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Epidemiology of Common Parasitic Infections of the Skin In Infants and Children

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Members of three taxonomic groups—protozoa, helminths, and arthropods—cause parasitic infections of the skin. Protozoans cause trypanosomiasis and leishmaniasis, whereas cutaneous larva migrans and cercarial dermatitis are attributed to infections with certain helminths. On the other hand, cutaneous myiasis, tungiasis, scabies, and allergic and toxic reactions are caused by arthropods. These conditions, their significance, and their recent epidemiological developments, are reviewed in this article.

The term "parasite" is derived from the Greek *parasitos*, to denote an uninvited person who has no place at the table but sits aside and receives leftovers. It refers usually to an animal or animallike protistan that lives on (ectoparasite) or in (endoparasite) another animal. In this animal-to-animal association, the parasite is benefited while the other animal, normally referred to as the host, is harmed, and the association is termed parasitism. The host unwillingly provides the parasite with a relatively stable biotic environment where nutrients, shelter, or both are provided. The host, however, does not sit idle but fights back, mainly through tissue reactions, digestive enzymes, and cellular or humoral responses. It is postulated that the longer the evolutionary relationship between the parasite and the host, the more adapted they are to each other.[1]

The degree of association between the parasites affecting the skin and their hosts varies. Some spend their whole life cycle in the skin as is the case with *Sarcoptes scabiei*, but others come in contact with the host for a very short period of time as is the case with a female mosquito that comes to take a blood meal within a minute. In between these two examples, there are many parasites that vary in the duration of their association with the hosts.

The parasites that affect the skin of infants and children are many and belong to either of the following three groups:

1. Protozoa: These are unicellular heterotrophic protistans that have animallike characteristics (eg, can not synthesize their own food). These include the well-known *Trypanosoma* and *Leishmania* flagellates.
2. Helminths: They are multicellular animals that include two taxonomic groups of worms; phylum Platyhelminthes which includes the cestodes and the trematodes, and phylum Nematoda, or the roundworms. The trematodes and the nematodes are the two main groups of worms having members that can cause skin infections in humans.
3. Arthropods: These include many species of insects (mosquitoes, fleas, bugs) and arachnids (ticks, mites, scorpions and spiders) that are of relevance. They may either infect the skin, inject into the skin material that can initiate pathogenesis, or take blood and body fluids through the skin causing blood loss and dermatoses and transmitting in the process different types of pathogens.

Protozoa

Two important skin-related diseases are caused by protozoans; trypanosomiasis and leishmaniasis.

Trypanosomiasis

Protozoans of the genus *Trypanosoma* cause the widespread tropical disease trypanosomiasis. There are two forms of the disease: the African and the American forms.

The African Form

It is endemic in a belt running across Africa. *Trypanosoma gambiense* is the cause in West Africa and *T. rhodesiense* in East Africa to the east and south of Lake Victoria.[2] Gambiense sleeping sickness is an endemic illness, affecting rural communities, while rhodesiense sleeping sickness causes sporadic infections especially in hunters, honey and beeswax gatherers and tourists.[3]

Man is the main natural host of *T. gambiense* while *T. rhodesiense* is zoonotic and man acquires the infection as

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he intrudes into the cycle that normally involves only the vectors and game animals.[3] The disease is transmitted by blood-sucking tsetse flies of the genus *Glossina.* The important vectors are *G. palpalis* and *G. morsitans*. Age, sex, race and occupation have no influence on the susceptibility to the disease; except in so for as they affect exposure to tsetse flies.

