

Cutaneous Leishmaniasis

Abstract

Cutaneous Leishmaniasis (CL) is endemic in over 70 countries worldwide. The effects of climate change, the increased popularity of eco-tourism and globalization has seen a rise of CL presentations in United Kingdom (UK) based travelers. Emergency nurses should be prepared to assess, recognize and treat patients who may present with CL. This article gives an overview of the epidemiology, pathophysiology, signs and symptoms and treatment of CL.

Introduction

Leishmaniasis is in 9th place on the league table of disease burden in terms of disease dispersion and mortality. However, it is mostly neglected in both tropical and sub-tropical areas and is considered a significant public health issue by the World Health Organization (WHO) (Soto et al, 2017). Cutaneous Leishmaniasis (CL) is a parasitic type disease that is endemic in more than 70 countries worldwide. In 2017, the WHO estimated that there were 1.5-2 million new cases and 70,000 deaths per year with over 350 million people at risk of being infected (WHO, 2004). CL is thought to be more prevalent in urban or peri urban environments due to the need for humans to be the reservoir for the parasite (WHO, 2018). The clear majority of CL cases have been reported in Afghanistan, Algeria, Brazil, Colombia, the Islamic Republic of Iran, Pakistan, Peru, Saudi Arabia and the Syrian Arab Republic, Mexico and Central America (WHO, 2018). CL can be found in densely populated areas such as large towns, cities and refugee camps in war and conflict regions (Markle & Makhoul, 2004; WHO, 2010). Interestingly, most cases diagnosed among non-military personnel in the United States (US) are acquired in Mexico and Central America (Ergen et al, 2015). Climate change has seen CL expand its reach as more arid habitats allow CL to flourish (Gonzalez et al, 2009).

The last 20 years has brought with it a change in transmission cycles thus the disease is spreading into non-endemic areas due to continued deforestation, migration patterns and urbanization (Reithinger et al, 2007). The traveler or certain at risk populations such as members of the British Armed Forces are most likely to encounter the disease (Bailey & Lockwood, 2007). Generally, the British Armed Forces tend to see a rise in CL when deploying into a jungle environment such as Belize or Afghanistan (Bailey, 2011; Wall et al, 2012). Due to the rise in popularity of international travel and ecotourism to endemic locations there is a likelihood

that CL presentations may increase in the UK healthcare system (Pavli & Maltezou, 2010). This article aims to develop emergency nurses' awareness and knowledge of the recognition, diagnosis and treatment of CL.

Cutaneous Leishmaniasis

CL is classified into Old World CL and New World CL. This classification is significant due to the differing causes of the disease (Wall et al, 2012). Mucosal disease (ML) is triggered by New World CL, most typically *Leishmania (Vianna) spp.* and requires systemic therapy. The associated skin lesions are most commonly ulcerated or can be keratotic in nature (Ergen et al, 2015). See Table 1 for the causative agents of Endemic CL related to geographical location. The disease vector is the sand-fly See Figure 1. The parasite that infects the sand-fly is a promastigote form that matures into a metacyclic infection over a 10-day period (Markle & Makhoul, 2004). Generally, following the bite of a sand-fly the parasite enters the human host as part of the inflammatory process. The parasite is pulled into macrophages by their digestive processes (Markle & Makoul, 2004). After entering the cell, the *Leishmania* can survive the lysosome driven acidity and develop into amastigote forms causing the disease in the human host. The amastigote forms measure 2.5 to 7 microns in width (Wall et al, 2012). The sand-fly measures approx. 2mm long and is from either the *Phlebotomus* genus from the Old-World type or the *Lutzomyia* genus in the New World variant (Ergen et al, 2015).

Table 1.

Causative Agent	Geographical Location
<i>Leishmania Infantum</i>	Spain and Portugal
<i>Leishmania Infantum, major and tropica</i>	Cyprus and Turkey
<i>Leishmania major and tropica</i>	Iran, India and Pakistan
<i>Leishmania aethiopica, major and infantum</i>	Ethiopia and Saharan Africa
<i>Leishmania (Viannia) spp.</i>	Central and South America

Presenting Signs & Symptoms

Several species of leishmania cause CL. Clinical presentation is influenced by the virulence of the causal species as well as differences in the immune responses of infected individuals (Ergen et al, 2015). The incubation period for symptomatic CL ranges from a few weeks to many months and mucosal involvement may arise after a latent period of years (Oryan & Akbari, 2016). Leishmania infection may, in many instances, be completely symptomless (Oryan & Akbari, 2016) however common symptomatic presentations include localised CL, CL with mucosal involvement (MCL) or systemic visceral leishmaniasis (VL).

