, secondary syphilis, and pityriasis lichenoides chronica. Due to the perifollicular distribution, other conditions such as keratosis pilaris, lichen nitidus, lichen spinulosus, and *Malassezia* folliculitis should be evaluated. Differentiation from the micronodular form of sarcoidosis may be clinically and histopathologically difficult.

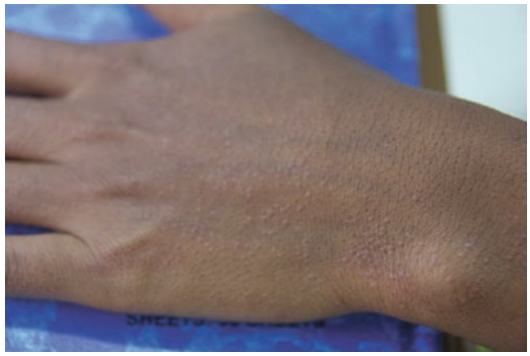

**Fig. 19.7** Lichen scrofulosorum

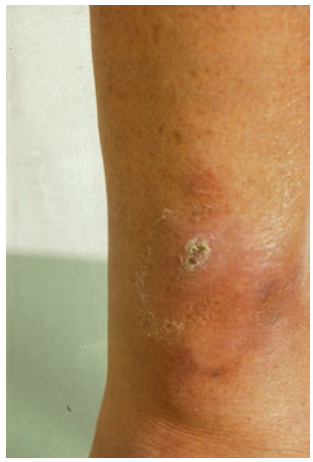

**Fig. 19.8** Nodular vasculitis (erythema induratum of Bazin)

#### 19.3.2.10 Immunological Reactions to Tuberculosis: Nodular Vasculitis

At present it is the most prevalent tuberculid [4]. It is also known as erythema induratum of Bazin, described by Bazin in 1855. It can however be induced by numerous antigenic or infective triggers including tuberculosis. Erythema induratum presents during early adolescence and perimenopause as recurrent subcutaneous poorly defined erythematous plaques and tender violaceous nodules, sometimes ulcerating, in particular on the calf of the legs of otherwise healthy, often heavy-set, women (Fig. 19.8) [11]. Differential diagnosis includes erythema nodosum, cutaneous polyarteritis nodosa, pancreatic panniculitis, lupus profundus, subcutaneous sarcoidosis, and cutaneous T-cell lymphoma.

#### 19.3.2.11 Immunological Reactions to Tuberculosis: Erythema Nodosum

Erythema nodosum [4] was frequently associated with tuberculosis in the past, while today it is most frequently caused by streptococcal infections, sarcoidosis, drug reactions, and inflammatory bowel disease. But tuberculosis still should be considered as a cause among migrants. Painful erythematous nodules present on the lower legs, especially on the shins (Fig. 19.9). Sometimes the extensor sides of the arms are involved. The histopathological picture is a panniculitis with vessel involvement. Differential diagnosis includes panniculitis, polyarteritis nodosa,

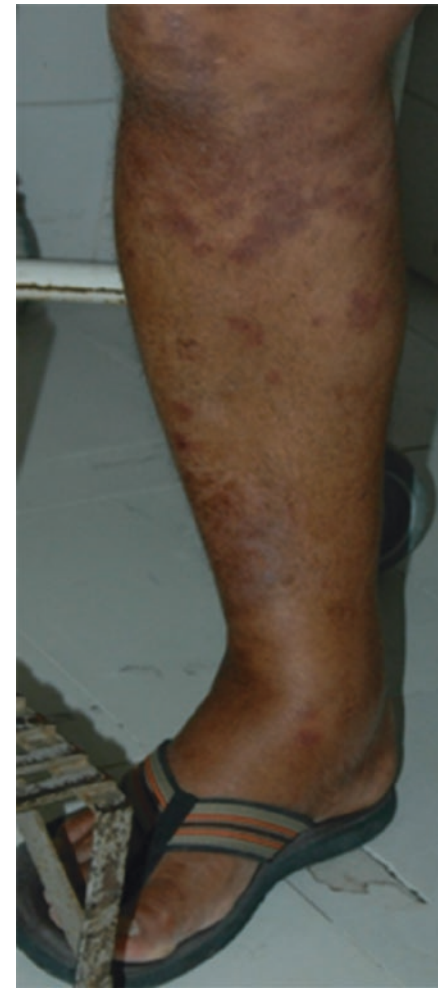

**Fig. 19.9** Erythema nodosum

erythema induratum, nodular lymphangitis, and erythema nodosum leprosum.

#### 19.3.2.12 Reaction to BCG Vaccine

BCG vaccination, with an attenuated strain of *M. bovis*, is practiced in many areas of the world. The vaccination provokes a CMI reaction in susceptible persons. This is clinically observed as an infiltrated papule which develops in 10–14 days at the site of inoculation. It enlarges into an ulcerative lesion of approximately 1 cm at 10–12 weeks. It heals which scarring. There may be lymph node enlargement (primary complex). After approximately 3 months, the tuberculin skin test reverses from negative to positive. In immunosuppressed children it may lead to non-healing ulceration and ulcerating lymph nodes.

### 19.3.3 Diagnosis

The clinical diagnosis can be confirmed by smear, biopsy, culture, and/or polymerase chain reaction (PCR). A PCR assay has been validated for detecting *M. tuberculosis* and rifampicin resistance in microscopy-negative samples. A molecular line probe assay has been validated for detecting drug resistant TB (DR-TB) in microscopy-positive samples and culture isolates in DR-TB suspects. However, despite a strong suspicion of tuberculous etiology in many cases, there is often no microbiological support for the involvement of mycobacteria.

### 19.3.4 Treatment

TB treatment should be delivered according to local regional or national guidelines. Pulmonary TB is treated using a 6-month course of a combination of antibiotics. The usual course of treatment is two antibiotics–isoniazid and rifampicin (HR)—every day for 6 months and two additional antibiotics, ethambutol and pyrazinamide (EZ), every day for the first 2 months. Extrapulmonary TB, e.g., cutaneous TB, can be treated using the same combination of antibiotics. However, the treatment may take longer, 12 months. The US recommendation is 2HREZ/7HR.

Unfortunately at present MD-resistant (MDR) TB is becoming a significant problem [12]. In addition there is even an extensively drug-resistant form of tuberculosis (XDR-TB), which is defined as resistance to at least RMP and INH (the definition of multidrug-resistant tuberculosis (MDR-TB)), in addition to resistance to any fluoroquinolone, and at least one of the three injectable antituberculosis (TB) drugs capreomycin, kanamycin, and amikacin [13]. About 4.1% of new tuberculosis (TB) patients in the world have multidrug-resistant strains (MDR-TB) [14]. Drug resistance in migrants with TB may certainly be present, as they come from and through areas where the drug resistance is more prevalent than in the West.

## 19.4 Leprosy

### 19.4.1 Introduction

Leprosy [4], or Hansen's disease, is a chronic infection caused by *M. leprae and/or M. lepromatosis*. There is a real possibility that it is present among immigrants. It is primarily a disease of peripheral nerves, skin, and mucosa, in particular the upper respiratory tract. Skin lesions are usually the first sign noticed. Left untreated, leprosy can be progressive, causing permanent damage to the skin, nerves, limbs, and eyes. Tissue and certainly nerve damage may be caused by a primary infiltration of *M. leprae* and/or its antigens, but most of the damage is secondary to immunological phenomena: reactions. Secondary infections can result in tissue loss causing fingers and toes to shorten, and the nose to collapse, as the bone and cartilage are resorbed. In 2005 WHO stated that leprosy was eliminated as a worldwide public health problem. Unfortunately this is not the case. To this day worldwide the incidence remains stable at about 250,000 new patients annually. Often children are affected, and new cases present late with permanent disabilities indicating

continuing infection, transmission, and failing detection rates. Due to increased travel, patients are diagnosed everywhere in the Western world, unfortunately often after long delay.

### 19.4.2 Clinical Features

Leprosy is highly infectious, but the attack rate is low. The major reason for this low attack rate is that most people are genetically unable to either admit the live mycobacteria into their cells or supply them with what they need to survive, because the cells lack the necessary genes. Only an estimated 20% of the infected persons are able to harbour an infection. In order to predict complications and to stratify according to the CMI, the Ridley-Jopling classification is important (Fig. 19.10), with on the one side of the spectrum polar tuberculoid (TT) leprosy (Fig. 19.11), characterized by single well-described lesion or enlarged nerve, no bacilli detectable, and high CMI against *M. leprae* antigenic determinants, and, on the other side, polar lepromatous (LL) leprosy, characterized by nodules and/or plaques (Fig. 19.12). Moreover, there is even only a generalized infiltrated skin (lepra bonita) (Fig. 19.13), characterized by symmetrically enlarged nerves, total absence of CMI against *M. leprae* antigenic determinants, and presence of many bacilli. Between the TT and LL leprosy is the borderline group, which comprises the majority of the patients: borderline tuberculoid (BT) with predominantly tuberculoid features or borderline lepromatous (BL) (Fig. 19.14) with predominantly lepromatous features. Between

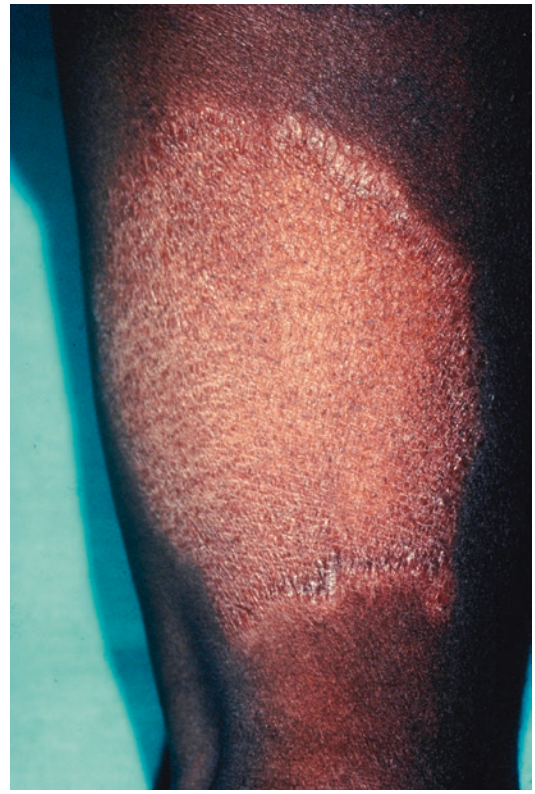

**Fig. 19.11** TT leprosy

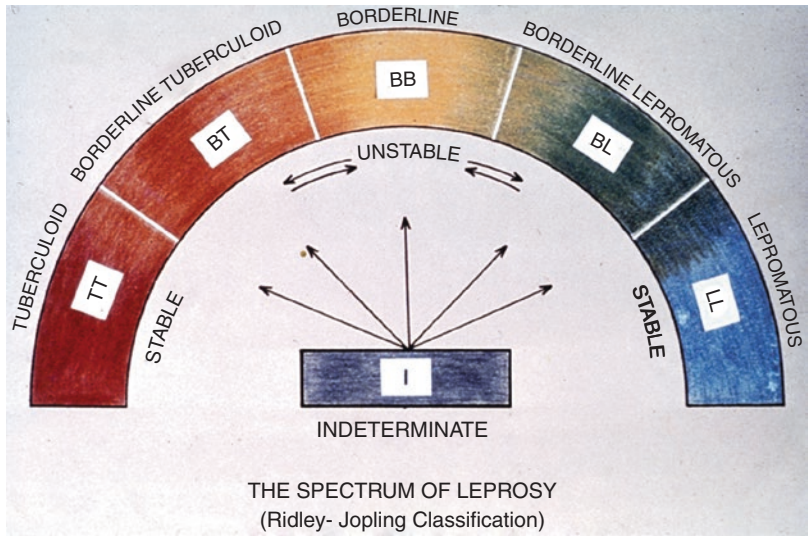


**Fig. 19.10** Classification of Ridley (courtesy dr D.L. Leiker)

**Fig. 19.12** LL leprosy

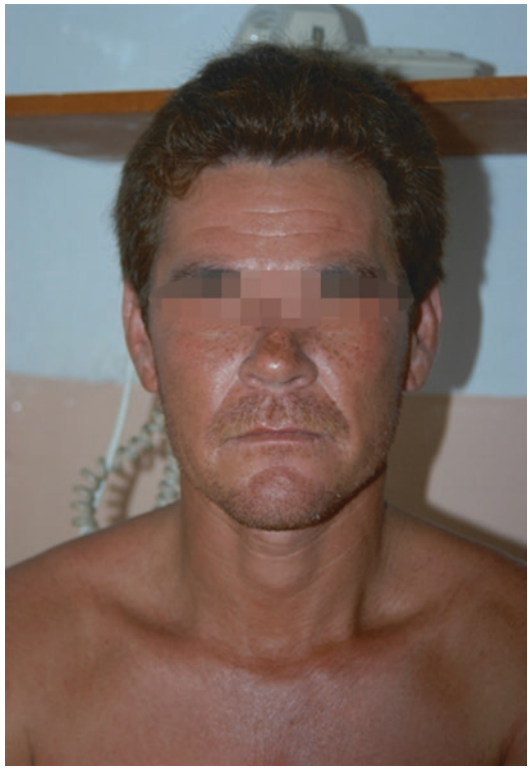

**Fig. 19.13** Lepra bonita

those two groups, there is a small group of mid-borderline (BB) (Fig. 19.15) patients with typical punched out or dome-shaped lesions. Sometimes it is not possible to classify leprosy. The lesions in those cases are then clinically and histologically indeterminate. The WHO classified leprosy into just two groups for practical purposes in the field. According to the number of the lesions, WHO identified paucibacillary leprosy (PB leprosy), if five or less lesions, and multibacillary leprosy (MB leprosy), if more than five lesions. Although this is a very practical approach, several reports have shown that by just counting, up to 30% of the patients may be wrongly classified as PB and therefore undertreated. However, when inexperienced and dealing with people on the move, this way of classification is acceptable.

### 19.4.3 Diagnosis

Patients may complain of loss of sensation in skin lesions or at hand or foot. They may have aches and pains in the face or limbs or describe a numb, sleepy, or dead feeling or sensations like "ants running under their skin" in the affected areas. Skin lesions are usually hypopigmented or erythematous macules or papules, nodules, and plaques which are skin colored or slightly red. The most important for the diagnosis is awareness. Clinically, leprosy is diagnosed when the patient shows two out of three cardinal signs. In patients on the move, one cardinal sign should be considered enough. Not treating may risk permanent disability and treatment side effects are minimal. The three cardinal signs of leprosy are:

1. Loss of sensation in a skin lesion
2. Enlarged peripheral nerve
3. Positive skin smears

*Loss of sensation* is tested with a wisp of cotton wool. The area in the lesion is tested by touch. With closed eyes the patient points to where he is touched. To make sure, the area outside the lesion is tested as well (Fig. 19.16). *Enlarged nerves* can be cutaneous nerves, subcutaneous nerves in

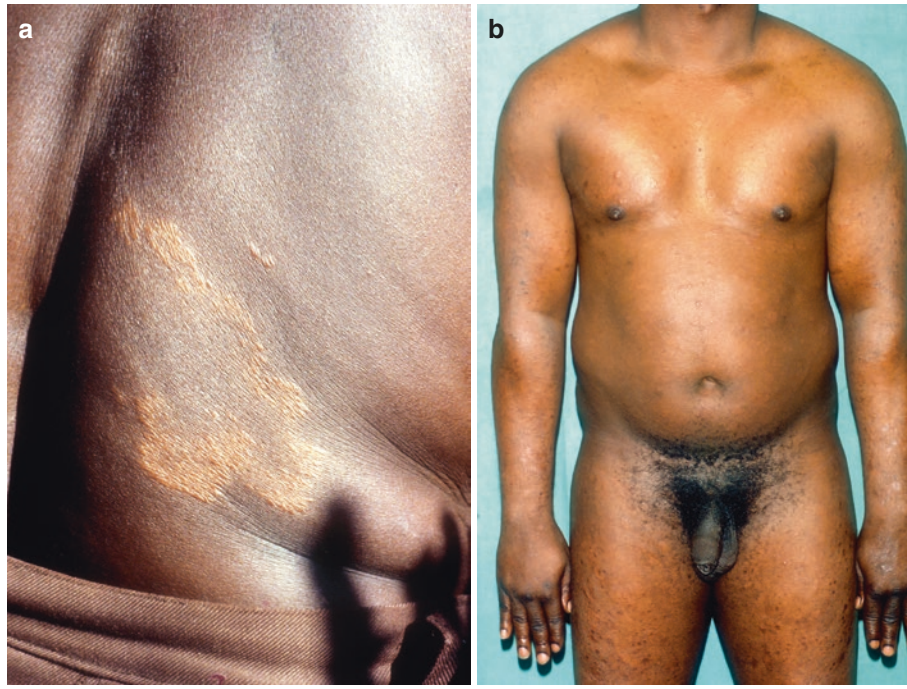


**Fig. 19.14** (**a**) BT Leprosy (active rim, with streaming), (**b**) BL Leprosy (small nodules)

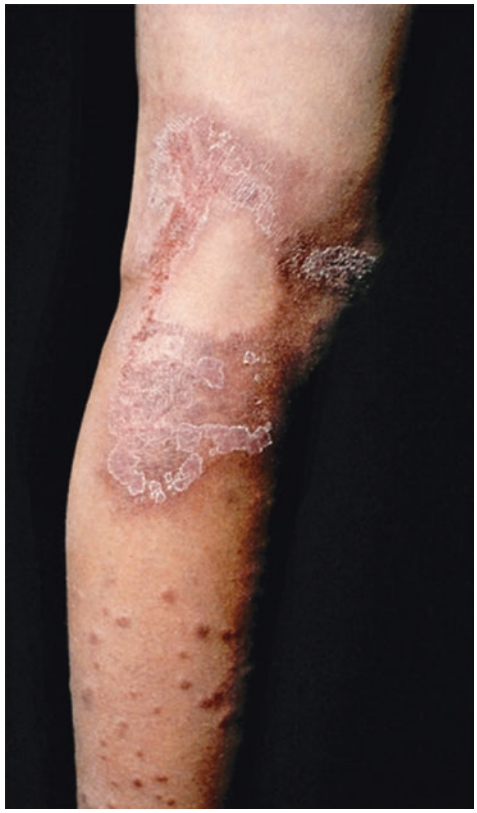

**Fig. 19.15** C Mid Borderline BB leprosy (Courtesy of Dr. D.L. Leiker)

the vicinity of skin lesions (Fig. 19.17), or nerve trunks. At least the posterior auricular, the ulnar, the radiocutaneus, the median, the lateral popliteal, and the tibial posterior nerves should be palpated. Nerve thickness, consistency, and tenderness should be appreciated. In some centers an echo Doppler is available which may replace palpation. *Smears* are taken to detect acid-fast bacilli from the earlobes and other cooler areas and from the rim of the lesion in paucibacillary (PB) patients and from the center of the lesion in multibacillary (MB) ones. The smear is taken while squeezing the skin, to numb and to diminish the bleeding while incising the dermis. Only tissue fluid is required. The laboratory can read the BI, bacillary index, and the MI, morphological index [15]. Be aware that the laboratory follows the protocol for *M. leprae*. *M. leprae* is less acid-fast than *M. tuberculosis* which most labs are used to staining routinely. Another way to detect bacilli is by PCR or NASBA, which, like the smear, is often negative in PB patients. Smears and molecular techniques can however be very useful in the diagnosis of MB leprosy, in follow-up, and in detection of relapses. Other laboratory investigations may help in the diagnosis of leprosy, but

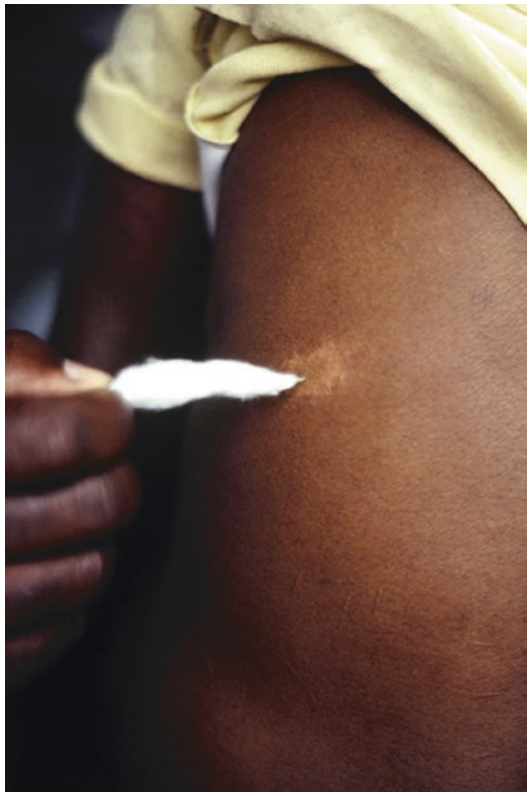

**Fig. 19.16** Loss of sensation

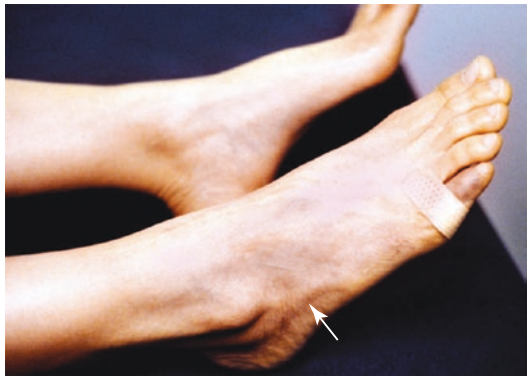

**Fig. 19.17** Enlarge nerve (skin leasion small toe)

none will be diagnostic in all cases. The antibody titer against phenolic glycolipid 1 (PGL-1), a cell wall species-specific glycolipid, is useful in MB leprosy. However, this can be positive in contacts and negative in PB leprosy. It helps to classify leprosy into PB and MB, and it can be used to follow the effect of treatment in MB patients and to detect relapses. The value of the recently introduced "LID" test is hardly more than that of the anti PGL-1 test. Lymphocyte transformation tests against different antigenic determinants have been a disappointment up to now. The lepromin test (Mitsuda), an old test, is positive in PB leprosy and negative in MB leprosy. But in healthy people, it can be positive and negative. Thus, it again helps only with the classification. Since it is made from biological material, theoretically it may sensitize; therefore, many oppose its use. Histopathology, as well as immunopathology, can be very helpful, but the latter is still experimental. A problem is that even within lesions, the histopathology of one spot may differ from the other [4].

### 19.4.4 Treatment

After the discovery of dapsone, or diaminodiphenyl sulfone (DDS), in the mid of the twentieth century, a number of regimens were recommended. Several treatment combinations, mainly based on previously proven effective tuberculosis therapy, were proposed to combine with DDS, such as rifampin, thioamide drugs, and isoniazid. The latter is however not active against *M. leprae*. But it was not until 1982 that the WHO's Chemotherapy Study Group recommended the combined use of RMP and DDS with or without clofazimine. WHO-MDT is the current standard treatment and continues to be widely administered.

#### 19.4.4.1 Multidrug Therapy (MDT)

Paucibacillary leprosy: 600 mg rifampicin once monthly, under supervision, and daily 100 mg dapsone for 6 monthly doses within a 9-month time. The dose is for a 60 kg patient.

Multibacillary leprosy: 600 mg rifampicin and 300 mg clofazimine once monthly, under supervision, and 100 mg dapsone and 50 mg clofazimine daily. Twelve monthly doses should be given within 18 months for low-BI patients and 24 monthly doses in 36 months for patients with a BI of 4 or more. The doses are for 60 kg patients.

These treatment regimens have proved effective and consistent; hardly any relapses (4%) are seen. However, it is important to be careful with dapsone in Papuans, Nepalese and Chinese patients who have a greater risk of developing

dapsone hypersensitivity syndrome. In Celtic and Nordic people, dapsone may also cause anemia. This is independent of G6PD, but is also probably genetically determined. In patients with another ethnic background, anemia due to dapsone is unusual. Fifty mg of dapsone is effective in the majority of patients and causes little anemia. As an alternative for daily treatment and as once-only treatment for single-lesion leprosy, ROM, a combination of RMP, ofloxacin, and minocycline, has been advocated. For BT and LL leprosy, it was given once per month, but it was shown to be less effective than WHO-MDT. But it could be considered in patients on the move.

#### 19.4.4.2 Reactions

During the course of treatment, but also before or after treatment, exacerbations of the disease may occur. These episodes are part of the normal course of a leprosy infection. Treatment can prevent or precipitate them. There are three types of reactions:

- Type I leprosy reaction (T1R), also called reversal reaction (RR) (Fig. 19.18)
- Type II leprosy reaction (T2R), also called erythema nodosum leprosum (ENL) (Fig. 19.19)
- Lucio's phenomenon, a reaction occurring specifically in untreated patients from Mexico (Fig. 19.20)

T1R is a CMI reaction, in particular a type IV Gell and Coombs reaction against *M. leprae* antigenic determinants. Clinically, there is increased inflammation of lesions, which become more visible and erythematous, are raised and may enlarge, and may also ulcerate. Nerves may be inflamed, enlarged, and tender, causing diminish-

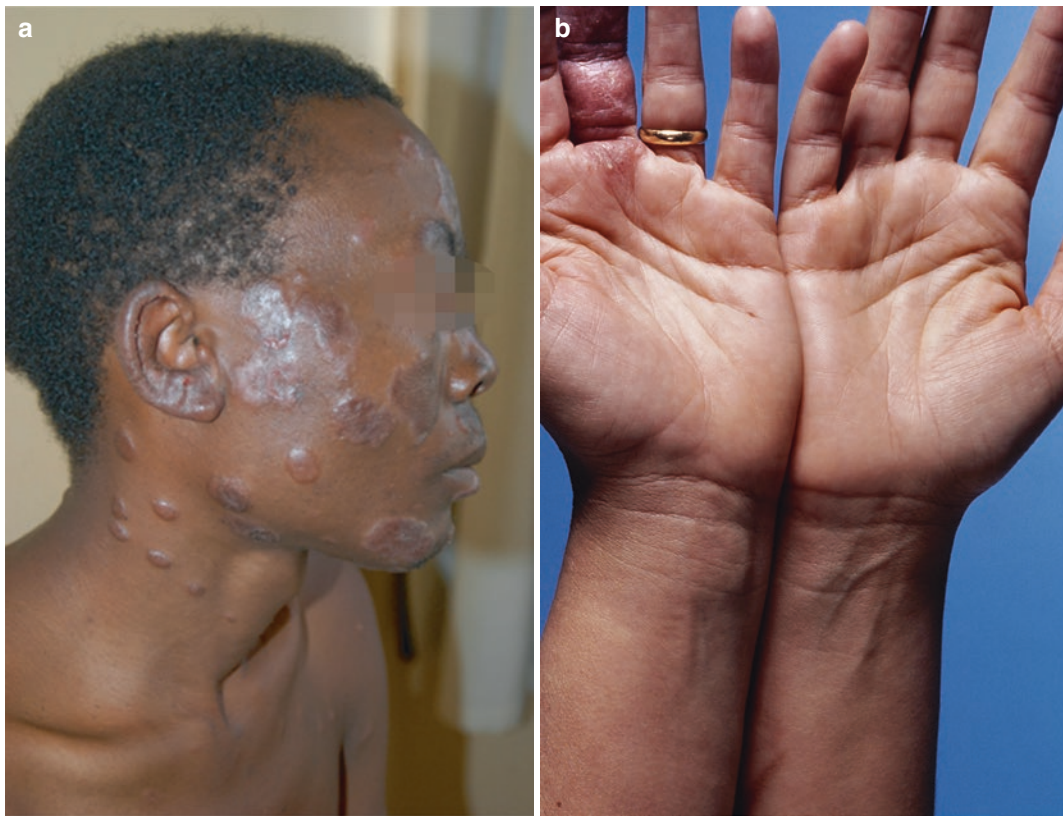


**Fig. 19.18** T1R. (**a**) inflamed leasions, (**b**) inflamed left median nerve (skin leasion on middle finger)

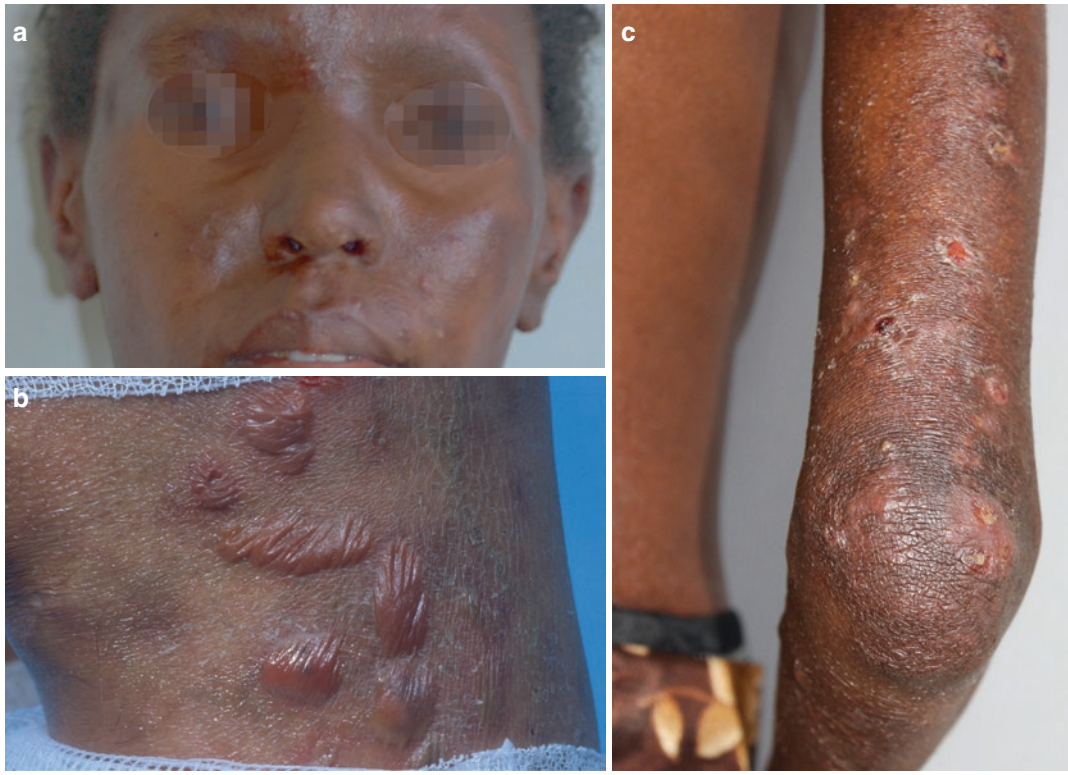


**Fig. 19.19** T2R. (**a**) ENL, (**b**) bullous, (**c**) ulcerating

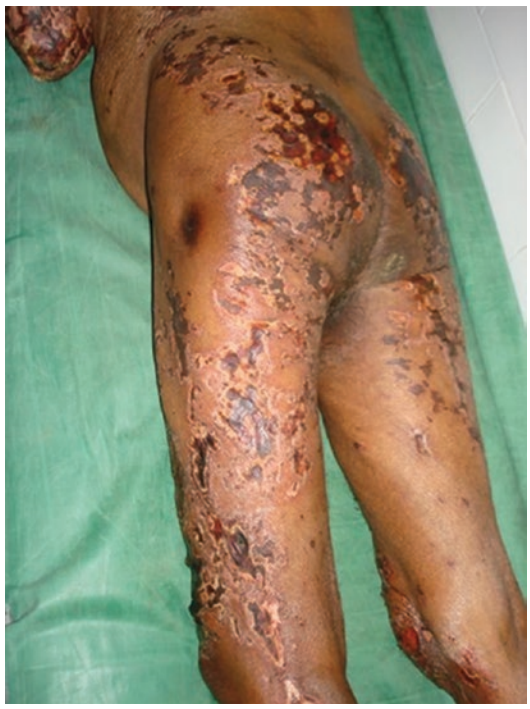

**Fig. 19.20** Lucio's phenomenon

ing strength, sweating, and sensitivity. There may be acroedema [16].