A skin chancre develops at the site of the tsetse fly inoculation. The clinical illness occurs with the time of blood stream invasion. Lymph nodes develop at the draining sores, with occurrence of lymphocytosis, and plasma cells. Late in the disease, meningitis occurs, followed by cerebral atrophy. The chancre develops after 10–14 days from the infected bite. It is round, raised, red, hot and tender, of 2–5 cm in diameter. The chancre occurs in 70–90% of people infected with *T. rhodesiense,* and less with *T. gambiense.* Edema of hands, feet and face, with erythema and urticarial rashes occur on the trunk. The rash may be hemorrhagic. Diagnosis is made by the demonstration of trypanosomes in blood film.[2]

The American Form

It is also called Chagas' disease, and Trypanosomiasis cruzi. It occurs in rural tropical zones of the American continent. The acute forms of the disease are more frequently observed in children, with equal sexes. It is caused by *T. cruzi,* which multiplies in the tissues. Blood-sucking insects called assassin or kissing bugs of the family Triatomidae transmit it.[3]

The disease is zoonotic and has many animal reservoirs, such as cats and dogs. Transmission occurs by contamination through small skin cuts and abrasions or through contact of mucous membranes of eyes and lips with bugs feces containing the infective stages of the parasite. The early signs appear on the fifth day after inoculation shown by "eye" or "Romana's sign," which is a unilateral edema of the eyelids and lacrimal glands inflammation.[2]

Cutaneous inoculation leads into adenopathy, fever, myalgia, and weakness, particularly in children in whom the disease may cause death due to meningoencephalitis or myocarditis. The spleen, the nervous system, and intestines may also affected. The prognosis of illness is serious in children.

Cutaneous Leishmaniasis

It is caused by protozoan parasites of the genus *Leishmania*. Human leishmaniasis is classified as cutaneous, visceral, and mucocutaneous, with the cutaneous leishmaniasis (CL) being the most common.

Old World cutaneous leishmaniasis (OWCL) is endemic in 66 countries, and New World cutaneous leishmaniasis (NWCL) is endemic in 22 countries. OWCL is caused mainly by three species of *Leishmania: L. tropica, L. major,* and *L. aethiopica. Leishmania infantum,* which causes visceral leishmaniasis in infants and children, can also produce a mild, self-healing cutaneous lesion in adults leaving a disfiguring scar.[4] On the other hand, NWCL is mainly caused by *L. braziliensis* (*L. b. braziliensis, L. b. guyanensis, L. b. panamensis)* and *L. mexicana*.[3]

The majority of CL infections are zoonotic and the reservoirs are small rodents or large mammals.[5] The vectors belong to a single subfamily, the sandflies Phlebotominae.[3] The vectors of NWCL are diverse and belong to the genus *Lutzomyia* whereas zoonotic OWCL is mainly transmitted by *Phlebotomus papatasi.* Anthroponotic CL is restricted to The Old World where it is basically urban or suburban.[6] It is caused by *L. tropica* and its main vector is *Ph. sergenti*.

The disease is endemic in five continents. The endemic zones have a surprising degree of climatic and ecological variety. They occur at altitudes from 400 m below sea level in the Jordan Valley up to 3200 m in the Andes Mountains in South America that extend along the West Coast from Panama to Tierra del Fuego.[7] So, CL is found in all countries of the tropical and subtropical regions of the world, except New Zealand, Australia, and the island nations of the pacific. The estimated annual incidence of CL is 1 to 1.5 million cases and 500,000 cases of visceral leishmaniasis with 350 million people at risk.[6] The number of cases occurring around the world is clearly far more than officially reported.

The recent increase in the prevalence of CL is due to several factors, most of them are related to development. These include large-scale migration of populations and labor force; development of new agroindustrial projects bringing nonimmune people to endemic areas; fast-growing and/or unplanned urbanization; massive rural-urban migration; and man-made environmental changes (eg, building of dams, irrigation systems, and wells).[6]

In addition to wars that involve movements of army personnel, maneuvers operations, establishment of camps, and the disruption of health services, cross-border movement of refugees and the termination of campaigns of residual insecticide spraying for malaria control have increased the risk of the spread of the disease.[6,8] AIDS and other immunosupressive conditions increase the risk for *Leishmania* infected people to develop and manifest visceral illness.

