DISEASE WATCH | IN THE NEWS

Polio: first eradication of 21st century?

At a recent meeting, representatives from the WHO and the six countries where polio remains endemic declared their intention to eradicate the disease by the end of 2004. According to the WHO, the success or failure of this initiative rests with the individual governments. Nigeria, India and Pakistan account for more than 95% of polio cases worldwide. The country causing greatest

CDC/Dr Joseph J. Esposito

concern at the moment is Nigeria, where vaccination in the north of the country was halted in late 2003 by the fears of local religious leaders that the vaccine was contaminated. However, in a recent interview with the BBC, Eytayo Lambo, the Nigerian Health Minister, commented that he expected vaccination to resume by the end of March 2004. **WHO/BBC News**

Trialling mass vaccination for cholera

The WHO and collaborating agencies are trialling the mass use of the oral cholera vaccine as a strategy to control the disease in Mozambique. The oral vaccine has been available for ten years but has never been used in a mass campaign. The disease is caused by the bacterium *Vibrio cholerae*, and spreads by the consumption of contaminated food and water. Cholera epidemics are therefore generally

linked with poor hygiene, overcrowding and inadequate sanitation and water supplies. The official death toll from cholera each year is 5,000, but there is believed to be significant under-reporting. This latest vaccination campaign will focus on the town of Beira, and the aim is to vaccinate at least 50,000 individuals. **WHO**

Hepatitis 'time bomb' in UK

The UK Health Protection Agency (HPA) has expressed concern at the significant rise in the prevalence of hepatitis C infection in injecting drug users. The latest report revealed that by the end of 2002, 39% of injecting drug users surveyed were infected with hepatitis C. The statement from the HPA coincides with the launch of a public campaign in the United Kingdom by the Hepatitis C Trust to raise awareness of two major routes for transmission

DISEASE WATCH | FOCUS

Human African trypanosomiasis**BACKGROUND**

Causative agents. Human African trypanosomiasis (HAT), also known as sleeping sickness, is caused by single-celled parasites, *Trypanosoma brucei*, which are transmitted to humans by infected tsetse flies. Two sub-species of *T. brucei* cause different forms of the disease. *T. b. gambiense* causes chronic infection, whereas *T. b. rhodesiense* generally causes a more acute infection. The parasites first develop in the blood, lymph and peripheral organs (stage 1), then spread to the central nervous system (stage 2), where they cause serious neurological disorders. Without treatment, the disease is fatal.

Distribution. HAT is known to occur in rural areas of 36 countries in sub-saharan Africa, where tsetse flies are endemic. *T. b. gambiense* is found in central, west and some parts of eastern Africa, whereas *T. b. rhodesiense* is found in southern and eastern Africa.

Current global status. The disease has re-emerged in epidemic proportions in several foci over the past 30 years. As the disease occurs in very remote areas, often where there is civil conflict, it is difficult to estimate the number of cases. In some villages, the prevalence has been reported to be as high as 20–50% and, in these places, HAT has emerged as a greater cause of morbidity and mortality than HIV/AIDS¹. Since the 1970s, serious epidemics of the gambiense form of the disease have occurred in Angola, the Democratic Republic of Congo, southern Sudan, and Uganda. Failure rates of 26.9% have been reported after treatment of gambiense infections with melarsoprol in some foci in Uganda, Angola and Sudan².

RECENT DEVELOPMENTS

New basic knowledge. The genome sequence of *T. brucei* is near completion, but the pathogenetic mechanisms involved in HAT are not fully understood. The methods by which trypanosomes cross the blood–brain barrier (BBB) remain speculative, but it is hypothesized that the loss of cells that participate in the BBB (for example, microglial and endothelial cells) might be important in the brain lesions of stage 2 HAT³; synaptic changes in neurons of the suprachiasmatic nuclei could also be important in the neuropathogenesis⁴. Several reports describe programmed cell death (PCD) in the non-dividing trypanosomes that develop in the blood and are infective to the tsetse. The role of PCD in trypanosomes is unclear⁵, but characterization of the pathway could provide information about pathogenesis. Recent research indicates that, like *T. b. rhodesiense*, *T. b. gambiense* might be zoonotic. In addition, further understanding of the symbiotic organisms *Wigglesworthia* and *Sodalis* sp. that are found in the tsetse midgut and which influence tsetse physiology and reproductive biology, also promises new control strategies⁶.

New tools and intervention methods. A serological card agglutination test for trypanosomiasis (CATT) is used for mass screening for gambiense HAT, but there is no satisfactory screening tool for *T. b. rhodesiense*. A LATEX test (latex particles coated with three variable surface glycoproteins of *T. b. gambiense*) was found to have higher specificity than the CATT⁷. Saliva testing has also been found to be possible using an indirect enzyme-linked immunosorbent assay to detect trypanosome-specific antibodies, thereby providing an alternative to blood testing⁸.

