DISEASE WATCH | IN THE NEWS

Clinton cuts cost of AIDS drugs

An initiative led by former US president Bill Clinton will cut the cost of drugs to treat AIDS in developing countries by more than 60%. Advisors from the Clinton Presidential Foundation sealed the deal by working with generic drug companies and securing funding from Canada, Ireland, the World Bank and the Global Fund to Fight AIDS, Tuberculosis and Malaria. Companies based in India and Mozambique will make two triple-drug regimes available for less than 40 cents a day, compared with the usual price of $1.50. Lee Jong-Wook, Director General of the WHO remarked that 'Providing AIDS treatment to those who most urgently need it in poor countries is the most urgent health challenge the world faces'. About 2 million people should be treated by 2008. **BBC News**

New drug hope for hepatitis C sufferers worldwide

A new drug called BILN 2061 has been designed to specifically inhibit replication of the hepatitis C virus. This drug could help the 170 million people worldwide that are infected with hepatitis C virus, which can cause permanent liver damage. Long-term trials are still required but initial results are promising, with virus levels dropping 1,000-fold in treated patients. Variants of the inhibitor molecule, which targets a viral protease, might be required to inhibit the virus successfully and avoid selection of resistant virus strains. **Nature Science Update**

Kenyan factory to produce bacterial pesticides to combat malaria

Kenya plans to open a factory that will manufacture bacterial insecticides to combat malaria by killing the mosquito vector. *Bacillus thuringiensis* subsp. *israelensis* was first isolated in 1976 from a mosquito breeding site in Israel, and proved highly insecticidal to

DISEASE WATCH | FOCUS

Onchocerciasis

BACKGROUND

Causative agent. Onchocerciasis (river blindness) is a parasitic disease caused by the filarial worm *Onchocerca volvulus*. It is transmitted through the bite of infected black flies of the genus *Simulium*, which carry the immature larval form of *O. volvulus* (known as microfilaria). The disease manifests as a reaction to the presence of microfilaria in the skin (itching, acute and chronic papular onchodermititis, fibrosis, atrophy and depigmentation), and the eye (acute and chronic lesions in the anterior and posterior segment). The most devastating effect is blindness.

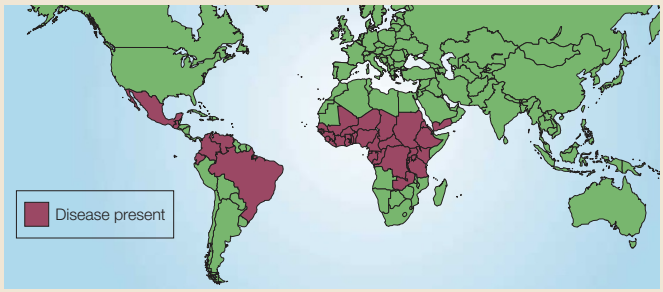
Distribution. Onchocerciasis is found in 28 countries in Africa — in the savannah as well as in the forest zone — from Senegal to Malawi, 6 countries in Latin America and in the Yemen. At present, the World Health Organization estimates that there are more than 17.7 million people infected with onchocerciasis — approximately 500,000 with visual impairments, 270,000 of whom are blind[1,2]. 99% of the cases are, however, found in Africa.

Current global status and impact. Owing to a fear of blindness, there has been a depopulation of the fertile river valleys of the west African savannah — making onchocerciasis an obstacle to socio-economic development. A combination of vector control in West Africa, the use of ivermectin, large-scale Community Directed Treatment (ComDT) and the use of ONCHOSIM[2] (a microsimulation model for onchocerciasis transmission) has allowed the continuous annual treatment of more than 30 million people. Interruption of transmission of *O. volvulus* and reduction of the burden of visual impairment and blindness has been achieved in most of the West African region and in the six Latin American countries affected by this parasite, and in these areas onchocerciasis is no longer a disease of public health importance. However, the skin disease, with its adverse psycho-social and socio-economic effects, continues to be a problem in the rest of Africa[3].

RECENT DEVELOPMENTS

New basic knowledge. Gene discovery in *O. volvulus* has been based on the generation of expressed sequence tags (ESTs); 12,269 ESTs from *O. volvulus* (six stage-specific libraries) have been clustered to form 4,208 groups[4]. The pathogenesis of onchocerciasis is poorly understood. Recent studies have indicated that the endosymbiotic bacterium *Wolbachia* might play a role in the ocular and skin disease[5]. Post-treatment reactions might also be related to *Wolbachia* products that mediate inflammatory responses[6].

