INVITED SUBMISSION

Not to be missed! Differential diagnoses of common dermatological problems in returning travellers

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Summary After systemic febrile illnesses and diarrhoea, dermatological disorders are the third most frequent health problem of returning travellers consulting travel clinics. While most travel-related dermatological problems are mild, self-limiting and rather harmless, the challenge is to pick up on dermatological clues to potentially severe or even life-threatening diseases. This article provides an overview of the most common and the ‘not to be missed’ dermatological diagnoses in international travellers.

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Introduction

The three most common reasons for returning travellers to seek medical help are systemic febrile illnesses, acute or chronic diarrhoea and dermatological disorders [1]. Various studies have recently reviewed the spectrum and the frequencies of travel-related dermatological disorders observed in travel clinics [1–4]. The spectrum of dermatological diagnoses in travellers is broad and dominated by insect bites, bacterial skin infections, creeping eruptions and allergic skin reactions (Table 1).

This article addresses the most frequent dermatological disorders and their differential diagnoses in returning travellers, and highlights the dermatological clues to severe and potentially life-threatening diseases, which should not be missed: ‘When you hear hoofbeats, think horses, not zebras’… but make sure not to miss out on zebras.

(Those dermatological disorders that are not confined to travelling — e.g. herpes zoster, pityriasis rosea, syphilis and sun- and heat-related skin pathologies — also frequently occur in travellers, but are beyond the scope of this review).

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Methods

This review is based on the most frequently reported skin pathologies in travellers (see Table 1), on the relevant literature and on personal experiences from daily practice at our travel clinic.

Ectoparasites

Insect bites

Consultations for insect bites are frequent and the clinical presentations vary widely. One insect may cause different types of skin lesions and each type of skin lesion may be caused by different kinds of insects, thus it is difficult and often impossible to infer from a skin lesion the causative insect. However, in some cases, the clinical aspect and the distribution of the skin lesions may be suggestive: for example, pruritic lesions caused by fleas and bed bugs are more frequently papular and typically clustered or linearly grouped, which is rarely seen with mosquito bites [5–7]. The typical evolution of insect bites is the initial formation of wheals and flares (with a peak within 20 min), a delayed reaction manifesting as itchy indurated erythematous papules (with a peak at 24–36 h) and the gradual resolution of the lesions within days to weeks [8]. However, the clinical picture may include ecchymoses or vesicles and severely allergic patients may develop haemorrhagic bullae, necroses or ulcers that heal with residual scarring [7]. In a few cases, insect bites may cause systemic symptoms like generalised urticaria, angioedema, anaphylaxis or the rare ‘Skeeter syndrome’ (a large local inflammatory reaction accompanied by fever, which can be differentiated from cellulitis by its peracute onset within hours) [8–10]. Sequelae of insect bites include bacterial superinfection, post-inflammatory changes in pigmentation, prurigo simplex-like lesions, prurigo nodularis and atrophic scarring [5,7].

Diagnosis

Diagnosis is based on the patient’s history and clinical picture.

Treatment

Insect bites are primarily treated with topical steroids and oral antihistamines. Patients suffering from agonising nocturnal pruritus may benefit from the use of older, sedative antihistamines. In severe, disseminated or refractory cases, the oral intake of steroids may be required.

Myiasis

The maggots/larvae of various flies (mostly Dermatobia hominis [human bot fly – Central and South America] and

Table 1  Spectrum and frequency of travel-related dermatological disorders.

