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Global Strategies for Elimination of Leprosy: A Review of Current Progress

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Introduction

Of the various 'ancient diseases', one of the longest lasting (and arguably notorious) is leprosy (leprosy was recognized in the ancient civilizations of China, Egypt and India). Notwithstanding its long history, the disease is one that should be relatively straightforward, with tangible political support, to eliminate as a global health concern. The current strategy being implemented by the World Health Organization (WHO) is discussed below. This paper also reviews some of the current research into leprosy, focused on the areas of diagnosis and treatment.

There has been a global reduction in cases of leprosy over the past twenty-years due to the combined efforts of WHO, local governments, health professionals, and non-governmental organizations. Nonetheless, the number of cases remains relatively high. Data compiled by WHO indicates that approximately 182, 000 people, mainly in Asia and Africa, were affected with the disease at the beginning of 2012, with approximately 219, 000 new cases reported during 2011. These numbers represent significant reductions from the 5 million cases estimated during 1985 and the estimated 3 million cases in 1995. Despite the reduction, some areas of high endemicity remain in some regions of Brazil, Indonesia, Philippines, Democratic Republic of Congo, India, Madagascar, Mozambique, Nepal, and the United Republic of Tanzania. Of these countries, India reports over 50% of the world's leprosy cases.

Anatomy of the Disease

Leprosy (or Hansen's disease) is a chronic disease caused by the bacteria *Mycobacterium leprae* and *Mycobacterium lepromatosis. (M. Lepromatosis)* is a relatively newly identified mycobacterium isolated from a fatal case of diffuse lepromatous leprosy in 2008) [1]. Leprosy is primarily a granulomatous disease of the peripheral nerves; disease also affects the skin, mucosa of the upper respiratory tract and the eyes [2]. The main symptoms are disfiguring skin sores, lumps, or bumps that do not go away after several weeks or months, and which can become permanent if left untreated. The skin sores are pale-colored. There are three main types of the disease: Tuberculoid (a mild, less severe form of leprosy); Lepromatous (a more severe form of the disease, where the nose, kidneys, and male reproductive organs may also be affected); and Borderline (people with symptoms of both the tuberculoid and lepromatous forms).

A further subdivision of the disease relates to patient reactions. Around 20-50% of all leprosy patients present reactional states during the course of the disease, which occur most frequently after the start of polychemotherapy. Leprosy reactions are divided into type 1 reaction (or reversal reaction), and type 2 reaction (or erythema nodosum leprosum) [3]. In relation to other bacterial diseases leprosy is unusual in terms of the time taken for the infection to become apparent. The causative agent, *M. leprae*, multiplies very slowly and the incubation period of the disease is about five years; moreover, symptoms can take as long as twenty years to appear.

Leprosy is not a highly infectious disease. It is probably transmitted via droplets, from the nose and mouth, during close and frequent contacts with an untreated case [4]. Nasal secretions from lepromatous patients could yield as much as 10 million viable organisms per day [5]. Not all people who become infected develop leprosy (for genetic factors are considered to be influential). At highest risk are those living in endemic areas with poor conditions such as inadequate bedding, contaminated water, and insufficient diet, or subject to other diseases that compromise immune function.

Whilst the outward signs of the disease can be characterised, the bacteria are difficult to identify. This is because *M. leprae* and *M. lepromatosis* are unculturable in the laboratory using standard culture techniques. Instead, the bacterium is grown in other animals prone to leprosy, including grown in mouse foot pads and nine-banded armadillos.

Treatment

Early diagnosis and treatment with multidrug therapy (MDT) are the key elements in eliminating the disease as a public health concern. The MDT approach, in place since 1981, consists of three drugs: dapsone, rifampicin and clofazimine. Of these, dapsone (diaminodiphenylsulfone) was the first leprosy drug developed and it remained effective for a couple of decades until the bacteria developed resistance. To be effective, MDT needs to be taken over a twelve month period. In addition, to suppress the cellular immunological response, Immunosuppressant's such as azathioprine and cyclosporine A can be used in association (or not) with corticosteroids [6].

Current Research

The study of leprosy remains an active area of scientific and clinical research. One strand of research is focused on detection of the disease (to enable earlier treatment); for this, researchers are seeking to identify suitable markers for lepra reactions [7]. Presently, there are no uniformly acceptable laboratory markers for lepra reactions. However, genetic and serum markers in human host may predict susceptibility to reactions as well as progression of nerve damage in leprosy [8].

Other research is orientated towards the assessment of patients post-treatment. Surgical nerve decompression in leprosy is indicated to prevent or treat nerve damage, and to improve sensory motor function and quality of life. Matrices are being considered by some researchers to add to the standard battery of tools used to assess health and well-being and to identify patients' needs whilst in rehabilitation [9].

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The ultimate aim is the development of a prophylactic vaccine, to protect against both drug-susceptible and drug-resistant strains. However, immunoprophylaxis in leprosy continues to be largely speculative. This is due to problems with culturing the infectious agent [10]. This nonetheless remains an area which is being examined and where a breakthrough would be of great significance.

Global Strategy

The global strategy for combating leprosy has been developed, in various waves, by the WHO. In 1991 the World Health Assembly (WHA) passed a resolution to eliminate leprosy by the year 2000 (where 'elimination' is defined as less than 1 case per 10 000 persons). This was achieved in a number of territories, although leprosy cases remain high in some regions.

The current WHO phase is the global leprosy strategy 2011-2015 [11]. Part of the strategy is reliant upon the pharmaceutical company Novartis and its charitable arm, the Novartis Foundation for Sustainable Development, for providing the MDT drug combination to the WHO for distribution. However, the combination of biological and epidemiological evidence suggests that the leprosy cannot be eliminated by MDT alone. It is on this basis that there are other aspects to the strategy, which include [12].

- Integrating leprosy treatment into general health services within affected nation states.
- Encouraging those affected to come forward and to seek treatment.
- Encouraging political commitment.
- Working with partner organizations to provide financial aid.
- Providing educational materials to reduce the stigma associated with the disease.
- Monitoring the performance of MDT in the event of any cases of drug resistance.
- Requiring people who live in the same household to be examined for leprosy and only be treated if symptoms are present [5,13].

Although the strategy is making progress, there remains a need to adopt local problem-specific strategies at sub-national levels (provinces, districts, municipalities) to address diverse factors influencing the leprosy. The major risk to the strategy is the potential emergence of bacterial strains that are rifampicin resistant. Some cases have been reported (most recently by Engström in relation to tuberculosis) [14]. Should this occur then treatment will be affected pending the development of new combinations of drugs.

Conclusion

This paper has reviewed the current state of leprosy worldwide and has presented the current global health strategy and some of the research projects. Contrary to expectations, use of MDT has not solved the problem of persistence of *M. leprae* and there are risks with any strategy that is solely dependent upon the use of the combination drugs. It is important, in terms of global action and research activities, to consider the eventuality of MDT resistance developing.

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