DISEASE WATCH | IN THE NEWS

Antibiotic cuts childhood AIDS-related deaths

A trial in Zambia has shown that administering the antibiotic co-trimoxazole to HIV-infected children reduced fatalities by more than 40% over a 19-month period. The team was led by Dianne Gibb (MRC, UK), who noted that "reducing the secondary complications and infections, which can be just as fatal as HIV, is also important". This cheap treatment was successful in spite of widespread resistance to co-trimoxazole in Zambia, and shows that treating respiratory infections in HIV-sufferers can save lives and reduce the burden of admissions in local hospitals. Children suffered no ill-effects from prolonged antibiotic therapy. Guided by this research, the WHO, UNAIDS and UNICEF have agreed to modify the current recommendations for co-trimoxazole prophylaxis in children.

SciDevNet/*The Lancet*

GM go-ahead for smallpox

An expert committee reporting to the WHO has recommended that researchers should be allowed to engineer variola virus variants for the first time since smallpox (caused by variola virus) was certified as eradicated in 1980. Scientists hope to insert GFP into the variola genome to speed-up testing of anti-smallpox drugs by automation. Other proposals include allowing researchers to use fragments of the genome (up to 20%) in experiments, raising concerns over reconstruction of this deadly virus. New research using variola virus has been spurred on by fears about bioterrorism, but these proposals have yet to be approved by the WHO.

The Scientist

Combination therapy for malaria

A recent report of a randomized trial in *The Lancet* indicated that the recommended frontline combination therapy of chloroquine and sulfadoxine–pyrimethamine for malaria in Uganda performed poorly when compared with several other combination therapies. A combination of amodiaquine and sulfadoxine–pyrimethamine was the optimal treatment for malaria in Uganda, taking into

DISEASE WATCH | FOCUS

Meningococcal meningitis

BACKGROUND

Causative agent. Meningococcal meningitis is a severe acute infection of the meninges caused by the Gram-negative bacterium *Neisseria meningitidis*. The meningococcus is a commensal of the human naso-pharyngeal mucosa that is carried by at least 10% of the population and is transmitted from person to person by upper-respiratory tract secretions. Occasionally, *N. meningitidis* will cross the mucosal membrane and enter the bloodstream, causing various clinical syndromes — acute meningitis is the most common. Meningitis is characterized by a sudden onset of headache, fever and neck stiffness. Despite treatment, at least 10% of patients die within 1 or 2 days of onset and 10–20% of survivors develop significant neurological sequelae. Meningococci remain highly susceptible to penicillin, which is the drug of choice for treatment, although a single dose of oily chloramphenicol is often a preferred alternative in outbreaks. Although 13 serogroups of meningococcus have been identified, only five (A, B, C, W135 and Y) account for nearly all reported disease[1–3].

Distribution. More than 700,000 meningitis cases were reported to the WHO between 1995 and 2003. Ninety percent of cases occurred in sub-Saharan Africa's 'meningitis belt' (FIG. 1), a savannah region extending from Senegal to Ethiopia with a total population of 400 million. Epidemic disease occurs in the dry season, when the nasopharynx is exposed to extreme heat, dryness and dust. Annual incidence rates can reach 1,000 cases per 100,000 population (1%). During 1996–1997 more than 250,000 cases and 25,000 deaths were reported in this area. In comparison, annual reported incidence in developed countries ranges from 1 to 3 cases per 100,000 population[2,4–6].

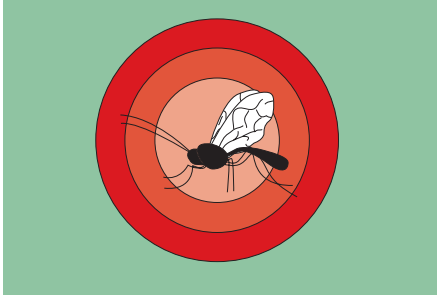
Current global status. Serogroup A meningococcus is the main cause of epidemic meningitis in sub-Saharan Africa. However, serogroup C meningococcus has been isolated from some epidemics and serogroup W135 was recently identified as the main pathogen during a 2002 out-break in Burkina Faso. This epidemic followed cases of W135 meningitis among Hajj pilgrims and their contacts in 2001–2002 (REFS 4,5,7–9).

Although serogroups A and C predominate in Asia and Africa, serogroups B and C are responsible for most cases in Europe and the Americas. Serogroup B epidemics have developed gradually and per-sisted for a decade or more in Europe, the United States, Central and South America, and New Zealand. Since the mid-1990s, there has been an increase in serogroup Y meningitis in the United States and Europe. Recently, several outbreaks of serogroup C have been reported in Canada, the United States, Spain and the United Kingdom.

RECENT DEVELOPMENTS

New basic knowledge. Serological methods have been used to classify meningococci according to antigenic variation of the capsular poly-saccharide (serogroup) and of the outer membrane proteins (serotypes and subtypes). Recently, analytical tools have been developed that allow more accurate global monitoring of strains. Among them, multilocus enzyme electrophoresis (MLEE) and multilocus sequence typing (MLST) enable genetic grouping of meningococci into clone complexes that are associated with different epidemiological patterns. In the future, DNA microarray technology might become the standard for molecular typing[3,7,8].

