*Clinical Review identifies issues in the medical literature of interest to clinicians in Africa. Essential references are given at the end of each section*

# AIDS REVIEW

## Clinical update on AIDS

This paper re-emphasises some of the issues covered in an editorial article entitled 'HIV/AIDS: The long haul ahead', published in *The International Journal of Tuberculosis and Lung Disease*.[1]

### Global epidemiology

According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), there were an estimated 33.2 million adults and children living with HIV worldwide in 2007.[2] During that year, 2.7 million people were newly infected and 2.0 million people died due to AIDS. Sub-Saharan Africa continues to bear the greatest burden of this pandemic, housing 68% of global HIV prevalence and incidence, bearing 76% of global AIDS mortality and 90% of the global HIV burden in children. Nine countries in Southern Africa, where less than 2% of the world's population resides, bear more than one-third of the global HIV/AIDS burden.

This knowledge is useful for guiding resource allocation and ensuring that countries with the highest burden of infection and disease such as in Eastern and Southern Africa receive proportional allocation of funding to combat the disease. Although the HIV epidemic is a multitude of diverse epidemics, in terms of responses it is useful to think of two broad epidemiological patterns: (a) generalised epidemics occurring mainly in countries in sub-Saharan Africa and defined as HIV prevalence rates >1% in adult populations and (b) concentrated epidemics affecting specific high-risk population groups (e.g. men who have sex with men (MSM), injecting drug users, commercial sex workers and their clients, and prisoners). Generalised HIV prevention approaches should be implemented in countries with generalised epidemics, and tailored context-specific services targeting high-risk groups implemented in countries with concentrated epidemics. This implies that countries with concentrated epidemics and limited resources should avoid the tendency to invest in generalised prevention approaches such as nationwide school education programmes, or mass condom distribution campaigns that are likely to have little impact on the epidemic. Countries and donors should heed the UNAIDS call of 'Know your epidemic, know your response'.[3]

### The response

The theme of the 2008 XVII International AIDS Conference in Mexico was 'Universal action now'. There were disappointments about efficacy failures in the field of HIV vaccine research, microbicide research, and herpes suppressive therapy while male circumcision was promoted as an important health sector intervention that reduces the risk of heterosexually acquired HIV among men. The 2007 UNAIDS report estimated that for every one person who receives antiretroviral treatment (ART), 4–6 other people acquire HIV.[2] Current efforts to scale up ART must thus be accompanied with similar efforts to boost prevention strategies. Achieving universal access to prevention, care, and treatment of HIV/AIDS remains a global health priority. At country level the following constitute the main elements of delivering an essential HIV/AIDS package.

### Increasing knowledge of HIV status

Although HIV testing services have expanded tremendously in the last few years, the gap in level of knowledge of HIV status is unacceptable with nearly 80% of HIV-infected adults in sub-Saharan Africa not knowing their HIV status and more than 90% not knowing their partner's status.[4,5] Knowing one's HIV status is the gateway to prevention, care, and accelerated treatment strategies. Knowledge of HIV status combined with access to ART is also a way to 'normalise' and de-stigmatise HIV. Investment and energy need to be put into the testing of couples, and home-based counselling and testing in communities. In generalised epidemics, provider-initiated testing and counselling offered through health facilities is recommended as part of antenatal care, clinical care of tuberculosis (TB), hepatitis B and C, management of sexually transmitted infections, paediatric services (including Expanded Programme of Immunisation (EPI) clinics), and general in-patient wards. We also need to learn from the experiences of HIV testing being implemented at country or community level such as Uganda's home testing in villages, Lesotho's 'Know your status' campaign, and Malawi's HIV testing week.[5]

### Scaling-up HIV prevention

HIV prevention must be maximised by promoting interventions that work and tailoring services for high-risk population groups. In sub-Saharan Africa, where heterosexual intercourse is the dominant means of HIV transmission, male circumcision has been shown to effectively reduce HIV acquisition by 60%. The challenge now in Africa is how to develop and scale-up male circumcision services and link these to broader prevention strategies, and to obtain accurate information on the limits of its protective effect. In clinical trials, various interventions around prevention of mother-to-child transmission (PMTCT) of HIV have been proved to reduce HIV infection in infants and children. Yet, in 2007, in low- and middle-income countries only 33% of HIV-infected pregnant women received antiretroviral prophylaxis. Only 12% were assessed for eligibility for combination ART and less than 10% of infants were tested for confirmed HIV infection within 2 months of birth.[5] This has to be improved. Offering ART to all HIV-infected pregnant women, regardless of clinical stage and CD4 count, is a potentially attractive option that simplifies some of the difficulties around implementation of PMTCT by enrolling mothers and children into