T2R is an antigen-antibody immune complex reaction in the tissues, particularly in the skin and nerve [17]. The skin shows the characteristic red painful, tender nodules. It is a multi-organ disease; all types of tissues can be inflamed. There may be malaise, fever, leukocytosis, and acroedema.

Lucio's phenomenon presents as an infarction in the skin, when huge numbers of bacilli are blocking the venous return in the small venules. This is only seen in untreated diffuse lepromatous leprosy and may be triggered by sudden cold. Some researchers are of the opinion that a special strain, *L. lepromatosis* [18], is responsible. Ulcerating ENL is frequently confused with Lucio's phenomenon.

The treatment of T1R primarily consists of corticosteroids: 30–40 mg prednisone as starting dose, tapering down, guided by graded sensory testing, in 4–12 months. When the dose is down to 15-20 mg it can be given for a longer time. This adequate immunosuppression (>0.25 mg/kg) should be given at least for 1–3 months in BT leprosy and

for at least 6 months in BL leprosy. In some cases dapsone helps to prevent a reaction [19].

T2R treatment is difficult. The reaction is episodic; 95% of ENL episodes last less than 1 month. Mild reactions can be treated with NSAIDs and arthritis with antimalarials, but severe reactions need high-dose steroids (60–120 mg) for a short period, diminishing to zero in a month or less. A new attack should be treated the same way. Clofazimine may prevent a T2R or can even be used as treatment. Thalidomide (100–400 mg) as treatment is superior and can be used as prophylaxis. But even thalidomide may not be effective in all T2R [20]. The combination of low-dose steroids with low-dose thalidomide is counterproductive. When thalidomide is not available, for the prevention of new ENL episodes, methotrexate (MTX) can be used.

When nerves continue to deteriorate despite proper medical treatment, a nerve release operation needs to be considered. This has also shown to be effective for nerves without a reaction that remain tender after medical treatment [20].

The treatment for Lucio's phenomenon, when not confused for ulcerative ENL, is easy: MDT with RMP as crucial drug.

The results of nerve damage, loss of sensation, and muscle strength are the sequelae or the stigmata of leprosy. These should be countered with supplying special padded tools, utensils, and shoes. Sometimes in order to increase grip or to improve foot movement, a tendon transfer may be considered, but always with an experienced physiotherapist present.

### 19.4.5 Prevention

Despite many efforts to develop a universal active vaccine, involving DNA techniques, BCG vaccination remains the best prophylactic in many areas. Protection ranges from less than 20% in some areas to up to 80% in other, probably depending on the presence and characteristics of environmental microorganism [21, 22]. Treating of contacts with a single 600 mg dose of rifampicin has proven to be effective for a few years, and BCG vaccination may extend this [23]. But it obviously is not the solution.

## 19.5 Buruli Ulcer

### 19.5.1 Introduction and Epidemiology

Buruli ulcer (BU) [4], also known as Bairnsdale, Searls, or Daintree ulcer, is an infectious disease caused by *M. ulcerans*. The disease was named according to the area of the first large epidemic in Uganda (1961), "Buruli," near Lake Kyoga. *M. ulcerans* grows optimally at 30–32 °C and contains a large plasmid that encodes for enzymes to produce a polyketide-derived macrolide toxin called mycolactone which mediates tissue necrosis, immunosuppression, and apoptosis [24, 25]. BU is a public health problem, mainly because of the severe disabilities it causes when diagnosed late and the stigma it carries. Since 1998, WHO has highlighted the growing problem of BU and developed improved treatment and control programs [26]. BU afflicts all age groups but most cases occur in children younger than 15 years of age. There is no gender preference. It is occasionally seen in immigrants. It is very much a disease of the poor. Most lesions are on the lower extremities, a relatively cooler site which is also prone to trauma. BU is focally endemic in the rural wetlands of tropical countries of Africa, America, Asia, and Australia. BU is most common in West Africa, with highest incidences in Benin, Ghana, and Côte d'Ivoire. The disease has been reported in over 33 countries. In 2015, 2037 new cases were reported from 13 countries [27]. A few cases also have been reported in non-tropical areas of Australia, Japan, and China. In the Americas, BU seems most common in French Guyana, with about 200 cases reported since 1970. The incidence of BU is low in Asia and Oceania. Since 1971, about 400 cases have been reported in Papua New Guinea, whereas in other Asian countries, very few cases have been confirmed. In Australia, the main focus is North Queensland, with 92 cases reported over the past 44 years [4]. BU is directly related to environmental factors and thus considered noncontagious. The epidemiology of BU is strongly associated with wetlands, especially with slow-flowing or stagnant water. A plausible mode of transmission is a minor, often unnoticed skin trauma that permits inoculation of *M. ulcerans* [28].

### 19.5.2 Clinical Features

Like in other mycobacterial diseases, exposure of the skin to *M. ulcerans* may lead to one of three outcomes: clearance of the infection, clinical disease soon after infection (primary BU), or subclinical or asymptomatic infection (latent BU) that may later reactivate and produce disease. It is most likely that many individuals exposed to *M. ulcerans* clear the infection and never develop disease [4]. The incubation period of primary BU is estimated to be 2–3 months. Delayed onset of disease, i.e., ≥3 months after leaving an endemic area, may represent activation of latent infection. When the incubation period is short (≤15 days), with lesions developing proximal to a bruise or sprain, without clinically detectable damage to the skin, this could be an activation of latent *M. ulcerans* infection caused by the local trauma [24]. BU presents with a spectrum of symptoms, which may depend on time of consultation, host immune status, inoculum size, inoculation depth, geographic area, and strain virulence (Fig. 19.21). There can be a striking discrepancy between the complaints and the symptoms as even impressive lesions may be painless. Together with stigma and fear of hospital admittance and surgery, this led as to delayed care-seeking behavior. Delayed care results in more ulcerative forms.

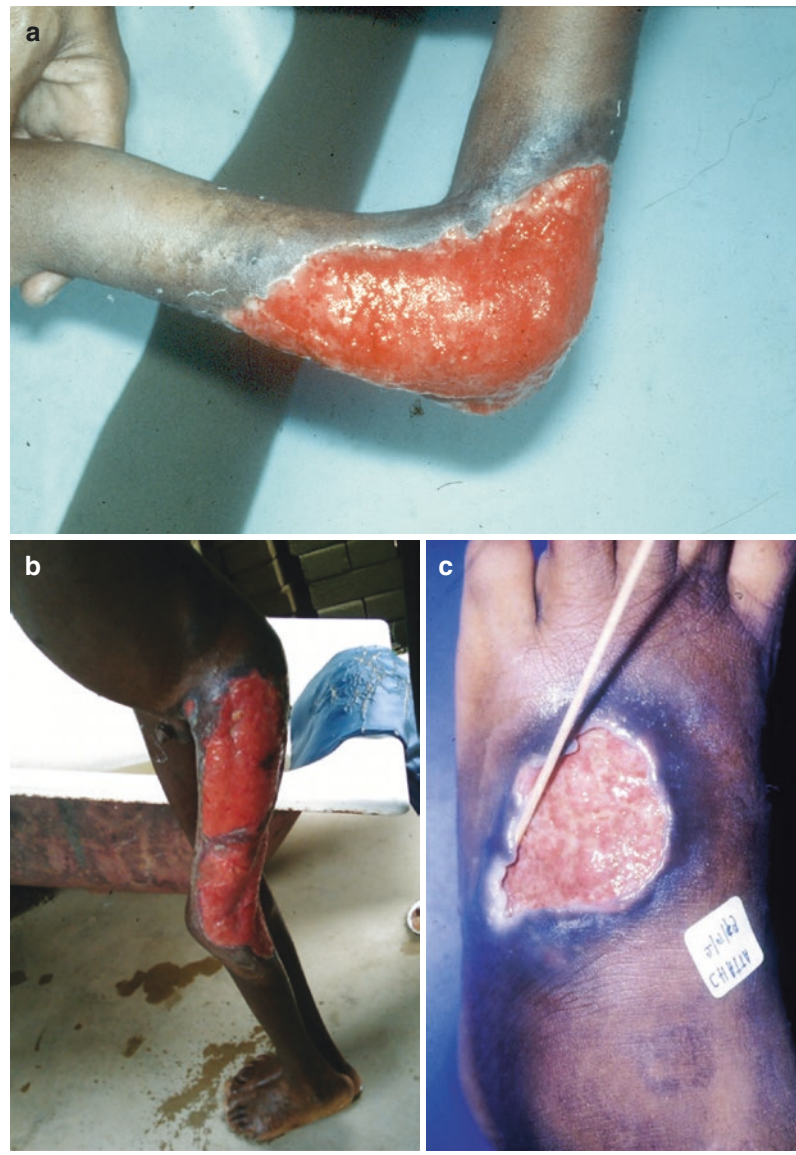


**Fig. 19.21** (**a-c**) Buruli ulcer. (B) courtesy father George Abraham; (C) courtesy Dr. PA Niemel

The disease develops through two active stages, non-ulcerated (edematous) and ulcerated lesions to the third stage, the healed or scarred lesion. There may be mixed forms however, with different stages presenting in the same site or at a different body site. Also disseminated forms occur, through spread by continuity or by lymphohematogenous spread. Bone involvement presents as osteomyelitis and occurs in up to 10% of patients in Africa [26]. This should be kept in mind seeing a migrant with osteomyelitis, in particular when he comes from West Africa. As such, it is important to examine patients thoroughly, looking for new and old BU lesions. The patient may be unaware of scars from healed BU. HIV seropositivity may be associated with aggressive BU. Non-ulcerative forms often occur in early stages and may heal spontaneously [4]. Non-ulcerative lesions may progress to ulcers after a few weeks to months.

### 19.5.3 Diagnosis

Clinical criteria supporting the diagnosis of BU include [24]:

- ≥1 painless ulcers lasting at least several weeks, undermined edges
- Nodule, plaque or wheal, or depressed scar
- Swelling over a painful joint, suggesting bone involvement
- No fever or regional lymphadenopathy (assumes there is no bacterial superinfection)
- Patient <15 years of age
- Patient who has lived in, or travelled through, a BU-endemic region

The disease may also be classified in three categories, according to lesion size:

- Category I: single lesion, <5 cm in longest diameter
- Category II: single lesion, 5–15 cm in longest diameter
- Category III: single lesion, >15 cm in longest diameter, multifocal lesions, lesions at critical sites (eye, breast, genitalia), or bone involvement [24]

Many conditions resemble BU. Differential diagnosis includes bacterial and other mycobacterial infections, deep fungal or parasitic infections, inflammatory lesions, and tumors. For ulcerative and edematous BU, the differential diagnosis includes tropical ulcer, leishmaniasis, and even anthrax and necrotizing fasciitis. Most of these conditions however, unlike BU, are painful, and tropical ulcer emits an unpleasant odor [4]. However, a painful BU may exist and it may indicate secondary infection.

Collection, when it is possible, of Clinical Specimens for Laboratory Testing should be performed.

For routine assessment and collection of specimen for culture and/or PCR, ulcers should be swabbed or scraped at the undermined rims. Fine needle aspiration can be used for suspected BU. Lesion biopsies, punch or excisional, are appropriate. If surgery is conducted, specimens should be collected.

Curetted bone samples should be cultured to determine the cause. Sampling of at least two sites of each lesion is suggested, which may increase sensitivity over a single sample by up to 25% [29].

#### 19.5.3.1 Laboratory Confirmation

Confirmation of BU is important because treatment may involve a moderately toxic antibiotic (streptomycin) and sometimes surgery. Two out of four laboratory tests should be positive in order to confirm the diagnosis. Lesion swabs or preferably scraping material or material obtained by biopsy may be used for:

- Direct smear examination for AFB, i.e., Ziehl-Neelsen or auramine stain.
- In vitro culture on selective media, at 30–32 °C.
- PCR of insertion sequence 2404 (IS 2404), which is considered to be specific for *M. ulcerans*. PCR may be also performed as single test.
- Punch biopsy for histopathologic examination.

Laboratory tests vary in sensitivity. Sensitivity is 60–80% for direct smear examination for AFB,

20–80% for culture, and >90% for PCR and histopathology. PCR and histopathology provide >90% sensitivity for all forms. Histopathology may confirm BU or suggest another diagnosis. Culture can be useful for tracking treatment response [30]. At basic level, the level on which migrants are usually quickly screened or seen, direct smears are useful, but rapid diagnostic tests are needed, like simple tests to detect mycolactone or *M. ulcerans*-specific proteins in lesions or other fluids [27].

### 19.5.4 Treatment

Historically, BU treatment consisted mainly of wide excision. Antibiotics were generally considered ineffective, although, already by the 1970s, Meyers indicated that RMP could be used for early lesions [31]. In 2004 WHO advocated a provisional antibiotic regimen, composed of oral RMP (10 mg/kg) + intramuscular streptomycin (S) (15 mg/kg), given daily for 8 weeks under supervision, with surgery as needed [32]. The current WHO recommendations for treatment [33] include:

- A combination of specific antibiotics for 8 weeks as first-line treatment for all forms of active disease
- Wound care
- Prevention of disability
- Surgery to remove necrotic tissue, cover large skin defects, and correct deformities

In general, recurrence rates in Category I and II disease after completing an RMP+S-based regimen are low (1–2%). Despite the encouraging success of antibiotics for BU, extensive disease still requires surgery. However, the point in time at which surgery should be performed in relation to antibiotic treatment is not clear. Physiotherapy, especially for Category III disease, should be suggested to prevent contractures.

While awaiting further confirmation of efficacy, the WHO has stated that an alternative regimen, based on vast clinical practice, may be:

- Rifampicin (10 mg/kg PO daily) for 8 weeks and clarithromycin (7.5 mg/kg PO twice daily) for 8 weeks
- Rifampicin (10 mg/kg PO daily) for 8 weeks and moxifloxacin (400 mg PO daily) for 8 weeks (for adults only)

Sometimes BU worsens at the start of antibiotic treatment, and this may be due to an increased CMI response. Lesions developing after treatment is completed may represent immune responses to subclinical foci of *M. ulcerans*, treatment failures, or reinfections. Sometimes steroids are needed [4].

## 19.6 Non-tuberculous Mycobacteria

### 19.6.1 Introduction

Non-tuberculous mycobacteria (NTM) (synonyms atypical mycobacteria (ATM) and mycobacteria other than tubercle bacilli (MOTT)) are implicated in cutaneous infection. NTM are usually transmitted from environmental sources by ingestion, inhalation, or inoculation. These environmental sources may include aerosols, water (surface water, ponds, streams, municipal waters), soil, dust, food products, and contaminated medical equipment [4].

### 19.6.2 Diagnosis

This is often not possible on only clinical criteria. But the most important is awareness (Fig. 19.22). Culture is the golden standard in the diagnosis of NTM. Culture may be negative if the laboratory is not informed of the clinical suspicion because specific conditions are required for culture. Mycobacterial infections usually have some specific features in a skin biopsy, so this may help direct suspicion [4]. The histologic findings of an infection vary by the age of the lesion. Scanning a developed lesion shows a typical granulomatous dermatitis, which forms an extensive inflammatory nodular

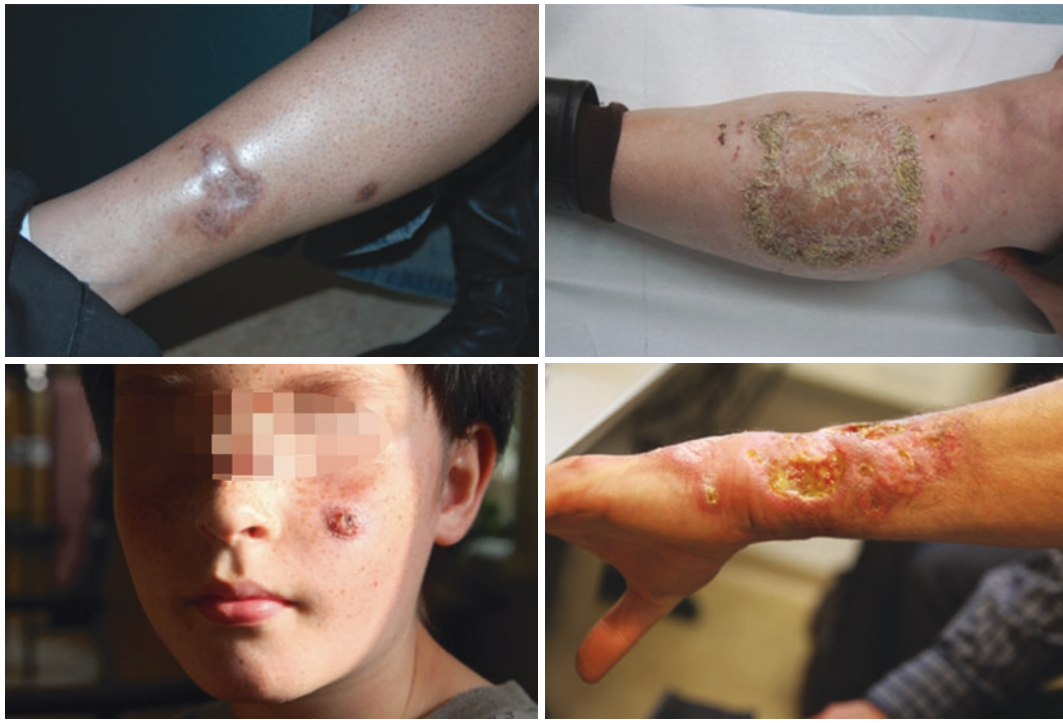

**Fig. 19.22** Non-tuberculosis mycobacterium lesions. Different etiology may give a similar clinical picture. PCR gives the proper diagnosis

infiltrate within the dermis. Early lesions may show acute suppurative inflammatory processes with little granuloma formation and sometimes extensive neutrophils. The epidermis may show pseudo-epitheliomatous hyperplasia with or without ulceration. Sometimes there are tuberculoid granulomas with varying degrees of abscess formation. The principal infiltrate however is mixed lymphohistiocytic with a few multinucleated giant cells and scattered neutrophils. Acid-fast bacilli may be scarce and are often not found [4]. A positive tuberculin test is not specific for tuberculosis but may point toward NTM as well. Molecular techniques are now available but sensitivity and specificity vary. To narrow down the possibilities in such cases, interferon gamma release assays (IGRAs) may also be performed. However, these may cross-react with other NTM: *M. kansasii*, *M. marinum*, and *M. szulgai* (and also with *M. leprae* and *M. tuberculosis*). It is not a standard test in skin disease. PCR led to new classifications and when one suspect a mycobacterial infection should always be done [34]. For example, diseases which were formerly always attributed to *M. tuberculosis*, such as lichen scrofulosorum, papulonecrotic tuberculid, lupus vulgaris, and scrofuloderma, could also be caused by *M. avium*, *M. kansasii*, *M. xenopi*, and *M. haemophilum*, respectively [34]. A natural division occurs between slowly and rapidly growing species. Mycobacteria that form colonies clearly visible to the naked eye within 7 days on subculture are termed rapid growers, while those requiring longer periods are termed slow growers. However all this is not practical in people on the move. If there is the clinical suspect of a mycobacterial infection, PCR negativety does not exclude it.

The most common slow growers that cause skin disease are *M. marinum*, *M. avium* complex, *M. haemophilum*, and *M. kansasii*. The common rapid-growing species are *M. abscessus*, *M. chelonae*, and *M. fortuitum*.

The diagnosis of *M. marinum* infection is based on the preferential localization in combination with a history of aquatic activity coinciding with skin

trauma. Histopathology can be nonspecific in the early stage of the disease. After 6 months a granulomatous reaction develops. Acid-fast bacilli may be seen; the absence does not rule out *M. marinum* infection. Cultures can be performed from aspirates or biopsies. Cultures should be maintained for 6 weeks. PCR techniques from biopsy material may provide a diagnosis within days [4].

PCR may confirm infection by *M. haemophilum*, *M. kansasii*, and *M. fortuitum*. Also in the rapid growers PCR may confirm the diagnosis.

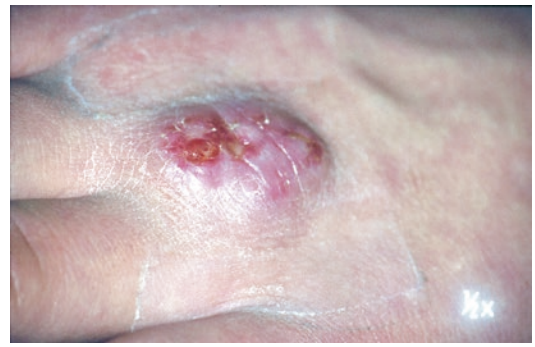

**Fig. 19.23** Granuloma by *M. marinum*

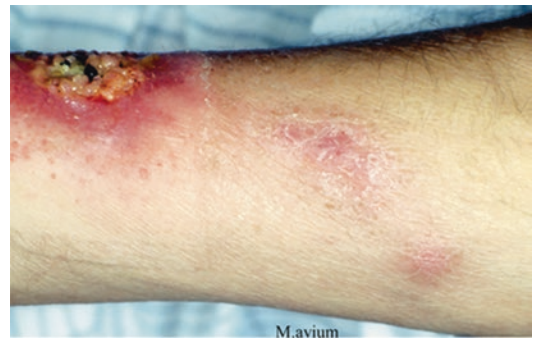


**Fig. 19.24** Lesion by *M. avium*

## 19.6.3 Clinical Features

### 19.6.3.1 Slow Growers: *Mycobacterium marinum* [4, 8]

In swimming pool or fish tank environment, granuloma is caused by *M. marinum*, a mycobacterium which causes disease in fresh, brackish, and saltwater fish and occasionally in humans (Fig. 19.23). It is found in aquariums, pools, natural water supplies, and salt water and is among the most common NTM known to cause opportunistic infection in humans. It has an incubation time of 2 weeks to several months.

The infection is preceded by trauma; often there is history of cleaning a fish tank or swimming in open water. The initial lesion starts as an inflammatory papule after an incubation period of 2–6 weeks. The papule then gradually enlarges into violaceous nodules or plaques which may ulcerate or show a warty surface. These lesions are painless. They may heal spontaneously in the course of months to years. *M. marinum* infections are one of the causes of nodular (also called sporotrichoid after the lymphatic spread of sporotrichosis) lymphangitis where nodules and/or ulcerating lesions are seen along the lymphatic vessels. Deep infections such as tenosynovitis, osteomyelitis, arthritis, and bursitis may occur. These are unusual but more common in immune-deficient patients [4]. *M. marinum* infection should always be included in the differential diagnosis of patients with poor-healing plaques, nodules, or ulcers on the upper extremities and a history of exposure to water with fish.

### 19.6.3.2 Slow Growers: *Mycobacterium avium*

This group of mycobacterial species (*Mycobacterium avium-intracellulare* complex (MAC)), with several closely related species, occurs worldwide. It is the most common group of NTM infections associated with AIDS in the West. The infection is caused by two closely related and difficult to distinguish bacteria, *M. avium* and *M. intracellulare*. These two bacteria can be found in drinking water, dirt, and household dust. MAC may be isolated in more than 30% of fecal samples [35]. It primarily causes opportunistic infections in the immunosuppressed people. *M. intracellulare* tends to cause lung disease, and *M. avium* causes lung disease and lymphadenitis in children and disseminated disease in the immunocompromised (Fig. 19.24). Symptoms of disseminated *M. avium-intracellulare* infection include fever, night sweats, weight loss, abdominal

pain, fatigue, and diarrhea [35]. Skin involvement occurs in the course of disseminated disease, rarely by inoculation. Depending on the degree of immunosuppression, widespread skin involvement may present as papules; nodules; plaques, with possible abscess formation; and ulcers. Lymph node involvement can occur. PCR may confirm the diagnosis [4].

#### 19.6.3.3 Slow Growers: *Mycobacterium scrofulaceum*

*M. scrofulaceum*was widely distributed in tap water and soil but has become very rare in the last decades. It is included in the "MAIS group" which consists of *M. avium*, *M. intracellulare*, and *M. scrofulaceum*. *M. scrofulaceum* causes pulmonary infection, and it may be the cause of cervical lymphadenitis in children. Cutaneous infection has been described as multiple subcutaneous abscesses and sporotrichoid infection (Fig. 19.25). Again PCR confirms the diagnosis [4].

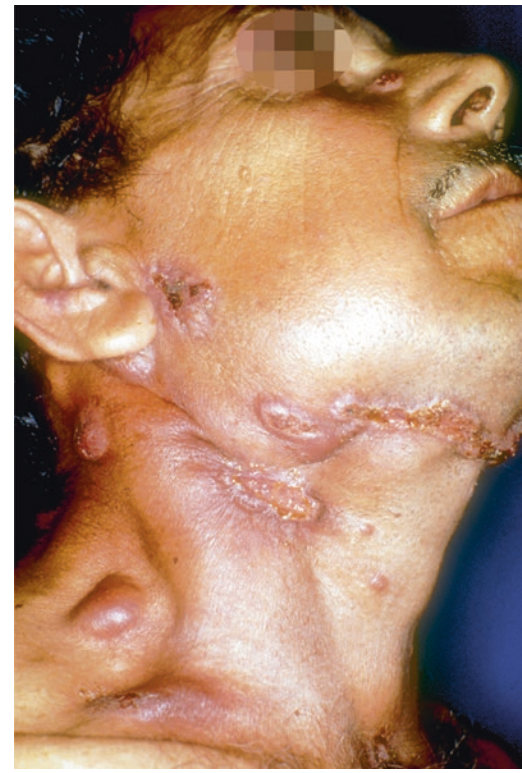

**Fig. 19.25** Scrofulaceum with subcutaneous abscesses

#### 19.6.3.4 Slow Growers: *Mycobacterium kansasii*

*M. kansasii*causes disease in humans throughout the world, and it is often associated with AIDS. It has been isolated from cattle and swine. However, water is most likely its true habitat. It affects people of all ages.

The most common manifestation is a chronic pulmonary disease. Inoculation of the skin is in general through a small wound. Cutaneous lesions include erythematous to violaceous papules and plaques but may be pustular, crusted, or verrucous papules or nodules. Lesions can resemble pyogenic abscesses, cellulitis, or sporotrichosis. Cervical lymphadenitis is reported in children [4].

#### 19.6.3.5 Slow Growers: *Mycobacterium haemophilum*

*M. haemophilum* causes skin, joint, bone, and pulmonary infections in immunocompromised people and submandibular lymphadenitis in children. Most infections occur in patients with AIDS and in transplant recipients. *M. haemophilum* skin infections have been associated with permanent eyebrow makeup and tattoos. Infections with *M. haemophilum* have been reported in a broad geographical range. The natural habitat and route of infection are unknown [4].

#### 19.6.3.6 Slow Growers: *Mycobacterium fortuitum*

*M. fortuitum* has been isolated from water, soil, and dust. Primary cutaneous disease is seen at all ages. It has been implicated in numerous outbreaks of hospital infections. The clinical manifestations are localized cellulites, frequently with draining abscesses and nodules. Mostly, history of a penetrating injury with possible soil or water contamination is reported. Postoperative infections, in general, develop 3 weeks to 3 months after surgery or trauma [36].

#### 19.6.3.7 Rapid-Growing Mycobacteria: *Mycobacterium chelonae* and *M. abscessus*

The two closely related species *M. chelonae* and *M. abscessus* (which consists of two subspecies) cause similar diseases worldwide. The skin disease caused by these opportunistic pathogens can be localized, similar to *M. fortuitum*, or may present as a disseminated disease with cellulitis and multiple often draining (sub)cutaneous nodular lesions in immunocompromised patients. The localized infection may occur at all ages, typically after a trauma or a surgical incision. Inoculation may also follow tattooing, implicating contaminated water for the dilution of ink, or cosmetic procedures such as dermal filling, where contaminated ice used to cool the skin may be the cause [4].

#### 19.6.3.8 Rapid-Growing Mycobacteria: *Mycobacterium szulgai*

The natural habitat of *M. szulgai*is unknown. It has, however, been isolated from snails and tropical fish. The predominant localization of infections is pulmonary. Cases of skin infection particular in the immunosuppressed even after minor trauma have been reported: cellulitis and inflamed tender nodules leading to draining abscesses [4].

### 19.6.4 Treatment

The treatment is not easy because mostly the cause is not known. The treatment depends upon the infecting organism, the severity of the infection, and host immunity. PCR may be of great help. In most cases a course of antibiotics is necessary. These include rifampicin, ethambutol, isoniazid, minocycline, ciprofloxacin, clarithromycin, azithromycin, and co-trimoxazole. Treatment of cutaneous localized disease is generally continued until 1 month after clinical recovery and for pulmonary and generalized infection even longer for 18–24 months. Treatment in general should consist of a combination of drugs. For treatment of cutaneous infections by NTM, it is preferable to select the drugs based on the antimicrobial susceptibility profile. In vitro susceptibility testing is useful for rapid-growing mycobacteria (RPM) but not for slow-growing NTMs, e.g., MAC, *M. haemophilum*, and *M. szulgai*, as in vitro results do not correlate with in vivo response to treatment [37]. Empiric therapy is sometimes necessary in the case of strong suspicion with negative culture and no identification by means of PCR. Duration of treatment is not fixed and is based on clinical judgment and will require in general 6–9 months. For the treatment of rapid-growing mycobacteria, it is important to follow the results of in vitro tests. For slow growers, that is not the case since in vivo and in vitro results often are not related.

Since drug resistance of *M. marinum* [38] varies, a combination therapy of usually two or three drugs is recommended. Ciprofloxacin has shown considerable effectiveness. In cases of severe infection, including those with a sporotrichoid distribution pattern, a combination of RMP and ethambutol (ETM) is the recommended regimen. Response to treatment is slow. Treatment is continued until 4 weeks after clinical recovery and usually takes 4–9 months. Surgical treatment is not usually recommended. Cryotherapy, X-ray therapy, electrodessication, photodynamic therapy, and local hyperthermic therapy have been reported as effective alternatives.

In general, MAC infection is treated with two or three antimicrobials for at least 12 months. Commonly used first-line drugs include macrolides (clarithromycin or azithromycin), ethambutol, and rifamycins (rifampicin, rifabutin). Aminoglycosides, such as streptomycin and amikacin, are also used as additional agents as is ciprofloxacin although supportive evidence for the latter is absent [39]. When lymphadenitis occurs in children, surgery is suggested.

For childhood cervical lymphadenitis due to *M. scrofulaceum*, surgery is the recommended treatment, in which the lesion is excised without chemotherapy. The success rate for this treatment is 95%. Drugs which are used in treatment include isoniazid, rifampin, and streptomycin. Good results were described with a combination

of isoniazid, ethambutol, rifampin, and ofloxacin [40]. Clarithromycin is a good addition.

*M. kansasii* shows good in vitro susceptibility to rifampicin, rifabutin, ethambutol, ethionamide, amikacin, streptomycin, clarithromycin, sulfamethoxazole, and ciprofloxacin. However, when monotherapy is given, drug resistance is common. Therapy usually consists of isoniazid, rifampicin, and ethambutol or rifampicin, ethambutol, or a macrolide [40]. When lymphadenitis occurs in children, excision is suggested. *M. haemophilum* appears to be susceptible in vitro to ciprofloxacin, clarithromycin, rifabutin, and clofazimine but resistant to isoniazid [40]. In vitro observations may not relate to outcome of treatment in vivo and should be interpreted with extreme caution. Susceptibility test assays have not been properly standardized, because of the fastidious nature of *M. haemophilum* [37].

