DISEASE WATCH | IN THE NEWS

Self-help for malaria in chimps

Chimps are thought to self-medicate when they are ill, but the scientific benefits of the foods that chimps choose have remained unclear. Researchers observing a community of chimps in Kibale National Park, Uganda, noticed that several plants that have no apparent nutritional benefit were specifically eaten by sick chimps or occasionally by other individuals. Extracts of one of these plants, *Trichlia rubescens,* and bioassays led to purification of two limonoids

that had significant antimalarial activity *in vitro*. Chimps might lead humans to new antimicrobial compounds. **Antimicrob. Agents Chemother.**

China gets TB under control

The DOTS initiative that was implemented a decade ago, and was supported by the World Bank and the WHO, has reduced TB incidence by 30% in regions of China. TB incidence in China — 1.4 million new cases annually — is second worldwide only to India. DOTS combines political commitment, microscopy services, drug supplies, surveillance and monitoring systems with highly efficacious drug regimes and direct observation of treatment. Implementation of the DOTS strategy throughout China, and the rest of the world, should proceed, but a careful appraisal of what is needed to make DOTS work is essential, cautioned S. Bertel Squire (Liverpool School of Tropical Medicine, UK). **The Lancet**

Network to fight bird flu

A south-east Asian 'bird flu' network just launched by the UN Food and Agriculture Organization will train veterinary officials in poverty-stricken regions of Asia so that vets can more easily recognize the symptoms of the disease. The network should enable better coordination between individuals in the field, between laboratories in different regions and between countries in Asia to ensure that bird flu is carefully monitored and contained. The UN will publish new guidelines for avian influenza in August, including recommendations on the use of vaccines in poultry farming. Vaccination is increasingly seen as a useful way to help control a disease that is becoming endemic in wild birds. The hope is that these measures will reduce the likelihood of a bird epidemic leading to outbreaks of a new influenza strain in humans. **Reuters**

DISEASE WATCH | FOCUS

Leishmaniasis

BACKGROUND

Causative agent and disease burden. Protozoan flagellates of the genus *Leishmania* are transmitted by the phlebotomine sandfly and cause different clinical forms of leishmaniasis — visceral leishmaniasis (VL) is often fatal if untreated, muco-cutaneous leishmaniasis (MCL) is a mutilating disease, diffuse cutaneous leishmaniasis (DCL) is disabling and cutaneous leishmaniasis (CL) can result in an unaesthetic stigma if multiple lesions occur. Disability-adjusted life years (DALYs) lost due to leishmaniasis are close to 2.4 million, there are 1.0–1.5 million cases of CL and 500,000 cases of VL each year, and a population of 350 million is at risk. Despite the scarcity of reliable data, there is little doubt that the case-load worldwide is considerably higher than official reported figures[1].

Distribution. Leishmaniasis affects 88 countries, of which 72 are classed as developing countries, including 13 of the least developed countries. 90% of VL cases occur in just five countries — Bangladesh, India, Nepal, Sudan and Brazil. 90% of CL cases occur in just seven countries — Afghanistan, Algeria, Brazil, Iran, Peru, Saudi Arabia and Syria[2] (FIG.1) The epidemiology of leishmaniasis is diverse with 20 *Leishmania* species that are pathogenic for humans and 30 sandfly species that have been identified as vectors. In several regions there is a clear and worrying increase in the number of cases. For example, the incidence of CL in Brazil increased from 21,800 cases in 1998 to 60,000 cases in 2003; in Kabul, Afghanistan, the incidence increased from 14,200 cases in 1994 to 67,500 in 2002; and in Aleppo, Syria, the incidence increased from 3,900 cases in 1998 to 6,275 in 2002. Increases have mainly been attributed to behavioural and environmental changes, including the development of new settlements, intrusion into primary forest, deforestation, massive migration from rural to urban areas, fast and unplanned urbanization, and the building of dams and new irrigation schemes. However, individual risk factors such as malnutrition and immunosuppression owing to HIV co-infection also have important roles[3].

Current global status. Although tools for leishmaniasis control were formerly inadequate owing to expense, or were too complex for local deployment, new research and development by the TDR and others mean that better tools are now available[4].

RECENT DEVELOPMENTS

New basic knowledge. The completion of the *Leishmania major* genome sequence was a landmark that enabled the identification of genes and processes that might represent good targets for new drugs, diagnostic tests or vaccines. Use of DNA microarrays allows comparative genomics between species and analysis of the expression of parasite genes at different infectious stages. In addition, host cell gene expression profiling allows the host response to infection to be monitored. DNA microarrays have identified differentially expressed mRNAs at several stages of the *Leishmania* life cycle and among different species[5]. Studies during a VL outbreak in Sudan showed that one locus on chromosome 22q12 and probably two loci on chromosome 2q22-23 control susceptibility to VL[6,7].