Malnutrition represents a permanent risk for the populations of rural areas. The relationship between nutritional status and CL was evaluated in 230 children living in a rural subtropical rain forest in Northwest Ecuador, and showed low dietary iron intake in infected children. Stunting growth was also noticed in such children.[9]

The disease occurs commonly among children and in particular school children who live near endemic areas. In a hyperendemic area in the Jordan Valley, 83% of children below the age of nine were found to have

evidence of past infection.[10] The epidemiologic factors of the disease and the ecological risk factors are almost similar all around the Middle East and the Arabia. At present, hopes for the control of CL are not optimistic, and the disease still remains a major challenge for health authorities and a health threat to community development, and the environment in developing countries.[11,12] Control is hindered by the wide variety of foci of the disease and the different animals that can act as reservoirs, as well as the complex relationship between the parasite, the reservoirs, and the vectors.[5] There are new foci appearing all the time, and the disease affects different developmental aspects. Thus, further work is needed to understand the distribution, ecology, and population dynamics of the animal reservoirs, the sand fly vectors and the transmission cycles. Strict surveillance, health education, and collaboration between health and other governmental sectors are also important for effective control and prevention of the disease.[3] Vaccination should also be considered as another strategy for prevention and control.[13]

Helminths

Nematodes

Cutaneous Larva Migrans

Creeping eruption, Sandworm eruption, Plumber's itch, and Duckhunter's itch are all synonyms for cutaneous larva migrans which is an intensely pruritic serpiginous eruption caused by the infestation of human skin by animal hookworm larvae, which burrow through the epidermis.[14] The prime feature, as the name suggests, is the presence of lesions that creep or migrate, due to the movement of the parasite in the skin. The foot is a typical site for origination of this infection which is usually self-limiting lasting normally for 8 weeks, but may persist for a year or more if misdiagnosed.[15,16]

Cutaneous larva migrans is a clinical term of distinctive eruption that has numerous causes.[2] The prime features are due to the presence of moving parasites in the skin.[17] It is produced by a variety of the skin-penetrating larvae of nematodes, mainly the dog hookworms, *Ancylostoma brasiliense* and *A. caninum.* The incubation period is approximately two weeks. The adult hookworms live in the intestines of dogs and cats and their ova are discharged in the animal feces. Under favorable conditions of humidity and temperature, the ova hatch into larvae that molt into infective filariform larvae that will penetrate human skin when a person comes in contact with infected soil. The infective larvae migrate in the skin for a period of 2–50 weeks producing visible, irregular, erythematous tunnels before they die. Rarely, some larvae reach the lungs, causing Loeffler's syndrome and patchy pulmonary infiltration.[18] Patients become often infected when walking or lying on beaches and other moist and sandy areas contaminated by feces of infected dogs and cats. The feet, legs and hands are the most common sites. It is virtually impossible to remove the larvae from the skin. The incidence is equal in both sexes, and it affects both adults and children. *Ancylostoma brasiliense* is found in Southern United States, Central America, the Caribbean, tropical South America, Africa and the Far East especially the Malay Peninsula.[14]

Various therapeutic modalities have been advocated for the treatment of cutaneous larva migrans, but the recommendations for the treatment are not uniform.[19,20] Thiabendazole, which is the first line of treatment, is given po, 25 mg/kg body weight per day for two days, and is usually effective.[21,22] If not, the dose can be double and repeated, but with caution as the drug has some side effects. New safer drugs are albendazole, 400 mg/day for 3 days, and ivermectin (mectizan) in a single dose of 200 mg/kg po.[23,24,25] Several practitioners consider topical application of thiabendazole effective and without side effects,[2,20,25] but others reported unsatisfactory results.[26] Topical thiabendazole is sprinkled on Elastoplast or in a 15% cream in a hyposoluble base. Physical treatment in the form of cryotherapy with liquid nitrogen has recently been used with good results.[27] The last two methods of treatment are better used for children.

The incidence of the disease in travelers and holidaymakers has increased over the past few years in Europe and Middle Eastern countries due to the growing number of people traveling to temperate endemic areas.[28] Thus, travelers to these areas should be alerted to this infection and are advised to have protective footwear to reduce the possibility of infection, especially among children.

Primary health care could be used in the prevention and treatment of zoonotic diseases in humans, as such diseases are more prevalent in disadvantaged communities.[29] The successful use of primary health care principle in the treatment and control of cutaneous larva migrans in people and in particular children in a semi-rural, low-income community is essential. This can only be done if the epidemiology of the disease is understood, and there has been an interinstitutional cooperation.