Ciprofloxacin, amikacin, and cefoxitin are considered as first-line drugs. Alternative drugs are doxycycline, imipenem, ethambutol, and cotrimoxazole. A combined regimen, preferably with three drugs, should be used for 2–4 weeks, followed by ciprofloxacin and a companion drug (e.g., clarithromycin despite the bacteria becomes easily resistant to this drug) for 3 months [4, 41].

The use of monotherapy is not recommended for *M. chelonae*. Tobramycin and clarithromycin are drugs of choice for *M. chelonae*. In general, cefoxitin and amikacin are active against both subspecies of *M. abscessus*. Clarithromycin is only active against *M. abscessus* subsp. *bolletii*, as it possesses an erm gene that induces resistance in vitro and in vivo [37].

Against *M. szulgai* triple-drug therapy with rifampicin, ethambutol, and clarithromycin guided by sensitivity testing is suggested. It is recommended to use multiple drugs to reduce development of resistance. The treatment may take up to 1 year [42].

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# Abuse, Self-Harm, Torture Signs, and PTSD

20

Aldo Morrone and Maria Lucia Dell'Anna

## 20.1 Introduction

"The WHO Constitution was the first international instrument to enshrine the enjoyment of the highest attainable standard of health as a fundamental right of every human being ('the right to health'). The right to health in international human rights law is a claim to a set of social arrangements—norms, institutions, laws, and an enabling environment—that can best secure the enjoyment of this right" [1].

Ibrahim Salama, Director of the Human Rights Treaties Division of the Office of the High Commissioner for Human Rights of United Nations, remarked that this is a time where the human rights agenda was losing ground in many parts of the world, but also at a time of powerful movements for human rights. It was therefore essential that the human rights treaty body system was efficient and produced concrete outcomes for the victims. With the recent accession of Samoa to the Convention against Torture and Other Cruel, Inhuman or Degrading Treatment or Punishment, the number of state parties now stood at 166. The 2020 review of the human rights treaty body system by the General Assembly was of utmost importance to ensure its sustainability and impact on the ground.

At an international and institutional level, torture has been unconditionally condemned in all international human rights documents, such as the Article 5 of the Universal Declaration of Human Rights adopted in 1948, the Article 3 of the European Convention for the Protection of Human Rights and Fundamental Freedoms adopted in 1950, and the Article 7 of the International Covenant on Civil and Political Rights adopted in 1966 [2–4].

## 20.2 San Gallicano Dermatologic Experience (2002–2007)

The first consideration to make is that there are no illegal migrants, because no human being can be defined as such in the universe. Gypsies and wanderers, low-income retired elderly people, women who are the victims of prostitution, unaccompanied minors, asylum seekers, and torture victims were sheltered (Table 20.1).

They are people, with their stories, illnesses, anguish, dreams, plans, and emotions. Hundreds of thousands of meetings have been held with a group of healthcare experts, physicians, nurses, psychologists, social workers, cultural mediators, sociologists, clerks, and cleaning staff—all

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**Table 20.1** The experience of San Gallicano Institute Rome (reported as % lesions observed)

| | Cause of scars | Reported torture |
|---|---|---|
| Cutting | 16 | – |
| Weapons | 11 | 8 |
| War | 26 | – |
| Burns | 5 | – |
| Other | 42 | – |
| Beating | – | 92 |
| Electrical | – | 17 |
| Frozen water | – | 23 |
| Sexual | – | 8 |
| Psychological | – | 4 |
| Falaka | – | 14 |

of them have helped welcome these people, each for his or her own part—to try to understand and assess them with the respect that every human being deserves and in compliance with the different cultural and religious needs that each of them brings. The disregard of the public administration over these long years has become evident on several occasions: whenever it has been able and wanted to, the administration has stepped in by skillfully mixing threats with "administrative suggestions" to make stop any activity dubbed as "extra-institutional." The text of the Hippocratic Oath did not forbid to assess anyone. Actually the opposite was true. Thus, the initial activity was carried out in absolute secrecy, not being possible to publicize a service that was essentially not only irregular but also clandestine, within a public facility, i.e., open to everyone.

Maybe it was exactly that "extra" that eventually thrilled and involved about a hundred other specialists from the most diverse fields, without knowing at all where it would have led. It is not Odysseus' voyage, but rather Abraham's, the ongoing journey of a person who is too old to leave and who abandons his certainties and his position relying solely on an incredible promise, upon the stars.

This sea voyage allows to meet not patients but people, sometimes sick, sometimes the victims of torture or of sex trade, yet human beings. Some words have the power to kill. Drug addicts, patients, detainees, and prostitutes do not exist; they are persons addicted to drugs, sick persons, detained persons, and persons who are victims of the sex trade.

Each therapeutic relationship should be based upon the uniqueness of every human being and not upon a "diagnostic categorization" representing a "cultural and symbolic categorization."

By identifying individuals by the name of the pathology they are affected by, we do not consider them as a whole; we focus on their problem and ignore their peculiarities, resources, and potential.

The multidisciplinary and transcultural service includes not only physicians, nurses, and psychologists but also anthropologists, sociologists, cultural mediators, and the victims of torture themselves. The limit of activity often lied in the necessity for direct assistance, treatment, and study in order to attain a final report for the purpose of requesting the refugee status. This was a very important task, the only opportunity for those people to start a new life, but it risked making lose the memories of a large number of meetings, histories, thoughts, and feelings.

As Filippo Gentiloni states in his beautiful book *Abramo contro Ulisse*, indignation is today part of those minor and useless things which seem to have gone lost. Indignation is an unusual feeling today, in the age of homologation, weak thought, and fear of marginalizing differences [5].

Too many times indignation is the only solution, but it may often appear useless and personal. Indignation is today considered an outdated and ineffective feeling. It is no longer popular even among the culture and attitudes of the political

side that has apparently forgotten it, along with the rage that filled the hearts of the labor movement for decades. It is indignation at a world that is larger than imagined, which tortures its opponents, in the indifference of those governments and movements that persistently refuse to see beyond their borders.

## 20.3 Taking Care

"Taking care" is a more complex clinical and anthropological experience than "caring." The lack of care, or, better yet, of taking care, is a dreadful feature of present times. Especially after September 11, 2001, there are too many symptoms of the lack of civilization. Dreams of generosity are disregarded and neglected, undermined by the supremacy of a new liberalism, matched by the ensuing individualism and the extolling of private property as well as with the remarkable security issues that affect everything. Traditions of solidarity are despised. Ideals of freedom and dignity for all human beings, starting from those who appear to be useless, are not taken into account. What prevails is the society of show business, of appearing, of having, as opposed to being or knowing to be.

As stated by Leonardo Boff in *Il creato in una carezza*, this new social contract is rooted in the respectful participation of the majority of persons and peoples, in valuing differences, in the acceptance of the various complementary issues, and in the agreement built on the diversity of cultures, of means of production, of traditions, and of meanings of life [6]. We feel the urgency for a new *ethos* that, in its original ancient Greek meaning, also refers to the burrow of an animal or to the human dwelling, namely, that part of the world used to organize, take care of, and create our *habitat*.

According to Heidegger, care refers to a fundamental existential-ontological phenomenon, or, in other words, a phenomenon that provides the foundation for human existence as such, namely, in relations, as nothing exists outside them. Human beings take care, or, better yet, their essence is in the care; this is all the more true for physicians, nurses, psychologists, and healthcare practitioners [7].

Taking care of people means having intimacy, feeling them in yourself, welcoming them, respecting them, and giving them rest and peace. Taking care means establishing a synchronicity with them, listening to their rhythm, and tuning in with them. Analytical and instrumental reasoning gives way to cordial reasoning, to the *esprit de finesse*, the spirit of finesse, the profound feeling. The *logos*-rationality does not take center stage any longer, but is replaced by *pathos*-feeling. We all feel connected to one another, forming a unique whole that is diverse and always inclusive, never exclusive.

Care has been slandered as a feminization of human practices, as an obstacle to objective understanding and to efficiency. Yet this is not the case. We have lost the notion of the human being as a being of relations and unlimited relations; a being of creativity, tenderness, care, and spirituality; and a carrier of an endless project.

It is thus evident that the originary fact is not *logos*, rationality and the structures of understanding, but rather *pathos*, feeling, the ability to sympathize and empathize, dedication, kindness, and communion with others. *Pathos*, in the original meaning of the Greek word, indicates sharing of the feelings.

Surely everybody remembers the secret that the fox discloses to Antoine de Saint-Exupéry's Little Prince, before leaving for its small planet for good: "It is only with the heart that one can see rightly; what is essential is invisible to the eye." It is the feeling that makes people, things, and situations meaningful to us. This profound feeling is called "care" [8].

As pointed out by Boff, more than the Cartesian *cogito ergo sum*, i.e., "I think, therefore I am," it is *sentio ergo sum*, "I feel therefore I am," that applies.

We should increasingly develop a listening attitude and not only toward those who are speaking to us, but we should also experience a profound, attentive feeling toward the environment and, essentially, toward nature. Human beings should feel themselves as nature. The more they immerse themselves in nature, the more they feel

how much they have to change and how much they have to preserve of the vital breath of the universe in their lives and relationships. There is an aspect of human relations that is often neglected, especially among those who provide healthcare in all its meanings and the people, either the patients or the sick, who rely on us: it is tenderness.

Vital tenderness is synonymous with essential care. Tenderness is the affection that we devote to people and the care that we apply to existential situations.

Tenderness is care without obsession: it also encompasses work, not as a mere utilitarian form of production, but as workmanship that expresses the creativity and self-fulfillment of people. It does not refrain from rigor in knowledge. It is a feeling of affection that, in its own way, is also knowledge. We actually know something only when we have affection for and are involved with what we wish to know. Tenderness can and must go side by side with extreme commitment to a cause, as was perfectly demonstrated by Che Guevara. From him we inherit the inspiring phrase: *Hay que endurecer pero sin perder la ternura jamás* [9].

Blaise Pascal introduced an important distinction to help us better understand care and tenderness: *l'esprit de finesse* and *l'esprit de géometrie*. *L'esprit de finesse* is the spirit of finesse, sensitivity, care, and tenderness. *L'esprit de géometrie* is the spirit of calculations and workmanship, which is interested in efficiency and power. This fact is where the terrifying emptiness of our "geometric" culture comes from, along with its plethora of sensations without deep experiences [10].

The fundamental difference between the experience with torture victims at the "San Gallicano" and similar experiences in other places lies in the attempt to perceive the victims as fragments of the universe, of the vital energy coming from the stars that others have sought to destroy. The practice of torture entails not only the attempt to annihilate the other but also the negation of life, as it has been developing over the past billions of years, from the Big Bang. Therefore, the reception of the other and the face of the other recall the sparkle of life that blossomed with considerable difficulty on our planet 4.5 billion years ago. At any time, torture means destroying life, in all its forms.

The face of the other precludes any indifference. The face of the other forces me to take a position because it speaks, provokes, evokes, and convokes: especially the face of the poor, the sick, the marginalized, and the excluded. The face and eyes always launch a proposal in search of a response. Thus, responsibility arises, the obligation to give responses. Here we find the birthplace of ethics, which lies in the relation of responsibility when met with the face of the other, especially with the face of those who are all the more "the other," such as the oppressed, the *illegal* migrants, the homeless, asylum seekers, and victims of the sex trade and torture.

## 20.4 Torture in History and Nowadays

The Convention against Torture and Other Cruel, Inhuman or Degrading Treatment or Punishment, adopted in 1984, is entirely devoted to banning these practices and provides for the liability to punishment before all courts where the perpetrator is, regardless of the place where torture was committed. In addition, no exceptional circumstances whatsoever, whether a state of war or a threat of war, internal political instability, or any other public emergency, may be invoked as a justification of torture.

The debate on torture probably dates as far back as the origin of humankind. This issue was discussed by philosophers since the Classical Age and Modern Age and in the twentieth and twenty-first centuries. However, the debate developed with greater continuity and incisiveness in the course of the Enlightenment.

Nowadays plenty of issues have radically changed if compared with the eighteenth century. The historical context is different. The jurists and the philosophers of the eighteenth century worked in a context where criminal procedure in both the civil and the ecclesiastical courts set detailed rules for the practice of torture and considered it, first of all, legitimate and useful. Today human rights

documents and international legislation openly and unanimously condemn these practices. However, torture is forbidden but not prevented. The cultural context is extremely different if compared with the eighteenth century, but not a day has passed without the international debate being focused on security issues, prevailing over the respect and protection of human rights. After the 9/11, there has been a debate in the USA and throughout the world on the use and legitimacy of torture in the framework of state security and war against and roused by terrorism.

In the eighteenth century, too, the debate was very intense between those considering torture useful for the security of society, though submitted to procedural rules limiting and regulating it, and those advocating its complete abolition. In fact, the victory of the abolitionist theory that acknowledged the unlawfulness of torture led to its elimination. Torture was abolished in 1740 in Prussia under Frederick II; in 1776, in Austria under Maria Theresa; in 1780 in France under Louis XVI, at least for some of its manifestations; and in 1784 by Joseph II in the Duchy of Milan. In Russia, too, under Catherine II, its elimination was called for in 1765.

Many authors, through their own texts and the debate following their publication, have contributed to spreading the culture of tolerance and led sovereigns to a greater attentiveness for the individual's reasons, human rights, and the unlawfulness of torture. It is impossible to forget Christian Thomasius in Prussia and his dissertation *De tortura ex foris Christianorum proscrivenda* in 1705; Cesare Beccaria and his dissertation *Dei Delitti e delle Pene* in 1764; Pietro Verri and his dissertation *Osservazioni sulla tortura* in Italy; Voltaire and his *Treaty on Tolerance* in 1767; and Montesquieu and Joseph von Sonnenfels among others [11–16].

In the past, torture had the function to certify and confirm the truth of the perpetrating power. Therefore, the person submitted to torture had to confess what he was accused of. The perpetrating power claimed to own the truth that had to be confirmed also through torture. Little mattered whether it was the sovereign's or the Church's power or both. The power of torture consisted in making the person confess the "truth" that the power already thought it possessed. Torture was not inflicted without distinctions, and its function was discretionary, extraordinary, and selective. In ancient Greece it was not known and in ancient Rome it was not inflicted on free-born men, but only on slaves who were considered neither as citizens nor as human beings. Historically, the practice of torture would spread later on, to coincide with the concentration of power in the emperors, followed by the progressive corruption of the republican political system that led to despotic governments.

At the end of the eighteenth century, when the practice started to be eliminated, there were social categories, such as magistrates, that were exempted from it, regardless of the offence. Torture and murder were turned into a spectacle, shown to the masses in order to deliver them that exemplary, symbolic, and dreadful message that exalted the sovereign's power. Punishment had to comply with a particular requirement: it had to be exemplary and evident. However, the exemplary ad evident character of the punishment contributed to showing the inherent partiality, that is to say the unfeasibility to punish everybody. In fact, the sovereign could not punish everybody; it was not in his power, interests, and wishes. He had to show that he could virtually punish everybody, and he demonstrated it in a clear and exemplary way, punishing someone with torture, extreme suffering, and finally death. Torture not only confirmed and certified the truth of the power, but it also possessed the power of truth. In some legal systems, this power was legalized to the point that the person resisting torture was considered innocent and hence released. Torture coincided with the punishment. The penal system was not characterized by detention centers that started to spread in the course of the nineteenth century. At a certain point, the evidence of the punishment started to lose importance, and torture started being abrogated, but this practice was not entirely eradicated. Being abrogated implies that it is not inflicted in a legal, exemplary, and evident way.

Torture starts being inflicted in a covert manner, hidden from the legality of the systems of power. What makes torture disappear from laws

and what leads it to hide in the niches of the criminal system? Absolute powers, both of the sovereign and of the Church, show signs of faltering. The powers that have gradually been legitimated no longer need to demonstrate their cruelty to subjects; rather, they have to prove their legality, normality, and rehabilitation to citizens. It is no coincidence that the reformation movement spread from the top, that the abolition of torture was endorsed by sovereigns themselves, and that it was not infrequent for intellectuals and magistrates to be adamantly opposed to such claims. The system of power changes, along with the system of punishments, and terror is replaced by discipline and thus by control, which is perhaps an even more subtle and fearful tool, as it is duly camouflaged.

The relationship between authority and control, between barbarism and civilization, was further examined by Alessandro Manzoni: while paying tribute to Verri's remarkable work and to the aim pursued in *Observations on Torture*, Manzoni also warned against a hasty dismissal of the problematic relationship between violence and power. Manzoni forcefully drew attention to a much needed recourse to more refined analytical tools, in order to avoid the risks of conceiving history as too linear [17]. Accordingly, the non-rational components of action should be taken into account in a holistic view of human nature while being aware of the unfathomable human soul as well as of the role played by passions. Manzoni's criticism foreshadows an explanation for the inhuman events of barbarism and torture that extensively occurred again in the civilized world during the twentieth and twenty-first centuries.

Nowadays, torture has made a powerful comeback on the world stage, especially with the pictures of the naked bodies in the Abu Ghraib prison. This worked as a sort of massmedia wakeup call for a distracted society that did not want to see and had already forgotten Via Tasso in Rome; Franco's Spain; Salazar's Portugal; the war in Algeria with the statements by General Massu; the Colonels' Greece; Pinochet's Chile; Videla's Argentina; former Yugoslavia with Srebrenica, Tuzla, and Mostar; and today's Myanmar of the coup generals and Libya's detection centers.

Books such as *The Question* (1958) by Henri Alleg, on the war in Algeria; *The Confession* (1970) by Artur London, on Czechoslovakia in the 1950s; or *La Punition* by Tahar Ben Jelloun seem to belong to a different time and to a different world [18–20]. Yet the debate over torture, which was triggered by the shameful images from Abu Ghraib, is looming on the horizon.

When the pictures of the naked, humiliated bodies piled in the Abu Ghraib prison were released in 2004, it could no longer be denied that US Armed Forces in Iraq used torture, but attempts were made to downplay and minimize it. Donald Rumsfeld stated: "My impression is that what has been charged thus far is abuse, which I believe technically is different from torture." Because of these "abuses," only few soldiers were identified and mildly punished, while General Janis Karpinski was demoted to colonel. The shame was due to not only the torture carried out in the Abu Ghraib and Guantanamo prisons but also the fact that official, secret prisons existed in many countries around the world.

On September 18, 2006, Gustavo Zagrebelsky stated in the Italian newspaper *La Repubblica* "Torture and death penalty turn men into mere living matter, without any defence, and consenting to the use of violence on reasons of security means allowing for the development of hate and barbarism" [21]. Irene Khan of *Amnesty International* wrote that torture "dehumanizes the victim and the perpetrator. It is the ultimate corruption of humanity"; the constantly vigilant fight against the practice of torture is the foundation of civilization. "If the international community allows this fundamental pillar to be eroded, it cannot hope to salvage the rest" [22].

## 20.5 Security and Freedom

After 9/11, the strategists of the war on terrorism have once again raised the age-old controversy on the legitimacy of torture and supported the need for a lenient—if not tolerant—conception of the rule of law, in which the relationship

between security and freedom has increasingly more ambiguous contours. Usually, security and freedom are inversely proportional. Where there is more security, there is less freedom. Thus, those who want freedom are to provide security and, conversely, those who want to take freedom away start spreading insecurities and fears. It is absolutely true that this relationship exists at a largely complex level.

Can the relationship between security and freedom justify surveillance of communications, investigations into the origin and destination of wealth of unknown origin, restrictions to the movement of people, searching of houses, use of public force, detention of suspects, and prison isolation for certain periods, and to what extent? It could be discussed, but, as pointed out by Zagrebelsky, "when it comes to torture, it is not possible to talk of striking a balance for two main reasons concerning morality and effectiveness. For once, they go along with one another" [21, 23, 24].

Torture is usually associated with slavery and genocide, and, along with them, it is condemned as a crime against humanity. There is crucial common ground between these crimes, which explains and justifies why they are commonly abhorred. Borrowing Giorgio Agamben's words, they are forms of degradation of the human being to "naked" biological "life," to mere living matter, without any autonomy and protection, helpless facing the authority of those who exert unlimited and unrestrained power for their own purposes. For those who believe in the "moral progress of humanity," rejecting slavery, genocide, capital punishment, and torture is the minimum—and thus inalienable—proof of civil conscience in progress. Capital punishment, too, is to be included in this list: the last moments before the execution are the most morally hideous, as the convicts, lacking any defense and hope, made unconscious by the drugs administered, become mere organic matter, and inert in the hands of human beings who decide upon their death. Accepting moral compromises and justifying the condition of people completely bereft of any dignity and literally left in the hands of others who can do whatever they please would mean going back to the time of slavery and mass exterminations, when the agonies and barbarities of torture were not only tolerated, but even imposed and justified as natural rights of the strongest. It would be like betraying humanity, its efforts, and the sufferings endured in order to step out of a condition ruled only by the law of the strongest. Those who try to relativize torture by allowing for its limited use against terrorists do not understand that crimes against humanity include also those concerning terrorism, and even terrorists regard human beings as naked life, to be destroyed for their own purposes. Nevertheless, one abomination (terrorism) does not justify another (torture).

The other major issue that has been raised with increasing force, especially after 9/11, concerns the role that torture could play to extort information from a terrorist who knows where and when a bomb has been placed to explode among the crowd, thus preventing a slaughter. What if many innocent lives could be saved from an attack, thanks to a confession extorted by violence? Undoubtedly, this is a serious and complex issue. These questions pose inevitable ethical dilemmas, but, at the same time, they do not prove what they planned to, namely, that the rule of law, in these cases, is powerless and, therefore, its principles have to be curtailed to the benefit of security. The presence of grave and imminent dangers for oneself and others justifies the acts that are deemed necessary to prevent them, including what would otherwise be serious crimes, not only morally but also legally. This is based on the principle of the "state of necessity," which is common to all legal systems. Therefore, it is totally useless, in these cases, to call for legality to be suspended or mitigated. However, these questions tend to justify another one: they talk about violence to foil present and certain dangers (because of which the legal system does not need to be modified) and aim at justifying violence as a tool for inquisition to extort information and bring about confessions to be used during trials. Violence as defense caused by pressing actual circumstances is one thing, yet it is another as a device to carry out police investigations. But is torture really effective

for the latter purpose? Historically, the likely gray and ambiguous areas have been extremely significant.

The notorious manual on interrogations, "Kubark manual," compiled by the CIA back in 1963 and declassified in 1977, made one thing clear to everyone: regardless of the drug or pseudo-scientific method used during interrogations, their outcomes were different for every subject. It was important for US experts to define specific personality types and find out what methods worked best for each of them, but the division into categories or groups of prisoners was a ridiculous approximation. The categories were useless, as each person and each situation are different. The "Kubark manual" indirectly confirmed the risk that torture set free those terrorists who were particularly strong while condemning weak innocents, as Verri or Beccaria had claimed. Saint Augustine himself motivated the denunciation of torture by shifting the attention of the debate from the unreliability of the findings to the unacceptability of torture at a juridical and philosophical level. In *De Civitate Dei*, he made reference to the inequality between a generic allegation with insufficient evidence to prove the guilt of a defendant and the painful reality of the corporal punishment inflicted in order to fill, through that procedure, the gap of doubt and uncertainty that made conviction possible [25]. This reversed the rationale, as the punishment inflicted became a direct consequence of the inadequate evidence:

He is tortured to discover whether he is guilty, so that, though innocent, he suffers most undoubted punishment for crime that is still doubtful, not because it is proved that he committed it, but because it is not ascertained that he did not commit it. Thus the ignorance of the judge frequently involves an innocent person in suffering.

Beccaria, too, was against the use of torture as an instrument of inquisition and evidence and regarded it as an expression of a force that was legitimated by law, as he stated that "No man can be judged a criminal until he be found guilty; nor can society take from him the public protection until it have [*sic*] been proved that he has violated the conditions on which it was granted. What right, then, but that of power, can authorize the punishment of a citizen so long as there remains any doubt of his guilt?" [12].

Torture would not only absolve but also give value to violence and sadism that debase the victims and all the more the perpetrators; it entails that people are illegally taken and segregated in secret detention places (the "black holes"); it requires "experts" trained in the technical use of violence; it needs special courts, trials without audience, and defendants without any defense and faced with "evidence" obtained through inquisition methods; it often ends with the physical elimination of the subjects at the end of the procedures, when they are no longer useful: all these implications show how absurd and dangerous it is to accept "torture with legal guarantees."

The purposes would thus be perverted: torture, justified by security reasons, would end up instilling violence and terror; those who were not terrorists before are likely to become such afterward. Torture seems to aim precisely at increasing hatred, spreading it also among those who did not feel it, and turning it against those who brought it up. It is true that, when flags are waved and trumpets are played, minds are no longer able to think rationally.

Zagrebelsky concludes by saying "It is an immoral stupidity. Yet there are people who do not withdraw, scared, when faced with the idea of a power with license to torture, perhaps because they believe, either consciously or unconsciously, that this will not concern themselves or their beloved ones, but just the 'others', people like them, but of other ethnic groups, creeds, or political beliefs. It is just under these terms that 'cold' speeches can be delivered about violence and its usefulness. If this is the case, we should realize that behind the apology of torture there is a false notion: it is a matter of security, as much as of racist, religious, class, or ideological discrimination. Thus an even more ominous light would ignite" [21].

## 20.6 Laws of Torture in Italy: Between Hypocrisies and Lack of Interest

Italy ratified the United Nations Convention against torture in 1988. The obligations to be fulfilled following the ratification included the immediate introduction of a specific crime of torture in the Italian criminal code [26].

This obligation has explicitly been pointed out to the Parliament by *Amnesty International* since 1992. Italy is not beyond suspicion, as shown by annual reports and other periodic documents published, in particular, by Amnesty International: abuses are reported to this organization on an annual basis, and in some cases, they emerge as torture proper. Between 2002 and 2004, most of these cases concerned blows and beatings during demonstrations, inside police and *Carabinieri* stations, and, increasingly, in centers for the reception of foreigners.

Concerns were also raised by the treatment of convicts in some prisons; there have been striking cases, such as the beating that occurred in the "San Sebastiano" jail in Sassari in April 2000. Following this event, the judge for the preliminary hearing, who examined the position of the defendants who had chosen the summary trial, delivered sentences ranging from a fine to an 18-month sentence. Serious events also took place in the detention facility in Bolzaneto (July 2001), as a result of which a trial started, despite considerable difficulties, with 47 defendants including police officers and physicians, alongside 28 policemen involved in the night raid on the "Diaz" school. This is a key occasion to look for the truth and trigger a wider debate in Italy on institutionalized violence and torture.

Faced with such cases, the reaction of Italian institutions is undoubtedly inadequate. The poor outcomes of the trials, also as a result of the mild charges, further show that the present system does not work properly. Many organizations, such as *Medici contro la Tortura* and *Amnesty International*, have frequently voiced their concerns about the fact that different penal procedures, concerning alleged abuses by police and prison officers, were excessively long and, in some cases, the relevant investigations were not exhaustive enough. In addition, when law enforcement officers were deemed responsible of abuses suffered by convicts, sentences were often symbolic.

The Law introducing the crime of torture in the Italian Penal Code was approved just in 2017 (Law 110/2017) and considered crime both of torture and of incitement to torture [27].

The UN Committee expressed its "concern about the detention policy applied to asylum seekers and other non-citizens, also based on reports by which these people often have to face long detention periods in Temporary Stay Centres (*Centri di Permanenza Temporanea*—CPT)."

## 20.7 Toward a Law on the Right to Asylum in Italy

Italy still has no organic law on the right to asylum. Yet a major step forward was taken on November 9, 2007, thanks to the decrees that implemented two European Directives, namely, 2004/83/CE and 2005/85/CE, on the procedures and recognition of the refugee status. These decrees abolish the role of filter currently played by the police and police headquarters, which will now have to accept the applications of asylum seekers in any case, while the assessments will be carried out by the territorial commissions.

In addition to "humanitarian protection," there will be "subsidiary protection" for those who would risk suffering "serious harm" if they returned to their countries of origin, although they are not eligible for asylum. Both protections will entitle to 3-year residence permit, reunification, and engagement in employed and self-employed activities, as well as to the enrolment in professional boards. The refugee permit will last 5 years instead of 2 and will also grant access to public employment under the same terms as EU citizens.

At the moment, all the patterns of the arrivals seem to have radically changed, as increasingly more complex routes are adopted: Libya-Lampedusa-Sicily, Egypt-Sicily, and Turkey-Calabria.

The project named SPRAR (*Sistema di protezione per richiedenti asilo e rifugiati*, i.e., Protection System for Asylum Seekers and Refugees) has been joined by more than 100 municipalities and coordinated the reception activities of local bodies.

How can we assert the superiority of the Western world, if any war—localized, ethnic or not, inter-African, and inter-European—uses military technology and weapons banned or not

by the Geneva Convention, devised and produced in highly civilized Europe or in the USA, China, and Russia?

It is the same old paradox. When it comes to declaring important, basic principles and uttering noble statements, no institutional representative steps back, especially under the spotlight of the mass media. When it comes to reassembling characters and life stories already destroyed and when it comes to giving hope and trust back to the victims of war, ideological oppressions, and racial discriminations, we are alone, terribly alone, without any facilities, without any investments, and, in particular, without any network, constantly running the risk of burn-out, solitude, and bitterness.

What happens to asylum seekers, refugees, and torture victims when their applications are rejected? What happens to their lives?

The percentage of rejected applications out of those submitted in 2006 was 40.3%, while 44.5% were rejected yet with humanitarian protection. Months of anguish and commitment pass, in order to organize thoughts, testimonies, and evidence of the life threats at home, as well as of the brutalities and persecutions suffered; yet it often happens that the future is lost during the few minutes of the interview in which it is impossible to "persuade" the commission of the risks. After some time, the letter, notifying refusal, arrives.

Now, the current Italian "Yellow-Green" Government (President of the Council of the Ministers Giuseppe Conte, Minister of Internal Affairs Matteo Salvini) aims to limit the access to the recognition of asylum seeker or refugee and invokes the national security as an excuse to close SPRAR and to not receive people migrants.

The asylum seeker people in Italy are 95,000 in 2018, but the 66% of the requests are rejected, with the peak of 82% at December 2018. Currently, the refugees and the asylum seekers in the world are 68,500,000.

## 20.8 Some Critical Situations

### 20.8.1 Afghanistan

The UNAMA (UN Assistance Mission in Afghanistan) report stressed as conflict-related detainees in Afghanistan continue to face torture and ill-treatment in government detention facilities. The report also says that the Government of Afghanistan has committed to fully eliminating the practice according to the national plan promulgated in 2015, as reported by Tadamichi Yamamoto, the Secretary-General's Special Representative for Afghanistan [28].

The report by the UNAMA and the OHCHR (UN Human Rights Office) is based on interviews with 469 conflict-related detainees conducted from January 1, 2015, to December 31, 2016, in 62 detention facilities administered by the National Directorate of Security (NDS), Afghan National Police (ANP), and other Afghan National Defense and Security Forces (ANDSF) across the country.

Among other findings, 45% of those interviewed who had been detained by police said they had been tortured or ill-treated—the highest level documented since UNAMA began its current monitoring program in 2010. Of 85 child detainees interviewed, 38 gave credible accounts of being subjected to torture or ill-treatment while in the custody of the Afghan security forces.

Overall, the majority of detainees said they had been tortured to force them to confess and that the torture and ill-treatment stopped once they did so. "Many of those interviewed stated that they did not understand or could not read what was written on the 'confession' which they signed or thumb-printed," the report notes.