New tools and interventions. Current meningococcal polysaccharide vaccines are poorly immunogenic in infants, fail to induce immunological memory and have little effect on colonization[1,10,11]. Consequently, the recommended WHO strategy for epidemic control in hyperendemic countries is based on detecting, confirming and vaccinating at-risk popula-tions, while improving case management. The development of conjugate vaccines (capsular polysaccharides conjugated to protein antigens) offers hope for a more effective prevention strategy. Effective conjugate C vac-cines have been introduced in Europe for the prevention of serogroup C



account cost-effectiveness and efficacy. Lead author Philip Rosenthal commented that "…although the lifespan of an amodiaquine and sulfadoxine–pyrimethamine combination might be limited by resistance, this regimen could be appropriate for regions of Africa where resistance to the individual drugs remains low…pending the introduction of artemisinin-containing combinations".

The Lancet

Call to improve health delivery systems

Research can only make a difference if it is applied, and translating research into effective and simple treatments deserves to be given a higher priority, according to the WHO. The *World Report on Knowledge for Better Health* noted that malfunctioning health systems are at the heart of the problem of effective care in many countries. If 2% of the health budget of each country was spent on research into health systems significant improvements could be made — currently less than 0.1% of the health budget is allocated for this research in developing countries.

SciDevNet

AIDS vaccine on test in China

Just before the seventeenth World AIDS day on 1 December, China approved testing of a domestically developed AIDS vaccine that protected a monkey from HIV infection. However, a campaign to distribute free condoms at Beijing's top two universities was halted by authorities only last week, owing to concerns over educating students about premarital sex. China claims to have 840,000 people infected with the AIDs virus, but AIDS prevention work in China is being hampered by bureaucracy and traditional taboos.

Reuters

Cholera outbreaks

In the past two weeks, 42 fatalities from cholera have been confirmed from a total of 629 cases in northern Nigeria. Plus, heavy rains in the western province of Bujumbura Rural, Burundi, have led to a cholera outbreak of 15 cases with 3 fatalities. The cholera outbreak in Dakar, Senegal, which claimed 6 lives from more than 850 cases, has now abated, with no new cases since 10 November. More than 1,600 Africans have died from cholera so far this year.

Reuters/WHO

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

disease. These vaccines were found to be immunogenic in infants, to induce immunological memory and to decrease carriage such that non-vaccinees were protected (herd immunity)[12]. Several vaccine manufacturers are developing multivalent A/C/W135/Y meningococcal conjugate vaccines. Hopefully, when delivered in early infancy, these polyvalent conjugate vaccines will not need additional booster doses[12]. Design of a vaccine against serogroup B meningococci has proven difficult, but vaccines based on outer membrane vesicles (OMV) have been successfully used to control outbreaks in Cuba, Brazil, Chile and Norway, and are currently under trial in New Zealand[13].

New strategies, policies and partnerships. New initiatives aim at improving access to vaccines. The Meningitis Vaccine Project (MVP), a partnership between the WHO and PATH, was created in 2001 with support from the Bill & Melinda Gates Foundation with the goal of eliminating meningococcal epidemics in sub-Saharan Africa through the development and use of conjugate vaccines[14]. MVP is developing a meningococcal A conjugate vaccine at a target price of US$0.40 per dose. Clinical trials will begin in 2005 and it is expected to be licensed in 2008–2009 for use in routine infant immunization and 'catch-up' campaigns. Until then, countries must optimize their use of current vaccines. Emergency access to vaccines is coordinated by an international group that was established after the 1996–1997 African epidemics. More recently, the WHO initiated a public–private partnership to produce an affordable A/C/W135 meningococcal polysaccharide vaccine for use in epidemic response and established an emergency vaccine stockpile for use in future epidemics. Similarly, the current OMV group B vaccine being tested in New Zealand was developed as a public–private partnership[13].

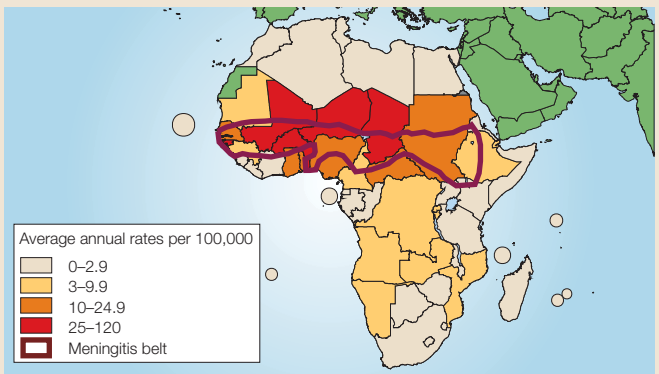


Figure 1 | Incidence of reported meningitis among total population, 1995–2003.

CONCLUSIONS AND FUTURE OUTLOOK

The successful introduction of a meningococcal C conjugate vaccine in the United Kingdom has given new hope that epidemic meningitis in Africa can be prevented with the use of appropriate conjugate vaccines. The creation of innovative partnerships has facilitated the development of new products that will result in more effective preventive strategies.

Information source: T. Aguado, E. Bertherat, M. Djingarey, D. Kandolo, M. P. Kieny, K. Kondé, F. M. LaForce, C. B. Nelson, W. Perea, M. P. Préziosi. e-mail: aguadom@who.int; bertherate@who.int; djingareym@oncho.oms.bf; kandolod@oncho.oms.bf; kieny@who.int; kondek@who.int; fmlaforce@path.org; nelsonc@who.int; pereaw@who.int; preziosim@who.int WHO, 20 Avenue Appia, CH-1211 Geneva, Switzerland. PATH, 13 chemin du Levant, 01210 Ferney, France.

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Online links

FURTHER INFORMATION
Meningitis Vaccine Project: http://www.meningvax.org
WHO Communicable Disease Surveillance and Response: http://www.who.int/csr/
WHO Global Atlas of Infectious Disease: http://www.who.int/globalatlas/
WHO Initiative for Vaccine Research: http://www.who.int/vaccine_research/
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