formal ART follow-up structures, making breast-feeding safer, potentially reducing the risk of HIV transmission to spouses and partners, and in the long term preventing orphans. Recent mathematical modelling has shown that annual voluntary and universal HIV testing with immediate ART to all high-risk populations, regardless of clinical stage of CD4 count, could have a significant impact in eliminating HIV transmission.[6] There are many practical issues to be considered in the implementation of these bold approaches such as regimen toxicity in women with high CD4 counts, ensuring adherence in HIV-infected people who might generally feel well, and the development of drug resistance, but they certainly deserve to be looked at under study conditions.

**ART scale-up**

Access to ART for advanced HIV infection is accelerating in low- and middle-income countries, where the number of patients on treatment has risen from 400 000 in 2003 to nearly 3 million in 2007.[5] In sub-Saharan Africa, an estimated 2.1 million patients were receiving ART by December 2007. Despite this progress, global ART coverage remains low with only 31% of people in need receiving ART by the end of 2007. The World Health Organization's (WHO) public health approach based on simplified decision-making, standardised regimens, and decentralised delivery of services for both adults and children works,[7] and must be supported.

Enhancing collaboration to respond to the dual epidemic of TB and HIV and offering ART as well as cotrimoxazole prophylaxis to HIV-positive patients with TB is particularly important in sub-Saharan Africa where TB remains a major killer. In addition, concerted attempts must also be made to scale up the three 'I's' (infection control, intensified case finding, and isoniazid preventive therapy) to prevent, diagnose, and treat TB associated with HIV and avoid the emergence of multi-drug resistant and extensively drug-resistant TB.

There is consensus that all infants less than 12 months of age with confirmed HIV infection should start ART.[8] In resource-limited settings, infants acquiring HIV at or around delivery end up with rapid disease progression in the first few months of life, often leading to death. Over 80% of HIV-infected infants rapidly become eligible to start ART before 6 months of age[8] and, in the absence of ART, about half of such children do not live to see their second birthday. The challenge to this approach will be the identification of these infants who are truly HIV-infected.

Consideration is also being given for starting ART at higher CD4 counts than is currently the practice (see section above). In resource-limited settings technical issues remain, and include: (a) concern about first-line regimens (long-term toxicity of stavudine and better access to tenofovir); (b) the general unavailability of tools for early HIV diagnosis in infants; (c) the monitoring of virological and immunological responses as well as adverse reactions. Without these tools, there are difficulties in knowing when the first-line regimen is failing and when to switch to a second-line regimen. As increasing numbers of people develop resistance or toxicity to first-line regimens, better access to second-line regimens needs to be achieved in resource-limited settings.

**Strengthening of health systems**

What little evidence exists to date suggests that ART scale-up has done more to strengthen health systems than otherwise.[9] Great attention must be paid to ensuring that availability of treatment and care for people living with HIV is not compromised because of the push towards integration. The lack of human resources, particularly in sub-Saharan Africa, needs to be addressed through better conditions of service, decentralising services, and task-shifting. Ensuring high retention in treatment programmes is a challenge and greater involvement of communities and patient associations will be needed for patient tracking. Strategies for strengthening procurement and supply management systems to ensure uninterrupted access to antiretroviral drugs are also necessary.

**Strategic information**

Finally there is recognition of the importance of strategic information that can only be acquired through robust monitoring and reporting systems. There will be a need to invest in standardised patient monitoring and to use these data to track progress and improve the effectiveness of HIV programmes. Fostering a spirit of operational research with results clearly linked to improving national policy and practice is also essential.

**Conclusion**

With HIV prevention, care and treatment, progress has undoubtedly been made, although there are grumblings about too much money and too many resources being given to HIV/AIDS to the detriment of general health services. 'The creation of relative islands of excellence within seas of insufficiency' is not deliberate and the problem is not the island, but the insufficiency that surrounds it.[10] If the progress that has been achieved so far is to be sustained, there must be adequate and sustained funding for all the major challenges in global health and the systems that will aim to address them.

