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It is possible to envision human leishmaniasis control encompassing several levels: vector transmission; identification of parasites more likely to be transmitted to man or more difficult to treat; control of disease in other animals which may harbor the parasite; early recognition of infection in man; the development of effective drugs, and availability of vaccines. Examining how scientific research can contribute in each of these areas is a daunting task. The purpose of this text is rather presenting a personal (and probably biased) view on the subject, and so no references cited.

Vector transmission in leishmaniasis is a neglected area. There are several Phlebotomine species with a large diversity in geographical distribution, and in their relationship with Leishmania species. Additionally, the rate of natural infection of *Lutzomyia spp* with *Leishmania* in endemic areas is very low. Sand fly populations tend to be clustered and there is evidence that higher rates of infection are found in areas with higher number of human cases. Such a non-homogeneous distribution of Leishmania-infected vectors may have implications in control strategies against leishmaniasis.

Phlebotomine species also vary in their feeding habits (including the sources of blood feeding) and in their salivary composition. Sand flies salivate on their hosts during blood feeding. Saliva of blood sucking vectors contains a large array of molecules that modulate their hosts' hemostatic, inflammatory and immune responses. Maxadilan, present in the saliva of the New World sand fly *Lutzomyia longipalpis* is a vasodilator and an immunomodulator. A large body of evidence demonstrate the production by humans and other vertebrates of antibodies against salivary components of blood sucking animals. Human immune response against sand fly saliva may be used as epidemiological markers of vector exposure or may help in devising more effective vaccines. Identification of human antibodies to sand fly saliva components could be useful to indicate the distribution of sand flies in a particular region, adding information to the clustered distribution of vectors. This may help directing vector control efforts. There are experimental indications that host immune response against sand fly saliva influences the course of leishmaniasis in mice. If similar findings are true in man, it is possible that stimulating the appropriate immune response against vector saliva may help in vaccination against leishmaniasis.

On the parasite side, science can boost control efforts by identifying Leishmania isolates which present higher virulence or drug resistance. It is known that some Leishmania strains are preferentially involved in some severe forms of the disease. *L. braziliensis* is the main agent of mucocutaneous leishmaniasis, and it is the only Leishmania isolated from lymph nodes in cutaneous leishmaniasis patients. *L. donovani* is the predominant agent of visceral leishmaniasis, and this aspect may be related to its capacity of multiplying at higher temperatures than other Leishmania which infect man. Exploring the characteristics of these parasites involved in such particular behaviors may be useful to control. An early identification of a virulence marker may direct therapy and follow-up, reducing the time the parasite is available for transmission.

As a matter of fact, a method capable of identifying low numbers of Leishmania, with or without indicating virulence, may be of great interest in Leishmaniasis control. A molecular biology-based test has the potential of amplifying the Leishmania material of few parasites available in a clinical sample. Such a test is likely to be faster than any approach based on parasite growth. It would also have advantages over immunologically-based tests as being a direct identification of the parasite, and not an indirect estimation. Such a molecular test could be useful in identification of early cases of infection, in therapeutic failures and relapses. In the last two situations the capacity of discriminating between live and dead parasites will most likely be a requirement.

Presently used drugs for leishmaniasis treatment are toxic, and there are indications of the increased presence of drug-resistance parasites. An effort for new drug development is needed but not envisioned. The market is not economically attractive for the commercial pharmaceutical companies, and no concerted effort of state-laboratories in the endemic areas is being conducted. Approaches for more effective drug delivery are also possible, following the lead of the use of liposomes.

Vaccination is viewed as the ultimate measure in leishmaniasis control. Candidates antigens for leishmaniasis vaccination are legion. None of them proved highly superior to the others. More than searching for new antigens the actual emphasis is on optimizing conditions for increasing cell-mediated immunity. New adjuvants or naked DNA technology are intensely pursued and may contribute to the finding of the Holy Grail. It should be pointed out however that the availability of a new experimental highly effective vaccine preparation is only a step in leishmaniasis control. Several factors, some of them outside the scope of scientific effort, will influence its outcome.

Table 1 summarizes our current views on the probable role of scientific pursues important for leishmaniasis control and likely to successful in the near future. In each case we have listed the technical approach likely to deliver the answer to the problem. It is our hope that our list proves to be modest and much more important contributions are brought to this field in the rising of the new millennium.

Table 1 - Selected objectives important to leishmaniasis control and possible scientific contributions envisioned in a new future.

Objective	Rationale	Approach	Implication in control
Determination of infected vectors	Possible clustering of infected sand flies, i. e small regions in the endemic area exhibit a higher density of infected phlebotomines than others	PCR	Identification of areas with higher risk of transmission may help identifying ecological factors involved in sand fly infection
Determination of human exposure to vectors	Identifying human immune response to sand fly salive may serve as an epidemiological marker of exposure. Immune response to phlebotomine saliva may alter the course of infections or disease	ELISA	Identification of populations at higher risk of infection/disease may help devise control strategies
Identification of virulence markers in Leishmania	Certain parasite characteristics may be implicated in more severe cases of leishmaniasis	Differential display Microarray DNA chips	Parasites with higher virulence may indicate patients to the submitted to special treatment schedules and/or special follow-up, decreasing availability of parasites for vectors
Identification of drug resistance in Leishmania	Drug resistance is rising in Leishmania		Correct drug regimens instituted early may shorten therapy decreasing availability of parasites for vectors
Detection of low parasite numbers	Molecular tests of high sensitivity for identification of parasites are prone to be faster than parasitological tests, and more reliable than immununological tests for early diagnosis	PCR	Such a test could be used for early diagnosis or faster identification of relapses, in addition to evaluation of treatment effectiveness identifying treatment failures
More effective drugs	Present drugs are toxic and resistance is beginning to rise	Development of new drugs, or other approaches for drug delivery (as liposomes are used today)	More efficient treatment will increase patient compliance and curtail drug resistance. These measures lead to reduced availability of parasites fo vectors.
Effective vaccines	Several candidate antigens are under tests but no vaccine is available for human or canine routine use. The need to reinforce cell-mediated immunity is a limiting factor in vaccines against leishmaniasis	New approaches for increasing cell-mediated immunity include: DNA vaccines. New adjuvants	An effective vaccine may decrease drastically the number of cases, representing the ultimate objective of control