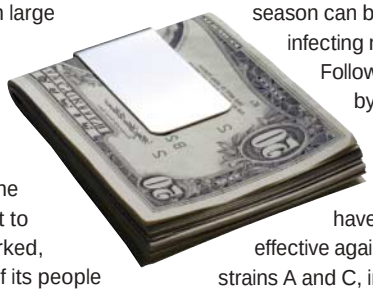
DISEASE WATCH | IN THE NEWS

$168 million from Gates Foundation to fight malaria

The Bill and Melinda Gates Foundation has announced grants totalling $168 million to fund malaria research. The Malaria Vaccine Initiative will receive $100 million, $40 million will go to the Medicines for Malaria Venture (a Geneva-based not-for-profit organization developing new anti-malarial drugs) and $28 million will be spent on large multi-centre trials of a new prevention strategy that combines the use of antimalarial drugs in the first year of life with routine vaccination. Announcing the funding boost during a visit to Mozambique, Gates remarked, 'Malaria is robbing Africa of its people and its potential'. 90% of the 1 million deaths from malaria each year occur in Africa, with most deaths in children. **(TDR) Nature**



WHO makes urgent appeal for meningitis funds

In the 'African meningitis belt', which stretches from Ethiopia in the east to The Gambia in the west, outbreaks of meningitis during the dry season can be devastating, frequently infecting more than 10,000 individuals. Following a severe outbreak caused by the emergence of *Neisseria meningitidis* strain W135 last year, GlaxoSmithKline, in partnership with the WHO, have produced a trivalent vaccine, effective against W135 and meningococcal strains A and C, in a record 6 months. 3 million doses of the vaccine are available at just €1 per dose, however, according to the WHO, unless sufficient funds are donated to purchase the vaccine soon, it will not be distributed in time for this year's dry season. Dr Anarfi Asamoa-Baah, Assistant Director-General in charge of Communicable Diseases at the WHO said, 'This is an urgent health situation which forces quick action'. **WHO**

Serious measles outbreak in the Pacific

CDC representatives are working with health officials on the Marshall Islands in the central Pacific to contain a serious measles outbreak. More than 600 cases of measles have been reported on the islands, which fall under US jurisdiction, with at least 3 deaths. It is believed that the measles virus was introduced from Asia,

DISEASE WATCH | FOCUS

Leprosy

BACKGROUND

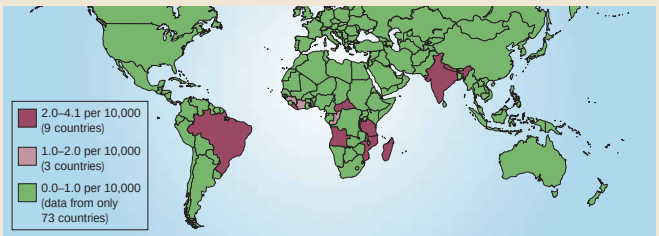
Causative agent. Leprosy is a chronic disease caused by the non-cultivable, slow-growing, acid-fast bacterium *Mycobacterium leprae*. It is thought to be transmitted from human to human by nasal droplets, as distinct from the transmission of *Mycobacterium tuberculosis*. Leprosy lesions have been reported to develop at the site of skin abrasions. Naturally occurring *M. leprae* infection has been reported in wild animals, including the nine-banded armadillo in the New World, and several species of monkeys in Africa. In humans, *M. leprae* primarily infects macrophages, endothelial cells and Schwann cells. The unique tropism of *M. leprae* for peripheral nerves leads to the classical deformities that have been described over the ages.

Distribution. In 1992, 88 countries reported more than one leprosy patient receiving treatment per 10,000 population. In 2003, leprosy is still found in nine high-burden countries, which report prevalence rates between 2.0–4.1 per 10,000 population. In an additional three countries, the prevalence rates are between 1 to 2 cases per 10,000 population. The recent prevalence figures represent a drastic reduction from the World Health Organization (WHO) estimates of 10–12 million cases globally in the early 1980s — the time when multi-drug therapy (MDT) was recommended to treat leprosy. More than 12 million leprosy patients have been cured by MDT treatment since 1981.

Current global status. The implementation of the WHO-recommended MDT for leprosy treatment has been very successful over the past 22 years. At present, more than 99% of registered patients are receiving MDT, and no drug resistance or significant relapses have been reported. As the average incubation time from initial infection to clinical disease is unknown, it is assumed that a significant number of 'subclinical' or asymptomatically infected individuals are present in those countries endemic for leprosy. The degree of infectivity of such individuals remains undetermined, so it is difficult to predict when there will be a significant decrease in the new cases detected. Indeed, for some countries, the detection rates of new cases have remained approximately stable over the past decade. In January 2003, there were 534,311 cases globally, and during 2002, 620,672 new cases were reported. The global mortality from leprosy is estimated to be ~4,000 individuals per year.

RECENT DEVELOPMENTS

New basic knowledge. The inability to cultivate *M. leprae in vitro* and the lack of a suitable animal model have hampered leprosy research. However, the availability of the *M. leprae* genome sequence[1] has stimulated several research studies and new approaches to improve our understanding of leprosy[2]. On the basis of recently available human genome sequence data, gene expression patterns associated with an ongoing host immune response in lesions of human leprosy have been defined[3]. Recently, a genome-wide search for loci controlling susceptibility to leprosy in a Vietnamese population provided evidence for a susceptibility gene on chromosome region 6q25 (REF. 4). A relationship between single-nucleotide polymorphisms in the genes encoding tumour necrosis factor-α and interleukin-10 and the development of paucibacillary leprosy has been shown[5]. We now have a greater appreciation of the functions of mycobacterial lipids, including the knowledge that mycobacterial lipoproteins can trigger host-defence mechanisms through Toll-like receptors[6–8] and that the *M. leprae*-specific phenolic glycolipid has a specific role in determining tissue tropism, leading to Schwann cell infection[9,10].