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Number of cases (n = 4158) %</td>
<td>16.8</td>
<td>8.2</td>
<td>9.7</td>
<td>18.7</td>
</tr>
<tr>
<td>Ectoparasites</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Arthropod/insect bite</td>
<td>16.8</td>
<td>8.2</td>
<td>9.7</td>
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</tr>
<tr>
<td>Scabies</td>
<td>2.3</td>
<td>–</td>
<td>10.0</td>
<td>2.2</td>
</tr>
<tr>
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<td>0.8</td>
<td>–</td>
<td>7.2</td>
<td>3.5</td>
</tr>
<tr>
<td>Tungiasis</td>
<td>0.6</td>
<td>–</td>
<td>4.0</td>
<td>–</td>
</tr>
<tr>
<td>Tick bites</td>
<td>0.6</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Myiasis</td>
<td>0.8</td>
<td>14.5</td>
<td>21.2</td>
<td>12.4</td>
</tr>
<tr>
<td>Rickettsial disease</td>
<td>1.3</td>
<td>–</td>
<td>0.6</td>
<td>–</td>
</tr>
<tr>
<td>Leprosy</td>
<td>–</td>
<td>–</td>
<td>2.4</td>
<td>–</td>
</tr>
<tr>
<td>Helminths</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Larva cutanea migrans</td>
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<td>9.8</td>
<td>4.8</td>
<td>12.9</td>
</tr>
<tr>
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<td>–</td>
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<tr>
<td>Filariasis (Loiasis)</td>
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<td>–</td>
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<tr>
<td>Gnathostomiasis</td>
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<td>–</td>
<td>1.8</td>
<td>–</td>
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<tr>
<td>Protozoa</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cutaneous leishmaniasis</td>
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<td>–</td>
<td>3.8</td>
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<tr>
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<td>3.4</td>
<td>7.2</td>
<td>–</td>
</tr>
<tr>
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<td>4.0</td>
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<tr>
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<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
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<td>–</td>
<td>3.6</td>
<td>–</td>
</tr>
<tr>
<td>Injuries</td>
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<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Terrestrial animal bites</td>
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<td>4.3</td>
<td>–</td>
<td>&gt;4.7</td>
</tr>
<tr>
<td>Maritime animals</td>
<td>0.7</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Pruritus of unknown origin</td>
<td>–</td>
<td>–</td>
<td>9.1</td>
<td>–</td>
</tr>
<tr>
<td>Unknown skin disorder</td>
<td>16.3</td>
<td>5.5</td>
<td>–</td>
<td>6.6</td>
</tr>
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*Including skin abscesses, impetigo, erysipelas, superinfected insect bites, etc.*
Cordylobia anthropophaga [tumbu/mango/putzi fly — Sub-Saharan Africa] can cause infection in humans [76]. African tumbu flies lay their eggs in faecal-contaminated soil or on damp clothing hanging to dry. Direct contact activates the hatched larvae to penetrate the skin. American human bot flies attach their eggs to the body of captured mosquitoes, to reach the human host.

Diagnosis
Diagnosis is based on the pathognomonic clinical picture, which is characterized by itchy, slowly enlarging (Ø 1–3 cm) subcutaneous furuncular (boil-like) skin lesions. On close inspection, a central aperture, permitting the maggot to breathe and to drain waste products, is visible (Fig. 1).

Treatment
The maggots can be removed by gently squeezing the boil, assisted by first covering the aperture with a layer of paraffin oil or petroleum jelly to stop the oxygen supply. While mature larvae are easily extracted by these measures, early lesions are best left to develop for a few days, as immature maggots are reluctant to emerge. If surgical removal is applied, rupture of the larvae has to be avoided, as this can lead to a severe inflammatory reaction.

Tungiasis (‘Sand flea’, ‘Jigger’)
Tungiasis is endemic in parts of Africa, Central and South America, and India. Tunga penetrans is the smallest of all fleas, measuring around 1 mm in length, and lives in the soil near pigsties and cattle sheds [77]. The female T. penetrans flea burrows into the soft skin regions of suitable hosts (humans and various animals) and remains there for up to five weeks, during which time it feeds on blood, matures, and produces and releases eggs, before finally dying [76].

Diagnosis
The lesions are commonly located at the feet and the clinical picture is pathognomonic: the flea’s round whitish abdomen shines through the overlying dermis around a central aperture (Fig. 2). The lesions may be pruritic and painful.

Treatment
Extraction of the parasite after removal of the overlying skin is straightforward.

Scabies
Scabies, caused by the mite Sarcoptes scabiei, is a cosmopolitan ectoparasitic disease, most commonly seen where hygiene standards are low and acquired by direct contact with infected individuals. Scabies mites (≤0.5 mm) burrow a mostly invisible S-shaped tunnel of up to 4 mm into the superficial layer of the epidermis, where they live and lay eggs [77]. The resulting skin lesions (Fig. 3) are most commonly found on the fingers, especially in the web spaces, anterior wrists, upper limbs, axillary lines, the periumbilical region, external genitalia and buttocks [78]. As a result of a hypersensitive reaction to mite proteins, patients typically complain about intense itching, typically worst at night while in the warm bed. Scratching itchy areas may result in bacterial superinfection. Diagnosis is frequently delayed, as the lesions are mistaken for eczema, tinea, or atopic dermatitis [79].

Diagnosis
Diagnosis is mainly based on the clinical picture. The lesions are best identified by a handheld dermatoscope.