"As this important report makes clear, torture does not enhance security. Confessions produced as a result of torture are totally unreliable. People will say anything to stop the pain," said UN High Commissioner for Human Rights Zeid Ra'ad Al Hussein. "It is essential that there is proper monitoring of detention facilities in Afghanistan and meaningful investigations to ensure that those accused of torture are brought to trial and held accountable for this abhorrent crime. Ensuring accountability for such acts sends a strong message and helps to prevent future violations," he added.

The report contains several key recommendations from UNAMA to the Government of Afghanistan, focusing on compliance (prohibition of torture), accountability (prompt impartial,

independent, and thorough investigations of all reports of torture or ill-treatment), effective remedy (access to an effective domestic legal remedy and reparation), prevention (establishment of National Preventive Mechanism foreseen under the *Optional Protocol on the Prevention of Torture*), and training and capacity building (technical skills to carry out detection, investigation, and prosecution of conflict-related crimes in accordance with international human rights standards) [28].

### 20.8.2 Libya

Libya has long been a destination for migrants seeking work as well as a transit country for migrants, asylum seekers, and refugees seeking to reach the EU. People with different backgrounds and motivations travel together along the same routes, often with the help of ruthless people, smugglers, and criminal gangs. They include refugees, asylum seekers, economic migrants, unaccompanied minors, environmental migrants, victims of trafficking, and stranded migrants, among others.

A study of mixed refugee and migrant flows by UNHCR, the UN Refugee Agency, has found that around half of those traveling to Libya do so believing they can find jobs there, but end up fleeing onward to Europe to escape life-threatening insecurity, instability, difficult economic conditions, plus widespread exploitation and abuse.

In recent years, the number of people crossing by sea from North Africa to Southern Europe has increased. The indications are that this trend is likely to continue. Of the three main routes used by refugees and migrants to reach Europe—the Western Mediterranean route, the Central Mediterranean route, and the Eastern Mediterranean route—Libya has become the most commonly used one and also the deadliest.

The study commissioned by UNHCR found that the profiles and nationalities of people arriving in Libya have been evolving over the past few years, with a marked decrease in those originating in East Africa and an increase in those from West Africa, who now represent well over half of all arrivals to Europe through the Central Mediterranean route from Libya to Italy (over 100,000 arrivals in 2016).

Refugees and migrants in Libya are predominantly young men (80%), aged 22 on average, and traveling alone (72%). Women tend to transit toward Europe over a short period of time, and many of them, particularly those from West and Central Africa, are victims of trafficking. The number of unaccompanied and separated children traveling alone is rising and now represents 14% of all arrivals in Europe via the Central Mediterranean route. These children come mainly from Eritrea, The Gambia, and Nigeria.

Refugees and migrants in Libya tend to have a low level of education, with 49% having little or no formal education and only 16% having received vocational training or higher education. They come mainly from Niger, Chad, Sudan, Egypt, and Tunisia. Most of them travel to Libya for economic reasons, and many engage in seasonal, circular, or repetitive migrations. Nationals of West and Central Africa countries are mainly from Nigeria, Guinea, Côte d'Ivoire, Gambia, Senegal, Ghana, Mali, and Cameroon. They report having left largely for economic reasons. Some are victims of trafficking, in particular Nigerian and Cameroonian women, and some might be in need of international protection.

People of Eastern Africa countries are from Eritrea, Somalia, Ethiopia, and Sudan, making the journey for political persecution, conflict, and poverty.

Individuals from other regions are Syrians, Palestinians, Iraqis, Moroccans, and Bangladeshis. Some flee conflict and violence, while others are looking for livelihood opportunities.

In addition to Libya's strategic location, the conflict and instability in the country have contributed to create an environment where human smuggling and criminal networks flourish. At the same time, the collapse of the justice system has led many armed groups, criminal gangs, and individuals to participate in the exploitation and abuse of refugees and migrants [29].

Human Rights Watch stated without compromise that European Union policies contribute to a cycle of extreme abuse against migrants in Libya.

The EU and Italy's support for the Libyan Coast Guard contributes significantly to the interception of migrants and asylum seekers and their subsequent detention in arbitrary, abusive detention in Libya.

In July 2018, Human Rights Watch researchers visited four detention centers in Tripoli, Misrata, and Zuwara where they documented inhumane conditions that included severe overcrowding, unsanitary conditions, poor-quality food and water that has led to malnutrition, lack of adequate healthcare, and disturbing accounts of violence by guards, including beatings, whippings, and use of electric shocks.

Migrant children are as much at risk as adults of being detained in Libya. Human Rights Watch witnessed large numbers of children, including newborns, detained in grossly unsuitable conditions in Ain Zara, Tajoura, and Misrata detention centers [30]. They and their caretakers, including breast-feeding mothers, lack adequate food. Healthcare for children, as for adults, is absent or severely insufficient. There are no regular, organized activities for children, play areas, or any kind of schooling. Almost 20% of those who reached Europe by sea from Libya in the first 9 months of 2018 were children under the age of 18 years. Because it is indefinite and not subject to judicial review, immigration detention in Libya is arbitrary under international law.

Already in November 2017, EU migration commissioner Dimitri Avramopoulos said "We are all conscious of the appalling and degrading conditions in which some migrants are held in Libya." He and other senior EU officials have repeatedly asserted that the EU wants to improve conditions in Libyan detention in recognition of grave and widespread abuses. However, Human Rights Watch interviews with detainees, detention center staff, Libyan officials, and humanitarian actors revealed that EU efforts to improve conditions and treatment in official detention centers have had a negligible impact.

Instead, EU is providing support to the Libyan Coast Guard to enable it to intercept migrants and asylum seekers at sea; they take them back to Libya to arbitrary detention, where they face inhuman and degrading conditions and the risk of torture, sexual violence, extortion, and forced labor.

Since 2016, the EU has intensified efforts to prevent boat departures from Libya. EU policymakers and leaders justify this focus as a political and practical necessity to assert control over Europe's external borders and "break the business model of smugglers." Italy, the EU country where the majority of migrants departing Libya arrive, has taken the lead in providing material and technical assistance to the Libyan Coast Guard and abdicated virtually all responsibility for coordination of rescue operations at sea in a bid to limit the number of people arriving on its shores.

While Mediterranean departures have decreased since mid-2017, the chances of dying in waters off the coast of Libya significantly increased from 1 in 42 in 2017 to 1 in 18 in 2018, according to UNHCR.

Clashes in Tripoli between competing armed groups in August–September 2018 presented further problems and risks for detained migrants. During the clashes, which illustrated the Government of National Accord's fragile hold on power and caused civilian deaths and destruction to civilian structures, guards abandoned at least two detention centers as fighting drew near, leaving detainees unprotected inside. Authorities eventually transferred hundreds to other detention centers in the capital, contributing to even greater overcrowding in those centers. The current (Spring 2019) very serious political and military status in Libya represents further risk for the safety of detained migrants and for all the people trapped in Libya during the journey toward Europe and other countries.

Since the end of 2017, the UNHCR and the International Organization for Migration (IOM), also a UN agency, have accelerated EU-funded programs to help asylum seekers and migrants safely leave Libya, a country with no refugee law and no asylum system [31]. By the end of November 2018, UNHCR had evacuated 2069 asylum seekers from Libya to a transit center in Niamey, Niger, for refugee status determination and, ultimately, resettlement to Europe and other

countries. However, the program suffers from UNHCR's limited capacity and mandate in Libya as well as from a gap between the number of resettlement places and the number of refugees in need.

The IOM had assisted over 30,000 to return from Libya to their home countries through its "voluntary humanitarian program" between January 2017 and November 2018. While the program can be valuable in assisting people without protection needs who wish to return home safely, it cannot be described as truly voluntary as long as the only alternatives are the prospect of indefinite abusive detention in Libya or a dangerous and expensive journey across the Mediterranean.

However, at July 2018, there were between 8000 and 10,000 people in official detention centers, up from 5200 in April 2018.

In addition to the migrants and asylum seekers in official detention, the UN estimates that more than 680,000 migrants and asylum seekers live in Libya outside detention, while an unknown number are held in warehouses and other informal detention centers operated by smuggling networks and militias. The UN refugee agency UNHCR had registered 55,912 asylum seekers and refugees in Libya, primarily from Syria, Iraq, and Eritrea, as of mid-October 2018.

Human Rights Watch has documented abuses by smugglers, militias, and criminal gangs against migrants in Libya for over a decade, including rapes, beatings and killings, kidnapping for ransom, sexual exploitation, and forced labor.

There is significant evidence that smugglers operate in varying degrees of collusion with government officials and militias. In September 2018, the UNHCR reiterated its call on all countries "to allow civilians (Libyan nationals, former habitual residents of Libya, and third-country nationals) fleeing Libya access to their territories." The refugee agency urged all countries to suspend forcible returns to any part of Libya, including anyone rescued or intercepted at sea, and stated that Libya should not be designated as a "safe third country" for the purpose of rejecting asylum applications from people who have transited Libya. UNHCR has not, however, taken a clear position on EU capacity-building programs for the Libyan Coast Guard. Foreigners, regardless of age, without authorization to be in Libya are detained on the basis of laws dating back to the Gaddafi era that criminalize undocumented entry, stay, and exit punishable by imprisonment, fines, and forced labor.

The EU has allocated €266 million from the EU Emergency Trust Fund for Africa for migration-related programs in Libya and an additional €20 million through bilateral assistance. EU financial assistance has supported positive efforts including training, improved registration of migrants and asylum seekers, and help getting a limited number of people out of abusive detention. Nevertheless, this funding has not helped to diminish the widespread and systematic violence and abysmal conditions in migrant detention centers. Building the capacity of the Libyan Coast Guard and Navy is a central plank in the EU's containment policy. The EU's anti-smuggling operation EUNAVFOR MED, also known as "Operation Sophia," included a training program, begun in October 2016, for Libyan Navy and Coast Guard officers, petty officers, and sailors at least nominally under the Libyan Government of National Accord's Defense Ministry. As of June 2018, 213 Libyan Coast Guard and Navy personnel had participated in training courses, out of 3385 total personnel. However, a classified 2018 report from the EU's Border Assistance Mission to Moldova and Ukraine (EUBAM) in Libya indicated that LCG staff includes an "unknown number" of former revolutionary fighters. None of them had any training at all, according to the report.

Italy has taken the lead in EU efforts to build the capacity of Libyan authorities to secure Libya's borders and patrol the Mediterranean. Italy has deep historical, political, and economic ties with the country and engaged in significant migration cooperation agreements with the Gaddafi government. The majority of migrants and asylum seekers departing Libya reach Italian shores. More than any other EU country, Italy is investing significant material and political resources to enable and legitimize Libyan authorities to intercept and subsequently detain anyone trying to leave the country by sea.

Italy is carrying out an EU-funded project to assist Libya in setting up a maritime rescue coordination center (MRCC), which is expected to be operational in 2020. In the meantime, a Libyan operations room has been set up aboard an Italian Navy ship docked in Tripoli. The Libyan Coast Guard does not have capacity to provide continuous coverage or rapid response in every case of distress in the entire area that Libya unilaterally delineated as its search and rescue zone. Libyan units have inadequate and insufficient boats, chronic maintenance problems, and fuel shortages that limit their ability to patrol even Libyan territorial waters and quickly reach boats in distress. Relying heavily on technical and surveillance assistance from Italy, the LCG increased the number of interceptions in the first half of 2018. The LCG intercepted 12,490 people in the first 7 months of 2018, a 41% increase over the same period in 2017. By the end of 2018, the LCG had intercepted 15,235 people according to UNCHR data, a slightly lower number than in the preceding year.

In June 2018, the International Maritime Organization (IMO), a UN inter-governmental organization, acknowledged a vast Libyan SAR (Search and Rescue) region. In April 2018 a senior IMO official argued that coordination among MRCCs was sufficient and that "you can't make a blanket statement that Libya is not a place of safety" under the terms of existing maritime law. He explained that the IMO's role was to register declared SAR regions when the declaration is in conformity with IMO stipulations and is agreed to by neighboring states.

Statistical analysis carried out by the Italian Institute for International Political Studies (ISPI) on the basis of IOM and UNHCR data demonstrates that the rate of deaths at sea compared to the number of people attempting the voyage rate surged in the absence of NGO rescue patrols from 2.3% to 7%. Moreover, some interviewees described acts of intimidation or violence by members of the Coast Guard during interceptions.

Children represent a small but particularly vulnerable part of the migrant population in Libya, in detention centers, and on the sea crossing. A UNICEF survey among children along the Mediterranean migration route through Libya found that 75% reported experiencing violence, harassment, or aggression by adults. Most reported verbal and emotional abuse; half reported physical abuse. Almost 20% of those who reached Europe by sea from Libya in the first 9 months of 2018 were children under the age of 18 years [32].

Exposure to the harsh conditions in detention, in addition to traumas experienced in their home countries and along the migration journey including abuses by smugglers and traffickers, can have a profound impact on children's mental health (see "Post-traumatic Stress Disorder").

In March 2018, the IOM tracked 29,370 unaccompanied children in Libya but said the real figure could be "much higher." UNICEF, IOM, and UNHCR established in 2018 a protocol for joint protection of unaccompanied children in Libya. The agencies set up a Best Interest Determination (BID) panel to address particularly complex cases of children outside detention.

Article 16 of the International Law Commission's Articles of Responsibility of States for Internationally Wrongful Acts provides that a state is accountable for human rights violations if it knowingly aids or assists another state to commit abuses. Explanatory notes clarify that assistance can trigger state responsibility if it contributes "significantly" to the commission of a wrongful act and when a state provides material aid subsequently used to commit human rights violations. Providing substantial assistance to the Libyan Coast Guard units to intercept people in international waters, when it is known that they will return those people to cruel, inhuman, or degrading treatment in arbitrary detention in Libya or, for children, where there are substantial grounds for believing that there is a real risk of irreparable harm, can constitute aiding or assisting in the commission of serious human rights violations.

Nils Melzer, UN special rapporteur on torture, has noted that "any participation, encouragement, or assistance provided" for pullback operations leading to exposure to the real risk of torture and ill-treatment "would be irreconcilable with a

good faith interpretation and performance of the prohibition of torture and ill-treatment, including the principle of non-refoulement." Melzer has also said that "If European countries are paying Libya to deliberately prevent migrants from reaching the safety of European jurisdiction, we're talking about complicity in crimes against humanity because these people are knowingly being sent back to camps governed by rape, torture and murder."

The EU and some of its member states, in particular Italy, are providing substantial support to Libyan authorities to enable them to intercept migrants seeking to leave Libya by sea. The support is given with the purpose of enhancing the capacity of Libyan authorities to intercept such migrants. The support comes in the form of equipment, funding, training, surveillance, intelligence, and coordination assistance. The EU and states including Italy know that migrants intercepted by Libyan authorities who are returned to detention in Libya are arbitrarily held in inhumane conditions, at risk of further prohibited abuses. Indeed, they acknowledge this in providing funds to ameliorate conditions in detention, but such funds have had minimal impact on the situation.

Stricter standards apply for children, including a prohibition on the detention children for migration-related reasons. The Committee on the Rights of the Child has reaffirmed time and again that children should not be detained on the basis of their or their parents' migration status. The absolute prohibition on torture and cruel, inhuman, or degrading treatment in international law is articulated in multiple treaties by which Libya is bound, in particular the UN Convention Against Torture (CAT), the Convention on the Rights of the Child, the African Charter on Human and Peoples' Rights, and the International Covenant on Civil and Political Rights (ICCPR) [33–35].

The Nelson Mandela Rules, the revised UN Standard Minimum Rules for the Treatment of Prisoners, call for, among other things, a limit to the number of people held in a room, depending on its size, appropriate sleeping arrangements, adequate facilities for personal hygiene, clothing and bedding, adequate food, and access to medical services. Women should be held in premises entirely separate from men and guarded by female staff. UN rules specifically for children in deprived of their liberty stipulate that children should never be detained with adults [36, 37].

The UNHCR guidelines, in conjunction with the UN Rules for the Treatment of Women Prisoners and Non-custodial Measures for Women Offenders, stipulate that facilities should accommodate women's specific hygiene needs, including the provision of sanitary pads, and ensure safeguards against sexual and gender-based violence. The use of female guards should be promoted, and there should clear remedies and protection measures for women in detention who report abuse. As a general rule, pregnant women and nursing mothers should not be detained. Survivors of sexual violence should have access to appropriate medical and psychological care, including pregnancy tests [29, 30].

### 20.8.3 Greece Experience

Doctors in Greece face the possibility of encountering a person that has suffered torture, especially since the high rates of refugees and migrants inflows that took place over the last years [38].

### 20.8.4 USA

"The USA government does not torture anybody. We respect the law and our international obligations," declared George Bush, former US President, during an unexpected speech delivered at the White House Oval Office, on Friday, October 5, 2007. After widespread accusations following *The New York Times* revelations on secret authorizations given by the former Justice Secretary, George Bush tried to defend his detention procedures and his administration's methods of interrogating terror suspects.

On Thursday, October 4, 2007, *The New York Times* newspaper revealed two top-secret Justice Department briefs dated 2005 [39]. In the first

one, then US Attorney General Alberto Gonzales, very loyal to Bush, authorized using head slaps, simulated drowning known as waterboarding, and freezing temperatures (below 0 °C) during the interrogation of terror suspects; these were a clear denial of the administration's official position, which in December 2004 defined torture as "detestable." The other brief confirmed the former, because it affirmed that CIA interrogation methods did not violate the law banning "cruel, inhuman, and degrading treatments."

In 2004, it was necessary to see the horrifying images of the Abu Ghraib prisoners in the media, to dramatically understand that torture, revenge, and use of inhuman and degrading actions are still relevant in our lives.

### 20.8.5 Argentina

Argentina is very sensitive to torture and violence. Plaza de Mayo is still the evidence of the mothers and grandmothers who, for many years, bravely struggled against the Argentine generals' dictatorship who turned torture, kidnapping, and murder into a daily practice, thanks to the silence of the governments of many, too many, world countries. Millions of Argentines who lost their *desaparecidos* mothers, wives, brothers, sisters, and children will remember General Videla as the perverse example of wickedness. This *Homo sapiens/demens* is so great in studies and scientific research, yet so contemptible in the use of scientific and torture techniques, implemented to destroy the lives and dignity of people, sometimes also with the involvement of physicians.

## 20.9 Post-traumatic Stress Disorder (PTSD)

Loss of social structures, cultural values, community rituals, relationships, and material features were experienced by forced migrants. Meeting the healthcare needs of those affected can help achieve safety and rehabilitation [40].

Individuals who have experienced multiple traumatic events in their home country, in transition to, and within the hosting country undergo elevated levels of stress linked with unmet basic needs and uncertainty about their own future and the safety of loved ones. Traumatic experience includes landmines, torture, or violent trauma, which may result in long-term disability.

Psychosocial stressors, experienced by many forced migrants, can increase pain intensification and sensitivity. Although somatic symptoms may be caused by underlying stress, it is important to rule out other causes. For example, headaches could be due to a neck injury, post-concussion syndrome, traumatic brain injury, or post-traumatic epilepsy, and abdominal pain could be a consequence of *H. pylori* disease or sexual assault. Integrating physical, psychological, sociological, and cultural models into a therapeutic approach to chronic pain and weakness (massage, physiotherapy, non-steroidal analgesics, and training in self-help techniques) can help with pain management [41].

These experiences cause huge personal losses, which are a major threat to identity. Accordingly, refugees and asylum seekers have higher rates of mental health conditions, particularly PTSD, anxiety, depression, and psychoses [42].

PTSD is a mental health condition triggered by a terrifying event—either experiencing it or witnessing it. Symptoms may include flashbacks, nightmares, and severe anxiety, as well as uncontrollable thoughts about the event. Most people who go through traumatic events may have temporary difficulty adjusting and coping, but with time and good self-care, they usually get better. If the symptoms get worse, last for months or even years, and interfere with day-to-day functioning, he/she may have PTSD.

Post-traumatic stress disorder symptoms may start within 1 month of a traumatic event, but sometimes symptoms may not appear until years after the event. These symptoms cause significant problems in social or work situations and in relationships. They can also interfere with the ability to go about your normal daily tasks.

PTSD symptoms, varying over time or from person to person, are generally grouped into four

types: intrusive memories, avoidance, negative changes in thinking and mood, and changes in physical and emotional reactions.

Symptoms of *intrusive memories* may include:

- Recurrent, unwanted distressing memories of the traumatic event
- Reliving the traumatic event as if it were happening again (flashbacks)
- Upsetting dreams or nightmares about the traumatic event
- Severe emotional distress or physical reactions to something that reminds of the traumatic event

Symptoms of *avoidance* may include:

- Trying to avoid thinking or talking about the traumatic event
- Avoiding places, activities, or people that remind you of the traumatic event

Symptoms of *negative changes* in thinking and mood may include:

- Negative thoughts about yourself, other people, or the world
- Hopelessness about the future
- Memory problems, including not remembering important aspects of the traumatic event
- Difficulty to maintaining close relationships
- Feeling detached from family and friends
- Lack of interest in activities you once enjoyed
- Difficulty experiencing positive emotions
- Feeling emotionally numb

Symptoms of *changes in physical and emotional reactions* (also called arousal symptoms) may include:

- Being easily startled or frightened
- Always being on guard for danger
- Self-destructive behavior, such as drinking too much or driving too fast
- Trouble sleeping
- Trouble concentrating
- Irritability, angry outbursts, or aggressive behavior
- Overwhelming guilt or shame

For children 6 years old and younger, signs and symptoms may also include:

- Re-enacting the traumatic event or aspects of the traumatic event through play
- Frightening dreams that may or may not include aspects of the traumatic event

PTSD symptoms can vary in intensity over time, also depending on environmental condition. Post-traumatic stress disorder can disrupt whole life, relationships, health, and enjoyment of everyday activities.

Having PTSD may also increase risk of other mental health problems, such as:

- Depression and anxiety
- Issues with drugs or alcohol use
- Eating disorders
- Suicidal thoughts and actions

The occurrence of PTSD in people refugees or asylum seekers affects in turn their ability to cope with the difficulties depending on unknown language, environment, laws, and habits of the countries of arrival. Moreover, considering the duration of the journey, it is possible the occurrence of the PTSD even in the transit country impairing the overall ability of the people to gain the final country. Finally, PTSD may further compromise the health and the life of the affected people because it impairs just the memories of the traumatic accident (frequently abuse or torture) even during the interview with physician or UN worker, lowering the possibility of obtaining the status of refugee. The rejected application will further affect the health and life itself of asylum seeker.

The conflict and forced migration disrupt several core elements, according to the ADAPT model: safety and security, interpersonal bonds and networks, justice, roles and identities, and existential meaning and coherence.

Depression among forced migrants is closely linked with poor social support, as well as with immigration processes, racial discrimination, and homelessness. A systematic review of the mental health implications of detaining asylum seekers

confirms that child, adolescent, and adult immigration detainees experience high levels of anxiety, depression, post-traumatic stress, self-harm, and suicidal ideation.

As already underlined, the events able to make refugees vulnerable to develop mental disorders may occur before or during migration.

Traumatic events experienced before migration may be related to exposure to war, persecution, or economic hardship and account for the decision to leave their home. Refugees can be exposed to war directly or indirectly, witnessing destruction and death, or have had traumatic experiences including torture and personal combat involvement. Persecution for political, ethnic, religious, or other reasons may involve torture, imprisonment, violations of human rights of the person, or death of family members. The psychological consequences of torture are more evident when the people fear for their life or if torture is enduring for a long time. Refugees may also have experienced extreme levels of poverty and economic hardship, including a lack of food, water, shelter, and other basic needs and resources. During migration many refugees have traveled in unsafe boats or in enclosed trains or trucks and may have walked on dangerous land routes. During their journey refugees have frequently experienced physical harm, sexual violence, infectious diseases, extortion, and human trafficking. Finally, displacement in itself is a risk factor for mental health.

Poor social integration will worsen risk for PTSD. In some cases, forced separation from family members and support networks occurs during migration or after resettlement, which further reduces social support for some refugees. This is particularly relevant for children and adolescents. The social isolation is linked with the poor acculturation, the cultural changes due to moving from one culture to another. This concerns mainly the refugees who have not chosen the country where they are displaced. The unemployment is itself a risk for mental disorders.

Refugees frequently encounter difficulties in accessing healthcare. This can result in delayed diagnostic assessments and treatments of mental disorders, which can then lead to a deterioration or chronicization of the condition.

Moreover, experiences of persecution before migration and fear of being reported to authorities in the host country may lead refugees—particularly asylum seekers and irregular migrants—to avoid accessing care or mistrust services and clinicians [43].

## 20.10 Self-Harm

In the literature, deliberate self-harm is often used interchangeably with the term "non-suicidal self-injury" (NSSI) and indicates the intentional injuring of own body without suicidal intentions. However, in some instances the term also includes possible suicidal intentions. Epidemiology of suicidal ideation, suicide attempts, and direct self-injurious behavior in adolescents with a migration background reported a higher prevalence of all three investigated variables than adolescents without a migration background.

Female adolescents reported a higher prevalence of suicidal ideation, suicide attempts, and direct self-injurious behavior [44].

## 20.11 How to Approach the People Alleged Victim of Torture

Physicians are involved in the investigation of torture or ill-treatment. They must act at all times in conformity with the highest ethical standards and, in particular, must obtain informed consent before any examination. The examination must conform to established standards of medical practice. In particular, it must be conducted in private under the control of the medical expert and outside the presence of security agents and other government officials. The medical expert should promptly prepare an accurate written report. This report should include at least the following items:

(a) The circumstances of the interview. The name of the subject and name and affiliation

of those present at the examination; the exact time and date, location, nature, and address of the institution (including, where appropriate, the room) where the examination is being conducted (e.g., detention center, clinic, house, etc.); and any appropriate circumstances at the time of the examination (e.g., nature of any restraints on arrival or during the examination, presence of security forces during the examination).

(b) The background. A detailed record of the subject's story as given during the interview, including alleged methods of torture or ill-treatment, the time when torture or ill-treatment was alleged to have occurred, and all complaints of physical and psychological symptoms.

(c) A physical and psychological examination. A record of all physical and psychological findings upon clinical examination including appropriate diagnostic tests and, where possible, color photographs of all injuries.

(d) An opinion. An interpretation as to the probable relationship of physical and psychological findings to possible torture or ill-treatment. A recommendation for any necessary medical and psychological treatment or further examination should also be given.

(e) A record of authorship. The report should clearly identify those carrying out the examination and should be signed. The report should be confidential and communicated to the subject or his or her nominated representative. The report should be provided in writing, where appropriate, to the authority responsible for investigating the allegation of torture or ill-treatment. It is the responsibility of the state to ensure that the report is delivered securely to these persons.

Because of the possible devastating sense of powerlessness, it is particularly important to show sensitivity to the alleged torture victim and other witnesses. The state must protect alleged victims of torture, witnesses, and their families from violence, threats of violence, or any other form of intimidation that may arise pursuant to the investigation.

Investigators should explain to the person the part of the procedure that will be public or confidential.

Special consideration should be given to the victim's preference for a person of the same gender, the same cultural background, or the ability to communicate in his or her native language. Consequently, this preferred person will be the referent for the alleged person victim of torture. If people are still imprisoned or in similar situations in which reprisals are possible, the interviewer should use care not to put them in danger. In situations where talking to an investigator may endanger someone, a "group interview" may be preferable to an individual interview. In other cases, the interviewer must choose a place for the private interview where the witness feels comfortable to talk freely.

Sufficient time should be allotted to interview the alleged torture victim. It is usual that not full story is reported during the first interview. The investigator must be sensitive in tone, phrasing, and sequencing of questions, given the traumatic nature of the alleged victim's testimony. The witness must be told of the right to stop the questioning at any time, to take a break if needed, or to choose not to respond to any question.

Most people consider sexual assault as meaning actual rape or sodomy. Verbal assaults, disrobing, groping, lewd or humiliating acts, or blows or electric shocks to the genitals are often not taken by the victim as constituting sexual assault. These acts all violate the individual's intimacy and should be considered as being part of sexual assault.

Very often, victims of sexual assault will say nothing or even deny any sexual assault. It is often only on the second or even third visit, if the contact made has been empathic and sensitive to the person's culture and personality, that more of the story will come out.

People may report physical injuries sustained in the course of the torture, and they may provide a description of weapons or other physical objects used. It is relevant to identify witnesses to the events. However, the investigator must use care in protecting the safety of witnesses. The investigator must encourage the person to use all

his/her senses in describing what has happened to him or her. Moreover, it is useful to ask what he or she saw, smelled, heard, and felt. This is important in situations where the person may have been blindfolded or experienced the assault in the dark. If the torture has allegedly taken place recently enough for such evidence to be relevant, any samples found of body fluids (such as blood or semen), hair, and fibers should be collected, labeled, and properly preserved. The investigator must consider whether the physical and psychological findings are consistent with the alleged report of torture, whether physical conditions contribute to the clinical picture, whether the psychological findings are expected or typical reactions to extreme stress within the cultural and social context of the individual, what is the time frame in relation to the torture events, and what other stressful factors are affecting the individual (e.g., ongoing persecution, forced migration, exile, loss of family, and social role). Color photographs should be taken of the injuries of persons alleging that they have been tortured.

A medical examination should be carried out regardless of the length of time since the torture, but if it is alleged to have happened within the past 6 weeks, such an examination should be arranged urgently before acute signs fade. The examination should include an assessment of the need for treatment of injuries and illnesses, psychological help, advice, and follow-up. A psychological appraisal of the alleged torture victim is always necessary. If it is evident that a large number of prisoners have been tortured in a given place, but they all refuse to allow investigators to use their stories because of fear, it is useful to set up a "health inspection" of the whole ward in full view in the courtyard. The physician and interpreter should provide their names and explain their role in conducting the evaluation. When the people have been tortured on multiple occasions, they may be able to recall what happened to them, but often they cannot recall exactly where and when each event occurred.

Forensic medicine and dermatology are often complementary sciences. A minimum knowledge of forensic terminology is useful in order to describe the process and mechanisms of injury resulting in the acute or healed skin signs of torture. Dermatologic description of primary and secondary skin lesions delivers additional information and clues to diagnoses.

During medical examination, for each form of abuse, it is relevant to note body position, restraint, and nature of contact, including duration, frequency, anatomical location, and the area of the body affected. In addition, it is relevant to take into account any bleeding, head trauma, or loss of consciousness and whether the loss of consciousness was due to head trauma, asphyxiation, or pain. The investigator should also ask about how the person was at the end of the "session" (Could he or she walk? Did he or she have to be helped or carried back to the cell? Could he or she get up the next day? How long did the feet stay swollen?). Disorientation of time and place during torture is a generally observed finding. Torture survivors may have difficulty recounting the specific details of the torture for several important reasons, such as blindfolding; drugging; lapses of consciousness; fear of placing themselves or others at risk; lack of trust in the examining clinician or interpreter; psychological impact of torture and trauma (PTSD); neuropsychiatric memory impairment from beatings to the head, suffocation, near drowning, or starvation; protective coping mechanisms, such as denial and avoidance; and culturally prescribed sanctions.

Survivors may be victims of physical and/or psychological torture (Table 20.2). The presence of psychological sequelae in torture survivors, particularly the various manifestations of PTSD, may cause the torture survivor to fear experiencing a re-enactment of his or her torture experience during the interview, physical examination, or laboratory test.

While it is essential to obtain accurate information regarding a torture survivor's experiences, open-ended interviewing methods require that patients should disclose these experiences in their own words using free recall. An individual who has survived torture may have trouble expressing in words his or her experiences and symptoms.

