Education is key to controlling visceral leishmaniasis

Costly and onerous treatment as well as resistance to drugs and pesticides are major challenges to the ambitious goal of eliminating visceral leishmaniasis. However, Dr Robert Killick-Kendrick is optimistic about recent advances in treatment and control.

Q: What is visceral leishmaniasis?

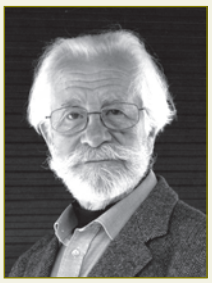
A: Visceral leishmaniasis (VL), also known as kala-azar (meaning black fever or deadly sickness in Assamese) on the Indian subcontinent, is an ancient parasitic disease that continues to resist modern control efforts. Transmitted by phlebotomine sandflies, it is most common in north-eastern Asia, eastern Africa and north-eastern Brazil, but cases also occur in southern Europe and elsewhere. Each year there are about 500 000 new cases and more than 50 000 deaths worldwide: however, as leishmaniasis is not a notifiable disease in many countries, these figures are underestimates.

Q: What happens if patients are not treated?

A: The blunt answer is almost all of them die. The time lapsed from being bitten by an infected sandfly and the appearance of first symptoms is variable but is generally between two and six months. The commonest symptoms are fever, swelling of the abdomen, with pain caused by enlargement of the spleen, diarrhoea, cough and bleeding. The immune system is compromised and patients have little resistance to other infections.

Q: In India, drug resistance and the high cost of medicines make treatment of this disease very difficult. Has there been any progress?

A: Until a few years ago, the treatment for VL was a long course of injections with a pentavalent antimonial. But the parasite in India has progressively developed resistance to this class of drugs and they are not much use there now. Fortunately, there are more options for treatment now than there were 10 years ago: AmBisome B® [liposomal amphotericin B] administered as two perfusions is perhaps the drug of choice. Until recently, it was prohibitively expensive but the World Health Organization is playing an important role in getting the price down. Miltefosine is the only orally administered drug available against VL but treatment takes time – it has to be taken twice daily for 28 days – and cannot be prescribed for women of childbearing age unless they are taking reliable contraceptive precautions.



Courtesy of Dr Robert Killick-Kendrick

Dr Robert Killick-Kendrick

Dr Robert Killick-Kendrick, Honorary Research Fellow at Imperial College, London, is a leading parasitologist whose early research was on African trypanosomiasis and malaria. In 1972, he set up a research unit at Imperial College funded by the Wellcome Trust and the Medical Research Council of the United Kingdom to study leishmaniasis and phlebotomine sandflies. His Doctorate of Philosophy was on the life-cycles and taxonomy of malaria parasites and in 1979 he gained a Doctorate of Science at London University for his published work on leishmaniasis. In 1991, he was awarded the Sir Rickard Christophers Medal of the Royal Society of Tropical Medicine and Hygiene and, in 2007, the Emile Brumpt International Prize.

Q: Is there much public awareness of the disease and its treatment?

A: In the state of Bihar in India, where 90% of Asian cases of the disease occur, there are three challenges. First, poverty and ignorance of the etiology of the disease mean few people with VL seek medical help for diagnosis and treatment. Second, compliance with long courses of treatment is extremely low. I think the answer to these challenges is health education and community participation – two activities that do not appear to be high priorities. The third challenge is the treatment of the 10% of patients who develop a skin infection after treatment – post kala-azar dermal leishmaniasis – that can persist for years. These patients don't feel ill and so are reluctant to spend weeks on treatment even though they are believed to act as a source of infection between epidemics. A proportion of infected individuals, perhaps as many as 30%, never have any symptoms at all.

Q: Do the challenges of diagnosis and treatment differ between countries?

A: Yes. Pentavalent antimonials can still be used in Brazil and countries around the Mediterranean. And the trickle of cases in southern Europe are readily diagnosed and treated because of well developed health-care systems. On the Indian subcontinent and in eastern Africa and Latin America, VL is mainly a disease of the poorest of the poor. Transport to a clinic or a hospital costs money: if you don't have the fare, you don't get treated.

Q: Have there been any advances in control of the vectors that spread this disease?