Treatment
For practical reasons, although possibly less effective, oral ivermectin has largely replaced the cumbersome topical treatment with permethrin, benzyl benzoate, crotonit and lindane as the first-line treatment [78–80]. The currently recommended treatment regimens are two applications (overnight) of topical permethrin 5%, 1–2 weeks apart or oral ivermectin (200 μg/kg body weight) OD on day 1 and after 1–2 weeks [78].

Pitfalls/not to be missed
- Non-healing or progressively ulcerating insect bites persisting over weeks or months should raise suspicions of cutaneous leishmaniasis (see below)
- Consider Myiasis or Tungiasis in lesions showing a central orification
- Scabies may present a wide range of clinical pictures
- Erythema chronicum migrans in Lyme borreliosis
- Rickettsioses (see below)
- African/South American trypanosomiasis/sleeping sickness (see below)

Bacterial skin infections
Bacterial infections are the most frequent skin disorder in travellers returning from tropical and subtropical countries. The majority of these cases concern superinfected insect bites, with Staphylococci and Streptococci being the primary causative pathogens. While most cases of erythema, erysipelas and cellulitis are caused by Streptococci, impetigo, folliculitis and abscesses are rather caused by Staphylococci [11]. While mitecillin-resistant Staphylococcus...
aureus (MRSA) infections were formerly considered to be a problem restricted to healthcare settings (‘hospital acquired’ HA-MRSA), ‘community acquired’ MRSA (CA-MRSA) infections have emerged as a global health problem, affecting international travellers [12,13]. Swedish surveillance data show that travellers returning from tropical and subtropical countries have an up to 59-fold higher risk of being colonised or infected with MRSA compared to travellers returning from countries in Western Europe [14].

In cases of skin and soft-tissue infections, linked to the rise in medical tourism (cosmetic injections [‘mesotherapy’] or plastic surgery) as well as tattoos acquired abroad, atypical mycobacteria (e.g. Mycobacterium chelonae, Mycobacterium fortuitum, Mycobacterium abscessus) should be considered [24–27].

Cases of cutaneous diphtheria [15,16], cutaneous bartonellosis/veruga peruana [17], cutaneous melioidosis [18,19], cutaneous tuberculosis [20], cutaneous atypical mycobacteriosis (e.g. buruli ulcer [21]), cutaneous anthrax [22] or leprosy [23] are only exceptional diagnoses in returning travellers.

**Diagnosis**

Diagnosis is based on the clinical picture and the bacterial culture of wound swabs.

**Treatment**

The selection of the antibiotic treatment regimen depends on the causative pathogen and should be guided by susceptibility testing.

**Pitfalls/not to be missed**

- With CA-MRSA emerging as a skin pathogen in travellers, microbiological work-up with culture and sensitivity testing should be performed, if antibiotic treatment of purulent skin lesions is indicated
- Bacterial superinfection of cutaneous leishmaniasis is common and should not distract from performing investigations for leishmania (see below)
- When symptoms (esp. pain and fever) and clinical findings of skin and soft-tissue infections are disproportional, the rare but rapidly life-threatening differential diagnosis of necrotic fasciitis should be ruled out before considering other diagnoses
- In skin lesions unresponsive to empirical antibiotic treatment, cutaneous leishmaniasis, cutaneous tuberculosis, atypical mycobacteria and leprosy should be considered

**Skin manifestations in febrile patients**

**Fever + generalised rash**

Causes of fever with generalised rash are copious and their discussion is well beyond the scope of this review. In returning travellers, arboviral infections like dengue and chikungunya and rickettsial infections (see below) are the primary infectious causes to consider (Fig. 4). However, cosmopolitan infections like measles, rubella, scarlet fever and acute HIV- and hepatitis B/C infection, as well as drug hypersensitivity reactions and connective tissue diseases, should not be forgotten in returning travellers presenting with fever and rash.

**Fever + insect bite: eschars & chancres**

In febrile patients returning from endemic regions, rickettsioses are common and, even though rare, the
potentially life-threatening cases of African sleeping sickness/African trypanosomiasis must not be missed. Therefore, in febrile patients returning from endemic regions, eschars and chancres should be actively sought after:

**Rickettsioses: ‘eschars’**

Rickettsial ‘spotted fevers’ are caused by various *Rickettsia* species worldwide and transmitted by ticks or mites. Most patients present with a mild-to-moderately severe flu-like illness (fever, headache, malaise, myalgia) typically accompanied by a cutaneous rash (maculopapular, vesicular, or petechial), lymphadenopathy and a characteristic inoculation eschar at the site of the tick bite [28, 29]. Eschars are morphologically characterised by a dry, dark (grey, brown, black) scab resembling a cigarette burn (Fig. 5) and lymphadenopathy of the locoregional lymphatic drainage is common. Most cases are mild, but severe complications (e.g. vasculitis, meningoencephalitis, pneumonia, myocarditis/pericarditis, nephritis, pancreatitis) and multi-organ failure can develop. Only a minority of infected travellers can recall a preceding tick bite. Even though not all rickettsioses show eschars and the absence of a rash or eschar does not exclude rickettsial infection, the finding of an eschar is often indicative. Among travellers, ‘African tick bite fever’ caused by *Rickettsia africae* is the most frequent rickettsiosis [30]. Especially among travellers to South Africa, the risk of becoming infected with ‘African tick bite fever’ is reportedly 4—5 times higher than the risk of contracting malaria [31]. Other rickettsioses regularly seen in travellers are ‘Mediterranean spotted fever’, caused by *Rickettsia conorii*, and ‘Scrub typhus’ (‘Tsutsugamushi fever’), caused by *Orientia tsutsugamushi* [30].

**Diagnosis**

In the absence of suggestive skin manifestations, the diagnosis of a rickettsial disease is often difficult as the most commonly applied serological tests are not useful before the end of the first week of illness and PCR diagnostic (from blood) is often not available (Note: Lacking sensitivity and specificity, the traditionally-used Weil-Felix [agglutination] test is no longer recommended). In these cases, the fast and universal response of rickettsioses to doxycycline treatment can help to corroborate the tentative diagnosis. If available, immunohistochemical detection of rickettsia in a biopsy specimen is an option, while the culture of rickettsia is well beyond routine diagnostics and restricted to specialised laboratories.

**Treatment**

Doxycycline is the drug of choice for all rickettsioses. In general, a seven-day course is given or until the patient has been afebrile for at least 48 h.

**African trypanosomiasis (sleeping sickness): ‘chancres’**

African trypanosomiasis, a blood protozoal infection, should be considered in safari tourists, hunters and wildlife researchers returning from East Africa and that present with a severe febrile illness, once malaria has been ruled out. To date, approx. 100 cases of African trypanosomiasis have been reported in travellers, with five cases published in 2012 [32—36]. Five to fifteen days after being bitten by an infected tsetse fly, a painful circumscribed inoculation chancre may develop, characterised by an indurated dusky-red papule 2—5 cm in diameter (Fig. 6) [37]. Accompanying regional lymphadenopathy may be present. The systemic dissemination of the parasite that follows leads to the ‘hemolymphatic stage’ of the disease, characterised by fever, headache, fatigue, malaise, lymphadenopathy, pruritus, skin rash, and gastrointestinal symptoms. Electrocardiography (ECG) may show signs of accompanying myopericarditis, which rarely leads to cardiac insufficiency but can lead to cardiac arrhythmias [38]. If diagnosis and treatment is delayed at this stage, the parasites may invade the central nervous system and cause the eponymous ‘meningoencephalitic stage’, characterised by neurological (e.g. headache, drowsiness, tremor, seizures) and psychiatric symptoms. With overlapping symptoms, neither stage can be clinically differentiated and staging of the disease has to be based on cerebrospinal fluid analysis. Neuropsychiatric disorders are only rarely seen in travellers and delayed treatment almost always entails multi-organ failure and death [39, 40].

South American trypanosomiasis (Chagas disease), which is transmitted by bloodsucking triatomine insects, is only very rarely seen in travellers [41]. Analogous to African trypanosomiasis, a chancré (‘chagoma’) may be seen in

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**Figure 4** Arboviral rashes left: maculopapular dengue rash middle: confluent dengue rash (‘white islands’) right: chikungunya rash.
acute Chagas disease. This oedematous lesion develops where the vector’s infective faeces enters (is rubbed) into the skin, which is mostly at or around the bite site. If the insect’s infective faeces is deposited close to or accidentally rubbed into the eye, a pathognomonic unilateral painless periorbital oedema with conjunctivitis (‘Románía’s sign’) can be seen. A generalised rash may also occur in acute Chagas disease.

Diagnosis
Diagnosis of trypanosomiasis rests on finding the parasite in body fluid or tissue by microscopy. All patients diagnosed with African trypanosomiasis must have their cerebrospinal fluid examined to determine whether there is central nervous system involvement, since the choice of treatment will depend on the disease stage. Serological tests are also available.

Treatment
Depending on the causative trypanosoma species and stage of the disease, pentamidine, eflornithine/nifurtimox, suramin or melarsoprol are the treatment options for African trypanosomiasis. In South American trypanosomiasis, benznidazole and nifurtimox are used.