New tools and intervention methods. A review of the impact of 10–12 years of ivermectin treatment reported that ivermectin was very effective in controlling the public health aspect of the disease. However, elimination of transmission proved more difficult[7]. It is unlikely that ivermectin treatment alone can provide a complete solution to onchocerciasis and a recent conference concluded that eradication is not feasible with the present tools[8]. So there is an urgent need for the development of new tools. First, modelling revealed that the use of drugs that would kill or sterilize the adult worm would be effective in eradication[9]. The endosymbiont *Wolbachia* has emerged as a potential drug target because the treatment of *O. volvulus*-infected individuals with doxycycline resulted in irreversible elimination of skin microfilaria, presumably through direct effects on the endosymbiont[10]. Although effective for individuals, the duration of

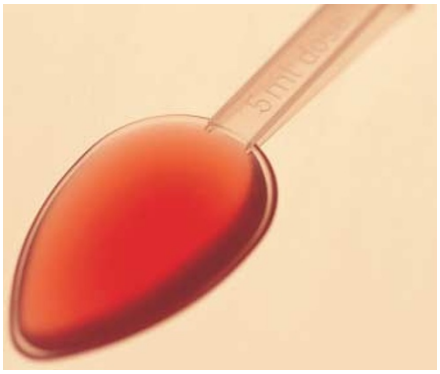


Global distribution of onchocerciasis.

mosquito larvae. Four commercial products based on this biopesticide are used in many countries to control mosquitoes and blackflies. However, the cost of these products has been prohibitive for use in Africa where malaria kills approximately 3,000 children per day. By producing about 7 tons of liquid *B. thurigiensis* subsp. *israelensis* annually at the facility in Kenya, the cost of the biopesticide to African countries could be reduced by a third. **Reuters**

Mass immunization to combat Nigerian polio outbreak

The WHO is coordinating a $10 million campaign to administer oral polio vaccine to 15 million children in Nigeria and neighbouring countries in just 3 days. Polio is still endemic in Nigeria, which now has the highest incidence of the disease worldwide. The polio strain



responsible for recent outbreaks in neighbouring countries Burkina Faso, Ghana, Togo and Niger is identical to the strain endemic in Nigeria, prompting the mass immunization programme. Chad and Cameroon are being targeted for action in mid-November. Polio eradication is at a crucial stage — with successful eradication measures the proportion of children who are susceptible has increased, making any disease resurgence a potential crisis. **WHO**

Typhoid outbreak in Tajikistan

Untreated drinking water piped from a mountain river to about a million city dwellers has led to an outbreak of typhoid in Dushanbe, the capital of Tajikistan. More than 745 patients have been admitted to hospital, and 256 cases confirmed. Poor sanitation has previously contributed to infectious disease outbreaks in this country, which remains the poorest ex-Soviet nation after years of civil war. In 1997, a typhoid epidemic affecting 17,000 people resulted in at least 80 fatalities. **Reuters**

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

the treatment is considered too long for mass treatment. Attention has been drawn to the milbemycin compound moxidectin, which has been shown to severely impair embryogenesis in most onchocerciasis animal models[11]. Second, diagnostic methods for surveillance that do not rely on taking skin samples to detect microfilaria are urgently needed. The use of specific antibodies, such as those directed to the Ov16 antigen, have been proposed as an alternative. Third, repeated treatments with ivermectin increase the risk of ivermectin resistance. Several cases of 'poor responsiveness' to ivermectin, as well as the detection of residual microfiladermia after treatment with ivermectin, have been reported[12,13]. Whilst the relevance of these observations has not been established, development of a test to detect ivermectin resistance is required. Attention has been drawn to neurological reactions in individuals with a *Loa loa* infection after treatment with ivermectin. This could pose problems for ivermectin treatment programmes in areas that are co-endemic for *L. loa* (Central Africa). Rapid mapping methods based on remote-sensing data and simple questionnaires have been developed to allow identification of high *L. loa* prevalence areas[14].

New strategies, policies and partnerships. In most of Africa, the principal control strategy is annual ComDT with ivermectin in high-risk areas to control onchocerciasis. The potential of ComDT for providing additional health services to the poor[15] and the impact on programme sustainability[16] has been assessed. Ongoing implementation research should determine the feasibility of using the ComDT approach for integrated delivery of community-based interventions, for example, mass treatment of other helminthic infections or home management of malaria. In the Americas, the control strategy involves 6-monthly treatments in all endemic areas with the aim to eliminate onchocercal morbidity and, where feasible, to interrupt transmission.

CONCLUSIONS AND FUTURE WORK

In West Africa, where there has been almost complete interruption of onchocerciasis transmission, the primary objective should be effective epidemiological surveillance to detect and control disease recurrence. A sustained annual treatment is needed in the rest of Africa if transmission is to be kept at the lowest levels possible and morbidity controlled. In African disease settings with more than 14 years of ivermectin treatment, field studies and modelling will determine the conditions under which ivermectin treatment can be stopped without risking recurrence. Therapeutic approaches to reduce the load of *L. loa* infections are also needed to achieve ivermectin coverage. As both the *O. volvulus* and *Wolbachia* genome sequencing projects near completion, new opportunities for the identification of new drugs, vaccines and diagnostic targets will emerge. This might transform the control programmes and make eradication a reality.

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Online links

FURTHER INFORMATION
River Blindness Genome OnchoNet:
http://www.math.smith.edu/~sawlab/OnchoNet/OnchoNet.html
TDR: http://www.who.int/tdr/
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