Localised CL is the most prevalent form of clinical leishmaniasis worldwide. It is characterised by localised skin lesions that occur on any exposed area of the body. Typically, localised CL begins with a small pink-coloured lesion or lesions that progressively enlarge to form one or more painless and chronically ulcerated areas. Multiple skin lesions often appear along the route of the lymphatic chain from the primary lesion. Lymphatic spread and node enlargement (nodular lymphangitis) may on occasion precede visible ulceration (Wall et al, 2012). Ulcerated areas gradually heal over variable amounts of time, depending on the infective species, and often leave areas of atrophy and scarring due to keratotic or fibrinous overgrowth. This process can result in unsightly deformity and ongoing psychological debility (Yanik et al, 2004). Spontaneous healing usually confers lifelong protection from further infection by the causative species (Reithinger et al, 2007) although lesions may reactivate.

MCL describes CL that is accompanied by mucosal involvement. This particularly affects the mucous membranes of the nasal, oral and pharyngeal mucosa. Systemic VL affects the internal organs, notably the liver, spleen and bone marrow and lymph nodes (WHO, 2018). This variant may produce fever and anaemia and can be fatal in the absence of appropriate management (De Vries et al, 2015).

Diagnosis

The diagnosis of CL is dependent on epidemiological awareness, consideration of presenting clinical features and laboratory tests. The gold standard of diagnosis is parasitological evaluation due to the high level of specificity with this test (Reithinger et al, 2007). These tests will include both a microscopic examination of Giemsa-stained biopsy smears and a histopathological review of the lesions (Bailey, 2011). It is important to differentiate between leishmaniasis and other

conditions that may present similarly (e.g. leprosy, tuberculosis, fungal infections and skin malignancies) and that are also prevalent in leishmaniasis endemic areas.

From an epidemiological perspective a diagnosis of leishmaniasis should be considered in circumstances when symptoms (e.g. skin lesions) occur in an individual, or cluster within an exposed group of otherwise healthy individuals, who have travelled or been domiciled in a leishmaniasis endemic area in recent weeks or months. Suggestive clinical features include the occurrence of painless, single or multiple chronic skin ulcerations on exposed areas of the body with evidence of inflammation and lymphatic nodules (Ergen et al, 2015).

In order to confirm a conclusive diagnosis of leishmaniasis a causative parasite needs to be identified in a tissue specimen by means of histology, parasite culture or molecular analysis techniques. Ideally, these techniques are used in combination to determine the causative species of leishmania. This helps to inform treatment decisions (IDAASTMH, 2016) however optimal diagnostic processes may be constrained by the available laboratory infrastructure.

Specimens of tissue should be collected from active, ulcerated lesions without evidence of secondary infection (IDAASTMH, 2016). After cleansing the lesion and removing any tissue overgrowth the base and margins are scraped gently with a sterile scalpel blade or brushed with a cytology brush. Contact impressions of ulcerative lesions using glass slides or tape may also provide useful samples for analysis. Alternative means of tissue sampling include aspiration of enlarged lymphatic nodules and punch biopsies of ulcerating skin lesions.

Management

ED nurses must refer all new CL presentations to their tropical medicine/infectious disease service in the first instance. CL is a non-fatal condition; however, treatment is necessary for persistent and/or multiple lesions of more than 6 months duration to reduce scarring to face, hands and torso and to prevent further parasite movement around the body or a subsequent relapse of symptoms (Reithinger et al, 2007). Current WHO recommendations are to treat CL with pentavalent antimonial drugs, such as sodium stibogluconate or meglumine antimonite. Target dosages are 20mg/kg per day for 20-28 consecutive days (WHO, 2018). See Table 2 for treatment regimen per geographical location.