Trematodes

Trematoda is a class of worms that are commonly referred to as flukes, and some of its members are associated with a clinical condition known as cercarial dermatitis (CD), or swimmer's itch. It is an allergic reaction that is accompanied by erythema of the invaded area of the skin with local or generalized urticaria. Larval stages of blood flukes of the family Schistosomatidae are responsible for this condition. Members of this trematode family infect the blood of animals, mainly

birds and mammals. They belong to several genera, including *Schistosoma, Schistosomatium, Heterobilharzia, Trichobilharzia, Gigantobilharzia*, and *Ornithobilharzia.* Man can be infected by only a few species of the genus *Schistosoma* (eg, S. *hematobium*, and *S. mansoni*) but humans are not a compatible definitive host for the other schistosomes. When specific larval stages of these nonhuman schistosomes, known as cercariae, come in contact with the skin of children or adults as they go into water, the cercariae attach to the skin. They are, however, unable to penetrate the germinal layer of the skin and reach circulation to complete their life cycle. They may die in situ or wonder in the skin before they eventually die. The higher the number of cercariae attempting to penetrate the skin, the more severe are the allergic reactions, and repeated exposure to the cercariae increases the intensity of the allergic reaction. Cercarial dermatitis, however, can also be seen in patients infected with cercariae of human schistosomes.[30]

The life cycle of these trematodes require the presence of the specific snail intermediate host. Adult females of schistosomes lay eggs in the veinules of their hosts. On reaching water contaminated with either feces or urine, they hatch, and the first larval stage, known as miracidium, swims in water for few hours. If it comes in contact with the appropriate snail intermediate host present in water, it penetrates its soft tissues, develops, and multiplies asexually in the snail's organs to eventually produce many cercariae. These leave the snail and swim in water looking for the appropriate final host to complete their life cycle. Infants and adults usually become infected when swimming in lakes and seawater where the infected snail intermediate hosts are present. These individuals are exposed to the cercariae of these nonhuman schistosomes and would likely develop CD. It can be acquired, however, by ways other than swimming. Farmers working in rice fields,[31] garden pools,[32] or even individuals who keep native fish and water snails in their aquaria[33] have contracted CD. Cercarial dermatitis responds well to treatment with topical antihistamines or cortisone but even without medication, the skin rash heals within 2–3 weeks.[34,35]

Cercarial dermatitis occurs in many parts of the world. Recent occurrences were reported from the United States (Delaware,[36] New England[37]), Russia,[38] Norway,[35] Austria,[34] Germany,[32] Byelarus,[39] and France.[40] de Gentile et al[40] reviewed the recent reports of CD in France and Europe, and based on their observations, they concluded that CD may be regarded as an emerging disease and its public health impact needs to be evaluated at the global level.

Arthropods

In addition to their importance as vectors of skin-related diseases, arthropods cause pathologic conditions related to the skin in both adults and children. The effect is related either to the presence of the arthropods or to their products. In either case, they are capable of causing adverse reactions that range from mild (itching) to sever and life threatening (anaphylactic chock and death). Scabies, cutaneous myiasis, tungiasis and allergic and toxic reaction to stinging and nonstinging arthropods are the most common of the conditions caused by arthropods.

Cutaneous Myiasis

Myiasis (*myia* in Greek means fly) refers to the infestation, by dipterous fly larvae, of tissues of either the skin (cutaneous myiasis), the eyes (ophthalmomyiasis), the intestine (intestinal myiasis) or any other organ. The females of myiasis-causing flies deposit their eggs or larvae in the tissues of humans and vertebrate animals to feed and complete their life cycles. In cutaneous myiasis (CM), the larvae penetrate into the unbroken skin, or enter wounds, causing skin abscesses or what looks as an insect bite.[41]

Flies usually reported to cause CM include *Dermatobia hominis*,[41–44] *Cordylobia arthropophaga*,[44–46] several species of *Chrysomya*,[47,48] and *Musca domestica*.[49]