Global distribution of leprosy, showing prevalence rates.

and was able to spread because of poor vaccine uptake — less than 75% of children under the age of 13 had been vaccinated against measles. In a press briefing, CDC director Dr Julie Gerberding remarked that measles is still a 'very real and important global health problem' and that the outbreak emphasized the importance of vigilance to ensure that adequate vaccination coverage is maintained. **CDC**

Hepatitis threatens tribes in Peru

The Minister for Health in Peru has turned to the United Nations Children's Fund (UNICEF) for help in halting the spread of hepatitis B in two remotes tribes. Local leaders fear that the tribes, which are located along the Pastaza and Morona rivers in the Amazon Basin, face extinction if the disease cannot be contained.

In response to the appeal, UNICEF has launched an emergency vaccination campaign. The hepatitis B vaccine is 95% effective, and vaccination requires 3 doses of vaccine. As infants and young children are most at risk of hepatitis B, the UNICEF team aims to vaccinate all newborn children within 24 hours of birth and to complete the vaccination regime before the children reach the age of 1. **UNICEF**

Cholera still a concern in Liberia

More than 10,000 individuals have been affected by the cholera epidemic in Liberia, which started in June 2003, with more than 100 deaths from the disease reported in the capital Monrovia. In the 14 years of civil war, an estimated 1.5 million people have been forced to leave their homes. In the most recent escalation in the conflict, more than 100,000 people are believed to have moved into temporary camps in and around the capital. The WHO and other non-governmental organizations have undertaken a mass chlorination of the capital's 5,000 wells in an effort to clean up water supplies and stop the spread of disease. The epidemic is now thought to have peaked, but is still a cause for great concern. **WHO**

In the News was compiled with the assistance of David Ojcius, Institut Jacques Monod, Paris, France.

New tools and intervention methods. The development of new tools to diagnose exposure to, or infection with, *M. leprae* has been boosted by the availability of the *M. leprae* genome sequence[1]. It has been shown that there are variable numbers of TTC repeats in a non-coding region of the genome of *M. leprae* strains[11]; strain differentiation based on these TTC repeats or single-nucleotide polymorphisms could be of great epidemiological value in identifying the infectious sources of leprosy and gaining a better understanding of transmission patterns. Leprosy-specific proteins and peptides are showing great potential as T-cell reagents that could be formulated either as skin-test reagents or as antigens to be used in *in vitro* testing, and which could be used to monitor exposure to *M. leprae* within communities. A simple, robust and rapid lateral-flow test for the detection of immunoglobulin M antibodies to the *M. leprae*-specific phenolic glycolipid I has recently been proposed for use in the classification of leprosy patients and the identification of contacts at a high risk of developing leprosy[12]. A genotypic method for the rapid detection of rifampicin-resistant isolates of *M. leprae* has been rigorously tested in the laboratory but remains to be validated under field conditions[13].

New strategies, policies and partnerships. The present WHO strategy for the elimination of leprosy as a public health problem is based on the early detection and cure of cases with MDT. An important problem is that leprosy diagnosis and treatment is often a highly centralized activity, conducted by specialized staff. Implementation of a more simplified approach to diagnosis and treatment is needed, using general health workers at the village level. A uniform MDT regimen of 6 months for the treatment of all leprosy patients would facilitate integration and help ensure the sustainability of leprosy control. Its evaluation is under way, but the results will not be available for at least 5 years. The concept of 'accompanied MDT' has been proposed as a means of helping integrate leprosy control activities, and would entail the patient taking some or all of their medication home to be taken under supervision. Again, this approach must be validated through formal research studies. The private–public partnership that presently exists between the WHO and Novartis to provide free anti-leprosy drugs to all leprosy patients globally provides an excellent example of teamwork in the public health arena.

CONCLUSIONS AND FUTURE OUTLOOK

The WHO-recommended MDT regimen has had a significant impact in reducing the global burden of leprosy. However, the risk remains that governments and health workers will become complacent, delaying or jeopardizing the final steps in the elimination strategy. Healthcare workers and researchers should continue to support the intensive implementation of the elimination strategy and address the issues related to the detection of *M. leprae*-infected individuals as a matter of urgency.

Leprosy research should be focused on developing new tools to support elimination efforts, in particular the development of tests for leprosy exposure (both skin tests and simple blood tests), tests for the prediction of reactions and a better means of controlling nerve damage. Leprosy researchers should strengthen links with the tuberculosis research community, as many of the concepts and challenges are the same. In the long term, research could provide tools for monitoring transmission, the reactivation of disease, the detection of sources of infection, and the emergence of drug-resistant leprosy strains.

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e-mail: DiseaseWatch.Leprosy@who.int
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Online links

FURTHER INFORMATION
M. leprae genome sequence: http://www.sanger.ac.uk/Projects/M_leprae
TDR: http://www.who.int/tdr and http://www.who.int/lep
Access to this interactive links box is free online.