DISEASE WATCH | IN THE NEWS

EC funding for resistance

The EC is to invest a further €6 million to support two important research projects looking at the growing problem of antimicrobial resistance. One project will investigate resistance to β-lactams and the other project will focus on the basic molecular mechanisms of antibiotic resistance in *Streptococcus pneumoniae*. Over the past four years, the EC has invested more than €100 million in this field and has supported more than 80 research projects on antimicrobial resistance. In a recent survey, 38% of EU citizens polled had taken antibiotics in the past 12 months. **EU Press Release**

Ebola update

A total of 36 cases of Ebola haemorrhagic fever (EHF), including 18 deaths, have been reported from the latest outbreak in the Mbomo district in the north west region of the Republic of the Congo. The WHO and supporting agencies have established an isolation facility, and contact tracing is ongoing to try to break the chain of transmission. The source of the outbreak is believed to be contaminated bushmeat. Also during November, the NIH announced the first human trials of an experimental Ebola vaccine. It is hoped that a total of 27 volunteers will participate in the trial, which will last 1 year, although the initial number of volunteers was low. There is no know cure for EHF, and vaccination is believed to be the best strategy to prevent or contain infection. **WHO/NIH**

Free trachoma treatment

Pfizer has announced that it will donate sufficient antibiotics over the next 5 years to treat 90% of the 150 million individuals currently suffering from trachoma. The antibiotic — Zithromax — treats the disease in a single dose. The donation, which amounts to 135 million doses, is in addition to the 8 million doses the company has donated since 1998 and will help the WHO achieve its goal of eliminating the

DISEASE WATCH | FOCUS

Schistosomiasis

BACKGROUND

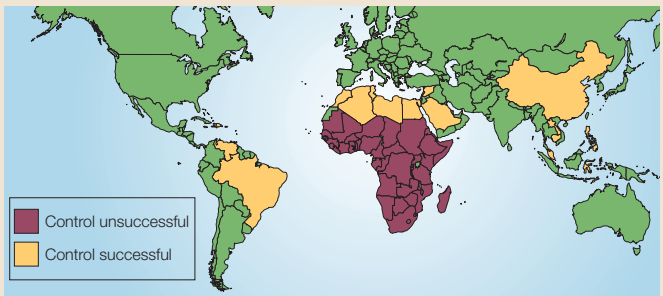
Causative agents. Human schistosomiasis is caused by the digenetic trematodes *Schistosoma haematobium, Schistosoma intercalatum, Schistosoma japonicum, Schistosoma mansoni* and *Schistosoma mekongi*. Infection occurs when larval forms of the parasites, known as cercariae, are released from aquatic snails (such as those of the genera *Bulinus, Oncomelania, Biomphalaria* and *Neotricula*) and penetrate the skin during water contact. Once inside a human host, cercariae transform into schistosomula and are transported to the portal circulation of the liver, where they mature and mate. Adult worms of *S. intercalatum, S. japonicum, S. mansoni* and *S. mekongi* migrate to the mesenteric vessels, and those of *S. haematobium* move to the veins that drain the urinary system. Parasite eggs are deposited in several tissues, primarily the liver, the bladder and the urinary tract. The presence of eggs in tissues elicits granulomatous reactions, causing disease. Chronic infection results in periportal fibrosis of the liver, calcification of the bladder and other sequelae. Genital schistosomiasis might increase the risk of HIV infection[1]. Eggs are released into the excreta and, on reaching water, hatch into miracidia (another larval form of the parasite), which infect the intermediate snail hosts.

Distribution. An estimated 200 million people in 74 countries have schistosomiasis, 85% of whom live in sub-Saharan Africa where *S. haematobium, S. intercalatum* and *S. mansoni* are endemic[2]. *S. haematobium,* and *S. mansoni* are also found in Egypt and the arabian peninsula. *S. haematobium* has been reported in the Mahgreb region (Morocco, Algeria, Tunisia and Mauritania). *S. mansoni* is endemic in north-east Brazil, and is also present in Venezuela, Suriname and the Caribbean. *S. japonicum* is endemic in China and the Philippines, and is also found in Sulawesi, Indonesia. *S. mekongi* is found in Cambodia and Laos.

Current global status. The burden of disease is disputed because original estimates[3] did not consider symptoms, sequelae and the chronic nature of schistosomiasis. A World Health Organization expert committee[4] concluded that yearly deaths could be as high as 200,000, compared with 15,000 as had been reported[5]. An analysis of these discrepancies indicates there is underestimation, making schistosomiasis second only to malaria among tropical diseases as a cause of morbidity (C.M. Michaud, W.S. Gordon and M.H. Reich, manuscript in preparation). A strategy of morbidity control through chemotherapy has resulted in successful control in Brazil, the Mahgreb region, the Middle East, China and the Philippines. There is a threat of resurgent transmission in China due to ecological changes owing to the construction of the 'Three Gorges' dam, and in the Philippines owing to inadequate support for public health interventions. Economic development has virtually eliminated transmission of the disease from the Caribbean and Mauritius.