**Table 20.2** Main types of physical and psychological torture

| | | |
|---|---|---|
| Physical | Positional | Suspension, stretching limbs apart, prolonged constraint of movement, forced positioning |
| | Burns | Cigarettes, heated instruments, scalding liquid or a caustic substance |
| | Electric shocks | |
| | Asphyxiation | Wet and dry methods, drowning, smothering, choking, or use of chemicals |
| | Crush injuries | Smashing fingers or using a heavy roller to injure the thighs or back, traumatic removal of digits and limbs, medical amputation of digits or limbs, surgical removal of organs |
| | Penetrating injuries | Stab and gunshot wounds, wires under nails |
| | Chemical | Salt, chili pepper, gasoline in wounds or body cavities |
| | Sexual | To genitals, molestation, instrumentation, rape |
| | Pharmacological | Toxic doses of sedatives, neuroleptics, paralytics |
| | Conditions of detention | Small or overcrowded cell, solitary confinement, unhygienic conditions, no access to toilet facilities, irregular or contaminated food and water, exposure to extremes of temperature, denial of privacy, and forced nakedness |
| | Deprivation of normal sensory stimulation | Sound, light, sense of time, isolation, manipulation of brightness of the cell, abuse of physiological needs |
| | Restriction | Sleep, food, water, toilet facilities, bathing, motor activities, medical care, social contacts, isolation within prison, loss of contact with the outside world |
| Psychological | Humiliation | Verbal abuse, performance of humiliating acts |
| | Threats | Death, harm to family, further torture, imprisonment, mock executions, attack by animals (dogs, cats, rats, or scorpions) |
| | Helplessness | Forced betrayals, accentuating feelings |
| | Exposure to ambiguous situations or contradictory messages | |
| | Violation of taboos | |
| | Behavioral coercion | Forced engagement in practices against the religion of the victim, forced harm to others through torture, forced destruction of property, betrayal of someone placing them at risk of harm, forcing the victim to witness torture or atrocities being inflicted on others |

**Table 20.3** Acute symptoms

| | |
|---|---|
| Crush and beatings | Bleeding, bruising, swelling, open wounds, lacerations, fractures, dislocations, joint stress, hemoptysis, pneumothorax, tympanic membrane perforation |
| Burn | Erythema, bulla or necrosis, sores |
| Electrical | Color and surface characteristics |
| Chemical | Color, signs of necrosis |
| General | Pain, numbness, constipation, and vomiting |

The individual should be asked to describe any symptoms that may have resulted from the specific methods of alleged abuse (Table 20.3). The intensity, frequency, and duration of each symptom should be noted. The development of any subsequent skin lesions should be described indicating whether or not they left scars. The people may also present chronic symptoms (Table 20.4). Although acute lesions may be characteristic of the alleged injuries, most lesions heal within about 6 weeks of torture, leaving no scars or, at the most, non-specific scars. This is often the case when torturers use techniques that prevent or limit detectable signs of injury.

During the physician examination (Tables 20.5, 20.6, and 20.7), facial tissues should be pal-

**Table 20.4** Chronic symptoms

| | |
|---|---|
| Crush and beatings | Skeletal deformities, incorrect healing of fractures, dental injuries, loss of hair, and myofibrosis |
| Electrical or chemical | Scars |
| Common to several different injuries | Headache, back pain, gastrointestinal symptoms, sexual dysfunction, and muscle pain |
| Common to several different injuries | Depressive affect, anxiety, insomnia, nightmares, flashbacks, and memory difficulties |

**Table 20.5** Physician examination of the skin

| | Acute | Chronic |
|---|---|---|
| Beatings and blunt trauma | *Abrasions:* scratches, brush-burn type or larger scraped lesions. Pattern reflecting the contours of the instrument or surface that inflicted the injury. Hypo- or hyperpigmentation after repeated or deep abrasions | Cicatricial alopecia: linear circular zone (with few hairs or hair follicles) around the arm or leg, usually at the wrist or ankle after prolonged application of tight ligatures |
| | *Contusions* and bruises (hemorrhage into soft tissue due to the rupture of blood vessels). Extent and severity depending on applied force, structure, and vascularity of the contused tissue. Their absence, however, does not exclude violence. Contusions may reflect the contours of the inflicting instrument | Bruises initially dark blue, purple, or crimson, gradually changing to violet, green, dark yellow, or pale yellow and then disappearing. It is very difficult, however, to date accurately the occurrence of contusions. Contusions in deeper subcutaneous tissues may not appear until several days after injury, when the extravasated blood has reached the surface |
| | *Lacerations* (tearing or crushing of skin and underlying soft tissues by the pressure of blunt force) on the protruding parts of the body, but with sufficient force, the skin can be torn on any part of the body | Scars, when resulting from whipping (depigmented and often hypertrophic, surrounded by narrow, hyperpigmented stripes), represent healed lacerations |
| Burns | Erythema. Edema | Cigarettes leave 5–10 mm, circular orovoid, macular scars with a hyper- or a hypopigmented center and a hyperpigmented, relatively indistinct periphery. Burning with objects (electrically heated metal rod or gas lighter) produces markedly atrophic scars reflecting the shape of the instrument and sharply demarcated with narrow hypertrophic or hyperpigmented marginal zones corresponding to an initial zone of inflammation. Hypertrophicor keloid scars (burning rubber) may appear. When the nail matrix is burnt, subsequent growth produces striped, thin, deformed nails, sometimes broken up in longitudinal segments |
| Nail lesions | | If a nail has been pulled off, an overgrowth of tissue may be produced |
| Cutting | Stab wounds, incised or cut wounds, and puncture wounds by knife, bayonet, or broken glass | If pepper or other noxious substances are applied to open wounds, the scars may become hypertrophic |
| Asphyxiation | Petechiae | |

pated for evidence of fracture, crepitation, swelling, or pain. The motor and sensory components, including smell and taste of all cranial nerves, should be examined. Computed tomography (CT) should be performed to diagnose and characterize facial fractures, determine alignment, and diagnose associated soft tissue injuries and complications. There are many forms of trauma to the eyes,

**Table 20.6** Physician examination of the bone

| | Acute | Chronic |
|---|---|---|
| Fractures | Direct fracture at the site of impact or at the site where the force was applied. Location, contour reflect the nature and direction of the applied force | Lesions vary according to age, sex, tissue characteristics, condition and health of the patient, and severity of the trauma |
| Direct head trauma | Scalp bruises are frequently invisible externally unless there is swelling | Possible cortical atrophy and diffuse axonal damage. In cases of falls, countercoup (in opposition to the trauma). Continuous headaches (initial symptom of an expanding subdural hematoma) |
| Violent shaking (usually brief, only a few minutes or less, but may be repeated many times over a period of days or weeks) | Edema, subdural hematoma, and retinal hemorrhages without any external marks<br>Bruises on the upper chest or shoulders where the victim has been grabbed | Recurrent headaches, disorientation, or mental status changes |
| Chest and abdominal trauma | Rib fractures. If displaced, lacerations of the lung and pneumothorax. Gross hematuria if kidney contusion. Occult abdominal hemorrhage at peritoneal lavage. On a CT, acute abdominal hemorrhage is isointense (acute central nervous system hemorrhage is hyperintense). Free air, extraluminal fluid, or areas of low attenuation represent edema, contusion, hemorrhage, or laceration. Peripancreatic edema as sign of acute pancreatitis. Ultrasound useful in detecting subcapsular hematomas of the spleen. Renal failure | Renal hypertension as a late complication of renal injury |
| Feet (falanga: repeated application of blunt trauma to the feet, or to hands or hips, usually with a truncheon, a pipe, or similar weapon) | CT or MRI for radiological documentation, but physical examination in the acute phase is diagnostic. On palpation, the entire length of the plantar aponeurosis tender and distal attachments of the aponeurosis torn, partly at the base of the proximal phalanges, partly at the skin. If aponeurosis is intact, the beginning of tension is felt when the toe is dorsiflexed to 20°; maximum normal extension is about 70°. Higher values suggest injury to the attachments of the aponeurosis | Closed compartment syndrome: muscle necrosis, vascular obstruction, or gangrene of the foot distal or toes<br>Fractures of the carpal and metacarpal bones and phalanges. Walking is painful and difficult. Tarsal bones fixed (spastic) or increased motion. Crushed heel and anterior foot pads: elastic pads under calcaneus and proximal phalanxes crushed directly or as result of associated edema; torn connective tissue bands through adipose tissue connecting bone to skin; atrophic adipose tissue deprived of blood supply; lost cushioning effect<br>Rigid and irregular scars involving skin and subcutaneous tissues due to partial or complete destruction of connective bands<br>Rupture of the plantar aponeurosis and tendons of the foot<br>Planter fasciitis |

(continued)

**Table 20.6** (continued)

| | Acute | Chronic |
|---|---|---|
| Suspension:<br>Cross suspension (by spreading the arms and tying them to a horizontal bar)<br>Butchery suspension (by fixation of hands upward, either together or one by one)<br>Reverse butchery suspension (by fixation of feet upward and the head downward)<br>"Palestinian" suspension (by suspending with the forearms bound together behind the back, the elbows flexed 90°, and the forearms tied to a horizontal bar, alternatively from a ligature tied around the elbows or wrists with the arms behind the back)<br>"Parrot perch" suspension (by suspending by the flexed knees from a bar passed below the popliteal region, usually while the wrists are tied to the ankles) | Extreme pain but little, if any, visible evidence (brachial plexopathy). If "Palestinian" suspension, rapid permanent brachial plexus. If "parrot perch," tears in knees cruciate ligaments. Victims will often be beaten while suspended or otherwise abused. Weakness of the arms or hands, pain and paresthesias, numbness, insensitivity to touch, superficial pain, and tendon reflex loss. Intense deep pain may mask muscle weakness<br>If "Palestinian" suspension, lower (deficiencies localized in the forearm and hand muscles; sensory deficiencies on the forearm and at the fourth/fifth fingers of the hand's medial side), middle (forearm, elbow, and finger extensor muscles; weak pronation of the forearm and radial flexion of the hand; sensory deficiency on forearm and dorsal aspects of the first/second/third fingers of the hand in radial nerve distribution; lost triceps reflexes), and upper (shoulder muscles affected, deficient abduction of the shoulder, axial rotation and forearm pronation-supination; sensory deficiency in deltoid region and outer parts of the forearm) plexus fiber involvement.<br>If "crucifixion" suspension, without hyperextension, damage to middle plexus fibers due to hyperabduction | For pain and tenderness around the shoulder joints to persist, as the lifting of weight and rotation, especially internal, will cause severe pain many years later<br>Weakness continues and progresses to muscle wasting. Numbness and paresthesia. Tears of the ligaments of the shoulder joints, dislocation of the scapula, and muscle injury in the shoulder region<br>"Winged scapula" (prominent vertebral border of the scapula) with injury to the long thoracic nerve or dislocation of the scapula |
| Other positions:<br>"Parrot suspension," "banana stand," "banana tie" over a chair just on the ground or on a motorcycle, forced standing, forced standing on a single foot, prolonged standing with arms and hands stretched high on a wall, prolonged forced squatting, and forced immobilization in a small cage | Pain in a region of the body, limitation of joint movement, back pain, pain in the hands or cervical parts of the body, and swelling of the lower legs | |

**Table 20.7** Physician examination of electric shock signs

| | Acute | Chronic |
|---|---|---|
| Electrodes placed on a toe of the right foot and on the genital region | Pain, muscle contraction, and cramps in the right thigh and calf muscles; excruciating pain will be felt in the genital region. Tetanic contraction of all muscles along the electric field route with dislocation of the shoulder, lumbar, and cervical radiculopathies. Burns as reddish brown circular lesion (1–3 mm) usually without inflammation. Biopsy controversial | Hyperpigmented scars |
| Use of water or gels (to increase the efficiency of the torture and expand the entrance point of the electric current on the body) | Undetectable electric burns | |

including lens dislocation; conjunctival, subhyaloid, retrobulbar, or retinal hemorrhage; and visual field loss. Nuclear magnetic resonance imaging (MRI) may be an adjunct for identifying soft tissue injury.

The ear canals and tympanic membranes should be examined with an otoscope and injuries described. A common form of torture, known in Latin America as *telefono*, is a hard slap of the palm to one or both ears, rapidly increasing pressure in the ear canal, thus rupturing the drum. It is relevant to note that tympanic membrane ruptures less than 2 mm in diameter may heal within 10 days. However, fluid may be observed in the middle or external ear. If otorrhea is confirmed by laboratory analysis, MRI or CT should be performed to determine the fracture site. The presence of hearing loss should be investigated. The nose should be evaluated for alignment, crepitation, and deviation of the nasal septum. For simple nasal fractures, standard nasal radiographs should be sufficient. When the cartilaginous septum is displaced, CT should be performed. If rhinorrhea is present, CT or MRI is recommended. Mandibular fractures or dislocations may result from beatings. Temporomandibular joint syndrome is a frequent consequence of beatings about the lower face and jaw. The patient should be examined for evidence of crepitation of the hyoid bone or laryngeal cartilage resulting from blows to the neck. Gingival hemorrhage and the condition of the gums should also be noted. During application of an electric current, the tongue, gums, or lips may be bitten. Lesions might be produced by forcing objects or materials into the mouth, as well as by applying electric current. X-rays and MRI are able to determine the extent of soft tissue, mandibular, and dental trauma. Examination of the trunk, in addition to noting lesions of the skin, should be directed toward detecting regions of pain, tenderness, or discomfort that would reflect underlying injuries of the musculature, ribs, or abdominal organs. The examiner must consider the possibility of intramuscular, retroperitoneal, and intra-abdominal hematomas, as well as laceration or rupture of an internal organ. Ultrasonography, CT, and bone scintigraphy should be used, when realistically available, to confirm such injuries.

Complaints of musculoskeletal aches and pains are very common in survivors of torture. They may be the result of repeated beatings, suspension, other positional torture, or the general physical environment of detention. They may also be somatic. While they are non-specific, they should be documented. They often respond well to sympathetic physiotherapy. Injuries to tendons, ligaments, and muscles are best evaluated with MRI. In the acute stage, this can detect hemorrhage and possible muscle tears. Muscles usually heal completely without scarring; thus, later imaging studies will be negative. Under MRI and CT, denervated muscles and chronic compartment syndrome will be imaged as muscle fibrosis. Bone bruises can be detected by MRI or scintigraphy. Bone bruises usually heal without leaving traces.

Genital examination should be performed only with the consent of the patient and, if necessary, should be postponed to a later examination. A chaperone must be present if the examining physician's gender is different from that of the patient. Ultrasonography and dynamic scintigraphy can be used for detecting genito-urinary trauma.

The neurological examination should evaluate the cranial nerves, sensory organs, and peripheral nervous system, checking for both motor and sensory neuropathies related to possible trauma, vitamin deficiencies, or disease. Cognitive ability and mental status must also be evaluated. Radiculopathies, other neuropathies, cranial nerve deficits, hyperalgesia, paresthesias, hyperesthesia, change in position, temperature sensation, motor function, gait, and coordination may all result from trauma associated with torture. In patients with ahistory of dizziness and vomiting, a vestibular examination should be conducted, and evidence of nystagmus noted. MRI is preferred over CT for radiological evaluation of the brain and posterior fossae.

For each lesion and for the overall pattern of lesions, the physician should indicate the degree of consistency between it and the attribution given by the patient. It is the overall evaluation of

all lesions and not the consistency of each lesion with a particular form of torture that is important in assessing the torture story.

Near asphyxiation by suffocation is an increasingly common method of torture, widely used in Latin America, that its name in Spanish, *submarino*. It usually leaves no mark, and recuperation is rapid. Normal respiration might be prevented through covering the head with a plastic bag, closure of the mouth and nose, pressure or ligature around the neck, or forced aspiration of dust, cement, hot peppers, etc. This is also known as "dry *submarino*." Beyond the cutaneous skin, nosebleeds, bleeding from the ears, congestion of the face, infections in the mouth, and acute or chronic respiratory problems occur. Forcible immersion of the head in water, often contaminated with urine, feces, vomit, or other impurities, may result in near drowning or drowning. Aspiration of the water into the lungs may lead to pneumonia. This form of torture is called "wet *submarino*." In hanging or in other ligature asphyxiation, patterned abrasions or contusions can often be found on the neck. The hyoid bone and laryngeal cartilage may be fractured by partial strangulation or from blows to the neck.

Sexual torture (Table 20.8) begins with forced nudity, which in many countries is a constant factor in torture situations. Nudity enhances the psy-

**Table 20.8** Physician examination after sexual assault

| | Acute | Chronic |
|---|---|---|
| Ano-genital area | Bleeding, vaginal or anal discharge, and location of pain, bruises, or sores<br>If clear evidence of rape on external inspection, unnecessary internal pelvic examination. Genital lesions include:<br>(i) Small lacerations or tears of the vulva (by excessive stretching), normally healing completely; if repeated trauma, scarring<br>(ii) Abrasions (by contact with rough objects such as fingernails or rings)<br>(iii) Vaginal lacerations (associated with tissue atrophy, by inserted sharp objects)<br>Men may show hyperemia, marked swelling, and ecchymosis. Urine containing erythrocytes and leucocytes. Hydrocele (excessive accumulation of fluid within tunica vaginal is due to testis inflammation), hematocele (blood accumulation due to a trauma), or inguinal hernia. If inguinal hernia, impalpable spermatic cord above the mass. Unlike the hydrocele, hematocele does not transilluminate. Testicular torsion from trauma to the scrotum: testis twisted at its base, obstructing blood flow to the testis, causing severe pain and swelling (surgical emergency; alternatively infarction of the testis)<br>Anal examination, beyond visual inspection, with local or general anesthesia | Urinary frequence, incontinence, or dysuria; irregularity of menstruation; pregnancy; abortion or vaginal hemorrhage; problems with sexual activity, including intercourse and anal pain; bleeding; or constipation<br>Where the alleged assault occurred more than a week earlier, lost signs of bruises or lacerations. Even when the woman has had subsequent sexual activity, whether consensual or not, or given birth, it may be almost impossible to attribute any findings to a specific alleged abuse<br>If scrotal torture, chronic urinary tract infection, erectile dysfunction, or atrophy of the testes<br>Anal scars of unusual size or position.<br>Anal fissures persisting for many years.<br>Rectal tears with or without bleeding.<br>Disruption of the rugal pattern as smooth fan-shaped scarring out of midline.<br>Purulent discharge from the anus |
| Skin | Bruises, lacerations, ecchymoses, and petechiae from sucking or biting | Scars on the skin of the scrotum and penis very difficult to visualize |
| Laboratory support | DNA testing on sperm for up to 5 days from samples taken with a deep vaginal swab and after up to 3 days using a rectal sample | Gonorrhoea, chlamydia, syphilis, test for HIV, hepatitis B and C, herpes simplex, and *Condyloma acuminatum* (venereal warts), trichomoniasis, *Moniliasis vaginitis*, *Gardnerella vaginitis*, and *Enterobius vermicularis* (pinworms), as well as for urinary tract infections |

chological terror of every aspect of torture, as there is always the background of potential abuse, rape, or sodomy. Furthermore, verbal sexual threats, abuse, and mocking are also part of sexual torture, as they enhance the humiliation and its degrading aspects. The groping of women is traumatic in all cases and is considered to be torture. Rape is always associated with the risk of developing sexually transmitted diseases, particularly human immunodeficiency virus. Currently, the only effective prophylaxis against HIV must be taken within hours of the incident, and it is not generally available in countries where torture occurs routinely. Electricity and blows are generally targeted on the genitals in men, with or without additional anal torture. Prisoners may be placed naked in cells with family members, friends, or total strangers, breaking cultural taboos. This can be made worse by the absence of privacy when using toilet facilities. Additionally, prisoners may be forced to abuse each other sexually, which can be particularly difficult to cope with emotionally. The fear of potential rape among women, given profound cultural stigma associated with rape, can add to the trauma. Not to be neglected are the trauma of potential pregnancy, the fear of losing virginity, and the fear of not being able to have children [45].

Not all skin lesions in patients alleging torture or ill-treatment are due to their treatment in detention. A comprehensive history is essential in order to differentiate inflicted from non-inflicted injuries. Moreover, knowledge of folk remedies and cultural practices is useful to avoid mislabeling those physical findings as abuse (additional photographs, see online repository material). Blue coloration of the skin can be drug-induced or hereditary. Drug-induced sideeffects are typically seen after treatment with minocycline, phenothiazines, amiodarone, or antimalarials and may leave a blue macula on the face. Hereditary causes, such as nevus of Ota, nevus of Ito, and Mongolian spots, might not always be clearly visible at birth as they are predominantly seen in darker skin types such as in Asian and Latino populations. Nevus of Ota is typically located around the eyes. Clues to differentiate them from bruises are indistinct borders, lack of inflammatory erythema, and absence of typical color changes associated with ecchymoses. Senile purpura, typically located on chronic sun-exposed areas, appears on the extensor surface of forearms. Steroid purpura is a direct consequence of skin atrophy due to prolonged intake or topical use of glucocorticoids. In both of the above, purpura is limited to the area of exposure, which makes it less likely to be mistaken for an inflicted injury.

Coin rolling is a commonly used practice in Southeast Asia to clear the body of "bad winds." Medicated coins are rubbed onto the skin until petechiae and purpura occur. Currently, it is a widely accepted form of alternative medicine practiced across the world as a remedy against various diseases.

The most important cutaneous infections caused by *S. aureus* and/or streptococci, which can mimic burns, are bullous impetigo, characterized by fragile bullae, erosions, and honey-colored crusting.

Scars from varicella, scabies, or other infections or secondary to acne can appear similar to cigarette burns. If scars are located on the calf, they should be differentiated from skin alternations due to venous insufficiency. Keloid scars following electrocution can be mistaken for a chondrodermatitis helicis, which is more painful and pale compared to postelectrocution scars.

Diseases such as lichen planus, lichen simplex chronicus, or allergic contact dermatitis can cause severe pruritus and erosions in the genital area and should be differentiated from the sexual assault. In chronic settings, caution is required not to overlook a squamous cell carcinomas when erosive mucosal lesions are long-lasting and non-pruritic [46].

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# Female Genital Mutilation

21

Aldo Morrone

## 21.1 Introduction

Some female migrant patients have come to clinics for diagnosis and treatment of sexually transmitted infections (i.e., molluscum contagiosum, viral warts, etc.) showing signs of previous genital mutilation. This prompted to investigate the phenomenon of female genital mutilation. This problem is of interdisciplinary relevance (dermatovenereological, gynecological, sociological, psychological, etc.), and the dermatological community should be aware of this [1–9].

The recent migration trends, which have caused millions of people to move from southern areas of the world toward affluent countries in search of a better future for themselves and their children or to escape war and persecution, have resulted in cultural and social changes, which have noticeable effects that also have an impact on health care. Migration has shown these countries realities and conditions that were previously unknown and have exposed host populations to different cultures and habits. Moreover, recently, western countries are also being confronted in their own land with the phenomenon of female genital mutilation (FGM): a term that describes several different traditional rituals.

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International migration [10–21] has brought the practice of female genital mutilation into industrialized countries, more particularly to the EU, the United States, Canada, and Australia: countries that were unfamiliar with these traditional practices. The presence of an increasing number of refugees and immigrants from countries where FGM is practiced has aroused in Australia, Europe, and North America much attention to this issue. As a result, several countries have passed laws against female genital mutilation even though little is known about the numbers and characteristics of local migrant communities where this is practiced. In some countries, programs have been started to develop awareness or to alert health and social services in order to protect girls at risk of genital mutilation.

## 21.2 Female Genital Mutilation

Female genital mutilation is a traditional cultural practice but is also a form of violence against the girl or the child, which will affect her life as an adult woman. Although this practice is illegal and prosecuted in many countries, the number of girls and women who have been subjected to genital mutilation is estimated to be around 132 million worldwide, and 2 million girls per year are considered to be at risk.



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It is known that the physical and psychological effects of the practice are often very extensive, affecting health, in particular sexual, reproductive, and mental health as well as general well-being. The damage done to female sexual organs and to their functioning is severe and irreversible. Furthermore, female genital mutilation reinforces the inequalities suffered by women in the communities where it is practiced. Despite recognition of the importance of this sensitive issue, and a realization that it must be addressed if health, social, and economic needs of women are to be met, there are still major gaps in our knowledge about the extent and nature of the problem and the kinds of intervention that can be successful in eliminating it. Current information on the types of mutilation and their prevalence derives from inadequate and often fragmentary data. FGM encompasses a wide range of procedures: the excision of the prepuce, the partial or total excision of the clitoris (clitoridectomy) and labia, the stitching and narrowing of the vaginal orifice (infibulation), and the excision of both the clitoris or of the clitoris and labia minora which is performed in approximately 80% of girls and women who undergo genital mutilation. Infibulation—the most extreme form of mutilation—involves the complete removal of the clitoris and labia minora, together with the inner surface of the labia majora.

## 21.3 Terminology

Terminology used for FGM procedures varies considerably, depending on regional (international versus local level terminology) and ethnic group. In the international arena, the term "female genital mutilation" is widely used. At local levels, "female circumcision" or referring to a woman as being "open" or "closed" are commonly used terms. In analogy with male circumcision, the term "female circumcision" could be used to describe excision of the prepuce. However, a number of researchers express disagreement with the definition because the term "circumcision" is used to describe a specific male procedure, which is less invasive. Analogous operations for men would involve the partial or complete removal of the penis rather than just removal of the foreskin. Others use the term "ritual female genital surgery" which refers to the non-therapeutic nature of the procedures and has a less emotional connotation than the phrase "female genital mutilation."

It is because of the severity and irreversibility of the damage inflicted on the girl's body that the procedure has been termed "female genital mutilation." This is the term currently used in all official documents of the United Nations.

We think that the term "mutilation" should be maintained, because this term clearly describes the severe physical impact of the practice, in comparison with the term "female circumcision" which obscures the more serious physical and psychological effects of the genital cutting on women [22].

## 21.4 Historical Data

Ritual cutting and alteration of the genitalia of female infants, girls, and adolescents have constituted a tradition since antiquity. The origin of the practice is unknown, and there is no certain evidence indicating how and when it began and propagated. Apparently in all communities where female circumcision is carried out, male circumcision is also present. Male circumcision is portrayed in some reliefs of the Egyptian tomb of Ankh-Ma-Hor (Sixth Dynasty, 2340–2180 B.C.) and other representations from different dynasties. It is not known whether excision and infibulation had a parallel development. However, within the first millennium, the practice was documented as existing in Egypt. The most ancient authority reporting circumcision is Herodotus (484–424 B.C.). He asserts that the Phoenicians, Hittites, and Ethiopians, as well as the Egyptians, practiced excision. About 25 B.C., the Greek geographer and historian Strabone relates that Egyptians circumcised boys and practiced excision on girls.

## 21.5 Definition and Classification

The traditional practice of female genital mutilation has attracted increasing international attention in the past 10 years. The joint statement on female genital mutilation issued in April 1997 by WHO, UNICEF, and UNFPA reported the following definition of the practice: *Female genital mutilation comprises all procedures involving partial or total removal of the external female genitalia or other injury to the female genital organs whether for cultural or other non-therapeutic reasons*.

The three agencies classified the different types of female genital mutilation as follows:

- Type I. Excision of the prepuce (clitoridectomy). It involves excision of the skin surrounding the clitoris with or without excision of part or the entire clitoris.
- Type II. Excision of the entire clitoris with partial or total excision of the labia minora. The vaginal opening is not covered in this type of procedure.
- Type III. Excision of part or all of the external genitalia and stitching/narrowing of the vaginal opening, known as infibulation, is the most severe form in which the entire clitoris and some or all of the labia minora are excised.
- Type IV. Unclassified. It encompasses a variety of procedures, most of which are self-explanatory. There is considerable evidence in literature that classifying these procedures can only be done theoretically. Categorizing the different types of FGM in an anatomically precise and simplified system is only an attempt to help clinicians and researchers standardize their descriptions of a multitude of operations (Figs. 21.1, 21.2, 21.3 and 21.4). The schematic drawings are examples only; considerable variations occur within FGM types [23–25].

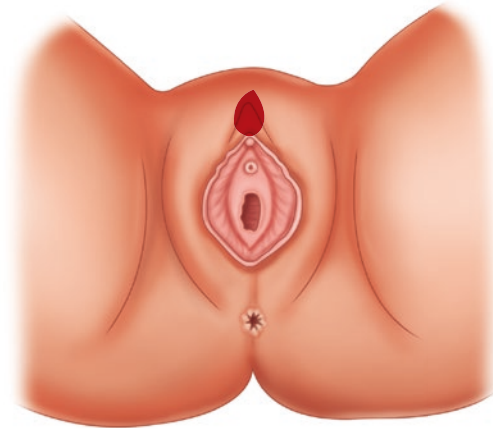

**Fig. 21.1** Type I female genital mutilation

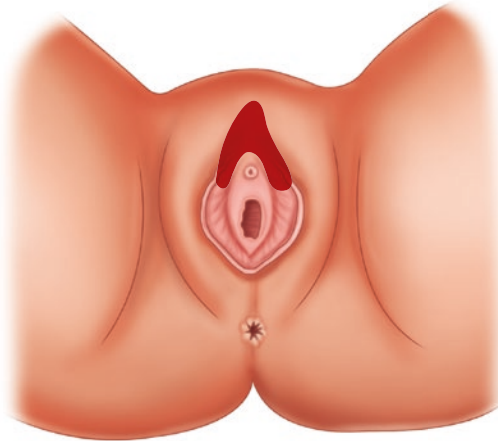

**Fig. 21.2** Type II female genital mutilation

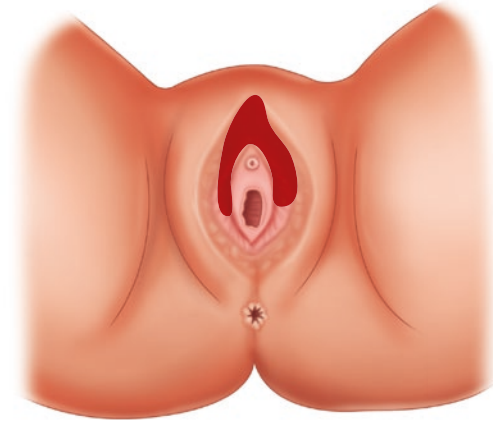

**Fig. 21.3** Type III female genital mutilation

## 21.6 Epidemiology

Documentation of the prevalence of different types of female genital mutilations began in the early twentieth century with reports of European travellers and missionaries. Since the 1950s,

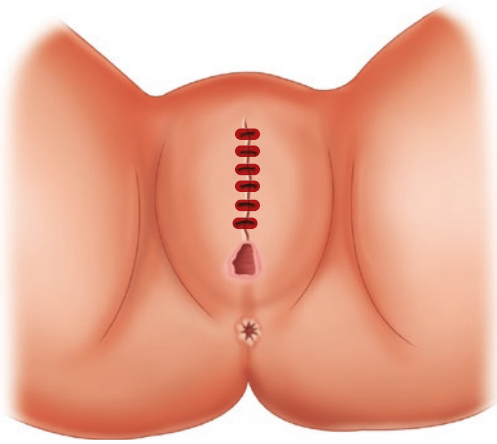

**Fig. 21.4** Type IV female genital mutilation

small studies have been undertaken by physicians and gynecologists in some countries, using clinical records or direct interviews with patients.

The first national survey ever to be undertaken was conducted by the Faculty of Medicine of the University of Khartoum in Sudan in 1979.

The Sudan Fertility Survey, also conducted in 1979, and the Demographic and Health Survey of Sudan in 1990 included questions on female genital mutilation. Sudan is the only country with comprehensive and reliable national prevalence data over time.