A: Progress is slow but there have been some recent advances. There have been encouraging results with insecticide-impregnated bednets. Between 1999 and 2001, Médecins Sans Frontières distributed 35 700 insecticide-impregnated bednets in 155 villages in a highly active VL focus in eastern Sudan. Seventeen to 20 months later, clinical cases had fallen by 59% and it was estimated that the intervention prevented 1060 new cases: the mean protection effect was 27%. Sadly, plans to cover a much wider area were discontinued in March 2009 when nongovernmental organizations were asked to leave northern Sudan. There is a new possibility of reducing the risk of infection in settings where domestic dogs are reservoir hosts. Dogs fitted with deltamethrin-impregnated collars are protected from the majority of sandfly bites for about six months. In Brazil, more than 22 000 dogs were collared in this way and followed from 2002 until 2005. The collars were renewed regularly. The prevalence of canine infections fell from 12.5% in 2003 to 3.9% in 2005. There was a concomi-

tant fall in the incidence of human cases from 34.1 to 5.4/100 000 over the same period. Earlier, a similar result was reported from a field trial in [the Islamic Republic of] Iran.

Q: Why hasn't house spraying been more successful in stopping the disease?

A: The vector on the Indian subcontinent is strongly endophilic (a species that remains indoors after taking a blood meal) and house spraying in the 1950s and 1960s to try to eradicate malaria was followed by a remarkable fall in the prevalence of VL. Unfortunately, when spraying was stopped, the sandfly population rapidly recovered and there were terrible epidemics in north-eastern India in the 1970s. Widespread house spraying with DDT [dichlorodiphenyltrichloroethane] is currently part of the action planned to eliminate VL in north-eastern India by the year 2015.

Q: But isn't DDT banned in most countries?

A: The choice of insecticide may indeed come as a surprise to people who remember the storm created by the publication in 1962 of Rachel Carson's *Silent Spring* that resulted in a ban on the manufacture of DDT in the United States of America and elsewhere. But its use is still permitted by the Stockholm Convention for spraying internal walls of habitations in developing countries when there is no practicable alternative. DDT is the insecticide chosen for the control campaign on the Indian subcontinent pending current investigations planned by the Convention to speed up its total ban. [Deltamethrin will be used in Bangladesh and Nepal, where DDT is banned.] There is no doubt that house spraying can work. However, it must be done properly. If not, it is almost certain that the vector will become resistant to DDT – as it did in Bihar in the 1970s. This is a real danger as indicated by a report that after five DDT spray-rounds in Bihar between 1992 and 1994, it was discovered that more than half the houses had not, in fact, been sprayed. This is a recipe for creating insecticide resistance, a risk that can be minimized by using more than one insecticide. Whatever insecticide is used, if spraying is stopped too soon, there could be a disaster: rapid recovery of the sandfly population followed by a devastating epidemic. To reduce this possibility in the north-east of the Indian subcontinent, active case detection and treatment of all cases of both VL and post kala-azar dermal leishmaniasis is planned, a tremendous undertaking.

Q: Do you believe that this disease can be eliminated?

A: Yes. But it depends what you mean by eliminated. No one likes to use the word "eradicate" with its inference of complete disappearance of an infection – a rare outcome of control. But if we go by the definition of "elimination" as control of a disease in a defined geographical area that nevertheless requires constant vigilance to detect any resurgence, in that sense, VL can be eliminated. It was done in eastern China after a campaign lasting 30 years. Domestic dogs were reservoir hosts in that part of China and control was by the total destruction of dogs, annual house spraying with two different insecticides and annual active case detection and treatment.

Q: What is required to make this happen?

A: There are five key factors that apply to all vector-borne diseases, not just VL. The first is peace: civil disturbances make it difficult to run a control programme. Second, long-term political commitment: even in the industrialized nations, health priorities change with changes of government. Third, finance: this again requires long-term commitment. Fourth, sound control methods likely to succeed are essential. And, lastly, public health education: if a mother doesn't think the disease is carried by a biting fly, why should her children sleep under a bednet? Why should she let the sprayers leave nasty spots all over her bedroom wall? Community understanding and participation increase the chances of success. Improvements in housing and standards of living will also make a big difference.

It's easy to sit in our armchairs and list the problems for the control of VL – or any other vector-borne disease. But I am optimistic: with adequate funding, long-term political support and energy coupled with a little imagination, it must be possible to tame this disease, if not get rid of it altogether. To be practical, we should remember VL has not been completely eliminated in the rich countries in southern Europe that border the Mediterranean.

Dr Killick-Kendrick was interviewed as a guest speaker of the World Health Organization's global health history seminar series. Access the seminars online at: http://www.who.int/global_health_histories/seminars/2009/en/index.html ■

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