



Cutaneous leishmaniasis

distribution

Approximately 90% of all cases of cutaneous leishmaniasis now occurs in Iran, Syria, Saudi Arabia, Afghanistan, Peru and Brazil.

□ **clinical features**

Various forms are clinically distinguished, the most important of which are :

- **Localised cutaneous leishmaniasis**
- **Diffuse cutaneous leishmaniasis**
- **Recurrent cutaneous leishmaniasis**

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A description from 1756 by a certain Alexander Russell is still relevant:

"... After it is cicatrised, it leaves an ugly scar, which remains through life, and for many months has a livid colour. When they are not irritated, they seldom give much pain... It affects the natives when they are children and generally appears in the face, though they also have some on their extremities... In strangers, it commonly appears some months after their arrival. Very few escape having them, but they seldom affect the same person above more than once."

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Localised cutaneous leishmaniasis

*After a bite by a sandfly infected with *L. tropica* (mainly urban infection), there is an incubation*

period of a few weeks or months, occasionally years. There is initially a small papula and usually only a single lesion, though sometimes there are several. This slowly spreads, can remain completely dry, become warty or nodular or develop into a painless, sharply delineated ulcer surrounded by a purplish raised border. Satellite lesions can occur. Spontaneous healing often occurs after 6 to 12 months, resulting in a depressed scar. Recurring cutaneous lesions - possibly with severe disfigurements - occasionally occur. There is usually immunity to any subsequent infection with the same organism. In infection with

L. major

(mainly rural infections, particularly from a rodent reservoir) the lesions are usually larger and develop more quickly, hence the name. There is a greater tendency to local spreading via the lymphatics and have to be distinguished from sporotrichosis. The lesions will eventually spontaneously heal with scar formation.

In South America the lesions often have their own local names and clinical expressions. Hence in Peru they are called "uta" (a solitary ulcer or a few restricted lesions brought about by *L.*

peruviana

, frequently on the face). In Guyana they are known as "bush yaws" or (French) "pian bois" (*L.*

guyanensis

) with raspberry-like lesions that resemble yaws. In Yucatan, Mexico an ulcer on the ear (usually caused by

L. mexicana

) is known as "chiclero" ulcer.

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Diffuse cutaneous leishmaniasis

Diffuse cutaneous leishmaniasis is a diffuse affection of the skin with extensive non-ulcerative nodules and is a very chronic disease. It is sometimes followed by chronic lymphoedema of an affected part of the body. This disease is poorly understood, but is probably caused by a diminished resistance to the parasite. This immunosuppression is possibly brought about by the parasite itself. In East Africa diffuse cutaneous leishmaniasis is often caused by *L. aethiopica* and in the New World frequently by

L. mexicana

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If there are generalised cutaneous lesions the condition has to be differentiated from lepromatous leprosy, keloids, neurofibromatosis and post kala azar dermal leishmaniasis (PKDL). Due to the low resistance of the patient very numerous amastigotes are present skin smears are always positive. Treatment is difficult, as the patient's immune system itself is functioning poorly. Differentiation from PKDL is important, as the latter can still be treated reasonably well. In Sudan 1 case of diffuse cutaneous leishmaniasis is found for every 100 cases of localised cutaneous leishmaniasis. The incidence varies greatly from district to district. It occurs frequently in South America, but in contrast to this it does not occur in India.

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Recurring cutaneous leishmaniasis

Recurring cutaneous leishmaniasis seldom occurs (Iraq, Iran). This disease, also known as leishmaniasis recidivans leads to significant tissue damage. Parasites are very difficult to detect in these very chronic lesions. Differentiation from cutaneous tuberculosis is important.

*Attempts should be made to detect the parasite microscopically in a biopsy or smear from the edge of the wound. The biopsy will, if possible, be divided up for pathology (seldom available, not very sensitive, is principally used more for exclusion of another cause) and cultures (bacteria, mycobacteria, fungi, Leishmania) and an impression preparation should also be made. Lesions on the face can be injected with 0.1 ml physiological saline and aspirated again while moving the small, thin needle back and forth in the skin. Serology is usually negative. Differential diagnosis includes ulcers due to mycobacteria, cutaneous diphtheria, tertiary syphilis, yaws, cutaneous carcinoma and deep or subcutaneous mycosis. Acid fast bacilli can be made visible using the method of Ziehl-Neelsen. Field sore (cutaneous diphtheria) and tropical ulcers (fusobacteria + *Borrelia*) are painful, particularly in the early phase.*

treatment

The response to treatment varies according to the species. Drugs for systemic and topical treatment can be used. There is an urgent need for better and cheaper drugs.