Pitfalls/not to be missed
- Fever + generalised skin rash:
  - Arboviral infection (dengue, chikungunya)
  - Acute HIV-, Hepatitis B-, Hepatitis C-infection
- Fever + insect bite/suspicious skin lesions:
  - Rickettsioses

- African/South American trypanosomiasis (sleeping sickness)

Cutaneous leishmaniasis
Leishmaniasis is caused by various Leishmania parasite species, which are transmitted through Phlebotomus (Old World) and Lutzomyia (New World) sandfly bites. The clinical manifestations of leishmaniasis vary widely (visceral-, cutaneous-, mucosal disease) and depend on the causative Leishmania species.

Cutaneous leishmaniasis (CL) manifests one to several weeks after the bite of an infected sandfly with a slow, progressively growing and ulcerating, granulomatous plaque (Fig. 7). Due to the high variability of the clinical picture and the overall low awareness of general practitioners, diagnosis is often delayed. In a few patients, mucosal leishmaniasis (ML), characterised by symptoms related to the progressive infiltration and ulceration of the mucosal membranes of nose and pharynx, may develop concomitantly or months to years after the appearance of the CL lesion(s). ML is mostly seen in patients infected by New World Leishmania species. As the treatment regimens used in ML differ considerably from the regimens used in CL, an ENT examination (inspection of the oral, pharyngeal and nasal mucosa) should be performed in all CL patients to rule out concomitant ML.

Imported CL cases among travellers returning from endemic regions have increased in recent years [42]. For international travellers, the risk of contracting CL depends on the region visited and is estimated to be 20 times higher...
in Central and South America, 10 times higher in Africa, and 5 times higher in Asia compared to visiting leishmanial endemic regions of Southern Europe [43]. The incidence rates of New World CL in travellers have been estimated to be between \(<1/1,000,000 in Mexico and 1/360 in the Amazonas region of Bolivia [44].

Diagnosis
Diagnosis is based on epidemiology, the clinical picture and direct or indirect detection of the parasite in biopsy material. Polymerase chain reaction (PCR) has a sensitivity of 89–100%, is fast, allows species determination and has become the diagnostic method of choice, likely to replace microscopy (sensitivity 9–77%) and culture (sensitivity 58–62%) [42,45,46].

Treatment
Treatment modality (local cryo- or heat-therapy vs. local drug therapy [topical or by injection] vs. systemic drug therapy) and the selection of an anti-leishmanial drug regimen depends on the causative *Leishmania* species and local drug susceptibility, as well as on the number, size and localisation of the lesion(s). Treatment is complex and should be discussed with a specialist or referral centre. Drugs currently in use include pentavalent antimonials (sodium stibogluconate and meglumine antimoniate), amphothericin B formulations, pentamidine, miltefosine, paromomycin, imiquimod, azoles (ketoconazole, itraconazole, fluconazole), allopurinol and adjunct pentoxysphillin and TNF-inhibitors.

Various recommendations for treating CL in travellers have been published at national level [46–50] and a European expert group (‘LeishMan’) is currently working on harmonising diagnostic and treatment recommendations for CL.

Pitfalls/not to be missed
- CL should be suspected for skin lesions that:
  - develop one to several weeks after a suspected insect bite
  - progress in size over days/weeks/months
  - persist over weeks/months
  - do not or only partially* respond to antibiotic treatment (* bacterial superinfection of CL lesions is common and should not limit investigations for Leishmania)
  - worsen under steroid therapy

- Consider mucosal involvement (ML) in CL patients with New World leishmaniasis
- PCR diagnosis should be enforced, as species determination is crucial for deciding the optimal treatment modality

Cutaneous larva migrans syndrome, creeping eruptions and migratory swellings

Various helminth parasites can cause ‘cutaneous larva migrans’ syndrome or ‘creeping eruptions’ (demarcated linear or serpiginous tracks beneath the skin) and ‘migratory swellings’ (less demarcated as the parasite migrates through deeper subcutaneous tissues). While Hookworm-related cutaneous larva migrans is always confined to the skin and shows a characteristic clinical picture, it is important to highlight that the clinical differentiation of other parasites (e.g. Strongyloides, Gnathostoma, Loa loa) is often not possible. Some parasites may migrate, unrestricted, through body tissues and organs, capable of causing severe symptoms and sequelae (e.g. CNS invasion of *Gnathostoma* or *Angiostrongylus*).