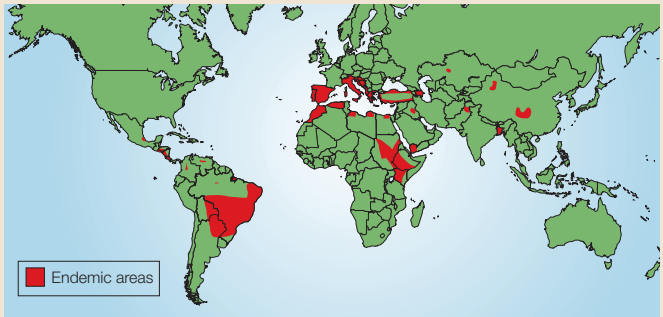

Figure 1 | The distribution of visceral leishmaniasis

Award for Hiroshi Nikaido

Hiroshi Nikaido, M.D., Professor of Biochemistry and Molecular biology at the University of California, Berkeley, has been selected to receive the fourteenth annual Bristol–Myers Squibb 'Freedom to Discover' Award for Distinguished Achievement in Infectious Diseases Research. Dr Nikaido was recognized for his pioneering work on bacterial solute transport systems — known as porins — and the role of these systems in both antibiotic function and resistance. His work on solute transport in bacteria opened a new field of research in microbiology and has led to important clinical applications in the fight against infectious diseases. **Freedom to Discover Foundation**

Outbreak news: update for September

The WHO have detected an outbreak of shigellosis using an early warning system set up in a camp that houses an estimated 63,000 displaced people in North Darfur, Sudan. Latrine building and education in handwashing are two strategies that are being implemented to try and reduce the impact of waterborne illnesses.

Yvette Bivigou, a UN WHO spokesperson, has expressed concern about the pertussis outbreak affecting 400 children, with 4 deaths, in the Helmand province of Afghanistan. Helmand is second only to the northern province of Badakhshan in whooping cough prevalence, with more than 1,500 cases reported in the past year. The WHO hopes to instigate a vaccination campaign for all children under 5, but the challenge is to obtain enough vaccine to achieve this objective.

Health officials in Ituri, a north-eastern district of the Democratic Republic of the Congo, reported 58 suspected plague deaths on 29 July. 90% of the cases are suspected to be bubonic plague. **IRINnews.org**

In the News was compiled with the assistance of David Ojcius, University of California, Merced, USA.

New tools and intervention methods. Cheap, reliable and easy-to-use tests for VL diagnosis have now been developed including: an immunochromatographic test that enables a quick differential diagnosis of malaria and leishmaniasis[8]; the direct agglutination test (DAT), which is a quantitative test that uses a freeze-dried antigen[9]; and a urine antigen-detection test that is particularly useful for immunocompromised patients and to evaluate treatment efficacy[10]. A TDR-supported multi-centre trial is ongoing in east Africa and on the Indian subcontinent to compare the three tests. Moreover, the development of species-specific primers have improved the specificity of molecular diagnosis tests based on PCR.

Miltefosine, registered for use in India in 2002, is an alkylphosphocholine that is the first oral drug for treatment of VL. Phase IV clinical trials that are aimed at evaluating the level of compliance were recently concluded. Owing to its teratogenic potential, the drug cannot be administered to females of childbearing age unless contraception is taken. With this exception, trials in India have confirmed the safety and efficacy of the drug[11]. Paramomycin, an aminoglycoside, is currently undergoing Phase III clinical trials in India — so far it has shown great promise and it has the potential for multidrug therapy[12].

Insecticide-treated nets (ITNs) seem to be a sustainable alternative to the traditional vector control approach of spraying houses with insecticide. ITNs are useful in areas where both leishmaniasis and malaria are endemic and in anthroponotic foci where only human-to-human transmission occurs. Long-lasting insecticide-treated bednets are currently being tested[13]. Finally, a new tool for canine leishmaniasis control — pyrethroid impregnated collars — has recently been validated[14].

Vaccine development against leishmaniasis remains a goal, but requires improved understanding of the pathogenesis of leishmaniasis and better animal models that more accurately reflect the human disease. Protective efficacy of a tandemly linked multi-subunit recombinant leishmania vaccine (Leish-111f) formulated in MPL adjuvant is under evaluation in the United States (Phase I trials have been completed)[15].

New strategies, policies and partnerships. Increased research and funds are needed for neglected diseases such as leishmaniasis. The WHO, together with several other institutions, will establish public–private partnerships to attract more funding for leishmaniasis research and disease control. The availability of a cost-effective package for case management and vector control should provide an opportunity to implement step-by-step elimination programmes in the main VL foci, which is the main priority.

CONCLUSIONS AND FUTURE OUTLOOK

The main challenge in leishmania research is to translate knowledge derived from research into cost-effective, accessible and affordable control tools that improve the outcome for those susceptible to this disease[16].

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TDR Reference Group on leishmaniasis: Boelaert, M., Sundar, S., Croft, S., Stuart, K., Tibayrenc, M., McMahon Pratt, D., Maroli, M., Reed, S., Dessein, A., Blackwell, J., Alvar, J., Davies, C., Saravia, N., Menne, B. & El Hassan, A. M.
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Online links

FURTHER INFORMATION
***Leishmania major*:** http://www.sanger.ac.uk/projects/l-major/
TDR: http://www.who.int/tdr/
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