CM is endemic in Central and South America and several parts of Africa, but has been reported from many other areas including Saudi Arabia.[46] It was recently reported to affect humans in France,[50] Israel,[42] Jamaica,[51] USA,[43,52,53] Australia,[44] Belgium,[54] Japan,[55,56] Canada,[41] and New Zealand.[57] These cases traveled to CM-endemic areas in the Senegal,[58] South America especially Brazil,[42,52–56] Sri Lanka,[59] South Africa,[44] and Thailand.[48,53] Thus, obtaining a history of recent travel to an endemic area is important for diagnosis and instituting appropriate treatment.[41] Treatment involves asphyxiation of larvae, forcing emergence, application of toxic agents, or surgical removal.[44]

Tungiasis

Tungiasis refers to the cutaneous infestation of humans by the gravid female flea *Tunga penetrans*.[60] The foot is usually the site of burrowing and the condition often mimics verrucae vulgaris.[61] Itching and ulceration are common.[62] Diagnosis is usually based on the typical picture and the history of inhabiting or visiting endemic areas.[63] Treatment is based on the extirpation of the flea, local and/or systemic antimicrobial therapy, and prophylaxis agaist tetanus.[63]

The burrowing flea is prevalent in Central and South America, the Caribbean, tropical Africa, India and Pakistan. Imported cases, however, have been encountered in several countries, including the United States,[60] United Kingdom,[61,64] and France.[65] In their prospective study on dermatoses associated with travel to tropical countries, Caumes et al[65] reported that 6% of the 260 cases presenting to their unit in Paris suffered from

tungiasia. The parasite is believed to be reappearing in several areas in Mexico especially in areas where poverty and poor hygiene conditions prevail.[63,66]

Allergic and Toxic Reactions

Various skin irritations are caused by arthropods as a result of either their bites or their invasion of the skin. The reactions of the host to substances present in oral secretions injected during the bite could be: (a) reactions to antigenic substances (b) reactions to nonantigenic irritating substances, or (c) reactions to antigenic and irritating substances.[67] Various species of mites cause skin irritations known as acariasis, including scabies mites, itch mites and chigger mites.[68] In addition, direct contact or inhalation of airborne material, including wing scales, exuviae, feces, or urticating hairs, and active injection of venoms (stings) or ejection of defensive secretions could lead to allergic reactions or toxic activity, including rapid paralysis, death, or intense pain.[69,70] The range of these reactions depends on many factors, including the type and source of the allergen or toxin, the route, intensity, duration of exposure and the immune response capabilities of the exposed person.[70]

Venoms are usually produced by glands associated with either a modified ovipositor, as is the case in hymenopterans and scorpions, or with the feeding apparatus, as in some insects and spiders. These venoms possess a variety of enzymes, peptides, small organic molecules, active amines and polysaccharides.[69,71] For example, the main allergens of bee venom are phospholipase A_2, hyaluronidase, and acid phosphatase as well as other biogenic amines and other low-molecular-weight substances, the most important of which is histamine.[71]

Venom allergy is often an immunoglobulin E (Ig)–mediated hypersensitivity leading to the release of mediators from activated mast cells, resulting in the observed clinical symptoms.[71,72] Venoms of some scorpions are neurotoxins that do not produce allergic reactions but cause convulsions, paralysis, and arrhythmia, and then death.[71] Venoms of bees, wasps, and scorpions cause thousand of deaths every year worldwide, and Ewan[71] estimates that at least 5000 deaths occur annually due to scorpion stings only.

Most bites of humans by arthropods are mainly caused by insects belonging to the taxonomic groups known as Diptera (mosquitoes, black flies, horse flies and other biting flies), Hemiptera (true bugs), Anoplura (sucking lice), Siphonaptera (fleas) and Chilopoda (centipedes). Other arthropods include the groups Acari (ticks and mites) and araneida (spiders). Reactions to the bites of these groups may vary from local swellings to sever reactions.