RECENT DEVELOPMENTS

New basic knowledge. The contribution of schistosomiasis to morbidity and mortality in sub-Saharan Africa has been quantified using reported symptoms, available and predicted prevalence of infection data, and associating the prevalence of infection to the prevalence of pathology[6]. Although co-infection with HIV-1 alters the cellular immune response[7], it does not affect the outcome of treatment[8,9]. The importance of genetic factors in disease is being elucidated — the relatedness of individuals might explain the variations in egg counts[10], and polymorphisms of the



Global distribution and control status of schistosomiasis.

disease by 2020. Trachoma is an infection of the inside of the upper eyelid caused by *Chlamydia trachomatis*. Repeated infections cause the eyelashes to curl under, which, over time, abrades the surface of the eye, causing blindness. **Reuters**

3 × 5 to tackle AIDS

The UN has pledged that antiretroviral treatment (ART) will be made available to 3 million people worldwide by 2005, with the World AIDS Day launch of a campaign called '3 × 5'. According to WHO estimates, only 400,000 of the 6 million individuals currently in need of ART have access to the therapy. To achieve the widespread coverage outlined in '3 × 5' will require increased manufacture and distribution of a combination therapy regime, which requires infected individuals to take just two pills a day. The AIDS epidemic update for 2003 revealed that an estimated 40 million people are now living with HIV worldwide and, in 2003 alone, 5 million people became infected with HIV and 3 million died from AIDS worldwide. **Reuters**

HepA outbreak

In the largest outbreak of hepatitis A in US history, 3 people have died and more than 500 people have been infected in Pennsylvania, USA. The hepatitis A virus attacks the liver, and is transmitted by the faecal–oral route. The source of the outbreak was identified as green onions (scallions) eaten at a Mexican restaurant. The genetic sequence of this outbreak strain is very similar to sequences obtained from hepatitis A outbreaks in three other US states earlier in 2003 that were also linked epidemiologically to green onions. A hepatitis A vaccine is available that is effective if given within 2 weeks of exposure to the virus. **AP**

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interferon (IFN)-γ gene are associated with periportal fibrosis[11]. Sequencing of the *S. mansoni*[12] and *S. japonicum*[13] genomes will further this work and provide information on new targets for diagnostics, drugs and vaccines, as well as being invaluable for understanding parasite biochemistry, development and diversity. Methods to manipulate gene expression and elucidate gene function are being developed. A fluorescent dye was used to localize gene activity in the excretory system of adult worms[14]. RNA interference with the SGTP1 gene reduces glucose uptake in the larval stage of *S. mansoni*[15].

New tools and intervention methods. Twenty years after introduction, praziquantel remains the drug of choice. It is efficacious even though treatment failure[16] and resistance have been reported[17]. Rapid diagnosis in the field, especially of intestinal schistosomiasis, continues to be difficult. As population-wide chemotherapy is the control strategy, identification of individuals with low intensity infection is problematic. The utility of new tests[18,19] in endemic settings remains to be determined. Vaccines might provide the long term solution to schistosomiasis, and many antigens that target schistosomula have been identified[20]. An antioxidant enzyme against the adult stage of the parasite also offers the possibility of a therapeutic vaccine[21]. In October 2003, a review of the status of candidate vaccines concluded that GST28 (REF. 22) and Sm14 (REF. 23) should continue towards clinical trial, and recommended a collaborative approach for antigen discovery.

New strategies and policies. After reviewing data on the use of praziquantel, and taking into account the possible risk of serious morbidity to women, the WHO now recommends that infected pregnant and lactating women be offered immediate treatment and should not be excluded from community-based treatment programmes[24]. All those at risk of morbidity and contributing to transmission should receive treatment. A Schistosomiasis Control Initiative (see Online links) is to be implemented in six African countries. One desirable outcome would be to convince policy makers and public health authorities in highly endemic countries that control is feasible by creating an infrastructure for public health interventions.

CONCLUSIONS AND FUTURE OUTLOOK

Sequencing of the *S. mansoni* and *S. japonicum* genomes, manipulating gene expression and understanding gene function, promise faster identification of targets for diagnostics, drugs and vaccines. Sequencing of the *S. haematobium* genome is also required. A collaborative approach to antigen discovery could also lead to a vaccine. It is expected that new drugs will be discovered and that the available tools for schistosomiasis control can be used to relieve endemic populations of the burden of schistosomiasis.

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Online links

FURTHER INFORMATION
Schistosomiasis Control Initiative: http://www.schisto.org/
TDR: http://www.who.int/tdr/
Access to this interactive links box is free online.