Hookworm-related cutaneous larva migrans
(‘ground itch’, ‘sandworm’)

Hookworm-related cutaneous larva migrans is caused by hookworm larvae from various animals (incl. domestic dogs and cats), with *Ancylostoma braziliense* being the species that most frequently affects humans [51]. Hookworms live in the intestines of animals and shed their eggs with the host’s faeces; left on the ground the infectious larval stage develops. Human infection results from larvae penetrating the intact skin on contact with contaminated soil (often sandy beaches). Humans are accidental dead-end hosts and the parasite lacks the enzymatic provisions to penetrate beyond the human dermis to complete its lifecycle. Therefore, the parasite migrates superficially, exclusively within the dermis, until the parasite eventually dies spontaneously (within 2–8 weeks). The track is 1–5 mm wide, extends slowly over days to weeks and classically shows a well demarcated linear or serpiginous pattern (Fig. 8). Sensitisation may lead to the formation of papules and vesicles and the (often) intense pruritus tempts patients to scratch, which may in turn cause bacterial superinfection.

![Figure 7](image) Cutaneous leishmaniasis.
Diagnosis
Hookworm-related cutaneous larva migrans can almost always be differentiated from other creeping eruptions by its distinct clinical picture and without the need for additional diagnostic investigations [52].

Treatment
Oral ivermectin and albendazole are the two first-line drugs for Hookworm-related cutaneous larva migrans, as this stage larva of the parasite. Gnathostomiasis is endemic to some regions of Asia and South America where raw fish is consumed as part of the local food tradition (e.g. 'sushi' in Asia and 'ceviche' in Central and South America). With increasing numbers of international travellers, gnathostomiasis has become recognised as an emerging parasitic disease in travellers returning from endemic regions [57–59].

Cutaneous gnathostomiasis may manifest as intermittent migratory swelling or subcutaneous creeping eruption, varying in size and duration (Fig. 9). The migratory tracks are often wider than 5 mm. The larvae are capable of migrating with a speed of up to 1 cm per hour and, if left untreated, for many (up to 10–12) years through the patient’s body [60]. The symptomatic episodes commonly last several days to weeks and the migratory swellings/creeping eruptions may be accompanied by pruritus, local pain and/or inflammation. In most cases, only one single migratory lesion is present at a time. Although most symptomatic infections are confined to the skin and subcutaneous tissue, severe manifestations due to visceral migration and invasion of the central nervous system may occur [61].

Diagnosis
Diagnosis is mostly based on the patient’s history (ingestion of raw or undercooked fish dishes), the clinical picture, blood eosinophilia (which is often, but not always, present) and positive serology (Western blot). If the parasite migrates very superficially, skin biopsy can be both diagnostic and therapeutic.

Gnathostomiasis
Gnathostoma is a helminthic parasite of dogs, cats and other (mostly fish-eating) mammals, with a complex life-cycle (involving copepods, freshwater fish and a wide range of potential paratenic hosts). Humans are accidental dead-end hosts and usually become infected by ingesting raw or inadequately cooked freshwater fish infected with the 3rd stage larva of the parasite. Gnathostomiasis is endemic to some regions of Asia and South America where raw fish is consumed as part of the local food tradition (e.g. ‘sushi’ in Asia and ‘ceviche’ in Central and South America). With increasing numbers of international travellers, gnathostomiasis has become recognised as an emerging parasitic disease in travellers returning from endemic regions [57–59].

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Strongyloidiasis ('Larva currens')
Strongyloidiasis is a human gastrointestinal helminthic parasite with global distribution. The prevalence is highest in tropical and subtropical regions and is related to poor hygienic conditions. Humans become infected by contact with soil containing infectious larvae. The larvae penetrate the intact skin and symptoms (e.g. pulmonary ['Löffler’s syndrome'], gastrointestinal [abdominal pain, diarrhoea]) accrue from the parasite’s migration through the host’s body, including the skin.

There are two types of skin manifestations in strongyloidiasis. One is a pruritic linear or serpiginous creeping eruption (mostly around the anus and anywhere on the trunk), which moves rapidly (2–10 cm per hour) and disappears within a few hours, hence the name ‘larva currens’ (Fig. 10) [67]. In most cases, the skin eruption has already completely disappeared when the patient is finally seen by the physician.

The second form is an urticarial rash in an individual who has already been sensitised. This urticarial rash occurs predominantly in the buttocks and around the waist, lasts 1–2 days and may recur at regular intervals [67].