Table 2. Local & Systemic Therapy

Leishmania Type	Local therapy	Systemic therapy
All Leishmania variants	<ul style="list-style-type: none"> • 15% paromycin and 12% methylbenzethonium chloride ointment twice daily for 20 days • Thermotherapy: 1-3 sessions with localized heat (50C for 30s) • Intralesional antimonials: 1-5 ml per session every 3-7 days (1-5 infiltrations) 	
L. Mexicana.		<ul style="list-style-type: none"> • Ketoconazole: adult dose 600mg oral daily for 28 days • Miltefosine: 2.5 mg/kg per day orally for 28 days
L. guyanensis. and L. panamensis.		<ul style="list-style-type: none"> • Pentamidine isethionate, intramuscular injections or brief infusions of 4mg salt/kg per dose every other day for 3 doses • Pentavalent antimonials: 20mgs/kg per day intramuscularly or intravenously for 20 days • Miltefosine: 2.5 mg/kg per day orally for 28 days
L. brazillensis.		<ul style="list-style-type: none"> • Pentavalent antimonials: 20mg/kg per day intramuscularly or intravenously for 20 days • amphotericinB deoxycholate: 0.7mg/kg per day, by infusion, for 25-30 doses

		<ul style="list-style-type: none"> • liposomal amphotericin B: 2-3mg/kg per day, by infusion, up to 20-40mg/kg total dose
L. amazonensis, L. peruviana. and L. venezuelensis.		<ul style="list-style-type: none"> • Pentavalent antimonials: 20mg/kg per day intramuscularly or intravenously for 20 days
Relapse treatment		<ul style="list-style-type: none"> • Amphoterecin B deoxycholate, as above • Pentavalent antimonials: as above plus topical; imiquimod every other day for 20 days • Liposomal amphotericin B: 3mgs/kg per day, by infusion, up to 20-40 mg/kg total dose may be considered

(WHO, 2018)

Psychological Support

When faced with non-healing skin lesions, the ED assessment should include details of the patient’s travel history and country of origin (Wall et al, 2012). CL is referred to as the year-long sore and can clearly negatively impact on the sufferer’s self-perception (Kassi et al, 2008). Research indicates that CL is directly linked to both self and social stigma, both of which have an adverse impact on quality of life, mental health and well-being (Bennis et al 2018). Skin lesions can be clinically indicative of atypical CL which is cases has been mis-diagnosed as indeterminate leprosy (Sota et al, 2017) which is marred by urban myths regarding pathology, cause and aligned to marginalisation of the subject. Similar social isolation emerged in 2014 with the Ebola Virus Disease outbreak in Sierre Leone and neighboring countries (Van Bortel et al, 2016). The effect of self-stigmatization is anxiety, and depression (Bennis et al, 2018) which can be worse for young single women, especially with facial scars [Chahed et al, 2016). This humiliation can be exacerbated if the person is deemed responsible for their appearance (Goffman, 2009), and in

marginalised groups from certain ethnic regions there is cultural stigma (Kassi et al, 2008). The patient may already be experiencing discriminatory attitudes and be worried of being rejected and socially excluded (Weiss, 2008). ED nurses must therefore be sensitive to the associated stigma.

CL (and skin disorders in general) cause high levels of fear. This is aggravated when there is a perception that it is difficult to treat and the cause for the unsightly scarring / boil was transmitted by a fly. The psychological distress may undesirably have impacted on the patient's help seeking behaviour and therefore needs to be attended too at the earliest opportunity through accurate and empathic communication. As with all causes of raised autonomic arousal and alarm there will be associated symptoms such as a dry mouth (See Table 3). As these symptoms are not part of the CL pathology, then the psychological cause should be relatively straight-forward in recognition.

Decisively, acknowledge that the assessment must allow time for every patient to provide their narrative of their beliefs, opinions, and concerns including the impact on their spouse, partner, friends, family and wider community. This knowledge will be fundamental in providing emphatic and constructive treatment. By obtaining the patient's perspective and understanding of CL the nurse is better placed to respond to the patient's trepidations with sensitivity. This will ensure that the ED nurse can maximise measures to reduce anxiety and circumnavigate the patient's potential reticence to discussing their condition. Normalizing of CL through reference to the commonality, the effectiveness of the treatment and how the visibility of the problem will reduce (after treatment) will assist in ensuring that the patient is not overwhelmed by subsequent information.