Hosken published the first comprehensive article on the epidemiology of female genital mutilation worldwide in 1978. In 1979, in the first edition of The Hosken report, the author presented a global review and country estimates of the prevalence of the practice. Although the report did not specify the exact methodology by which data were collected, these figures remain a major source for global estimates of female genital mutilation. A literature review of available studies by Toubia, published in 1993, modified Hosken's figures on the basis of more recent country studies and reports. These figures were updated again in 1995 and 1996 [26–39].

Current estimates of prevalence are based on an extensive review of the most recent published literature and unpublished reports and on the most recent results from completed Demographic and Health Surveys. In countries where results of studies with adequate sample sizes or regional representation were available, estimates are based on them. However, the majority of published studies and surveys had sample sizes that were too small, neither representative nor clinically based. In addition, some reports did not state clearly how samples were selected. The authors are also aware of a number of studies, including several Demographic and Health Surveys and a comparative study of the results obtained using the Demographic and Health Survey module in African countries, which are currently underway.

## 21.7 Geographical Distribution

There have been no comprehensive global surveys of the geographical distribution of female genital mutilation. Most of the girls and women who have undergone mutilation live in 28 African countries. It is practiced by many ethnic groups, from the east to the west coast of Africa, in the southern parts of the Arabian Peninsula and along the Persian Gulf, and increasingly among immigrant populations in Europe, Australia, Canada, and the United States. It has also been practiced by Daudi Bohra Muslims who live in India and among Muslims in Malaysia and Indonesia. Infibulation is widespread in Somalia, Northern Sudan, and Djibouti and has been reported in Ethiopia, Eritrea, Northern Kenya, some parts of Mali, and Northern Nigeria. Introcision has only been documented in some aboriginal communities of Australia, even though it is not considered to be a current practice among these groups.

On the basis of government reports, anecdotal evidence, and limited surveys with nonrepresentative samples, the prevalence of mutilations in countries where they are practiced is estimated to range from 5% to 98%. Sudan is the only country to have carried out nationwide surveys (the Sudan Fertility Survey, 1979; Sudan Demographic and Health Survey, 1989/1990). They were based on a national sample, which excluded the three southern provinces, where the practice is unknown (except by adoption or

through marriage with members of northern groups where mutilation is practiced), and indicated an initial prevalence of 89%, which subsequently declined by 8%.

A study by the Nigerian Association of Nurses and Nurse-midwives conducted in 1985–1986, using a sample of 400 women and men in each state, showed that 13 out of the 21 states had populations practicing some form of female genital mutilation, prevalence ranging from 35% to 90%. However, the data could not be extrapolated to give a national picture. Similar surveys exist for Chad, Ethiopia, Gambia, Ghana, Kenya, and Senegal.

The Central African Republic and the Ivory Coast have incorporated a few questions on the female genital mutilation in their National Demographic and Health Surveys (1994 and 1994–1995, respectively). A special questionnaire form on female genital mutilation containing 20 questions (DHS III) was tested in Mali and in Eritrea in 1995, and Egypt integrated 34 questions on female genital mutilation in its National Demographic and Health Survey in the same year. It is hoped that these attempts will generate more reliable incidence and prevalence data in future years [40–45].

## 21.8 Description of the Different Types of Female Genital Mutilation

Female genital mutilation is usually performed [47, 48] by traditional practitioners, generally elderly women specially designated for this task, or traditional birth attendants. FGM is done without anesthesia using a variety of instruments, such as knives, razor blades, broken glass, or scissors. In some countries, health professionals—trained midwives and physicians—are increasingly performing female genital mutilation. In Egypt, for example, preliminary results from the 1995 Demographic and Health Survey indicated that the proportion of women who reported having been "circumcised" by a doctor was 13%. In contrast, among their most recently "circumcised" daughters, 46% had been "circumcised" by a doctor.

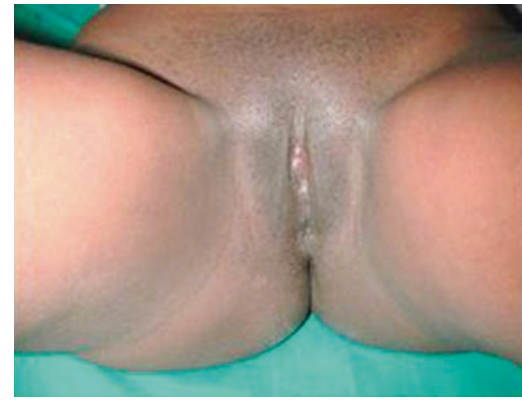

**Fig. 21.5** Type I female genital mutilation

Types I and II generally account for 80–85% of all female genital mutilations, although the proportion may vary greatly from country to country.

### 21.8.1 Type I

In the commonest form of this procedure, the clitoris is held between the thumb and the index finger, pulled out and amputated with one stroke of a sharp object. Packing the wound with gauze or other substances and applying a pressure bandage usually stop the bleeding. Modern trained practitioners may insert one or two stitches around the clitoral artery to stop the bleeding (Fig. 21.5).

### 21.8.2 Type II

The degree of the severity of cutting varies considerably in this type. Commonly the clitoris is amputated as described above and the labia minora are partially or totally removed, often with the same stroke. Bleeding is stopped with packing and bandages or by a few circular stitches that may or may not cover the urethra and part of the vaginal opening. There are reported cases of extensive excisions that heal with fusion of the raw surfaces, resulting in pseudo-infibulation even though there has been no stitching (Fig. 21.6).

**Fig. 21.6** Type II female genital mutilation

### 21.8.3 Type III

The amount of tissue removed is extensive. The most extreme form involves the complete removal of the clitoris and labia minora, together with the inner surface of the labia majora. The raw edges of the labia majora are brought together to fuse, using thorns, poultices, or stitching to hold them in place, and the legs are tied together for 2–6 weeks. A small opening is left at the back to allow the flow of urine and menstrual blood. The opening is surrounded by skin and scar tissue and is usually 2–3 cm in diameter but may be as small as the head of a matchstick. The healed scar creates a "hood of skin" which covers the urethra and part or most of the vagina and which acts as a physical barrier to intercourse. During sexual intercourse, the infibulated woman has to undergo gradual dilation by her husband over a period of days, weeks, or even months. This painful process does not always result in successful vaginal penetration, and the opening may have to be re-cut. At childbirth, the woman has to be cut once more (defibulation) to allow the passage of the baby. After birth, the raw edges are again stitched together to create a small posterior opening, often of the same size as that which existed before marriage (re-infibulation). This is done to create the illusion of virginity, since a tight vaginal opening is culturally perceived as more pleasurable to the man. Because of the extent of both the initial and repeated cutting and suturing, the physical, sexual, and psychological effects of infibulation are greater and longer lasting than those of other types of female genital mutilations. Although only an estimated 15–20% of all women who experience genital mutilation undergo Type III, in certain countries such as Djibouti, Somalia, and Sudan, the proportion rises to 80–90%. Infibulation is practiced on a smaller scale in parts of Egypt, Eritrea, Ethiopia, Gambia, Kenya, and Mali and may occur in other communities where information is lacking or still incomplete (Figs. 21.7 and 21.8).

### 21.8.4 Type IV

Type IV includes different practices of variable severity including pricking, piercing, or incision of the clitoris and/or labia; stretching of the clitoris and/or labia; cauterization by burning of the clitoris and surrounding tissue; scraping of tissue surrounding the vaginal orifice ("angurya cuts") or cutting of the vagina ("gishiri cuts," posterior or backward cuts from the vagina into the perineum, as an attempt to increase the vaginal outlet to relieve obstructed labor, that often result in vesico-vaginal fistulae and damage to the anal sphincter); and introduction of corrosive substances or herbs into the vagina to cause bleeding or for the purpose of tightening or narrowing it.

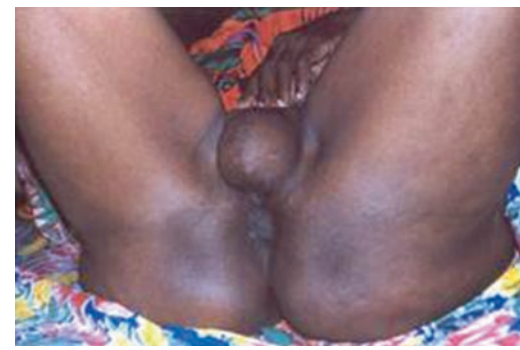

**Fig. 21.7** Type III female genital mutilation

**Fig. 21.8** Type III female genital mutilation

## 21.9 The Age of Female Genital Mutilation

The age at which female genital mutilation is performed varies widely, depending on the ethnic group and geographical location. In some groups, it is performed on babies; more commonly it is undertaken between the ages of 4 and 10 years, but it may also be carried out in adolescence or even at the time of marriage or during a first pregnancy. The operations, which last about 15–20 min, are carried out with special knives, scissors, scalpels, pieces of glass, or razorblades. The instruments [46, 47] may be reused without cleaning. Operations are usually undertaken by an elderly woman in the community specially designated for this task or by traditional birth attendants, although in some cases, the services of health personnel such as midwives and doctors are called upon. Anesthetics and antiseptics are not generally used, and pastes containing herbs, local porridge, or ashes are frequently rubbed on the wounds to stop bleeding. Involuntary additional damage is often caused because of the crude tools, poor light, poor eyesight of the practitioner, and septic conditions or because of the struggle of the girls or women during the procedure.

## 21.10 Religious and Health Beliefs

It is not known when or where the tradition of female genital mutilation originated and a variety of reasons (socio-cultural, psychosexual, hygienic, aesthetic, and religious) are given for maintaining it. Female genital mutilation is practiced by followers of a number of different religions, including Muslims and Christians (Catholics, Protestants, and Copts), by animists and Jews (Falashas in Ethiopia), and also by non-believers in the countries concerned. The practice is deeply embedded in local traditional belief systems [48–61].

In some countries, the practice does seem to be more common among Muslim groups, and many people falsely believe that FGM is required by Islam. In Côte d'Ivoire, 80% of Muslim versus 16% of Christian women have been genitally cut; in Burkina Faso, Muslim women have undergone FGM due to the belief that God does not listen to the prayers of uncut women. Debate has been ongoing among Islamic scholars regarding whether or not Islamic teaching mandates FGM. It is now generally conceded by many Islamic authorities that there are no authenticated Islamic texts requiring the practice.

It is important to stress, however, that even though communities are aware that it is not a religious requirement, the practice continues because it serves as a way of controlling women's sexuality. It is therefore necessary to work with women first, before approaching religious leaders, so that they become convinced of the need to stop FGM due to health consequences.

## 21.11 Consequences and Complications

The exact incidence of morbidity and mortality associated with FGM is difficult to measure. Until now, few studies have dealt with this subject. As mentioned above, only 15–20% of the

complications ever come to the attention of medical personnel due to the unavailability or distance of health care, ignorance, or fear of legal consequences. Most operators take care of the complications themselves, sometimes with devastating results. Only the more serious complications are referred to the health sector. Complications requiring hospitalization pose a significant constraint on already scarce resources [62–79].

Since many women underwent FGM as infants, they may not remember any immediate adverse effects. Women may not link complications arising during childbirth or later in life to genital cutting they underwent as children. Also, FGM-related complications may be considered normal and natural to women, especially among populations where FGM is nearly universal. The effects of female genital mutilation depend on the type performed (in general, infibulation is considered far more hazardous than other types of FGM), the expertise of the circumciser, the hygienic conditions under which the operation is conducted, and the cooperation and the health of the child at the time of the operation.

The effects of female genital mutilation may be divided into the following categories: physical consequences and sexual, mental, and social consequences.

### 21.11.1 Physical Consequences

Female genital mutilation causes severe damage to girls and women and frequently results in immediate-, short-, and long-term health consequences. The effects on health depend on the extent of cutting, the skill of the operator, the cleanliness of the tools and the environment, and the physical condition of the girl or woman concerned.

*Immediate Complications: Death*.

While anecdotal evidence is frequently mentioned, no study has ever been undertaken to determine the proportion of female child mortality that is attributable to female genital mutilation. Death can result from severe bleeding, from the pain and trauma, or from severe and overwhelming infection.

*Short-Term Complications: Pain.*

The majority of mutilation procedures are undertaken without anesthetic and cause severe pain.

*Short-Term Complications: Injury.*

Injury to adjacent tissue of the urethra, vagina, perineum, and rectum can result from the use of crude instruments, poor light, poor eyesight of the practitioner, or careless technique.

*Short-Term Complications: Hemorrhage.*

Excision of the clitoris involves cutting the clitoral artery, which has a strong flow and exhibits high pressure.

*Short-Term Complications: Shock.*

Immediately after the procedure, the girl may develop shock as a result of the sudden blood loss (hemorrhagic shock) and severe pain and trauma (neurogenic shock), which can be fatal.

*Short-Term Complications: Tetanus.*

Tetanus can occur due to the use of unsterilized equipment and lack of tetanus toxoid injection.

*Short-Term Complications: Acute Urine Retention.*

It can result from swelling and inflammation around the wound, the girl's fear of the pain in passing urine on the raw wound, or injury to the urethra.

*Short-Term Complications: Fracture or Dislocation.*

Fractures of the clavicle, femur, or humerus or dislocation of the hip joint can occur if heavy pressure is applied to the struggling girl during the operation.

*Short-Term Complications: Infection.*

It is very common for a number of reasons: unhygienic conditions, use of unsterilized instruments, and application of substances such as herbs or ashes to the wound, which provide an excellent growth medium for bacteria.

*Short-Term Complications: Failure to Heal.*

The wounds may fail to heal quickly because of infection, irritation from urine or rubbing when walking, or an underlying condition such as anemia or malnutrition.

*Long-Term Complications: Difficulty in Passing Urine.*

It can occur due to damage to the urethral opening or scarring of the meatus.

*Long-Term Complications: Recurrent Urinary Tract Infection.*

Infection near urethra can result in ascending urinary tract infections.

*Long-Term Complications: Pelvic Infections.*

They are common in infibulated women.

*Long-Term Complications: Infertility.*

It can result if pelvic infection causes irreparable damage to the reproductive organs.

*Long-Term Complications: Keloid Scar.*

Slow and incomplete healing of the wound and post-operative infection can lead to the production of excess connective tissue in the scar.

*Long-Term Complications: Abscess.*

Deep infection resulting from faulty healing or an embedded stitch can result in the formation of an abscess, which may require surgical incision.

*Long-Term Complications: Cysts and Abscesses on the Vulva.*

Implantation dermoid cysts are the commonest complications of infibulation.

*Long-Term Complications: Clitoral Neuroma.*

A painful neuroma can develop as a consequence of trapping of the clitoral nerve in a stitch or in the scar tissue of the healed wound, leading to hypersensitivity and dyspareunia.

*Long-Term Complications: Difficulties in Menstruation.*

These complications can occur as result of partial or total occlusion of the vaginal opening.

*Long-Term Complications: Calculus Formation.*

Calculus formationin the vagina can occur as a result of the accumulation of menstrual debris and urinary deposits in the vagina or in the space behind the bridge of scar tissue formed after infibulation.

*Long-Term Complications: Fistulae.*

Holes or tunnels between the bladder and the vagina (vesico-vaginal) and between the rectum and vagina (recto-vaginal) can form as a result of injury during mutilation, deinfibulation or re-infibulation, sexual intercourse, or obstructed labor.

*Long-Term Complications: Development of a "False Vagina".*

It is possible in infibulated women if, during repeated sexual intercourse, the scar tissue fails to dilate sufficiently to allow normal penetration.

*Long-Term Complications: Dyspareunia.*

It is a consequence of many forms of female genital mutilation because of scarring, reduced vaginal opening, and complications such as infection.

*Long-Term Complications: Sexual Dysfunction.*

Dysfunction can result in both partners because of painful intercourse, difficulty in vaginal penetration, and reduced sexual sensitivity following clitoridectomy.

*Long-Term Complications: Difficulties in Providing Gynecological Care.*

The scarring resulting from type III mutilation may reduce the vaginal opening to such an extent that an adequate gynecological examination cannot be performed without cutting.

*Long-Term Complications: Problems in Pregnancy and Childbirth.*

They are common, particularly following type III mutilation, because the tough scar tissue that forms causes partial or total occlusion of the vaginal opening and prevents dilatation of the birth canal resulting in obstructed labor.

### 21.11.2 Psychosexual, Mental, and Social Consequences

Little research about the psychological, sexual, and social consequences of FGM has been conducted. However, personal accounts of women who suffered ritual genital procedures recount anxiety before the event, terror at being seized and forcibly held during the event, great difficulty during childbirth, and lack of sexual pleasure during intercourse. Female genital mutilation can have lifetime effects on the minds and bodies of those who experience it.

*Sexual Consequences: Malfunctions of Female External Genitalia.*

The clitoris is a key to the normal functioning and mental and physical development of female sexuality. The clitoris and labia minora are supplied with a large number of sensory nerve

receptors and fibers, with a particularly high concentration in the tip of the clitoris.

*Sexual Consequences: Frigidity Due to Dyspareunia, Injuries Sustained During Early Intercourse, and Pelvic Infection.*

*Sexual Consequences: Lack of Orgasm Due to the Amputation of the Glans Clitoris.*

A study conducted on 651 circumcised Egyptian women showed that their sexual desire was not affected by the procedures, but the ability to achieve an orgasm depended on the severity of the operation and the extent to which social messages inhibiting sexual expression were internalized.

*Sexual Consequences: Coital Difficulty or Inability to Vaginal Intercourse.*

It occurs because the stenosis of the vagina may affect up to 35% of infibulated women.

*Mental and Social Consequences: Marital Conflicts.*

Psychological problems such as post-traumatic stress disorder, behavioral disturbances, psychosomatic illnesses, anxiety, nightmares, depression, psychosis, neurosis, and suicide are due to the painful FGM procedures, painful menstruation afterward, painful intercourse, recurring episodes of frigidity, formation of dermoid cysts, and urine incontinence. A syndrome of genitally focused anxiety and depression, characterized by a constant worry over the state of their genitals, intolerable dysmenorrhea, and fear of infertility, has been described in Sudan among infibulated women.

In communities where FGM has a high social value, girls and women who are not mutilated may be ostracized from their communities.

Genital mutilated women in immigrant communities may face problems concerning their sexual identity when confronted with non-mutilated Western girls and women and the strong opposition against FGM in their host country.

Genital mutilation is commonly performed when girls are quite young and uninformed and is often preceded by acts of deception, intimidation, coercion, and violence by trusted parents, relatives, and friends. Girls are generally conscious when the painful operation is undertaken—no anesthetic or other medication is used—and they have to be physically restrained as they struggle. In some instances, they are also made to watch the mutilation of other girls.

For many girls, genital mutilation is a major experience of fear, submission, inhibition and suppression of feelings, and thinking. This experience becomes a vivid landmark in their mental development, the memory of which persists throughout life.

The experience of genital mutilation is commonly associated with psychosomatic and mental problems, symptoms, and disorders that affect a wide range of brain functions.

## 21.12 Female Genital Mutilation in Immigrant Communities in Western Countries

Countries where female genital mutilation is not a traditional practice should be aware that it may be practiced in immigrant communities or that immigrant survivors who have undergone the procedure in their home countries may need special medical help. Of major concern are the possible adverse psychosocial consequences for women and girls who have moved from a country in which female genital mutilation has familial and social acceptance to one in which it is illegal and raises general community abhorrence. Because immigrant population groups practicing female genital mutilation are marginalized groups within Western nations, their needs may not be visible. State resources should be set aside for the education of immigrant groups practicing female genital mutilation and to investigate health needs of immigrant women and girls. Some such activities are already underway in certain Western nations (e.g., Australia, Canada, France, Sweden, Italy, and the United Kingdom).

Prevention of female genital mutilation should be integrated with broader national health-care policies. An attempt is the creation of a lead agency that acts as a bridge between local communities and the statutory agencies to find the best possible ways of developing a sensitive system for prevention, protection of girls at risk of genital mutilation, and the rehabilitation of women and girls who have already undergone it. A rapid survey can be undertaken to study the distribution of the problem and to examine the entry points within childcare law and health care

and educational systems through which prevention can be furthered. The approach should stress support to families through counseling and persuasion [80–103].

## 21.13 Leaving a Dangerous Practice Without Betraying a Culture

FGM is considered to be a barbaric practice inflicted on women and girls in remote villages of foreign countries. But is not so.

Dignity of the family, cleanliness, protection against sorcery, guarantee of virginity, and fidelity to the husband are the motivations sometimes brought forward for the practice. One of the most frequent explanations for FGM is the local cultural custom, and women are often unwilling to change this habit because of its long-lasting use. Moreover people using this kind of practice often ignore the true implications of FGM and the severe risks for health involved.

Owing to the great number of cases of FGM, followed sometimes by death, the practice is now forbidden in some European countries (the United Kingdom, France, Sweden, Switzerland) and in some African countries (Egypt, Kenya, Senegal). However it is important to note that even if FGM is illegal in many African and Middle Eastern countries, the number of girls mutilated every year has not decreased, as the governments of these countries cannot monitor the extent of the practice.

The United Nations, via UNICEF and the WHO, consider FGM a violation of human rights and recommend eradicating the practice. Also, many NGOs are trying to increase consciousness of the necessity of eliminating it [104–112].

## 21.14 What Can the International Dermatological Community Do?

FGM is a problem unfamiliar to most Western physicians and dermato-venereologists. Besides a lack of clinical knowledge of FGM procedures and complications, information about the underlying socio-cultural beliefs and traditions is incomplete. For example, in many communities where FGM is a traditional practice, women are reluctant to discuss sexual matters with health personnel and are reluctant to complain about painful intercourse or inability to consummate marriage. In Northern Sudan, women have a defibulation procedure performed immediately after marriage. This procedure is carried out by a local midwife or birth attendant and facilitates consummation of marriage. Many Somali women living in the UK experience difficulties in obtaining such a facility. Physiological, psychosexual, and cultural aspects of FGM should be incorporated in training of health-care personnel working with communities who practice FGM.

European politicians need to create an environment that does not contribute to increasing marginalization of refugees and immigrants. This means that they must evaluate current social policies and statements about immigrants in this context. For example, immigration and asylum laws should be assessed as to how they affect identity and to what are the potential links with immigrants in favor of FGM. Women should be able to request political asylum on their own and not only as dependants upon men. Girls should be made aware of the possibility of seeking help and refuge, e.g., through telephone helplines, social services, and battered women's shelters.

It is the responsibility of politicians to meet with communities; these consultations can identify important issues, which can be used as a basis for developing a policy framework that tackles the medical, economic, social, and legislative aspects of FGM. Immigrant and refugee workers will then have to receive systematized information on groups that still perform FGM and on groups that provide services to deal with FGM. Advocacy toward policy makers should stress that a holistic approach is needed toward immigrants and that immigrant women have rights too. Funds should be raised in order to tackle more than one aspect of immigrant women's lives. We consider FGM to be more than a health problem; it is also a social means of controlling women's sexuality. We therefore do not strive for eradication of FGM as such. Instead, we want to label it as social behavior, using gender as a basis. This means that our message is not only "don't do FGM"; we rather aim at

facilitating social change. We consider FGM as a form of gender-based violence, although it is recognized as not being an intentional and deliberate effort to produce injury.

Dermato-venereologists, anthropologists, educationists, social assistants, and health operators should be able to reach these villages and districts and simply inform the practitioners about the dangers of FGM. In order that the efforts to eliminate such practice are successful, it is necessary to act with great attention and delicacy, as the cultural beliefs have a very strong hold [113–127].

In order to eradicate FGM, we think the following will be necessary:

- Training and sensitization of dermato-venereologists and gynecologists, nurses, and health workers in Europe because international migration has increased the number of circumcised women in Europe.
- Health education programs for immigrant communities.
- Attempt of health-care workers to discourage women from performing FGM on their daughters.
- Education and prevention campaigns aimed for different target groups: adolescents, refugees, men and women of the communities involved, and health professionals who work with communities with a high FGM risk degree.
- Cultural mediators involved in working with immigrant communities.
- Intensive education on FGM included in the official curricula of midwives, nurses, and medical doctors, also through publications in medical journals.
- Consultation and interaction between health-care professionals and affected communities as a basis for preparing guidelines for dermato-venereologists, gynecologists, and other medical doctors and health workers.

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# Right and Agencies (Health)

# 22

Ottavio Latini and Francesca Vietti

## 22.1 Introduction

The term "international migration" encompasses a wide range of population movement, the reasons for that movement, and the legal status of migrants, which determines how long they can stay in a host country and under what conditions.

Approximately 258 million people, or 3.4% of the world's population, currently live temporarily or permanently outside their countries of origin [1]. This figure includes migrant workers, permanent immigrants, refugees, and asylum seekers, but it does not account for the growing irregular or undocumented movement that is coming to characterize migration everywhere.

## 22.2 Definitions

A distinction is made between regular and irregular (documented and undocumented) migrants. Regular or documented migrants are those people whose entry, residence, and, where relevant, employment in a host or transit country have been recognized and authorized by official state authorities. Irregular or undocumented migrants (sometimes referred to inappropriately as "illegal" migrants/immigrants) are people who have entered a host country without legal authorization and/or overstay authorized entry, for example, visitors, tourists, foreign students, or temporary contract workers.

There is also a distinction made between "voluntary" and "forced" migrants. Voluntary migrants are people who have decided to migrate of their own accord (although there may also be strong economic and other pressures on them to move). This includes labor migrants, family members being reunified with relatives, and foreign students. Forced migration refers to "movements of refugees and internally displaced people (those displaced by conflicts) as well as people displaced by natural or environmental disasters, chemical or nuclear disasters, famine, or development projects." Labor migrants are not generally considered to fall within the category of forced migrants. There is growing debate, however, as to the extent to which the lack of fulfillment of economic, social, and cultural rights also forces people to abandon their homes to seek possibilities of survival and sustenance elsewhere. In short, it is increasingly difficult to distinguish clearly between "forced" and "voluntary" migrants.

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## 22.3 Categories

### 22.3.1 Internally Displaced Persons (IDPs)

In conflict situations, displacement of populations often means that health personnel are also displaced, causing disruption of health services and interrupting vital access to care.

### 22.3.2 Refugees (Rs)

They are defined by the 1951 Convention Relating to the Status of Refugees as any person who is "owing to well-founded fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group or political opinion, is outside the country of his nationality and is unable or, owing to such fear, is unwilling to avail himself of the protection of that country." The 1951 Convention Relating to the Status of Refugees is the foundation for the international regime for the protection of refugees. The 1967 Protocol removed geographical and temporal restrictions from the Convention. UNHCR estimates that at the beginning of 2018, there were approximately 25.4 million refugees worldwide [2]. However, the number of de facto as opposed to registered refugees is probably higher, as refugees frequently find themselves in similar situations to undocumented labor migrants where they choose not to be documented for fear of rejection or other reprisal. In countries with poorly defined borders and where families may be living on both sides of borders, refugees may be taken in by relatives and not even come to the attention of local authorities.

### 22.3.3 Asylum Seekers (AS)

They are people who have fled to another country where they have applied for state protection by claiming refugee status but have not received a final decision on their application. The most recent UNHCR information estimated that there were almost 3.1 million asylum seekers worldwide. Refugees and asylum seekers arriving in countries of asylum have often experienced severe shock and trauma. Many are likely to be suffering from post-traumatic stress disorders (PTSDs), anxiety, and the loss of family members. In many cases, they may also have suffered torture and other abuses, including sexual abuse. Both short- and long-term psychosocial disability can be anticipated in displaced populations, and their capacity to insert themselves easily and actively in host countries may be limited.

### 22.3.4 Internally Displaced Persons (IDPs)

Like refugees, they are forcibly displaced by circumstances of war, civil conflict, and political persecution. However, unlike refugees, they do not cross international borders but rather remain in the territory of the state of their nationality and, technically, under the jurisdiction of the government of that state. According to UN Guiding Principles on Internal Displacement, IDPs are defined as "persons or groups of persons who have been forced or obliged to flee or to leave their homes or places of habitual residence, in particular as a result of or in order to avoid the effects of armed conflict, situations of generalized violence, violations of human rights or natural or human-made disasters, and who have not crossed an internationally recognized State border." Although it has been estimated that there are 40 million IDPs worldwide, the lack of registration and national authorities' reluctance to acknowledge the problem means that this number may be a gross underestimation.

### 22.3.5 Migrant Workers (MW)

They constitute a major category of migrants in general. The International Convention on the Protection of the Rights of All Migrant Workers and Members of Their Families has defined a migrant worker as "a person who is to be engaged, is engaged or has been engaged in a remunerated activity in a State of which he or she is not a

national," a definition similar to those enshrined in the relevant ILO Conventions. According to UN and ILO estimates, out of the 258 million migrants worldwide, 150 million are migrant workers and their families [3]. ILO estimates, there are roughly 9 million migrant workers across Africa, 37 million in North America, 4 million in Central and South America, 17 million in South and East Asia, 17 million in the Middle East, and 49 million across all of Europe.

### 22.3.6 Temporary Contract Workers (TCW)

They are the most common category of documented labor migrants. They are admitted to the host country for limited periods with the intention that they will return home when their contract expires. The majority is low-skilled and recruited to work in agriculture and construction, both of which are seasonal and in which market fluctuations can easily dictate changes in demand.

### 22.3.7 Smuggled Migrants (SM)

The introduction of more severe entry restrictions for migrants in general has given rise to an increase in the number of people trying to enter countries unofficially. Large numbers of migrants die each year while being smuggled by land or sea.

### 22.3.8 Victims of Trafficking (VT)

Trafficking in persons is a growing global problem with an estimated 40 million victims of international trafficking [4]. Trafficking in persons is defined by the protocol against trafficking as "the recruitment, transportation, transfer, harboring, or receipt of persons, by means of threat or use of force or other forms of coercion, abduction, fraud, deception, abuse of power or a position of vulnerability, or of the giving or receiving of payments or benefits to achieve the consent of a person having control over another person, for the purpose of exploitation". Traffickers use coercive tactics, including deception, fraud, intimidation, isolation, threat, and use of physical force and debt bondage to control their victims. Some of the negative health impacts endured by victims of trafficking, the vast majority of whom are women and children, include greater vulnerability to ill health and lesser abilities to implement healthy choices; exposure to health hazards and infectious diseases, particularly for those who experience poor living conditions; physical violence or conditions of labor servitude; impacts on reproductive and sexual health, including sexually transmitted infections, unwanted pregnancies, unsafe abortions, infertility, and HIV/AIDS; and emotional and mental health implications.

### 22.3.9 Permanent Immigrants (PM)

They are a major category of migrants, particularly for traditional countries of immigration. No common legal definition has been laid down in international law; national legislation and practice vary considerably in defining immigrant categories, qualifications, and treatment. Nonetheless, until non-nationals admitted for purposes of immigration have achieved permanent resident or citizenship status, they also may be subject to disadvantages or limitations in access to health care and health rights in relation to nationals of those countries. International labor migration is increasingly selective in terms of gender and age, and many national immigration and "temporary" labor migration policies legally proscribe families accompanying temporary migrant workers. Family reunification programs have been initiated to allow migrant workers' families to join them after a certain time. Family reunification constitutes a large proportion of all documented immigration into Western countries.

## 22.4 Agenda 2030

International migration is a critical concern for the implementation of the *Agenda 2030* for sustainable development. On September 19, 2016,

the General Assembly adopted the New York Declaration for Refugees and Migrants, in which UN member states agreed to implement well-managed migration policies. They also committed to sharing more equitably the burden and responsibility for hosting and supporting the world's refugees, protecting the human rights of all migrants, and countering xenophobia and intolerance directed toward migrants.

The World Health Organization Constitution states that "The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political, economic or social condition."