Repeated bites may elicit a definite sequence of events in the skin reactivity of the host. Based on their chronological progression, these events were classified by Feingold et al[67] as follows: (a) no observable reactions, (b) delayed reactions, (c) immediate followed by delayed reactions, (d) immediate reaction only, and (e) no reactivity. Each of these events is identified with a specific histopathological pattern,[67] and the reactions observed depend on the nature the immunogen, the route of presentation, the immune response capabilities of the host, and prior antigen exposure.[72] Most people are familiar with local cutaneous reactions to mosquito bites where immediate and delayed reactions or both may occur.[71,73,74] The immediate reaction to mosquito bite is consistent with an IgE-mediated reaction whereas the delayed (swelling) reactions are thought to be T-cell mediated or local IgG immune-complex reactions.[75]

Cross-reactivity between bites of different species of arthropods has been demonstrated and an individual who is sensitive to bites of one species may respond when bitten by another species of a different genus, family or order.[67] Cross-reactivity of venom from closely related insects has also been documented[76] and in bees and wasps it seems to be due to cross-reactivity between the hyaluronidases.[77]

Treatment of allergic reactions should be started immediately. Ice pads are usually applied at the site of the bite. Both local and systemic antihistamines and steroids are required if the patient develops systemic reactions. Other measures include the administration of atropine to counteract the cholinergic effects of venoms. Adrenergic blocking agents to antagonize effects on the cardiovascular system may be needed.

Scabies

It is a highly contagious skin infestation that affects some 300 million people world wide.[78] The disease occurs in developed as well as developing countries and affects all age groups. In some isolated Australian communities, the prevalence in children may reach 50%.[79] Epidemics have been reported in nursing homes,[80] hospitals,[81–83] prisons[84] and similar institutions.[85] The disease is caused by the mite, *Sarcoptes scabiei*, which also infests different mammalian hosts. It is not yet determined whether the forms of the mite associated with different animal hosts constitute separate species or merely variants of the same species (ie, *S. scabiei* var. *hominis*; *S. scabiei* var. *canis*, etc.) as they exhibit little or no morphologic differences.[86] However, scabies mites from different hosts are largely host-specific.[87,88] The transfer of these mites from one host species to another does not usually occur and most human and animal cross-infestations are probably self-limiting.[86]

Scabies mites are transmitted through skin-to-skin contact. The sharing of inanimate objects, however, (eg, fomites) leads to the spread of scabies in households and neighborhoods or to reinfestation.[86,89] The female

mite burrows under the surface of the skin to lay its eggs in a tunnel. Pruritis occurs after 2 to 4 weeks, and scratching leads to secondary skin lesions.[71] The different stages in the life cycle of this mite (ie, larva, nymphs, and adults) could leave their burrows and wonder on the skin and may subsequently leave the host to be picked up by another host.[86] In humans, the infestation sites are often the webs of the fingers, and the volar aspect of the wrists and arms,[71,86] but other sites may be involved including the feet, genitalia, armpits, buttocks, knees, elbows, and nipples. Diagnosis of scabies is confirmed by positive skin scrapings, and the use of polymerase chain reaction has recently been advocated to diagnose cases infested with few mites or having subtle or atypical manifestations.[90]

Mite infestations stimulate a wide range of immune responses including immediate and delayed hypersensitivity and precipitating antibody.[72] Falk and Bolle[91] demonstrated that hypersensitivity is IgE-mediated and Morgan et al[92] have recently reported that at least half of the patients with active scabies have IgE antibodies specific to *S. scabiei*.

Different treatment modalities have been used to treat scabies. These include lindane, sulfur, benzyl benzoate, permethrin, and ivermectin.[80,93–97] However, side effects are noted in some patients, and many physicians recommend the use of topical application of permethrin as well as ivermectin for safety considerations.[83,96–98] Treatment of asymptomatic family members and physical contacts of all cases of scabies and washing or disinfection of clothing and other fomites are significant in combating this infestation.[80,89]

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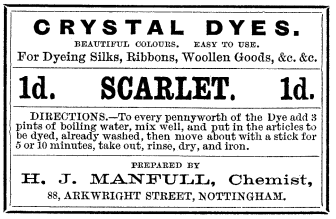

Pharmacy Labels—From the collection of Lawrence Charles Parish, MD, Philadelphia, PA.