The level of communication should be pitched at a level that the patient can understand whilst considering that any level of fear can impact on his / her comprehension. Therefore, address each point independently and ensure the patient acknowledges the facts that have been presented. If the patient is tearful or distressed, then offer compassionate support before continuing. It is key to be positive regarding the clinical outcomes by keeping to the empirical evidence. Another factor to be addressed is that the patient may be worried that the disorder may be contagious and therefore transmitted to their spouse, partner, family and friends. This may already have reduced the patient's interface with the very people who can offer them the best support. Therefore, (especially if working with populations where families or friends may have been exposed to sandflies) the ED

nurse's public health message should include positive messages to be passed onto their friends and family.

Table 3: Psychological management of cutaneous leishmaniasis in the ED department.

Ser Table 1

- 1 Keep calm, maintain good eye contact and be confident in responses.
- 2 Place patient in a comfortable position. They should be confident that he / she can speak securely.
- 3 Respond to symptoms indicating raised autonomic arousal such as hyperventilating, by encouraging the patient to take deep and slow breaths. Keep reassuring them and praise their efforts.
- 4 If the patient is highly anxious panicking, then explain to them calmly that that this is a normal reaction.
- 5 If the patient complains of a dry mouth, give him or her water.
- 6 Carefully explain what the treatment involves whilst ensuring that the patient does not feel overwhelmed by the information. Avoid using jargon or clinical terms unless it is clear that the patient understands them.
- 7 Explain that pain or does not necessarily mean harm.
- 8 Provide the patient with an opportunity to ask questions and respond to his or her concerns.

9 After you have explained the treatment, ask the patient to provide feedback and confirm that he or she understands the information they have received.

10 Provide the patient with direction to an approved National website so that can access further information once they get home. For example, the UK NHS: <https://www.nhs.uk/conditions/lyme-disease/>

11 If the patient is to be discharged, then ensure they are calm and relaxed if driving home. With their permission, contact a friend or relative if appropriate.

Adapted from McGhee et al, 2015

Public Health Promotion

The primary providers of emergency room facilities are influential in early detection and treatment of CL. Providing essential information about prevention and transmission is vital to ensure early detection and treatment. Due to the high incidence of sand fly activity between dusk and dawn, it is important to inform patients and families of the pivotal transmission times (CDC, 2018; Placinta et al, 2018). Delayed treatment of CL can result in progression toward mucocutaneous leishmaniasis (Burza, Croft, & Boelaert, 2018). Individuals must be cognizant of the various modes of transmission and the impact of traveling to cross-border locations with a high incidence (CDC, 2017; ECDC, 2018).

There are currently no vaccines or drugs that prevent the development of CL (CDC, 2018). However, there are several things that the at-risk person, such as a traveler or member of the British Armed Forces can do to decrease the risk of being bitten by the disease vector, the sand-fly. See Table 3 for further prevention and control measures.

Patient Advice

When Outdoors	When Indoors
<ul style="list-style-type: none">Minimize the amount of exposed uncovered skin.	<ul style="list-style-type: none">Stay in well-screened and/or air-conditioned areas

<ul style="list-style-type: none"> • Wear long-sleeved shirts and long trousers and socks, shirts tucked in • Apply insect repellent to exposed skin. Follow instructions on the product container. • Use a product that contains DEET (N,N-diethylethanolamine) 	<ul style="list-style-type: none"> • Sand flies are smaller than mosquitos and can access almost anywhere • Spray sleeping and living areas with insecticide to reduce sand fly activity • Use bed net treated with pyrethroid-containing insecticide. Treatment can also be applied to screens, curtains etc
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(Adapted from CDC, 2018)

Conclusion

CL is diagnosed through epidemiological awareness, symptomology and skin biopsy. The development of the WHO Leishmaniasis program in 2014 served as a first step towards facilitating the implementation of sustainable initiatives to reduce CL incidence and facilitate early detection and treatment. Early detection and vigilant surveillance by frontline nurses and other health care providers is essential for addressing the incidence of cutaneous leishmaniasis. Emergency Department nurses are optimally placed to ask patients about their recent travel history and to recognise common presenting symptoms. Creating a population level heightened awareness of the disease endemic areas and climates that are reservoirs for transmission is fundamental to addressing future spread of CL.

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Figure 1





Figure 2

