Journal of Infectious Diseases & Preventive Medicine

Sandle, J Anc Dis Prev Rem 2015, 3:2
DOI: 10.4172/2329-8731.1000e122

Editorial Open Access

Incidences and Treatments for Buruli Ulcer

Tim Sandle*

School of Pharmacy and Pharmaceutical Sciences, University of Manchester, UK

***Corresponding author:** Sandle Tim, School of Pharmacy and Pharmaceutical Sciences, University of Manchester, UK, Tel: 07808906409; E-mail: timsandle@btinternet.com

Received date: July 27, 2015; **Accepted date:** July 28, 2015, **Published date:** July 29, 2015

Copyright: © 2015 Sandle T. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Introduction

Buruli ulcer is a bacterial disease, alternatively called Bairnsdale ulcer, Searls ulcer, or Daintree ulcer. The tropical disease causes blood clots on the skin and, when untreated, leads to severe ulceration. The infectious disease caused by a bacterium called *Mycobacterium ulcerans*. It is the third most common mycobacterial disease after tuberculosis and leprosy.

The necrotizing disease occurs in parts of West Africa, Australia and Southeast Asia, affecting around 5,000 people each year [1]. Children aged under 15 are the most commonly infected demographic group and the region with the highest concentration of infections is, currently, Cote d'Ivoire. Until the late 1990s, when World Health Organization (WHO) programs began, the disease was a 'neglected disease' [2].

The current treatment option primarily involves courses of antibiotics. More serious or untreatable cases require surgical intervention. To improve current treatment regimes, scientists are investigating alternative approaches; this article assesses some of these approaches alongside current practices.

Analysis of the Disease

Infection with the *M. ulcerans* bacterium leads to skin nodules forming on the skin and within subcutaneous tissues. When unchecked these nodules and plaques lead to ulceration, of a characteristic white-yellow coloration. This can extend to 15% of the skin surface. If the ulcer progresses skin is lost to the extent that bone is affected. Unlike comparable diseases there is an absence of an acute inflammatory response.

The disease is manifest in different forms: indurated subcutaneous nodules, plaques, ulcers and oedema. The pain associated with the ulcer and be accompanied by fever. Many ulcers heal, however those infected can be left with scars and disabling contractures.

The common term applied to the condition - Buruli ulcer – relates to the former Buruli county (now Nakasongola) in Uganda where a number of cases of the disease were noted and studied [3]. The first cases of the disease were notified during the 1930s in the Bairnsdale District of Victoria, Australia, although accounts from the Victorian era recount probable infections [4]. Humans and animals are affected.

How someone becomes infected is unclear. Some researchers think that there is a connection between the bacteria and water sources (perhaps through water insect transmission via Naucoris or Diplonychus). Despite the association with vegetated stagnant waters, it remains that there is insufficient data to confirm this assumption. Nevertheless, the primary foci of cases are with wetlands found in tropical or subtropical countries. Cases are higher following environmental changes, including sand mining and irrigation There is a secondary relationship between the disease and physical damage to skin, in that those with braised skin are more likely to become infected compared to those with intact skin.

Causative Agent

Mycobacteria are associated with several ancient diseases, with virulence linked to extracytoplasmic proteins. One property that this family share is that they are relatively resistant organisms to many common antiseptics and disinfectants, as well as naturally resistant to several antimicrobials including penicillin. This is due to the relatively thick bacterial cell being protected by a hydrophobic waxy outer cell coat. Species of mycobacteria are the causative agents of tuberculosis (*M. tuberculosis*) [5] and leprosy (*M. leprae* and *M. lepromatosis*) [6]. The organism that leads to the Buruli ulcer - *Mycobacterium ulcerans* - is a typical microareophilic acid-fast bacterium of the Mycobacteriaceae.

While the organism can be cultured and identified, in terms of detection, there is a need for more effective methods and rapid diagnostic tools. Culturing can take between 6 and 8 weeks. Such tests are likely to be based on immunodiagnostic tools, based around identification of specific gene sequences.

Current Treatment and Approaches

With current antibiotics treatment of the disease is successful in 80% of cases, although treatment is of a relatively long duration, taking around 8 weeks. Typical oral antibiotics used are streptomycin and rifampicin, optimally in combination [7]. These carry risks in terms of toxicity. More serious conditions, or where antibiotic treatment is not successful, require surgery and skin grafting. Typical post-hospital stays, following surgery, are for three-months. Without antibiotics, post-surgery there remains a risk of reoccurrence of the infection.

With surgery the aim is to remove most infected tissue. Where antibiotics are administered, removing all infected tissue is not essential. As part of post-surgical care, addressing the joint mobility is important and this is aided through regular exercises and physiotherapy. Exercise can help to prevent permanent impairment.

Alternative Treatment Strategies

In relation to antibiotics, some patients are intolerant to streptomycin. Using an alternative regime of rifampicin and clarithromycin appears to deliver comparable results [8].

