Conference reports

HIV and associated infections

Infection with human immunodeficiency virus (HIV), which leads to the acquired human immunodeficiency syndrome (AIDS), presents with a number of opportunistic infections whose management remains a major concern. Understanding their pathogenesis and interactions with the HIV, and applying this knowledge to diagnostic and therapeutic procedures, were the main topics of the conference organised by the Royal College of Physicians, with support from Glaxo Wellcome. As the role of associated infections in HIV progression becomes clearer, prophylaxis becomes a possibility. Various antiviral therapies show promise of prolonging survival among patients and it seems almost certain that the future lies in multidrug therapy.

Cytomegalovirus and HIV

Professor Paul Griffiths (Royal Free Hospital, London) emphasised the value of knowing the natural history and pathogenesis of cytomegalovirus (CMV) in attempting to control it. The role of herpes viruses in HIV infection is underestimated. AIDS patients not only die with them, they die from them. Infection with CMV in HIV-positive patients is present in 66% at post mortem. Professor Griffiths stressed that we should try to identify patients with CMV viraemia and offer them treatment before retinitis or other systemic manifestations develop. Although recent studies on antiviral therapy in CMV appear to show improved patient survival, there is still a need for double-blind, placebo-controlled trials.

Herpes simplex virus and HIV

Treatment of sexually transmitted diseases is important in the control of HIV. Dr George Kinghorn (Royal Hallamshire Hospital, Sheffield) pointed to the synergy between HIV and herpes simplex virus (HSV) infections. HSV infection appears to be an important cofactor increasing HIV transmission and replication. Improved management of genital ulcer diseases (GUDs) is thus one of the priorities and includes better diagnosis, treatment and prophylaxis with antivirals and vaccines. This task is particularly important in developing countries where HSV is under-diagnosed. Combination therapy with the antiviral drug acyclovir and the antiretroviral drug zidovudine appears to prolong patient survival. Management options for HSV/HIV co-infection include: acyclovir or valaciclovir for suppression, or episodic antiviral treatment of clinical recurrence. Acyclovir resistance, which occurs in patients whose CD4 lymphocyte count is less than 100 or in those who have had previous repeated courses of acyclovir, can be managed with intravenous foscarnet.

Tuberculosis and HIV

Dr Kevin De Cock (London School of Hygiene and Tropical Medicine) spoke about HIV and mycobacterial infections. About 14% of global cases of tuberculosis (TB) are associated with HIV. There is a marked geographical variation in the causative organisms. African mycobacterial disease is mainly due to Mycobacterium tuberculosis (MTB) while in the UK the predominant infective organism is Mycobacterium avium complex (MAC). This, as well as costs, influences the management of TB in different parts of the world. Interactions between TB and HIV include: increased extrapulmonary and disseminated disease, diagnostic difficulties such as negative sputum samples, false negative skin tests, atypical radiological appearances and problems with antituberculous therapy. HIV-infected patients experience more side effects from antituberculous drugs and suffer more relapses of the disease. The latter is due to emergence of drug resistance often linked to poor patient compliance. Prophylaxis against MAC is still difficult, Rifabutin is better than placebo in prolonging patient survival. Recent recommendations for prophylaxis include rifabutin therapy when the CD4 lymphocyte count is less then 75, provided disseminated MAC and MTB have been excluded. In deciding on prophylaxis one must consider the advantages and disadvantages of drug therapy. Among the advantages are: reduction in morbidity, hospitalisation, blood transfusions and MAC bacteraemia; disadvantages include: side effects of antituberculous drugs, drug interactions and resistance, cost of therapy and unproved effect on survival and TB prevention. In summary, Dr De Cock said that tuberculosis is a well recognised HIV-related problem and should not be missed.

Epstein–Barr virus and HIV

Professor Dorothy Crawford (London School of Hygiene and Tropical Medicine) pointed out that 95% of adults show evidence of Epstein–Barr virus (EBV) infection and that it persists for life. It is associated with disease of lymphocytes and squamous epithelial cells, such as glandular fever, lymphomas, oral hairy leukoplakia and nasopharyngeal carcinoma. The pathogenesis of EBV-induced neoplasia in HIV infection is unclear but data suggest a genetic basis. EBV-associated lymphomas occur in 3% of AIDS patients, 60 times the incidence in the general population. Incidence is lowest in heterosexuals and increases with age. Men are more often affected than women, whites more than blacks, haemophiliacs more than intravenous drug users (IVDUs). Among EBV-associated

Rapporteur: BEATA CYBULSKA, MD, Staff Grade, Department of Genitourinary Medicine, St. Thomas’s Hospital, London

[100]
lymphomas the commonest are: primary cerebral lymphoma, immunoblastic lymphoma, Burkitt-like and non-Hodgkin’s lymphomas; the first two comprise 80% of all lymphomas and are also seen in other immunocompromised groups. The prognosis is poor, with survival times between two and three months.