An important feature of Strongyloides stercoralis is the parasite’s unusual ability to complete its lifecycle within the human body, leading to continuing cycles of autoinfection [68]. This is especially important as chronic or
persistent infection may remain asymptomatic over decades and culminate in severe and potentially life-threatening Strongyloides hyperinfection syndrome once an individual sustains immunosuppression (e.g. chemotherapy, organ transplantation, high dose steroid- or any other immunosuppressive therapy) [68,69].

**Diagnosis**

Diagnosis is based on the clinical picture, blood eosinophilia (which is often, but not always, present), positive serology (ELISA), and special stool investigations. Conventional stool microscopy is insufficient for diagnosing strongyloidiasis because the parasite load is generally low and the larval output irregular. Therefore, specific stool concentration methods (e.g. ‘Baermann’) or stool culture techniques (e.g. Harada–Mori filter paper culture, nutrient agar plate culture) have to be applied [70]. A novel, promising diagnostic tool is stool PCR [71].

**Treatment**

Oral ivermectin is the drug of choice for strongyloidiasis, and is more effective than albendazole (400 g BID for 7 days) [72]. A single dose of ivermectin may not completely clear the infection, thus the recommended regimen is 200 µg/kg body weight OD for 2 days [72].

**Loa loa/loiasis (‘eye worm’)**

Loa loa is a filarial disease (helminthic parasite) transmitted by bloodsucking flies in West- and Central Africa. The classical symptom of an adult worm (3–7 cm × 0.4 mm) migrating under the conjunctiva of the eye is rarely observed, as the visible passage of the worm only lasts 10–15 min [73].

The same applies to the fugitive creeping eruptions caused by superficially migrating adult worms (Fig. 11). The most frequent symptoms are recurrent subcutaneous soft-tissue swellings (‘Calabar swellings’) and chronic pruritus. Calabar swellings are painless, non-pitting angio-oedemas, most commonly observed on the hands, wrists and forearms (but possibly anywhere on the body), lasting a few hours to several days [73].

**Diagnosis**

Diagnosis is based on the epidemiological history, the clinical picture, blood eosinophilia (especially common in travellers), positive serology, and the microscopical detection of microfilaria in the patient’s blood. Because loa microfilariae exhibit a diurnal periodicity in the peripheral blood, the optimal time for taking a blood sample is around noon, when the concentration of microfilariae in blood samples is highest [73]. However, the absence of microfilaraemia does not rule out the diagnosis; in a study comparing the clinical symptoms in endemic and non-endemic populations, microfilaraemia was present in 90% and Calabar swellings in only 16% of the endemic patients. Conversely, only 10% of the expatriates were microfilaremic, while 95% complained of Calabar swellings [74].

**Treatment**

The drugs used to treat loa loa are diethylcarbamazin (DEC), ivermectin and albendazole, but only DEC is effective against adult worms and microfilariae (ivermectin and albendazole are microfilaricidal only). Therefore, a definitive cure requires DEC therapy. As 20–60% of the adult worms survive the three-week DEC therapy, repeated courses of DEC may be necessary [75]. Because treatment is complex and may cause severe complications (potentially fatal encephalopathy) in patients with high levels of microfilariae in the blood, therapy should be discussed with a specialist or referral centre.

**Other parasites causing creeping eruptions**

Other parasites able to cause creeping eruptions include dracunculiasis, dirofilariasis, fasciola, paragonimiasis, sparganosis, lagochilascariasis and migratory myiasis. However, these infections are only rarely seen in travellers.

**Pitfalls/not to be missed**

- Diagnosis of Hookworm-related cutaneous larva migrans is unlikely, if:
  - the lesion spontaneously disappears within 2–3 days

**Figure 9** Gnathostomiasis left: migratory swelling (thigh); middle: creeping eruption; right: Gnathostoma 3rd stage larva (3 mm long).

**Figure 10** Strongyloidiasis creeping eruption.
- the track is subcutaneously located
- the track is wider than 5 mm
- peripheral blood eosinophilia is present
- the lesion shows almost no migration

- Treatment of gnathostomiasis is mandatory, as severe and potentially fatal neuroinvasive disease may develop
- Treatment of strongyloidiasis is mandatory, as the infection may cause severe and potentially life-threatening hyperinfection syndrome in cases of immunosuppression
- Migrants from regions with high strongyloidiasis prevalence rates should be screened for asymptomatic chronic infection before initiating immunosuppressive therapy (e.g. chemotherapy, high dose steroid- or any other immunosuppressive therapy, organ transplantation)

