

# Management of HIV: still a long way to go

In June 1981 the US Center for Disease Control reported the occurrence, without identifiable cause, of an unusual pneumonia caused by *Pneumocystis carinii* (now *jirovecii*) in five apparently healthy men in Los Angeles. In that first year over 1600 cases of this new form of severe immunodeficiency were diagnosed with close to 700 deaths. Two years later, after much speculation, the human retrovirus HIV-1 was isolated and found to be the cause of this severe immune deficiency syndrome. Over a decade later effective treatment was discovered, so-called highly active antiretroviral therapy (HAART), consisting of usually three antiviral compounds. Ten years after the widespread introduction of HAART there are still 33.2 million people living with HIV globally and most have no access to antiviral treatment.

The commonest presenting illness for patients with HIV and AIDS in the developed world was *Pneumocystis jirovecii* pneumonia (PCP). Pre-HAART, management of PCP was an important area of research and prophylaxis with co-trimoxazole improved patients' quality and quantity of life. Physicians looking after ever-increasing numbers of immune deficient patients became more and more aware of the variety of different diseases which can affect the respiratory tract. Many of these had previously only been seen in transplant or chemotherapy patients but were now common in HIV-positive patients. The infecting organisms were usually opportunistic and depended on the level of immune deficiency and other factors such as age and geography. Although PCP was seen in the developing world this epidemic has been overshadowed by the rise of *Mycobacterium tuberculosis* especially in developing countries. Probably the greatest single factor hindering worldwide control of tuberculosis has been the HIV epidemic.

As patients live longer because of HAART, they may also be at more risk of developing carcinomas, and one of these associations is with lung cancer. The significant association of smoking with non-

malignant pulmonary diseases is exacerbated in HIV. Smoking cessation should be a priority in patients on successful HAART now that their life expectancy has been so prolonged by adequate antiviral therapy.

It is almost unbelievable that someone now starting therapy can take a single pill, consisting of three antiretroviral drugs, once a day for their HIV disease. There are four different classes of drugs and around twenty individual compounds to choose from so that patients can start or switch if they suffer intolerance, toxicity or development of resistance. The efficacy of many combinations has been proven but one of the major differences between drug regimens today are their side effects.

There has recently been a focus on the association of renal disease in HIV and HAART therapy and the potential for renal toxicity. The interest in tenofovir, a nucleotide reverse transcriptase inhibitor which can interact with the OAT-2 pathway in the renal tubule, has focussed attention on HIV and renal disease. Clinically relevant, tenofovir-associated renal tubular dysfunction is rare, however, occurring in <1% of patients and is reversible on stopping the drug.

Apart from this HIV patients are specifically affected by several disorders of the kidney – the most curious of which is probably HIV-associated nephropathy which mainly occurs in black patients. HAART does not seem to prevent many of these patients ending up with end-stage renal disease. As patients live longer, the incidence of diabetes and hypertension may rise over time and this may have an impact on their kidneys. It is important that patients seen for HIV care are screened for kidney disease and are treated appropriately. Haemodialysis and transplantation are now options for HIV-positive patients, although immunosuppression can be difficult because of the drug interactions with some of the antiviral agents, especially ritonavir, which is a potent inhibitor of cytochrome P450-3A4.

Although there have been great advances in managing HIV patients, the increasing number of new HIV diagnoses is a con-

cern. Even more worrying is the number of people who are unaware of their HIV diagnosis – detecting these patients is extremely important. However, even in patients who do know they are HIV infected there has been an increase in some sexually transmitted infections – most worryingly ulcerative diseases which enhance onward transmission of HIV such as syphilis and lymphogranuloma venereum. This is a major health issue and more effective public health education is required because transmission of these infections in HIV-positive men must reflect continuing unsafe sex. Other genital infections can have long-term sequelae. As HIV-positive patients live longer, the risk of anal cancers related to human papilloma virus type 16 and 18 is increased.

This symposium (p. 132) is timely and brings together many important aspects of HIV disease. These include infections associated with severe immune suppression, complications of drug therapy, and the indirect impact of prolonging life expectancy. The continuing increase in sexually transmitted infections reminds us that there is still a lot to learn about control and prevention and that there is still a long way to go. **BJHM**

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### KEY POINTS

- *Pneumocystis jirovecii* and *Mycobacterium tuberculosis* are common respiratory pathogens in patients with HIV especially if severely immunodeficient.
- As highly active antiretroviral therapy prolongs life, malignancies and other long-term conditions increase in importance for HIV-positive patients.
- Long-term toxicities of antiviral drugs are an important cause of morbidity.
- Increasing rates of some sexually transmitted diseases in HIV-positive patients is an important public health issue.