Papovavirus and HIV

Professor Michael Harrison (University College, London) gave an account of progressive multifocal leukoencephalopathy (PML), a white matter disease caused by the neurotropic JC (papova) virus (JC are the initials of the patient in whom it was discovered). The virus is present in 65% of 14 year olds in the United States and is believed to be associated with basal upper respiratory tract infection. After a blood-borne spread JC virus affects the white matter of the brain. PML occurs also in other conditions including leukaemia, lymphoma, sarcoidosis and TB. In HIV infection the condition is associated with CD4 lymphocyte counts less than 150. It is an AIDS defining illness in 1% of patients and it occurs in about 5% of cases overall. Presentation is with a motor abnormality, mental state impairment, hemiparesis or hemianopia. Headaches and seizures are uncommon as the cortex is not predominantly involved. Increased intracranial pressure, fever or seizures are more suggestive of other pathology. Diagnosis of PML can be made by magnetic resonance imaging (MRI), by demonstrating the presence of the JC virus in cerebrospinal fluid (CSF) and urine, or by brain biopsy. An MRI showing low density lesions affecting white matter including the gyrus, with no mass effect and no enhancement, is suggestive of the condition. The main differential diagnosis is HIV encephalopathy in which lesions are symmetrical, not homogeneous, do not extend to the gyri and are not associated with hemiparesis or aphasia. Prognosis is poor, with 70% of patients not surviving beyond five months. Of various treatments tried, antiretroviral combination therapy is the most effective. The condition can be monitored by clinical response, imaging volumes of the lesions, magnetic resonance spectroscopy and CSF/urine JC virus load. Professor Harrison commented that PML, once almost unknown, is now a well-recognised condition.

Mycoplasmas and HIV

Professor David Taylor-Robinson (St Mary’s Hospital, London) described studies using the polymerase chain reaction (PCR) technique which showed the presence of mycoplasmas in 49% of HIV-positive patients with fulminant disease. Species which seem important in AIDS are Mycoplasma fermentans, first found as a contaminant of tissue culture cells, and Mycoplasma penetrans. The first species appears to be associated with more rapidly progressive disease. It has been linked with AIDS nephropathy and was found in broncho-alveolar lavage specimens with other respiratory infections. It can also be found in joints. The question whether it is an opportunistic lung infection has yet to be answered. Professor Taylor-Robinson spoke briefly about M penetrans, the newly-found organism which is not uniquely associated with HIV and was shown not to be associated with Kaposi’s sarcoma.

Epidemiology of HIV

Dr Anne Johnson (University College, London) outlined the current global epidemic. In 1994 there were an estimated 17 million adults infected according to the World Health Organization. Eleven million were heterosexuals in sub-Saharan Africa, 3 million were reported from south-east Asia and an increase was noted in Latin America and the Caribbean. In Europe, the prevalence of HIV infection varied: Spain reported 156 AIDS cases per million population, Italy, France and Switzerland between 66 and 93, the UK 25 and Poland only 2 cases per million. North European HIV infection is mainly related to homosexual spread whereas south European infection is predominantly due to intravenous drug abuse. In the UK in 1994, the prevalence of HIV infection was 11.3% in homosexual men in London compared with 3.4% in England and Wales, and 3% in male IVDUs in London compared with 0.3% in England and Wales. The prevalence of HIV in women was higher in London (0.5%) than in England and Wales (0.03%). The same applied to infected female IVDUs of whom 4% were living in London and 0.6% in England and Wales, and to HIV-infected pregnant women of whom 0.2% lived in London and 0.01% in England and Wales. Trends in women based on antenatal blood testing showed a rising prevalence of HIV in London. The incidence of HIV in homosexuals peaked in the mid-1980s and early 1990s. This group was characterised by a rise in newly diagnosed individuals whose CD4 lymphocyte counts were above 700, a rising annual number of men having repeat HIV tests, and rising numbers of diagnosed HIV seroconversion illness. In heterosexuals in the UK HIV infection is linked to exposure abroad in 79%, to a high-risk partner (bisexual male or IVDU) in 12% and to exposure in the UK to a partner from abroad in 7%. The incidence of HIV infection in heterosexuals in the UK has not been as great as expected. Projections for 1995–1999 include reduction in homosexual HIV and an increase in heterosexual and childhood infection as well as that related to IVDU. AIDS deaths are predicted to rise to 16%, with AIDS prevalence reaching 15%. There is a need for further surveillance in general and high-risk populations.