Swimmer’s itch

‘Swimmer’s itch’ (also known as ‘lake itch’, ‘duck itch’, ‘cercarial dermatitis’, or ‘Schistosome cercarial dermatitis’) is a short-term, self-limiting immune reaction caused by penetration through the skin of various species of zoonotic schistosomatida larvae (cercariae of e.g. *Trichobilharzia* spp.), and is observed in patients who have bathed in freshwater. These zoonotic schistosomatidae must not be confused with the *Schistosoma* spp. that cause invasive human schistosomiasis/bilharziosis. Zoonotic schistosomatidae are found worldwide and human infection is well documented in Central Europe and North America. When the parasites’ larvae penetrate the skin, they cause mild itchy spots on the skin. Within hours, these spots become raised papules, which are intensely itchy. Each papule corresponds to the penetration site of a single larva (cercaria). As the parasites die off spontaneously, the symptoms are self-limiting and rarely last longer than a few days.

**Diagnosis**
Diagnosis is based on the clinical picture and on the patient’s history of freshwater contact.

**Treatment**
Depending on the severity, symptomatic treatment with antihistamines or glucocorticosteroids (topical or oral) may be considered.

Pitfalls/not to be missed
The history of exposure to freshwater is crucial in the differential diagnosis, as the skin manifestations may otherwise be considered representative of insect bites.

**Allergic skin reactions/urticaria**

Urticaria is frequently seen in returning travellers and its causes are copious, ranging from food allergies and jellyfish contact to parasitic infections. Depending on the travel history, parasitic infections should not be excluded as, in some cases, acute or chronic urticaria may be the only indicator of infection (e.g. *strongyloidiasis*, *gnathostomiasis*, *toxocariasis*, *filariasis*, *fascioliasis*, *giardiasis*, *amoebiasis*, *Blastocystis hominis*) [81]. Other frequently seen travel-related dermal hypersensitivity reactions include contact dermatitis (e.g. poison ivy), phytophotodermatitis (e.g. lime juice), drug induced phototoxic reactions (e.g. by doxycycline, which is used for malaria chemoprophylaxis) and other drug eruptions (Fig. 12).

**Diagnosis**
Diagnosis is based on the patient’s history, the clinical picture and (when indicated) laboratory investigations to rule out an underlying parasitic infection.

**Treatment**
Depending on the severity, symptomatic treatment with antihistamines or glucocorticosteroids (topical or oral) may be considered. If an underlying parasitic infection has been identified, specific treatment is indicated.

**Not to be missed/pitfalls**
In patients with urticaria (especially in chronic cases) rule out a potential underlying parasitosis by stool examination (for intestinal parasites) and serological test (for tissue invasive parasites), respectively.

**Fungal skin infections**

Although not confined to travelling, dermatomycoses are frequently seen in travel clinics but are almost exclusively limited to the superficial *tinea* (ringworm) and *pityriasis versicolor* infections [1,2]. *Tinea pedis* (athlete’s foot) is
probably the most common dermatomycosis in travellers, but is rarely seen in travel clinics, as the clinical manifestation is well known and most patients will either consult their general physician or perform self-treatment with over the counter products. Dermatomycoses caused by other fungi endemic to the tropics and subtropics or cutaneous manifestations of endemic mycoses (e.g. histoplasmosis) are only exceptionally reported in travellers [82].

Diagnosis
Diagnosis is based on the clinical picture and on microscopy and culture of skin scrapings.

Treatment
Depending on the severity and causative fungus, topical or systemic antimycotic drugs are applied.

Pitfalls/not to be missed
The diagnosis of fungal skin infections is mostly straightforward. However, some lesions may mimic other disorders, e.g. bacterial skin infections or cutaneous leishmaniasis.

Summary
Dermatological disorders in travellers returning from tropical and subtropical destinations are the daily business of travel clinics. Differential diagnoses largely depend on the patient’s travel history, the geographic background of the journey (local endemicity of certain diseases) and the clinical picture, with a focus on the evolution of skin manifestation(s). When evaluating dermatological pathologies in travellers, the main objective is to rule out potentially severe or even life-threatening diseases. In this regard, the presence or development of extra-cutaneous systemic symptoms (e.g. fever, generalised lymphadenopathy) may be suggestive (e.g. trypanosomiasis, rickettsiosis, etc.). If the pathologies are restricted to the skin, the differential diagnoses are best narrowed down by evaluating the progression/evolution of the skin manifestation(s) over time (e.g. cutaneous leishmaniasis, insect bites, etc.).

Conflict of interest
None.

References
Diagnoses of common dermatological problems in returning travellers