Every person, even the poorest of the poor, is entitled to human rights: a set of universally recognized inalienable entitlements and freedoms concerning the protection of the inherent dignity and equality of every individual without any discrimination. Every human being is entitled to enjoy all human rights codified in international, regional, and national human rights treaties that state parties commit themselves to implement in their policy making both at the national and international level through ratification. States have legally binding obligations to protect, to respect, and to fulfill the human rights of the individuals under their jurisdictions, and, in particular, they also hold responsibilities at international level. According to international human rights law, and in particular to article 12 of the International Covenant on Economic, Social and Cultural Rights, adopted in 1966, every human being is entitled to enjoy the right to the highest attainable standard of physical and mental health [5]. This implies much more than mere absence of disease. Because of its very nature, the right to health is indispensable for the exercise of the other human rights, and it is closely related to, and dependent upon, their realization as all these rights, whether civil, political economic, social, or cultural, are mutually reinforcing, inter-related, universal, indivisible, and interdependent [6]. For instance, the failure of a given state to provide people under its jurisdiction with the right to an adequate standard of living, including adequate food, clothing, and housing and the continuous improvement of living conditions, adversely affects individuals' health and makes people more vulnerable to diseases, as this contributes to strengthening the proliferation of vectors and the transmission cycle.

## 22.5 Human Rights Perspective

A human rights perspective contributes, first of all, to humanizing the disease, shifting attention from numerical statistics to *the persons* affected by the diseases and the burden they bear. Adopting a human rights lens, we realize that the persistence of common skin disorders constitutes major undeniable human rights violations, as it impairs health status and causes disability and death, preventing the affected individuals from enjoying the rights and the freedoms they are entitled to as human beings on the basis of their dignity and equality.

The independent expert monitoring committee overseeing the implementation of the Covenant on Economic, Social and Cultural Rights has extensively interpreted the right to health in order to enable states to operationally make use of human rights in their policy making. First of all, the right to health imposes three types of obligations on the states. The obligation to protect requires states to take measures that prevent third parties from interfering with the right to health; the obligation to respect requires states to refrain from interfering directly or indirectly with the enjoyment of the right to health; finally the obligation to fulfill requires states to take actions such as legislative, administrative, budgetary, judicial, and promotional measures toward the full realization of the right to health [7]. In particular, the obligation to fulfill in the realm of the right to health in developing countries implies to make the best use of scarce and limited resources and human capital. According to the interpretation of the committee, states are required to take specific steps to fulfill the right and to establish effective and integrated health systems encompassing medical care and the underlying determinants of health responsive to national and local priorities [8]. When planning

any intervention concerning the promotion of health, in order to give shape to holistic and omni-comprehensive and human-centered health systems, states are required to guarantee at least at a minimum level the satisfaction of the following core obligations in order to:

(a) To ensure the access to health facilities, goods, and services on a nondiscriminatory basis, especially for vulnerable and marginalized groups.
(b) To ensure access to the minimum essential food which is nutritionally adequate and safe, to ensure freedom from hunger to everyone.
(c) To ensure access to basic shelter, housing and sanitation, and adequate supply of safe and potable water.
(d) To provide essential drugs, as from time to time defined under the WHO Action Program on Essential Drugs.
(e) To ensure equitable distribution of all health, goods, and services.
(f) To adopt and implement a national public health strategy and plan of action, on the basis of epidemiological evidence, addressing the health concerns of the whole population; the strategy and plan of action shall be devised, and periodically reviewed, on the basis of a participatory and transparent process; they shall include methods, such as right to health indicators and benchmarks, by which progress can be closely monitored; the process by which the strategy and the plan of action are devised, as well as their content, shall give particular attention to all vulnerable and marginalized groups.
(g) To ensure reproductive, maternal (pre-natal as well as post-natal), and child health care.
(h) To provide immunization against the major infectious diseases occurring in the community.
(i) To take measures to prevent, treat, and control epidemic and endemic diseases.
(j) To provide education and access to information concerning the main health problems in the community, including methods of preventing and controlling them.
(k) To provide appropriate training for health personnel, including education on health and human rights.

This approach stems from the consciousness that people's health is conditioned by the satisfaction of a wide range of human rights. In addition, the right to health contains these interrelated and essential elements, namely, availability, functioning public health and health-care facilities, goods, services, and programs in sufficient quantity, including the underlying social determinants of health; accessibility which implies that health facilities, foods, and services must be easy to be accessed by all, with regard to physical, economic, and information conditions; acceptability which is respectful of medical ethics and culturally appropriate features; and quality which refers to good and appropriate scientific and medical standards. Because of the constraints due to the limit of available resources, the right to health is meant to be realized progressively, but states have however specific obligations of immediate nature and effects.

The first refers to the fact that states should take continuously, to the maximum of their available resources, deliberate, concrete, and targeted steps, to move as expeditiously and effectively as possible toward the full realization of the right to health, without retrogressing. Each state is required to adopt a comprehensive national plan encompassing the measures to be taken to develop its own health system including appropriate indicators and benchmarks. In particular, it reveals fundamental to distinguish between the unavailability of a given state to deliver services owing to economic and structural constraints and its unwillingness, by analyzing for instance the list of priorities set by governments with regard to public spending.

The second obligation that states should immediately comply with refers to the fact that the right to health must be exercised without any kind of discrimination. Equal treatment and nondiscrimination constitute the pre-condition for health equality. In particular, states bear the immediate obligation to ensure equality and nondiscrimination in laws, in policies as well as

in the distribution and delivery of resources, health services, and the underlying determinants of health. The principle of nondiscrimination entails, among other issues, that vulnerable groups are identified and subsequently targeted. In addition, authorities need to take steps to ensure that prevalence data, mass drug administration, and facility-based treatment are available to all at-risk and hard-at-reach population. Therefore, states must abstain from adopting discriminatory laws and are required to adopt and enforce laws for preventing discriminatory policies and practices by non-state actors and must take positive actions for effective protection of the most vulnerable in designing and implementing all the components of the right to health.

Furthermore, participation lies at the core of the human rights approach as it contributes to turning individuals from passive recipients into active subjects of the process of policy making. Giving importance to ordinary people's agency entails involving them not only in the implementation of top-down activities; it implies that individuals are actively present from the very design of any intervention at the local, regional, and national level to the phase of monitoring and therefore participating also in the process of accountability. It should be recalled that involving the concerned communities means empowering them, redressing their voicelessness; besides, participated interventions lead to effective and feasible solutions because they are bottom-up and responsive to the beneficiaries' real needs. In addition, grassroots participation, also through partnership of public institutions and non-for-profit organizations with donor or recipient governments, contributes to making states' action more effective.

The people affected by common skin disorders cannot be neglected any longer. Framing universal skin care as a human right, as advocated by many practitioners and academics, implies operationally integrating human rights standards into policy making. It is argued that making use of human rights normative criteria and standards in policy making turns pivotal in order to achieve universal skin care. It is suggested that the very respect, protection, and fulfillment of human beings' entitlements generate the vital lymph crucial to break the vicious circle of poverty and disease trapping the affected individuals and to turn it, progressively, into a virtuous circle, as health and human rights are mutually reinforcing. It is argued that human rights can make a very important contribution, as they indicate the way forward together with the practical steps that need to be taken in order to give realization to the right of every individual to the highest attainable standard of physical and mental health. This implies designing and implementing services respectful of, and tailored to, the needs of the local context, through partnership with the national institutions, the best use of scarce, limited resources, and the participation of all the stakeholders involved, according to a bottom-up and an integrated human-centered approach. This also implies making health services and treatment available, accessible, affordable, acceptable, and guaranteeing good quality and nondiscrimination. Moreover, a human rights approach prioritizes empowerment and ownership. For this reason, community health workers' training on the most common skin disorders reveals crucial in order to transfer know-how and making it available, accessible, and usable in the prevention, control, and treatment of common skin disorders. We share the beliefs expressed by the former UN Special Rapporteur on the right to health, Mr. Paul Hunt, that the global legitimacy of international human rights norms can help to ensure that these common diseases attract equitable levels of research and development and that existing drugs, vaccines, and other services reach all those who need them. It is in fact urgent to create pro-active, pro-development, and pro-people policies.

It is suggested that dermatologists can play a pivotal role in advocating and lobbying for universal skin care as they can provide technical assistance to government, national, and international organizations in order to monitor their policies and build together comprehensive national and international plans aimed at guaranteeing skin care through the integration of human rights into policy making. Monitoring allows assessing not only dis-

ease prevalence but also the policies and the institutions in the realm of health and development, in order to define which are working and which are not and why, with the objective of improving the realization of the right to health and skin care for all [9, 10]. Poverty should start being considered as a communicable disease, and because of the interdependence between the underlying social determinants of health and skin disorders, holistic and omni-comprehensive interventions should be realized. Furthermore, it should not be ignored that, since socially marginal and economically deprived groups have the greatest overall need for health care, services at subsidized, low fees should be provided; in fact, it is notorious that health services are sparser and of poorer quality in areas serving populations experiencing disadvantages, the so-called inverse care law [11].

Our mission is to take care of human mobile population, comprising migrants with irregular status, victims of torture, trafficked people, and unaccompanied foreign minors.

It is argued that developing partnership aimed at improving the living conditions in the countries of origin, in this particular case, health systems for the enjoyment of the right to health and the underlying socio-determinants of health, is a duty. This responsibility comes into two forms: first of all, every human being should live in dignity; second, human beings should not be forced to migrate because of human security; mobility should become a free choice, not the desperate attempt to escape, irregularly, hopeless living conditions with several risks for their own health during the travel.

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# Access to Care and Facilities for Care

23

Maria Lucia Dell'Anna and Aldo Morrone

## 23.1 Introduction

WHO spent consistent resource to evaluate and support the current status of the access to health facilities [1, 2]. Universal health coverage has been set as a possible umbrella goal for health in the Post-2015 Development Agenda. Universal health coverage will improve health and financial protection for households. More recently, attention has put on the actual goal to be gain: universal coverage or universal access. According to the universal health coverage, all people obtain the health services they need without risking financial hardship. It means coverage with good health services (health promotion, prevention, treatment, rehabilitation, and palliation) together with a form of financial risk protection. Universal health coverage is gained when people actually obtain the health services they need and benefit from financial risk protection. On the other hand, when the universal access is considered, this is the opportunity or ability to do both of these things. Hence, universal health coverage is not possible without universal access, but the two are not the same.

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## 23.2 How to Access

Access to health-care facilities implies several different aspects. The first one consists in the physical accessibility. The true efficacy of the health system depends on the availability of good health services, i.e., proximity to the people who need them, opening period, appointment systems, language and communications systems, and other aspects of service organization and delivery that allow people to obtain the services when they need them.

Another aspect concerns financial affordability. This is a measure of people's ability to pay for services without financial hardship. It takes into account not only the price of the health services but also indirect and opportunity costs, including those of transportation to and from facilities and of taking time away from work. Affordability is influenced by the wider health financing system and by household income.

Finally, it should be also considered—the acceptability. This captures people's willingness to seek services. Acceptability is low when patients perceive services to be ineffective or when social and cultural factors such as language or the age, sex, ethnicity, or religion of the health provider discourage them from seeking services.

Facilities become accessible when they are available, of good quality, and located close to people. The prerequisite for this is obviously represented by the availability and good quality of



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buildings, equipment, health personnel, health products, and technologies. Financial affordability can be improved by reducing direct, out-of-pocket payments through insurance prepayments and pooling (collection of government revenues and/or health insurance contributions to fund health services) or through demand-side stimuli (conditional cash transfers and vouchers). Social and cultural accessibility can be improved making sure that health system, through health workers, deals with all people seeking care, and their families, with dignity and respect.

The access to health facilities and care can be improved first of all through the reduction of poverty and income inequalities. Moreover, people able to access to school, and instruction in general, will be more able to access to health services and to demand and obtain the health services they need. Efforts to address these social determinants will help to reduce inequalities in income, service affordability, and access to services, and this, in turn, will help to attenuate differences in health service coverage and in financial risk protection.

These actions alone, however, will not guarantee that all people obtain the health services they need. Even if the services exist and people have access to them, they might not meet each other. People may be unaware that they need treatment, or they don't know that health promotion or preventive services can benefit them, or they are unaware that different types of health services or financial risk protection plans exist. Or they might not recognize that own decision about care or not care can affect the health of other people, as occur for a treatable communicable disease.

Overall universal health coverage is the obtainment of good health services de facto without fear of financial hardship. It cannot be attained unless both health services and financial risk protection systems are accessible, affordable, and acceptable. Yet universal access, although necessary, is not sufficient. Thus, universal health coverage and universal access to health services are complementary ideas. Without universal access, universal health coverage becomes an unreachable goal [1–17].

## 23.3 Migrant, Refugees, and Health Facilities

The most frequent health problems of newly arrived refugees and migrants include accidental injuries, hypothermia, burns, gastrointestinal illnesses, cardiovascular events, pregnancy- and delivery-related complications, diabetes, and hypertension. Female refugees and migrants frequently face specific challenges, particularly in maternal, newborn and child health, sexual and reproductive health, and violence. The exposure of refugees and migrants to the risks associated with migration itself (psychosocial disorders, reproductive health problems, higher newborn mortality, drug abuse, nutrition disorders, alcoholism, and exposure to violence) increases their vulnerability to noncommunicable diseases (NCDs). Migrant or displaced people often are forced to interrupt the care, due either to lack of access or to the decimation of health-care systems and providers; displacement results in interruption of the continuous treatment that is crucial for chronic NCDs.

More vulnerable individuals, mainly children, are prone to respiratory infections and gastrointestinal illnesses because of poor living conditions, suboptimal hygiene, and deprivation during migration, and they require access to proper health care. Poor hygienic conditions can also lead to skin infections. Furthermore, the number of casualties among refugees and migrants crossing the Mediterranean Sea has increased rapidly until 2016, with 3771 and 5096 people estimated to have died or gone missing at sea in 2015 and 2016, respectively; in the following period, there was a drastic reduction due to closure policy, agreement with Libyan authorities, and rejections carried out by the Europe, with 3139 and 2023 migrants who died in 2017 and in 2018, respectively [3]. The drastic reduction of the deaths during the journey in the Mediterranean Sea indicates that we do not know or do not see the death, which instead occurs in the countries before the boarding attempt.

Legal status is one of the most important determinants of the access of migrants to health services in a country. Each refugee and migrant

must have full, uninterrupted access to a hospitable environment and, when needed, to high-quality health care, without discrimination on the basis of gender, age, religion, nationality, or race. WHO supports policies to provide health-care services irrespective of migrants' legal status. As rapid access to health care can result in cure, it can avoid the spread of diseases; it is therefore in the interests of both migrants and the receiving country to ensure that the resident population is not unnecessarily exposed to the importation of infectious agents. Likewise, diagnosis and treatment of NCDs such as diabetes and hypertension can prevent these conditions from worsening and becoming life-threatening. However, migrant people provided with uncertain legal status fear to contact public facilities dreading to be imprisoned or expelled.

The health systems in the countries receiving migrants are usually well-equipped and experienced to diagnose and manage common infectious diseases and NCDs; they should also be prepared to provide such health care to refugees and migrants. While countries should remain vigilant, other challenge should be approached.

Responding quickly and efficiently to the arrival of large groups of people from abroad requires effective coordination and collaboration between and within countries as well as between sectors. A good response to these social and clinical requests applies for good vigilance, which represents the basis for setting up adequate capacity in the medium and long term, requiring robust epidemiological data on the refugees and migrants, careful planning, training, and, above all, adherence to the principles of human rights. The adequate addressing the influxes, even large, of refugees or migrants into a country will improve coordination among the numerous stakeholders, as well as resilience, and it will counteract possible deleterious overloading of health systems. The easy access of vulnerable groups to emergency health system for common and severe conditions must be assured, as children's health can deteriorate quickly if they do not have adequate care. It is possible that health workers must manage communicable diseases that are infrequent in Europe. In addition, they should learn to communicate with people who speak other languages and are from other cultural backgrounds (through interpreter services or other means). High-quality care for refugee and migrant groups cannot be ensured by health systems alone and much less the mere availability of technical device and support. The social determinants of health, such as education, employment, social security, and housing, all have a considerable impact on the health of migrants [3, 18–32].

## 23.4 How to Meet the Needs of Migrants and Refugees with NCD

During the early approach with migrant and refugee people, it is relevant to recognize the occurrence of NCD in order to provide the best access and management. The overall aim is to ensure non-interruption of treatment. When the early treatment is ensured, most of the life-threatening exacerbation and complications of NCDs can be avoided.

In any case, when treatments for NCDs are not immediately available, it is mandatory to define clear standard operating procedures for referral.

Finally, it is relevant to provide the primary health-care system with essential diagnostic equipment, core laboratory tests, and medication for routine management of NCDs.

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# 24 Understanding and Working with Traditional Beliefs, Cultures, and Practices (Cupping, Coining, and Other Ethno-Dermatoses)

Aldo Morrone

## 24.1 Cupping

### 24.1.1 Practice and Diffusion

Cupping is a traditional medical practice, performed by placing on the skin hot cups of different materials containing reduced air pressure, with subsequent "skin traction" due to suction by heated air, which results in trauma of the outer blood vessels of the papillary derma, followed by local hyperemia. This is expected to promote and help healing in the area. Cupping originates in Asia but is also practiced in other areas (Africa, Australia) and can be found among large communities migrated from the regions where the technique is widespread. Evidence has been found that the Chinese have been performing cupping for at least 3000 years. Metal and glass cups were found in archaeological excavations. In Western areas, it was certainly practiced in Egypt. In the Ebers Papyrus, it is stated that "the bleeding due to the use of wet cups removes foreign matters from the body." From there, the practice spread to the Ancient Greece and to Rome, where instruments called "cucurbital" (pumpkin-shaped) were used. Both Hippocrates and Galen were convinced of the efficacy of that therapy; Galen also condemned Erasistratus, a famous Alexandrian physician, because he did not use cupping. In 413 B.C., Herodotus wrote that this technique can remove harm from the head, reduce pain and inflammation, restore appetite, and strengthen weak stomach.

Through Alexandrians and Byzantines, the therapy was then transmitted to the Muslim Arabs—where it was called Hijama—and to the Persians. Also the prophet Muhammad recommended cupping, and the therapy became important and diffused in Unani medicine.

In China the famous Taoist alchemist and herbalist Ge Hong (281–341 A.D.) made the first description of cupping in his volume *A Handbook of Prescription for Emergencies,* recommending the use of animal horns for pustular lesions. Chinese traditional medicine linked health to the energy balance between Yin and Yang, and cupping was considered as a means suitable to force energy to leave the internal organs, to move toward the surface and help healing. Cupping could drive out evil spirits and chase them away, and it was as well able to draw out harmful "humors" from the affected organs.

With the consolidation of modern medicine, the practice was progressively neglected, although surviving up to present in some areas and in traditional ethnic cure systems. In the nineteenth century, cupping was still used to treat epilepsy in Western countries, particularly in England, and today it is practiced in African countries, such as

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Ethiopia, where it is called *wagemt*, to treat common thoracic pains or abdominal swelling, often due to kwashiorkor. In some areas of Europe and America, the therapy is obtaining new popularity, due to the action of acupuncturists and other holistic health professionals, who promote its use for antalgic and depurative purposes [1–5].

### 24.1.2 Technique

The most widespread practices are dry and wet cupping. Dry cupping consists in putting some alcohol in a round cup, burning the alcohol, and placing the cup on the skin.

Wet cupping consists in making an incision in the skin and in exactly positioning the cup on top of it in order to favor bleeding. In both cases, the procedure lasts about 15–20 min. Cups, which were originally made of animal horns, are now available in glass or plastic.

### 24.1.3 Clinical Features

Clinical manifestations include blue-red, circular erythematous spots, sometimes covered with crusts, consistent with recent cupping. Particularly in older lesions, atrophic-cicatricial irregular lesions, with normal, slate gray, or hypochromic color, were observed. Lesions were observed on the back, on the presternal region and, in case of pathologies causing abdominal swelling (i.e., kwashiorkor, intestinal parasitosis), on the abdomen. Skin hyperemia causes erythema, which induces edematous, ecchymotic, and bullous lesions, and can subsequently lead up to typical circular hypopigmentation. If lubricants were used to move the cups, purpuric linear striae may be found. Possible complications of the practice are burns, purpura, hematoma, and hypopigmented and atrophic scars, as well as bullous and keloidal lesions. Differential diagnosis should include lesions due to traumas or violence, later resulting in cupping-related outcomes or complications.

### 24.1.4 Use and Mechanism of Action

The most common diseases for which cupping is exploited, often together with acupuncture, are pain syndromes (i.e., myalgia, headache, rheumatic pains) and diseases of the respiratory system (i.e., fever, bronchitis). Other syndromes and diseases are also considered suitable to be treated with cupping, such as indigestion and menstrual disturbances. Other possible diseases treated with cupping are acne, psoriasis, herpes zoster, and urticaria. The theories underlying this practice and its action mechanisms are still quite obscure. The most widely accepted hypothesis holds that the suction effect created in the heated cup, which gradually cools down, favors blood circulation, relieves pain, and eliminates harmful and toxic substances trapped in the tissues. Also, a "counter-irritation" theory was proposed, according to which the stimulation of the skin, by producing local hyperemia and increase of superficial blood flow, decongests sick internal organs.

Other theories suggest involvement of hormonal or nervous mechanisms, producing positive circulatory or trophic effects on the internal organs. Lastly, a psychosomatic theory asserts that by displacing pain in parts of the body, which better tolerate it, positive psychological effects can be obtained.

### 24.1.5 Complications

A case of stroke subsequent to cupping in the cervical region has been reported, probably due to high increase of arterial pressure and to thermal stress in case of inner laceration of vertebral arteries and possible dissection. Also, cases of thrombocytopenia have been reported. It is of the utmost importance to highlight these cases, in order to spread attention on ethno-medical practices which, when not performed by expert health-care professionals, can entail severe complications involving both the skin and other organs.

## 24.2 Coining

Coining consists in vigorously rubbing a coin over the chest or back after applying hot oil or Tiger Balm, to the point of creating ecchymosis and linear petechiae. The idea is to "liberate the breath" and has a therapeutic goal in curing a myriad of adult disturbances, particularly fever in children. Superficial observation often causes coining lesions (cao-gio in Cambodian) to be mistaken for child abuse.

Coin rubbing is performed by scraping the skin with instruments such as a coin, comb, spoon, or the edge of a jar cap to improve circulation within the soft tissue to relieve the symptoms of flu, fever, and headaches. The scraping motion performed with the instrument can cause ecchymotic streaks on the skin [6–8].

## 24.3 Moxibustion

Moxibustion is performed by lighting an incense like material and applying it to the skin at certain acupuncture points. Moxibustion can lead to second-degree burns. Physicians who may not be aware of these cultural practices can confuse the effects of coin rubbing, cupping, and moxibustion as signs of physical abuse.

The material used takes the name of moxa. The Artemisia, a herbal stick commonly used, is placed inside burning cones, or moxa cigars are used, which may cause burns, generally in the abdominal, neck, or heel regions. It is often used when other methods have not been effective or for chronic respiratory illness [9–11].

## 24.4 Traditional Cosmetic Practices

The most used practices able to cause skin lesions include depigmentation, hair products, and greasy creams.

The use of depigmentation products containing hydroquinone can have as side effect the induction of ochronotic hyperpigmentation of dark skin. The pathogenic mechanism lies in the inhibition of oxidase, with a consequent local accumulation of the homogentisic acid in the skin and successive polymerization and production of ochronotic fiber [12–20].

The frequent xerosis of dark skin, particularly of the skin of Indians, induces them to use repeatedly greasy substances, with a consequent development of follicular occlusion. The clinical picture is often that of so-called pomade acne, made up of usually comedonic lesions, with few inflammatory elements, but which may leave pigmentary results for a long time.

## 24.5 Anthropological Ritual

Beyond the female genital mutilation (see Chap. 21), other practices to be considered are scarification (scraping, branding, cutting), tattoos, and perforation (lip plates, ear plates).

*Scarification* is the creation, through whatever technique, of one or more permanent scars in any area of the skin. It is used in African societies for decoration of the face or for medical reasons.

*Branding* is a particular form of scarification using heated metal instruments [21, 22].

*Cutting* is carried out by incision of the skin, repeated in the same spot over time, with the goal of obtaining a clear and visible mark. In other cases, the wounds are temporarily kept open in order to create a pronounced scar like a keloid.

*Cutaneous perforations* are common in ethnic groups from Central Africa. One of these is the lip disk. The women of the Mursi tribes in Ethiopia use a rounded disk made of clay, and the perforated lip is continually manipulated to make it more elastic and capacious. Sometimes, the lower incisors are removed to create more stability. In Sudan, Suma women use a rectangular plate made of light Balsa wood. The lower incisors are removed for greater stability. If the lip, freed from its plate, reaches up to the top of the woman's head, she will be especially prized and her dowry extremely large.

*Piercing* (perforation of the skin) is traditionally used to distinguish the roles of members within a tribe. It regulates the relations between individuals, both day to day and during ceremonies, establishing with a single glance the position of the individual in relation to the group. It often causes dermatitis due to contact with nickel sulfate.

## 24.6 PsychoculturalBehaviors

The term "culture-bound" means a psychopathological entity of defined geographic prevalence determined by the beliefs and paradigms of a specific cultural area.

### 24.6.1 Dhat Syndrome

The term "Dhat syndrome" was proposed by Wig in 1960 and describes a *culture-bound* syndrome common in the Indian sub-continent. It is related to a Hindu theory according to which seminal fluid is rich in a particular vital force and losing it impoverishes the physical and psychic energy of the individual.

The syndrome is characterized by profound anxiety over the loss of seminal fluid through ejaculation and wet dreams. Clinically it often mimics prostatitis, aspecific urethritis, or epididymitis, with consistent negative results of microbiological exams. Patients complain of anxiety, feeling unwell, burning sensations, weakness, psychic disturbance, and trembling. In Italy, an increasing number of cases can be seen in immigrants. A multidisciplinary approach is very important, with the presence of anthropologists, ethno-psychologists, and the help of linguistic-cultural mediators [23–26].

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# What Diseases Occur Where

# 25

Aldo Morrone and Maria Lucia Dell'Anna

## 25.1 Introduction

As stated in previous chapters (see, i.e., Chap. 22 or 23), the overall interaction, starting from the early instance, with migrant or refugee people, requires a holistic approach able to provide the people with clinical, social, and educational care. Among the initial health care, there aren't evidence of benefits (or cost-effectiveness) for obligatory screening for communicable and non-communicable diseases. In addition, it can cause anxiety in individual refugees, often from countries where the state's coercion and abuses are commonplace. However, according to WHO recommendations, the local health workers must offer and provide all health care for all the people requiring health protection. Checks should be performed for both communicable diseases and NCDs, while respecting the human rights, the dignity of refugees and migrants, and the different cultural and religious background. In any case, the collected data must never be used to discriminate or reject a refugee or a migrant from a country. Finally, but not less relevant, despite the common perception of the relationship between migration and arrival of infectious diseases, there is no systematic true association. Refugees and migrants are exposed mainly to the infectious diseases that are common in Europe, independently of migration. The risk that exotic infectious agents, such as Ebola virus, will be imported into Europe is extremely low; experience shows that, when it occurs, it affects regular travelers, tourists, and health-care workers rather than refugees or migrants [1, 2].

## 25.2 How to Start

Triage is recommended at arrival points to identify health problems in refugees and migrants as soon as possible. Proper diagnosis and treatment must follow, and the necessary health care must be ensured for specific population groups (children, pregnant women, and the elderly). All the people must have full access to an adequate health facility, according to the specific needs, and to vaccination program, without discrimination on the basis of gender, age, religion, nationality, race, or legal status. This is the safest way to ensure that the resident population too is not unnecessarily exposed to potential infectious risk.

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## 25.3 Communicable Diseases

The true association of communicable diseases is with the poverty. The economic and environmental conditions occurring in the origin countries, together with a dangerous and fatiguing journey, increase the risk for communicable diseases, particularly measles, and food- and waterborne diseases. The European Region has a long experience of some communicable diseases potentially lethal, such as tuberculosis (TB), HIV/AIDS, hepatitis, measles, and rubella; their burden was significantly reduced during economic development, through better housing conditions, access to safe water, adequate sanitation, efficient health systems, and access to vaccines and antibiotics. However, none of these diseases was completely eradicated in European Region, and this occurs without any association with migration process. This is also true of vector-borne diseases in the Mediterranean area, such as leishmaniasis, which is not based on interpersonal transmission and can be effectively treated. Typhoid and paratyphoid fever are also reported in the European Region. The risk for importation of exotic and rare infectious agents into Europe, such as Ebola, Marburg, and Lassa viruses or Middle East respiratory syndrome (MERS), is extremely low.

### 25.3.1 Tuberculosis

Tuberculosis can affect migrant people, and this is dependent on TB incidence in the country of origin, living and working conditions in the country of immigration (access to health services and social protection must be also taken into account), possible contact with infected people, and journey modality (overcrowded and poor ventilated spaces increase the risk). The incidence of TB in the countries of origin varies from as low as 17 new cases/100,000 population in the Syrian Arab Republic to 338/100,000 in Nigeria. The average TB rate in the European Region is 39/100,000 population. The transmission of TB is not easy, and just 10% infected people in HIV-infected group manifest active disease. Moreover, TB is not often transmitted from migrants to the resident population because of limited contact.

### 25.3.2 HIV

The prevalence of HIV infection is generally low among people from the Middle East and North Africa, and consequently there is a low risk that people from these countries infect resident population in European Region. However, migrants still constitute 35% of new HIV cases in the European Union, but they acquire HIV during the journey and after their arrival, often depending on sexual abuse or prostitution practice and on language and cultural barriers affecting the knowledge of correct behaviors.

### 25.3.3 Influenza and Other Respiratory Infections

The respiratory infections (influenza viruses, respiratory syncytial virus, adenovirus, parainfluenza virus) are very frequent in European Region, as well as in all high-income countries, but migrant people did not increase the risk of spread to the receiving populations. On the contrary, the poor living and working conditions can seriously affect the overall health status of the migrant and refugees people, exposing them to a greater risk of being infected, mainly those of fragile groups (pregnant women, children, elderly). Accordingly, the risk groups should be educated to and provided of seasonal vaccine, irrespective of legal status, according to WHO recommendations.

### 25.3.4 Vector-Borne Diseases

The risk for reintroduction of vector-borne diseases, including malaria and leishmaniasis, can be increased by a mass influx of refugees, as reported in Greece where outbreaks of malaria have been observed directly linked to an influx of migrants from Pakistan.

## 25.4 Antimicrobial Resistance

Antimicrobial resistance may occur when overcrowding, poor hygiene, and malnutrition favor spread of infections, and they are caused by resistant pathogens depending on their origin, which can be the environment, animals, food, or humans.

## 25.5 Prevention of Communicable Diseases

Hand hygiene with soap is one of the most effective methods for preventing transmission of pathogens. Hands should be washed frequently, especially before and after contact with sick people, before and after preparing food, before meals, and after using the toilet. The sanitation facilities represent the other modality of spread; accordingly, a clear separation between drinkable water, food, and sanitation system must be carried out mainly in overcrowding setting.

Moreover, in order to prevent respiratory infections, there should be good air flow in rooms and other space. Fresh air should be allowed to replace the contaminated air around a patient. The doors and windows on opposite sides of the room should be opened to ensure a good air flow. The larger the openings and the larger the difference in temperature between the inside and the outside, the better the air flow.

Although one toilet for no more than 20 people is recommended in emergencies, this standard cannot be respected in most circumstances. If it becomes necessary to install additional (mobile) on-site sanitation facilities that are not connected to centralized sewerage, close attention should be paid to safe collection and disposal of human waste to prevent contact between humans and human feces.