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Indications for local treatment

- ***lack of risk of developing mucosal lesions***
- ***Old World cutaneous leishmaniasis***
- ***small, single lesion***
- ***absence of lymph node metastasis***

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Indications for systemic treatment

- ***presence of mucosal lesion or lymph node metastasis***
- ***New World cutaneous leishmaniasis, except localised *Leishmania mexicana* infection***
- ***lesions unresponsive to local treatment***

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Overview topical treatment of cutaneous leishmaniasis

- **physical methods: cryotherapy (liquid nitrogen) for 15-20", repeated 2-3 times. Blistering will occur.**
- **application of local heat (e.g. infrared lamp). Heat-induced skin bullae are common.**
- **ointment with 15% paromomycin and 12% methylbenzethonium chloride in soft white paraffin (e.g. Leishcutan® ointment). Urea can be added as a keratolytic. Twice daily application is advised, for a duration of 20-30 days.**
- **skin infiltration with pentavalent antimony with a fine gauge needle. Blanching of the lesions should be obtained. Treatment is repeated every 5-7 days, in general 2-5 times, sometimes more.**
- **imiquimod crème (Aldara®). This immunomodulator activates macrophage killing of *Leishmania amastigotes*, but is best used in combination with systemic meglumine antimonate. Experience with this drug is limited. Local application of imiquimod crème (250 mg, 5% weight/volume), i.e. one individual packet every other day x 20 days is possible.**

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Overview systemic treatment of cutaneous leishmaniasis

- **Pentavalent antimonials (meglumine antimonate [85 mg Sb/ml, IM] or sodium stibogluconate [100 mg/ml, IV]. Duration of treatment is not standardised (e.g. 14 to 28 days).**
- **Pentamidine. First line against *L. guyanensis* (French Guyana). Check glycaemia. Several treatment schemes exist and the cure rate is dose-dependent. Some short-courses use 1200 mg as a total dose. In Guyana 3 mg/kg/day every other day is often used (4 injections).**
- **Imidazoles, triazoles. Fluconazole promising against *L. major*. Ketoconazole 600 mg per day x 28 days is moderately effective for *L. mexicana*, but much lower against *L. braziliensis*.**
- **Miltefosine. Still experimental.**

- **Amphotericine B and its liposomal formulation**
- **Allopurinol. Not as monotherapy, but associated with e.g. pentavalent antimony for *L. panamensis*.**

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Glucantime® (meglumine antimonate) or Pentostam® (stibogluconate) can be injected intralesionally (that is, into the edge of the lesion itself) as a treatment for cutaneous leishmaniasis. These can be given parenterally for extensive lesions. Varying results have also been reported with allopurinol (Zyloric®), which can be given orally. Topical treatments with heating (40° C to 42° C for 12 hours), freezing with liquid nitrogen and paromomycin ointment (15% aminosidine in methylbenzethonium BD x 15-30 days) have been used with varying success. Itraconazole (Sporanox®) gave good results in initial studies, but is still controversial. Ketoconazole is sometimes used, but its use is often complicated by hepatotoxicity, abdominal pain and nausea. Imiquimod 5% cream (Aldara®) is an immunomodulating substance, initially used for warts caused by papilloma virus. Its use in cutaneous leishmaniasis is still experimental.

Infections caused by *Leishmania major* can be successfully treated with oral fluconazole 200 mg/day for 6 weeks (cure rate of 80%).

The treatment of diffuse cutaneous leishmaniasis caused by *L. aethiopica* is problematical, as this parasite is less sensitive to Glucantime®. Pentamidine can be used against

. *aethiopica*

. A dose of 4 mg/kg/week which has to be continued for at least 4 months after disappearance of the parasites from the skin is an acceptable guideline here. Parenteral aminosidine sulphate is another therapeutic possibility. This is an antibiotic that is obtained from

Streptomyces chrestomyceticus

. It is an aminoglycoside and is thus potentially nephro- and ototoxic. It is chemically identical to paromomycin, which is obtained from a related

Streptomyces

strain. The compound is not resorbed from the intestine. Recurrences are frequently seen with aminosidine given as monotherapy. Aminosidine is, however, synergistic with stibogluconate and a permanent remission can be obtained with the combination of aminosidine with Glucantime® or Pentostam®. The dose is 14 mg/kg/day IM to be

continued for up to 60 days after all parasites have been eliminated. The total treatment period takes 6 months or more. Good results were obtained with amphotericin B.