Distribution of human African trypanosomiasis

of blood-borne viruses, including hepatitis C and B — intravenous drug use and body piercing. The National Institute for Clinical Excellence in the United Kingdom has recently published guidelines on the latest treatment options for hepatitis C, and the Department of Health is expected to translate these into an action plan for treatment and prevention. **HPA/Daily Telegraph**

Avian influenza

The outbreak of highly pathogenic H5N1 avian influenza in poultry in Asia continues to cause grave concern. The virus has been detected in flocks in at least 10 countries, including Vietnam, Thailand, China and South Korea. Millions of birds have been slaughtered in an effort to contain the epidemic. So far, the virus has been transmitted to humans in Vietnam and Thailand, where at least 16 people have died. The news that two cases of suspected human-to-human

transmission of the virus have been recorded in Vietnam has heightened worldwide concern. After a recent meeting, the UN and WHO approved the use of targeted vaccination of poultry. It is hoped that this strategy will create buffer zones around infected areas to prevent the further spread of disease. Development work on a vaccine for humans continues, with experts estimating it could be prepared for use within six months. **WHO/BBC News**

After diagnosis, it is necessary to determine the stage of the disease. Current methods all involve lumbar puncture, which is not ideal. In an evaluation of the PCR (which detects trypanosome DNA) and LATEX agglutination (which detects immunoglobulin M, indicating neuroinflammation) tests, the PCR test seemed the more sensitive, but the LATEX/IgM test seemed more appropriate for therapeutic decision⁹. Research to optimize the use of existing anti-trypanosomal drugs and/or minimize their toxicity is ongoing. Recently, a ten-day course of treatment for gambiense HAT with melarsoprol proved as effective as a standard 26-day treatment schedule^{10,11}. The growing number of cases that are refractory to melarsoprol treatment has driven clinicians to consider combination therapy, and initial data indicate this to be more efficacious^{12,13}. At present, the only drug in development is DB-289 (an oral diamidine pro-drug), for the treatment of stage 1 infection^{14,15}. New diamidines are being investigated as pro-drugs to pass the BBB and cure stage 2 disease¹⁶. Other research is focused on drug targets that are related to the biochemical peculiarities of the trypanosome — for example, its glucose metabolism pathway¹⁷. Antimicrobial peptides, which are being developed as antibiotics against bacterial and fungal infections, have also been examined for use in HAT¹⁸. Recent evidence for the presence of plant-like enzymes has opened new perspectives for the identification of new drug targets¹⁹. One novel control strategy under development involves reducing the ability of the tsetse to transmit trypanosomes by expressing anti-trypanosomal molecules in *Sodalis*, the commensal symbiont in the tsetse midgut which is in close proximity to trypanosomes²⁰.

New strategies, policies and partnerships. The governments of disease-endemic countries are committed to control of the disease, and several initiatives to coordinate efforts have begun. These include the Pan-African Tsetse and Trypanosomiasis Eradication Campaign, and the Programme Against African Trypanosomiasis. The field activities of non-governmental organizations, such as Médecins Sans Frontières, are also invaluable in the control of HAT, and an agreement between Aventis Pharma, Bayer and the WHO guarantees stocks of all trypanocides up to 2006.

Human metapneumovirus rises to prominence

A new study in the *New England Journal of Medicine* has revealed that human metapneumovirus is a significant cause of lower respiratory tract infections in young children. This RNA virus was first isolated in 2001 by investigators in The Netherlands. In a prospective survey of nasal wash samples from a longitudinal study of children conducted over 25 years, researchers found that human metapneumovirus could be identified in 20% of specimens that were negative for other pathogenic viruses. The seasonality of human metapneumovirus infection was similar to that of respiratory syncytial virus, and the severity of infection varied from year to year. **NEJM**

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

CONCLUSIONS AND FUTURE OUTLOOK

HAT remains a challenge for health services, medical personnel and researchers. The pan-African initiatives to coordinate control efforts provide some hope for the future, but epidemics could be amplified by war and civil conflict, so stability, growth and development in Africa will be important factors in disease control.

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TDR Reference Group on African trypanosomiasis: F. Kuzoe; J. Jannin; R. Brun; J. Ndungu; P. Büscher; C. Miaka Bilenge; S. Van Nieuwenhove; F. Doua; D. Mbulamberi; C. Burri; S. Aksoy. TDR/WHO, 20 Avenue Appia, CH-1211 Geneva, Switzerland. doi: 10.1038/nrmicro848

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Online links

FURTHER INFORMATION

TDR: <http://www.who.int/tdr>

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