It is important that people with food- and waterborne illnesses (i.e., cholera) have access to proper health care.

A clear education about potential toxic food, falsely similar to known plants and fungi, may prevent intoxication, such as that happened in Germany when refugees ate poisonous mushrooms.

## 25.6 Vaccination

Equitable access to vaccination is crucial to prevent most of communicable diseases, and it is one of the objectives of the European Vaccine Action Plan 2015–2020. The plan urges all countries in the region to ensure the eligibility and access of refugees, migrants, international travelers, and marginalized communities to culturally appropriate vaccination services and information.

Many countries, such as those receiving large influxes of migrants, are incorporating vaccination of migrants into their routine vaccination programs.

## 25.7 Non-Communicable Diseases

The prevalence of NCDs, including diabetes and hypertension in adults, is 25–35% in low- and middle-income countries. The occurrence of a NCD renders more vulnerable people migrants due to the lack of continuous medical care during journey and arrival in new country, to poor hygienic condition, to overcrowding, and to PTSD. It is more frequent the occurrence of potentially lethal complications associated with physical injuries (secondary infections and poor control of glycemia compromise management of acute traumatic injuries), loss of access to medication or devices as consequence of forced displacement, loss of shelter, shortages of water and regular food supplies and lack of income add to physical and psychological strain, interruption of power supplies or safe water, with life-threatening consequences, especially for people with end-stage renal failure who require dialysis.

## 25.8 What Disease Associated with Weather Conditions

The elderly, children, people with health problems, and alcohol abusers are particularly vulnerable to the consequences of cold weather. They can experience several different conditions often lethal: hypothermia (body temperature below

35.0 °C), due to exposure to extreme cold or immersion in cold water, characterized by shivering as first symptom; frostbite, when the skin and underlying tissues freeze due to exposure to cold air, wind, and humidity, most common in the fingers, toes, nose, ears, cheeks, and chin; fractures, sprains, and strains from falls and accidents as well as cardiovascular, respiratory, and mental health problems; and bacterial and viral infections.

On the contrary, due to exposure to extreme high temperature, the physiological compensatory mechanism, the sweating, could be impaired by high ambient humidity (greenhouses) or tight-fitting clothes. This may give rise to life-threatening heatstroke, exhaustion, heart attacks, or confusion and can worsen existing conditions such as cardiovascular and respiratory diseases [2–7].

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# 26 Essential Medicines for Immediate Care in Refugee Camps

Peter Bakker

## 26.1 Medicine as a Cause of Skin Symptoms

Medicines may be helpful to treat disease, but they may also be harmful. Side effects are not uncommon and may well affect the skin. Most of these are mild, but some may be serious or even lethal, such as toxic epidermal necrolysis and Stevens–Johnson syndrome. It is good practice to consider medication as a possible cause of skin reactions [1].

However, the evaluation of side effects is complicated. In the literature, there are reports of side effects or warning for them, but it is often difficult to ascertain that the suspected medicine actually caused the side effect reported. However, the number and nature of reported side effects may well help to determine the likelihood of a causative relation. Many countries have national or regional databases in operation that can help. The biggest and most comprehensive is VigiAccess, the database of side effects of the World Health Organization (WHO). It is maintained by the Uppsala Monitoring Centre and accessible online at http://www.vigiaccess.org/. VigiAccess allows you to find the number of times a specific side effect was reported for a specific medicine. A possible alternative is Sider, accessible online at http://sideeffects.embl.de/. Sider allows you to search for a specific side effect and find medicines associated with it (either through reports of side effects or indicated in product leaflets or packet inserts) and gives some indication of the magnitude of the risk. However, it is far less comprehensive, so you may well miss certain potential risks. Both should be used with caution as the fact that a specific side effect on a specific medicine has not been reported does not prove that it cannot exist. Also, be aware that a specific side effect may be listed under different descriptions.

## 26.2 Specific Issues in Dermatological Pharmacotherapy in Migrants

There are specific issues that must be taken into consideration when looking at treatment for migrants (not necessarily in order of importance!).

### 26.2.1 Migrants Are on the Move, and Their Movement May Be Sometimes Difficult to Predict

They may not be able to keep an appointment for follow-up. This calls for safe and robust treatment. Robust treatment is treatment that is most

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likely to be effective and least likely to pose any problems in terms of side effects, availability, stability, or need for follow-up, to name just a few. This also means such a treatment should not be susceptible to ineffectiveness or excessive risk if used in a suboptimal way, e.g., in case of poor compliance.

Using medication while moving and taking everything necessary is not always feasible. "One-stop shopping" and single-dose treatment would be preferable in such cases.

### 26.2.2 Migrants Have Often Moved into an Environment that Differs from Their Home Environment (Both in Cultural and in Environmental Context)

Migrants come from, and have moved through, different regions and cultures [2, 3]. This poses a challenge for diagnostics but may also be relevant for the selection of medicines. This again calls for robust and safe treatment.

They may have diseases that are uncommon in the region where they are received or that have a different presentation. Also, causative pathogens may show different antimicrobial resistance patterns.

They may be more susceptible to diseases commonly seen in the region where they are received.

They may suffer from the consequences of their travel (exposure to sun, cold, heat, crowded places).

Their expectations of medical care may differ.

Language (communication) and health literacy may be potential problems.

### 26.2.3 Migrants Often Have Had a Long and Difficult Journey and Often Have Encountered Hostilities and Abuse Before and During Their Journey

Safety and certainty are important issues. Any problem solved adequately may be beneficial; any new source of anxiety is to be avoided. This might mean one should reframe one's approach. For example, any medication that is ineffective, or that is used where non-drug treatment is as good as pharmacotherapy, should normally be avoided. However, under certain circumstances and assuming safety is not an issue, this balance may well change when a patient could be reassured with the prescription he expects.

### 26.2.4 There May Well Be Infrastructural Issues in Diagnosis and Treatment

Generally, in order to avoid attracting more immigrants, authorities tend to minimize care for migrants [4]. Several considerations could be said about that, but it is a political issue out of scope here. However, we must be aware of the consequences. These could involve the following:

- Limited availability of expert advice. This could be addressed using teledermatology that has elsewhere been shown to be a feasible option [5, 6].
- Limited availability of diagnostic tests. Smart diagnostic and therapeutic procedures might be used to minimize this problem, but there will be a need to provide for some sort of back-up diagnostic testing facility.
- Limited availability of medicines.

## 26.3 A Formulary for Dermatological Pharmacotherapy in Migrants

This book aims at providing health workers serving migrants with the necessary dermatological information. These health workers may come from, and operate in, different countries and under different circumstances. Any formulary that is to be useful under such conditions should aim at a set of medicines that are widely available and widely accepted. The WHO Essential Medicines List (2019 edition) may serve as first

reference [7]. However, it may be necessary to consider alternatives. Obviously, the usual selection criteria apply (see Sect. 26.5).

### 26.3.1 Systemic Medicines for Specific Diseases

Depending on the regions where migrants come from (or travel trough), specific systemic medicines may be needed, such as medicines for tuberculosis, HIV, leprosy, and leishmaniasis. The current national or WHO treatment guidelines should be adhered to.

### 26.3.2 Systemic Anti-Infective Medicines

Skin infections may begin superficial, but microorganisms that have penetrated the skin may cause deeper and more serious infections; they may become systemic. There should be an adequate choice of systemic anti-infective treatment. A specific formulary should be in line with relevant national or WHO guidelines. Systemic antibiotic treatment may cause systemic side effects, and microorganisms may be resistant or resistance may develop. Local antibiotic treatment is less likely to cause systemic side effects (although this remains a possibility) but more likely to cause local reactions. Also microbial resistance may be more likely to develop or to be already present. Microbial resistance is far less likely to develop against local antiseptics [8]. Therefore, local antiseptics such as povidone-iodine are preferred whenever possible, for example, in superficial impetigo. Systemic treatment is indicated if infection with a *Streptococcus* sp. is suspected, because of the potentially severe complications these bacteria may cause.

### 26.3.3 Systemic Corticosteroids

If treatment with corticosteroids is indicated, topical treatment is usually sufficient. Although there is always some absorption of corticosteroids through the skin, topical treatment greatly reduces the risk of systemic side effects, as compared to systemic treatment. However, in severe cases (e.g., severe inflammation), systemic corticosteroids may be indicated. Systemic corticosteroids such as dexamethasone (injection/tablet), hydrocortisone (powder for injection), and prednisolone (tablets) are included in WHO's Essential Medicines List 2019 (under several headings, such as 2. Medicines for pain and palliative care, 3. Antiallergics and medicines used in anaphylaxis, and 8.2.4 Hormones and antihormones) [7].

Intralesional injection of a corticosteroid such as triamcinolone (acetonide) may be useful to bring rapid relief in severe conditions. This is *local* treatment but with a greater risk of systemic side effects as compared to application on the skin. It is not included in the WHO Essential Medicines List 2019 [7].

### 26.3.4 Other Systemic Medicines in Dermatology

Several other systemic medicines are used in dermatology, most of them not included in the WHO Essential Medicines List 2019. One of them is methotrexate, used for its immunomodulator effects, for example, in psoriasis that does not respond to conventional therapy. Methotrexate is included in the WHO Essential Medicines List 2019, but for another indication (in Sect. 8: Immunomodulators and Antineoplastics) [7]. These drugs should be prescribed only by physician with specific expertise on their use.

### 26.3.5 Topical Dermatological Medicines

Table 26.1 represents the relevant topical preparations in the Essential Medicines List 2019 of WHO and may well serve as a guideline for selecting a set of dermatological preparations for the care for migrants. Those in bold typeface may be considered to form a basic set.

**Table 26.1** Essential medicines list 2019: Dermatological preparations

| Category WHO | Preparation | Indications and remarks |
|---|---|---|
| Antifungal | **Miconazole cream or ointment 2% or other imidazole topical preparation** | Against fungi but also *Candida*; some activity against gram-positive bacteria |
| | Selenium sulfide suspension 2%[a] | Against pityriasis versicolor and seborrheic dermatitis |
| | Sodium thiosulfate solution 15%[a] | Against pityriasis versicolor |
| | Terbinafine cream or ointment 1% | Against fungi |
| Anti-infective | Mupirocin cream or ointment 2% | Against gram-positive bacteria especially *Staphylococcus aureus*. Suspected streptococcal infection should be treated systemically because of the risk of serious complications. Superficial impetigo generally responds to hygiene and antiseptic. Deep infection, or patients at risk are an indication for systemic antibiotic treatment. Fusidic acid cream or ointment 2% may be an alternative but might be less effective |
| | Potassium permanganate solution 1:10.000[a] | Antiseptic bathing or soaking of foul wounds. Cave: Very dangerous when ingested, crystals and strong solutions cause severe chemical burns. Check for full dissolution of crystals before use, solution for use should have a light pink color and is best prepared by diluting stock solution immediately before use. |
| | **Silver sulfadiazine cream 1%** | Severe burn wounds, also useful for ulcers. Broad activity against bacteria |
| Anti-inflammatory and antipruritic | **Betamethasone cream or ointment 0.1% or other strong corticosteroid preparation** | Strong anti-inflammatory preparation for local use. For young children, weak corticosteroids are preferred |
| | **Hydrocortisone cream or ointment 1% or other weak corticosteroid preparation** | Weak anti-inflammatory preparation for local use |
| | Calamine lotion[a] | Antipruritic. |
| Skin differentiation and proliferation | Benzoyl peroxide cream or lotion 5% | Keratolytic for use in acne |
| | Coal tar solution 5%[a] | May be useful in various conditions, including eczema and psoriasis. Suspected carcinogen after chronic exposure, therefore not a preparation of choice. To be avoided in pregnancy |
| | Fluorouracil ointment 5% | Oncolytic preparation, use carefully. Do not use in pregnancy. Not for primary care |
| | Podophyllum resin solution 10–25%[a] | Caustic preparation for treatment of condylomata acuminata, serious warts, and some skin tumors. Do not use in pregnancy or lactation. Not for primary care. Application should be left to a professional. |
| | Salicylic acid solution 5%[a] | Keratolytic with little antiseptic activity. May be absorbed, especially in children or when used on large areas of skin |
| | Urea cream or ointment 5–10% | Moisturizer with keratolytic and antimitotic effects |
| Scabicides and pediculicides | Benzyl benzoate lotion 25%[a] | Must be applied twice at 24-h interval, may be repeated after 1 week. Do not use in children under 2 years of age |
| | **Permethrin cream 5%** | Scabies treatment of choice because of single application (may be repeated if necessary after 1 week). Also used for pubic lice |
| | Permethrin lotion 1%[a] | NOT for scabies, only for head lice (frequent combing and washing of clothes) |
| Antiseptics | **Chlorhexidine solution 5%**[a] | General antiseptic, usually well tolerated. Resistance is uncommon but possible. Stock solution: Dilute to 0.5% (1:10) for use on intact skin, dilute to 0.05% (1:100) for use on wounds, burns, and damaged skin |
| | **Alcohol solution 70%**[a] | General antiseptic, e.g., for hand disinfection. Resistance is unlikely to develop |
| | **Povidone-iodine solution 10% (1% available iodine)**[a] | General antiseptic, usually well tolerated but stings and stains. Resistance is unlikely to develop |

[a]Cave: liquid preparations may form a risk upon accidental ingestion

As stated in 26.3.5 preparations in bold typeface may be considered to form a basic set (of dermatological preparations for the care for migrants)

Apart from this set of preparations, there is need for a general soothing and moisturizing preparation that may serve several purposes. Such a preparation helps to establish or maintain good skin condition [9]. Any well-tolerated preparation may serve. Hydrophilic creams however may be less suitable as they may be more drying than moisturizing and may affect the skin barrier [10, 11].

More detailed information on the use of most of these medicines can be found in the WHO Model Formulary, available online via http://www.who.int/selection_medicines/list/en [12]. Note that the WHO Model Formulary is not updated with every new Essential Drugs List. This means it may not always be completely up to date.

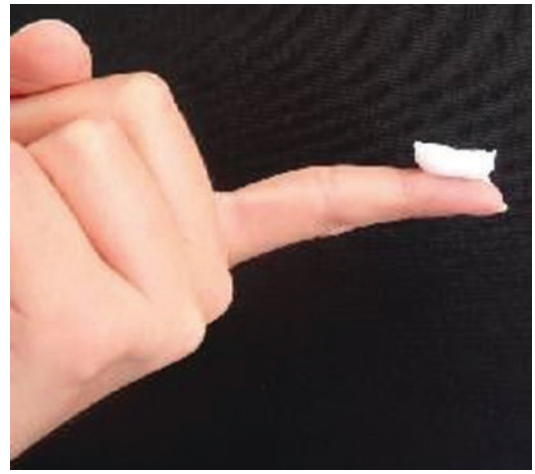

**Fig. 26.1** An FTU is a dash of cream with the length of a fingertip (reproduced with permission from [21])

## 26.4 Some Notes on Prescribing and Dispensing

### 26.4.1 Mixing and Dilution of Topical Preparations

Mixing or dilution of topical preparations, especially corticosteroid preparations, is sometimes advised and may in fact be helpful [13]. For example, a strong corticosteroid may be diluted with vegetable oil during application. However, one should always take into account that the vehicle has a paramount influence on the effectiveness and safety of a preparation. Mixing might well diminish the potency or the systemic absorption of the active ingredient, but an unexpected increase in potency or systemic absorption could also occur [14]. There is a risk of incompatibilities between the diluent and (ingredients of) the preparation resulting in loss of effect. Therefore the decision to mix or dilute should always be taken cautiously and only when the effects of the specific mix are known.

### 26.4.2 Amounts to Be Prescribed and Dispensed

Migrants are often on the move and may not be able to fill a repeat prescription. Especially in such cases, it may be preferable to give them a full treatment supply if safety and stability are not likely to be a problem.

It may be difficult to determine how much of a topical preparation should be prescribed and dispensed. The "fingertip unit" (FTU) is a practical aid for dosing [15]. An FTU is one dash of cream or ointment with the length of the distal bone of the forefinger of an adult (Fig. 26.1). One FTU equals approximately 0.5 g cream or ointment and is sufficient to cover 300 $cm^2$ skin. Depending on the part of the body to be treated, one or more FTUs are used (Table 26.2).

The quantity required for a particular patient can also be estimated from the dose and duration of the therapy and the area of the skin that will be treated (Table 26.3).

Creams are generally more economic than ointments or pastes because they are easier to apply. The amount of an ointment required for a specific treatment is 1.5–2 times as high as compared to the quantity of a cream for the same treatment. When a paste is used, 2–3 times as much is required as compared to a cream.

### 26.4.3 Information and Labeling

As stated above, language and health literacy may be potential problems, especially when serving

**Table 26.2** Fingertip unit dosing for ointments and creams per application (courtesy of [16])

| | Head and neck | Arm and hand | Leg and foot | Trunk (front) | Back and bottom |
|---|---|---|---|---|---|
| Age | Number of FTU per application | | | | |
| 3–12 months | 1 | 1 | 1½ | 1 | 1½ |
| 1–2 years | 1½ | 1½ | 2 | 2 | 3 |
| 3–5 years | 1½ | 2 | 3 | 3 | 3½ |
| 6–10 years | 2 | 2½ | 4½ | 3½ | 5 |
| Adult | 2½ | 4[a] | 8[b] | 7 | 7 |

[a]For only one hand of an adult, 1 FTU is required
[b]For only one foot of an adult, 2 FTUs are required

**Table 26.3** Standard quantities required for adults to treat a particular part of the skin two times daily for 1 week

| Part of the body | Cream/ointment/paste (g) | Liquid preparation (mL) |
|---|---|---|
| Face | 5–15 | 100 |
| Hand | 15–50 | 200 |
| Arm | 50–150 | 200 |
| Leg | 100–300 | 200 |
| Trunk | 200–500 | 500 |
| Whole body | 500–1500 | 500 |

The quantities are rounded off to the nearest standard quantity (courtesy of [16])

migrants. Medication should be used in a safe and effective manner. The patient can only do that if he knows how, so he must be adequately informed. The following may be relevant points of attention:

1. Advice should be specific. For example, "apply in the morning and evening to the right foot" is better than "apply twice daily to affected areas" [17].
2. Pictograms may be helpful but must be accompanied by verbal information [18]. The United States Pharmacopeia (USP) pictogram library is available at http://www.usp.org/download-pictograms. The International Pharmaceutical Federation (FIP) provides pictogram labeling software at http://www.fipfoundation.org/pictograms-download. Alas, the amount of dermatology-specific pictograms is limited.
3. It is good practice to check if the patient has understood, especially in more complex situations [19]. It is more effective to ask "how are you going to use this?" and in that way to let the patient explain to you what he/she has actually understood than to simply ask "do you understand?" The latter question will usually be answered in an affirmative manner and tells you nothing.
4. It may be useful to demonstrate the use of a preparation instead of just telling the patient how to use it [20]. Also, it may be useful to ask the patient to show you how she uses the preparation, rather than just to ask her.

## 26.5 Selection Criteria for Medicines

The selection of medicines for any specific situation is subject to national and international rules and regulations. Therefore, there may not be much degree of freedom for choices. Still, it is useful to have some general idea of selection criteria [16].

### 26.5.1 Need

The preparation must be effective for the treatment of skin diseases that affect many people. There is no need for medicinal treatment if it is not effective, or when non-medicinal treatment is as good as, or better than pharmacotherapy.

### 26.5.2 Benefit/Risk Ratio

The effectiveness of a medicine must be well documented, preferably with controlled clinical trials. In the case of equal effectiveness, the medicine that has the fewest side effects should be selected. If misuse or abuse of a medicine can result in major risks, the use of that medicine should be avoided. Whenever relevant, information such as tropical climate factors, referring to the specific context in developing countries or regions, should be considered when weighing the risk/benefit ratio, instead of looking only at relevant scenarios in Western countries. Specific conditions of the population that will be using the medication, i.e., the presence of malnourishment or endemic diseases, such as hepatitis, malaria, or AIDS, need to be taken into account in the risk/benefit assessment of that medication.

### 26.5.3 Benefit/Cost Ratio

Benefits and costs should be carefully evaluated. Cost estimates need to be based on treatment prices and not unit prices. Transport costs should also be considered. Estimates of treatment cost should include any additional costs, such as bandages used or hospital admissions. Also, non-financial costs and benefits should be taken into account, for example, the need for extra hospital visits.

### 26.5.4 Vehicle

Selection of medicines is incomplete if only active ingredients are considered. This holds true for any medicine but especially so for dermatologicals. These preparations should be washable, non-occlusive, and suitable for the given skin conditions. They should be easy to pack and simple to apply, even under tropical conditions.

### 26.5.5 Stability

Raw materials and preparations must show good chemical, physical, and microbiological stability under adverse storage conditions. When excessive chemical degradation of an ingredient or toxicity of degradation product(s) is expected, the preparation or ingredient should be avoided.

### 26.5.6 Packaging

A general requirement is that packaging should ensure integrity of the preparation and protection against adverse external effects. The packaging of medicines meant for use in tropical countries should also be light, reusable, and providing adequate protection for the preparation against evaporation, adsorption of water, and excessive exposure to light.

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# 27 How to Recognize Skin Signs of Potentially Life-Threatening or Disabling Diseases (Malnutrition-Driven Skin Disorders)

Ismael Maatouk and Aldo Morrone

## 27.1 Introduction

Pellagra, a disease first described by the Spanish Gaspar Casal in 1762, has been now eradicated from Europe and North America. However, sporadic forms arise, mostly in the Mediterranean area, maybe due to the sunlight exposure. sometimes pellagra may emerge as pellagra sine pellagra, as occurred during the Spanish Civil War (1936–1939). However, the disease appears as the most severe problem in developing countries and in refugee populations where war aggravates the perpetual distress. Kwashiorkor is also a disease of poor developing countries, and its combination with severe measles in Cambodian refugees produced a high mortality in children in Vietnam in the 1970s. The toxic form of porphyria occurred in Turkey in 1954–1955 when 0.2% hexachlorobenzene was utilized as pesticide for wheat and the consumption of it by humans provoked close to 5000 cases of porphyria ("*karayara*") with 10% mortality. People affected had photosensitivity, cutaneous blisters, hypertrichosis, and severe mutilations, and 30% developed hyperthyroidism. Related to "*karayara,*" a toxic dermatosis ("*pembeyara*" = pink sore) was seen in approximately 500 breast-fed children born from mothers who had toxic porphyria; the mortality of "*pembeyara*" was up to 95%.

There are other examples of toxic porphyria, such as the disease which Bantu aborigines developed in South Africa, due to the association of deprivation, drinking adulterated alcohol ("*skokiaan*"), and a very iron-rich diet (soup preparation, "*marewa,*" in metallic pots).

This is to illustrate that the group of diseases of this chapter is associated with poverty, war, and underdevelopment. If the man has been able to eradicate them in north-western developed countries, it would be possible to create the conditions permitting to control and eliminate worldwide these calamities that, as long as they exist, are a shame for rich and developed nations [1–6].

## 27.2 Kwashiorkor

### 27.2.1 Synonyms

It is also known as protein-energy malnutrition (PME), malignant malnutrition, nutritional dystrophy, kwashiorkor marasmus, and Eiweißmangelkrankheit.

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### 27.2.2 Definition

Kwashiorkor is a typical childhood pathology, which principally involves children between 6 months and 4 years old, characterized by severe hypoproteinemia, responsible for edema with facies lunare, which covers up the lack of fat, already consumed. It is characterized by growth retardation, anemia, muscular weakness, and some typical dermatological manifestations. The name kwashiorkor derives from the Ga dialect of Ghana and means "first child-second child." It indicates that the first child develops PEM when the second child is born and replaces the first child at the breast.

### 27.2.3 Distribution

WHO considers that more than 400 million children younger than 5 years old suffer from malnutrition in developing countries, and a great number of them suffer from severe protein deficiency like kwashiorkor.

### 27.2.4 Clinical Features

PME can appear under three clinical forms. The dry form, marasmus, is due to near starvation with absence of protein and non-protein nutrients. The wet form is called kwashiorkor, where child is fed a thin gruel of poor nutritional quality (compared with mother's milk) and fails to thrive. Accordingly to pronounced protein deficiency, edema develops. When dry and wet forms occur together, PEM is called marasmic kwashiorkor.

Children with this form have some edema and much body fat. Mucocutaneous alterations are frequent. The onset in many cases is insidious. It is possible to observe stomatitis, cheilitis, conjunctivitis, blepharitis, and a characteristic dermatitis, erythematous and cyanotic, with a "painted" (flaky paint dermatitis) aspect. Subsequently the cutaneous lesions became hyperpigmented; it is usual in the formation of rhagades, bullae, and erosions with well-defined borders. The most affected areas are the perineum, the regions under mechanical pressure, and the folds. In black children, hair assumes a characteristic large band pigmentation that varies from lucent brown to red and to white and develops in successive cycles (flag sign). General symptoms include anaemia, hepatomegalia, marasma, and mental retardation. Secondary infections and ulcerations may also be observed.

### 27.2.5 Diagnosis

It is based on patient's history, on the country of origin, on the clinical edema signs, and on cutaneous manifestations. Hypoalbuminemia in these cases is significant. Differential diagnosis includes pellagra, ankylostomiasis, edema and anemia, abdominal tuberculosis, nephritis, and coeliac disease. Hepatic biopsy shows a fatty degeneration. Skin histology shows epidermal atrophy together with hyperkeratosis or parakeratosis.

### 27.2.6 Therapy

The first therapy is to correct fluid and electrolyte abnormalities (hypokalemia, hypocalcemia, hypophosphatemia, and hypomagnesemia) and to treat infections with antibiotics. Children with PEM should be treated with I.V. fluids. The initial rehydrating fluid is Darrow's solution, containing 1:2:3 parts (V:V) of 0.17 M lactate: normal saline: 5% glucose, to which 50 mL of 50% D/W is added to each 500 mL. This solution provides with 78 mEq/L of sodium and 55 mM/L of glucose. The water deficit should be replaced over the first 8–12 h of therapy. The administration of i.m. iron or high doses of oral iron (100–200 mg/day of elemental iron) in children is very important. Iron immediately increases bone marrow iron stores when i.m. administrated. For oral rehydration in adults, a solution containing 90 mEq/L sodium, 20 mEq/L potassium, 80 mEq/L chloride, 30 mEq/L bicarbonate, and 111 mM glucose/L given in divided doses over 24 h is satisfactory.

Following the initial rehydration phase, it is useful to supply macronutrients. This step may be delayed 24–48 h in children (to avoid worsening the diarrhoea). Milk-based formulae are the treatment of choice. The amount is gradually increased during the first week; after a week, the full rate of 175 kcal/kg and 4 g of protein/kg for children and 60 kcal/kg and 2 g of protein/kg for adults can be given. When diarrhea is severe, the patient may be kept NPO (nil per os) for up to 48 h. When diarrhea subsides (usually during the first 48 h), the I.V. is discontinued, and oral feeding begins [7–10].

## 27.3 Vitamin A Deficiency (Hypovitaminosis A)

### 27.3.1 Synonyms

It is also known as retinal deficiency, phrynoderma, avitaminosis A, and Vitamin-A-Mangelkrankheit.

### 27.3.2 Definition

Vitamin A deficiency is characterized by various ocular disorders and mucocutaneous manifestations. Children and young adults are the most affected by the disease.

### 27.3.3 Distribution

It is ubiquitous but particularly frequent in the tropical and subtropical regions.

### 27.3.4 Diagnosis

The diagnosis is based on diet history, endemia in the country of origin, and cutaneous and ocular manifestations. Vitamin A dosage is indicative.

Differential diagnosis will include ichthyosis vulgaris, keratosis pilaris, and follicular keratosis, and Darier's disease has to be taken into consideration. The histologic evaluation shows sebaceous and sudoriparous gland atrophy.

### 27.3.5 Clinical Features

Skin appears dry and wrinkled, ichthyosiform, squamous, and xerotic. On the arms, head, shoulders, and trunk, follicular hyperkeratosis (phrynoderma), as well as sebaceous and sudoriparous gland atrophy, may be observed. Hemeralopia and keratomalacia are the typical ocular manifestations.

### 27.3.6 Therapy

Administration of adequate vitamin A amount (vitamin A palmitate in oil 60,000 IU daily for 2 days and once before discharge from the hospital after 7–10 days) is the usual therapeutical approach. Since xerophthalmia is the major cause of blindness among young children in most developing countries, prophylactic doses of 200,000 IU of vitamin A palmitate in oil orally once every 3–6 months are advised for all children aged 1–4 years old; the dose is halved for those under 1 year old. The diet should include dark green leafy vegetables and yellow fruits, such as mango and pawpaw. Bread, sugar, and monosodium glutamate are added with vitamin A. For secondary deficiency, vitamin A supplements should be given routinely. Infants suspected of being allergic to milk should be given adequate vitamin A in the alternative food. It is advisable to avoid excessive vitamin A dosage [11, 12].

## 27.4 Pellagra

### 27.4.1 Synonyms

It is also known as nicotinic acid deficiency, niacin hypovitaminosis, and pellagroid.

### 27.4.2 Definition

The complete syndrome of vitamin PP deficit includes dermatitis, diarrhea, dementia (the "three D syndrome"), stomatitis, and glossitis. It is often observed in rural populations that are

used to eating excessive quantities of corn and only assume very small quantities of animal proteins and fresh fruit. Corn, even if rich in nicotinic acid, is not able to provide the body with an adsorbable form.

### 27.4.3 Distribution

Pellagra was 7.8 times more common in women than in men. Poverty and consumption of corn were risk factors to develop pellagra at the beginning of past century in the USA.

Now it is very frequent in the tropical and subtropical regions of the developing countries. It still represents a severe problem in many African countries, in Latin America, and in India.

### 27.4.4 Clinical Features

The clinical manifestations are a triad, prevalently cutaneous, but with a gastrointestinal and at times neurological involvement. Cutaneous lesions are usually symmetrical and are represented by a dark red erythema, with well-defined borders, that rapidly appears on the exposed areas, accompanied by edema. Skin appears thin and fissured; later a bullous leak, with a sero-hemorrhagic content, may be observed, which slowly recovers leaving atrophic and pigmented skin. Diarrhea, stomatitis, and glossitis can at times precede the cutaneous manifestations. In the worst forms, apathy, depressive syndromes, sensitive disturbances, and dementia occur. Pellagra slowly progress.

### 27.4.5 Diagnosis

It is based on cutaneous lesions in endemic areas. A still valid diagnostic criterion is the ex-juvantibus test by vitamin load: after the therapy with PP vitamin, successful recovery may be observed. Differential diagnosis includes solar dermatitis, contact dermatitis, porphyria cutanea tarda, neurodermatitis, erythematous lupus, and Hartnup's disease. Skin biopsy is characterized by inflammatory infiltrates in the superior derma and bullae in the sub-epidermis. Later hyperkeratosis appears with parakeratosis, moderate acanthosis, melanin growth, edema, and chronic derma inflammatory infiltrate.

### 27.4.6 Therapy

The oral administration of nicotinamide or niacin usually is effective. Oral or preferably parenteral administration leads to a rapid improvement of the cutaneous manifestations and subsequent recovery of the neurological and gastroenterological conditions. Providing a diet high in protein and adequate in calories is very important. The addition of meat, milk, peanuts, green leafy vegetables, whole or enriched grains, and brewers' yeast can enhance the niacin intake. In patients with oral dysphagia secondary to glossitis, a liquid or a semisolid diet may be required. Long-term inclusion of milk, meat, and eggs in the diet ensures dietary adequacy of proteins essential for recovery. Alcoholic intake must be forbidden [13–16].

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