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## PAEDIATRICS REVIEW

### Tuberculous otitis media

Despite changes in prevalence and general improvement in health, tuberculous otitis media (TBOM) is still a devastating cause of deafness today.

**Epidemiology**

During the period 1907–1914, 1797 cases of chronic secretary otitis media (CSOM) in children under 15 years of age were treated at the ENT (ear, nose, and throat) department of the Royal Infirmary Edinburgh. Of these, 51 (2.8%) had TBOM including 43 of 86 patients (50%) up to 1 year of age.[1] It was considered that regurgitation of unpasteurised milk (harbouring *Mycobacteria bovis*) causing primary infection through the eustachian tube was the most important factor in this age group. At that time in Edinburgh 20% of milk was infected with the bovine bacillus which was responsible for 90% of tuberculous cervical nodes and 60% of bone disease.[1] A subsequent report from the same department for the period 1915–1924 found 55 cases of TBOM amongst 4285 cases of CSOM (1.3%), and of these 46 were children.[1] In the 1920s, in Europe and USA, around 3% of children with TB had TBOM and up to 15% of those with CSOM.[2] By the period 1950–1959, of 23 000 cases of suppurative otitis media seen in the Royal National ENT Hospital, London, only 12 (0.05%) were caused by TBOM.[3] A literature search for the period 1960–1975 found only 13 cases of TBOM in children, which reflected the marked decline of the condition.[4] This dramatic fall in prevalence relates to the availability of pasteurised milk, BCG, public health measures, and tuberculous chemotherapy. Isoniazid and streptomycin were in clinical practice by 1953. However there are still sporadic cases in children in industrial countries today.[5,6] The incidence of TBOM in all age groups in England and Wales is now approximately 0.04%.[7]

In the recent but pre-HIV era, TBOM has also become uncommon in developing countries. In the 5-year period 1967–1971, nine children with TBOM were diagnosed by the ENT department of Groote Schur Hospital, Cape Town.[8] One child was 6 months old and the others ranged from 2 to 11 years of age. Radical (7 patients) or cortical mastoidectomy (1 patient) was required for most of the patients.

CSOM is a feature of HIV-infected children, as TB is a complication. Isolated cases of TBOM have been reported in association with HIV but there have not been any systematic studies. Clinical records of 14 children admitted to Tygerberg Hospital, Cape Town between 1992 and 1997 with both HIV infection and culture-proven TB were reviewed. Ear swabs were the source of infection in three.[9] Due to the difficulties in diagnosing TBOM itself and TB in HIV-infected children many cases are probably missed.

**Pathophysiology**

Primary infection via the eustachian tube is now rare and generally occurs in the first months of life. This was associated with unpasteurised milk (see above), close contact with a case, e.g. the mother with open TB, or through congenital or neonatal infection. In infants, the eustachian tube is relatively short and wider than in adults.[1] Before the availability of tuberculous chemotherapy around 1% of adults with pulmonary TB developed TBOM from pooling of infected sputum in the pharynx and nasopharynx.[2] This was also a route of infection in older children. Much more common is haematological spread from a distant primary focus (nearly always the lungs) where mycobacteria reach the middle ear mucosa or the mastoid bone and there is subsequent reactivation.[1,10] In a patient with longstanding non-specific CSOM, the possibility of contracting TBOM through an additional systemic tuberculous infection has been considered but is very difficult to prove.[3] Primary infection through an existing perforated tympanic membrane has also been suggested.[11,12] TBOM may also present as a general bacterial infected otitis media (due to superinfection).

**Clinical features**

Most cases of TBOM are unilateral and present with usually painless otorrhoea (not responding to antibiotics) or painless swelling over the mastoid bone. Ear discharge may be present for months or years before TBOM is diagnosed and it may be intermittent. It usually resolves within 2 months of tuberculous chemotherapy. Facial palsy is common especially in young children. Regional lymph nodes may be enlarged particularly the preauricular nodes. There is perforation of a thickened, lustreless tympanic membrane. Copious grey or pink granulation tissue is seen and this may protrude through the perforation. There may be widespread destruction of the ossicles. Permanent, moderate-to-severe hearing impairment is usual and it may be profound. Owing to the healing process of TB, deafness may progress despite chemotherapy. Occasionally, in early diagnosed cases, it may improve