Diagnosis and Treatment of Leishmaniasis Remain a Big Challenge

Leishmaniasis, caused by protozoan Leishmania parasites and transmitted via infected female sand flies and possible reservoir hosts, like dogs, is endemic in 88 countries and 350 million people are at risk of contracting the disease. Leishmaniasis prevalence is >12 million cases/year and the incidence is >2.5 million cases/year. The estimated disease burden is 2.4 million DALYs. Leishmaniasis is a category 1 disease (“emerging or uncontrolled diseases”). The World Health Organization has acknowledged it as a severely neglected disease and urged intensified research programmes to improve vector control, diagnostics and therapeutic arsenal to contain further incidence and morbidity\(^1\).

An infection with Leishmania parasites can, depending on the infecting species, give rise to several distinct clinical manifestations, ranging from localized cutaneous leishmaniasis (CL) with single to multiple skin ulcers, satellite lesions or nodular lymphangitis or possibly mucosal involvement, muco-cutaneous leishmaniasis (MCL), to systemic visceral leishmaniasis (VL) with involvement of different organs (like liver and spleen) and bone marrow, which may be lethal. Early diagnosis and correct identification of the infecting parasite species causing disease are crucial to install effective treatment, as pathology and treatment are different depending on the infecting (sub-)species, and remain problematic\(^2\).

Traditionally, the diagnosis of leishmaniasis is based on clinical criteria and, in the best case, supported by conventional laboratory diagnosis, such as microscopical demonstration or culturing of Leishmania parasites from skin biopsies or aspirates from lesions, bone marrow, lymph node or spleen. However, these methods are rather insensitive, sometimes painful or even dangerous for the patient and culturing of parasites is time-consuming and laborious\(^2\).

There is thus an urgent need to enhance the diagnostic arsenal for this disease, but only few initiatives are focusing on the improvement of leishmaniasis diagnosis and funding is limited. Although molecular biology and genomics have proven to provide, or are promising to deliver, many answers to health problems, including diagnosis, in the industrialized countries, these developments do not translate into useful tools for developing countries\(^3\). A major obstacle preventing the implementation of these innovative tools is the fact that they rely on a constant supply of electricity and require investment in expensive equipment, which often needs dedicated maintenance. An innovative EU sponsored research consortium, Human African Trypanosomiasis and Leishmaniasis Diagnostics (TRYLEIDIAG; see: www.tryleidiag.org), in which research groups from Europe and disease endemic countries in Africa, strives towards the development of simplified molecular-based diagnostic tests that circumvent the use of sophisticated equipment and electricity. The TRYLEIDIAG consortium exploits a combination of simplified amplification methods, like for example nucleic acid sequence based amplification technology, with easy read-out
systems, like oligo-chromatography, which are promising sensitive and specific diagnostic tools for kinetoplastid disease. However, the implementation of such a tool in primary health care may be hampered due to relative high cost of the test. A test costing over $1 is not affordable for communities able to spend less than this amount of money per person on primary health care per day.

After diagnosis, adequate treatment must be installed promptly. Here we meet another challenge in leishmaniasis control. A wide variety of treatment modalities exist for the diverse spectrum of clinical disease. Traditional anti-leishmanial systemic agents such as antimonials, pentamidine and amphoterin are limited by toxic side effects, parenteral route of administration and emerging drug resistance. The latter is for example evident in India where sodium stibogluconate, once considered to be the standard first line drug for VL, has lost its efficacy because of the development of high resistance (>50%). Newer agents, such as liposomal amphoterin B (Ambisome) or oral miltefosine (Impavido), have shown efficacy and tolerability. However, daily use of these new pharmaco-therapies remains limited by their high cost in developing countries and despite advances in basic scientific research, there has been little progress in new drug development for what remains a neglected disease; but luckily there are some exceptions. The drugs for neglected diseases initiative (www.DNDI.org) is developing drugs for neglected diseases on a not-for-profit basis. A recent success of DNDI is Paromomycin (aminosidine), a low-cost parenteral formulation, which was registered in late 2006 in India and is currently in Phase III trials in East Africa. Recently, GlaxoSmithKline (GSK) has joint DNDI in a collaborative research effort targeting neglected tropical diseases which disproportionately affect the developing world and it is hope that this program will provide innovative projects yielding new drugs against leishmaniasis and other neglected diseases.

The challenge to improve the diagnosis of leishmaniasis and subsequent adequate treatment of the disease remains at this moment. It is a task of the scientific community to prioritize and conduct research towards this issue, but it is a duty of policy makers to place this high on the international research agenda and the obligation of international doners to secure funding for research and implementation of innovative diagnostics and new drugs in primary health care systems in developing countries. The best diagnostics and treatment options must be made available for those at need at all levels in society. We cannot afford to neglect diseases.

References

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