There may be ways to make antibiotics work more effectively. A histopathological feature of diseased skin in Buruli ulcer is coagulative necrosis. Thus Buruli ulcer causes a skin condition not unlike deep vein thrombosis, this similarity means that similar treatments can be considered, namely anticoagulant medicines. Trials, published in 2015,

have shown that anticoagulants promote healing faster than antibiotics alone [9]. Anticoagulants help to reduce the lesion size, providing a smaller target area for the antibiotic.

The research has found that *M. ulcerans* produces a macrolide toxin called mycolactone, which is a major virulence determinant [10]. Guinea pig studies have shown that mycolactone causes the extensive tissue damage and immunosuppression associated with a Buruli ulcer.

Mycolactone affects endothelial cells, which line blood vessels and form capillaries [11]. These cells function to prevent blood from clotting inside the vessels. Mycolactone functions to reduce the ability of endothelial cells to anticoagulate blood. This is through blocking the expression of the protein thrombomodulin. On this basis the researchers concluded that anticoagulants could improve response to antibiotics in patients.

In terms of prevention, research has been undergoing on developing a vaccine. A vaccine against *M. ulcerans* could be administered to protect people in at risk areas. A vaccine could also be used as to reduce treatment time and to guard against relapses of the disease [12]. There are three potential vaccine types: mycolactone-directed vaccines; attenuated live vaccines; and subunit protein vaccines. A probable vaccine candidate, and upon which most research has been centred, is live attenuated *Mycobacterium bovis* (also termed Bacillus Calmette-Guérin.) *M. bovis* causes tuberculosis in cattle [13].

Summary

Buruli ulcer is a damaging bacterial disease associated with tropical climates. The focal point for the cases and the current treatment points means that control of the disease is achievable and its elimination might one day be considered, provided that funding and resources are made available. New treatment options, such as the use of anticoagulants, can further help towards the realization of this goal.

A related area to addressing the disease and lowering incidences is with health promotion and education. Ensuring that the local population more fully understand the risks and causative factors will help lower the incident rate.

References

1. Chany AC, Tresse C, Casarotto V, Blanchard N (2013) History, biology and chemistry of Mycobacterium ulcerans infections (Buruli ulcer disease). Nat Prod Rep 30: 1527-1567.
2. World Health Organization (1998) WHO joins battle against a new emerging disease, Buruli ulcer. Indian Pediatrics 35: 581.
3. Lunn HF, Connor DH, Wilks NE, Barnley GR, Kamunvi F, et al. (1965) Buruli (Mycobacterial) ulceration in Uganda. (A new focus of Buruli ulcer in Madi district, Uganda): Report of A Field Study. East Afr Med J 42: 275-288.
4. MacCallum PTJC, Tolhurst JC, Buckle G, Sissons HA (1948) A new mycobacterial infection in man. The Journal of pathology and bacteriology 60: 93-122.
5. Sandle T (2014) The Possible Origins of Tuberculosis in South America. J Anc Dis Prev Rem 2: e116.
6. Sandle T (2013) Global Strategies for Elimination of Leprosy: A Review of Current Progress. J Anc Dis Prev Rem 1: e112.
7. Simpson C, O'Brien DP, McDonald A, Callan P (2013) Mycobacterium ulcerans infection: evolution in clinical management. ANZ Journal of Surgery 83: 523-526.
8. Nienhuis WA, Stienstra Y, Thompson WA, Awuah PC, Abass KM, et al. (2010) Antimicrobial treatment for early, limited Mycobacterium ulcerans infection: a randomised controlled trial. The Lancet 375: 664-672.
9. Ogbechi J, Ruf MT, Hall BS, Bodman-Smith K, Vogel M, et al. (2015) Mycolactone-Dependent Depletion of Endothelial Cell Thrombomodulin Is Strongly Associated with Fibrin Deposition in Buruli Ulcer Lesions. PLoS Pathog 11: e1005011.
10. Portaels F (1989) Epidemiologie des ulcères à Mycobacterium ulcerans. Ann Soc Belg Med Trop 69: 91-103.
11. George KM, Chatterjee D, Gunawardana G, Welty D, Hayman J, et al. (1999) Mycolactone: a polyketide toxin from Mycobacterium ulcerans required for virulence. Science 283: 854-857.
12. Huygen K, Adjei O, Affolabi D, Bretzel G, Demangel C, et al. (2009) Buruli ulcer disease: prospects for a vaccine. Med Microbiol and Immunol 198: 69-77.
13. Phillips RO, Phanzu DM, Beissner M, Badziklou K, Luzolo EK, et al. (2015) Effectiveness of routine BCG vaccination on buruli ulcer disease: A Case-Control Study in the Democratic Republic of Congo, Ghana and Togo. PLoS neglected Tropical Diseases 9: e3457.

This article was originally published in a special issue, entitled: **"Viral Infections"**, Edited by Marisa N Madison, University of Iowa, USA