Professor Taylor-Robinson was surprised at the low number of AIDS cases in Poland and expressed his doubts about reporting methods in Eastern Europe. Dr Johnson said that Centres for Disease Control make adjustments for that in their analysis.
Sexually transmitted diseases and HIV

Dr David Barlow (St Thomas’s Hospital, London) pointed out that HIV-positive patients suffer more frequent recurrences of some sexually transmitted diseases (STDs) (HSV and human papillomavirus infection) and that these were more refractory to treatment. Although STDs have long been suggested as cofactors for HIV transmission, it is only in recent years that properly constructed, prospective, longitudinal and interventional studies in Africa and the United States have provided evidence for this relationship. A controlled randomised trial by Grosskurth et al [1] showed that improved STD facilities and treatment reduced HIV incidence by 42%. The relevance of this finding to the UK is that those with STDs may be at greater risk if their contact has HIV, and if HIV positive themselves, may transmit HIV more easily. STDs are not evenly distributed in the population. Data presented by Dr Barlow’s clinic on gonorrhoea in heterosexuals showed that the local endemic has remained largely confined to a subgroup of clinic attenders.

Does sexual mixing among clinic attenders and travel outside the UK increase HIV risk? The results of HIV-linked serosurvey data from St Thomas’s Hospital show that STDs are significantly more common in the Commission for Racial Equality (CRE) category 2 (Afro-Caribbean) than in CRE 1 (white). This may in part be due to highly assortative sexual mixing. Travel patterns give greater potential for HIV in the CRE 2 category.

Hepatitis viruses and HIV

Dr Janice Main (St Mary’s Hospital, London) stressed that in HIV-positive patients infection with any of the hepatitis viruses aggravates their clinical and therapeutic problems. Hepatitis A, usually mild, is more severe in HIV. Hepatitis B is more likely to be chronic and to undergo reactivation, and responds poorly to interferon. Hepatitis C is characterised by more progressive liver disease and increased transmission of infection. Treatments under evaluation include: interferon, steroids, lamivudine, ribavirin and zidovudine. As cure is unlikely, emphasis should be on monitoring the declining liver function tests and assuring good quality of life. The role of maintenance therapy is still unclear but preliminary results of trials of lamivudine look promising.

Human papillomavirus and HIV

Dr Margaret Stanley (University of Cambridge) discussed the role of human papillomaviruses (HPV) in the development of cervical cancer. She described the differences between transient and persistent HPV infection and the immune response to each of them. The hypothesis that HIV infection induces neoplasia implies belief in reactivation of latent virus, increased viral replication and viral persistence, faster progression of low grade to high grade intra-epithelial lesions and direct effect of HIV-encoded proteins on HPV gene expression. HIV-positive women have a higher recurrence rate of cervical intra-epithelial neoplasia when their CD4 lymphocyte count is less than 500. Dr Stanley concluded that cervical cancer is an AIDS-associated disease but is not increased in early HIV infection.

Lumleian Lecture: Sex, sun and responsibility

The conference ended with a lecture by Professor Michael Adler (University College, London) in which he highlighted the global HIV situation and concentrated on problems encountered by Third World countries. He pointed to the importance of economic factors and their effect on health. So-called ‘Economic Structural Adjustment Programmes’ have led to a decline in rural economy, migration, urbanisation, development of transportation routes, and reduction in spending on health and social services. He talked about the importance of preventive measures, emphasising the role of health education, provision of condoms, and social, cultural and economic interventions. He listed promotion of health-seeking behaviour and early detection and treatment of infections as crucial tasks in those countries. He pointed to the role of women in society in the Third World and the need to increase their profile. Factors that have to be addressed include: male sexuality, abuse of women and moral corruption.

What about the responsibilities of developed countries towards the Third World? Professor Adler was critical of early Western research workers in Africa who often did their work without considering ethical issues or benefits for participants and the participating country. He stressed that we must not exploit developing countries. The situation is now changing, but there are still problems coordinating research, although there have been cuts in aid in recent years. We still have the moral and humanitarian duty to offer advice, expertise and help in developing suitable programmes, bearing in mind the best interest of the country for which they are designed.

Acknowledgement

I thank Dr R N Thin for his critical review of this report.

Reference

1 Grosskurth H, Mosha F, Todd J, Mwijarubi E, et al. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. Lancet 1995;346:530-6.