Since the first report of Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy individuals in the USA in 1981, the pandemic of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) has reached alarming proportions. The current WHO/UNAIDS (2004) report has estimated 38 million people living with this infection worldwide; ~60–90,000 in the UK. Almost 50% of these are females and the number of people living with HIV/AIDS continues to rise by 1.5 million every year.1

Management of HIV patients poses a significant challenge for healthcare providers. This article outlines the epidemiology and pathophysiology of HIV infection and its implications for anaesthetic and intensive care management.

Epidemiology

HIV belongs to the Lentivirus group of retroviral family. These are cytopathic and have a long latent period and a chronic course. Two distinct variants of HIV have been identified: HIV-1 and HIV-2. HIV-2 occurs almost exclusively in West Africa; it may be milder and less readily transmitted from mother to child.

The initial wave of infection was amongst white, homosexual males, followed by a second wave amongst i.v. drug users (IVDU). However, currently, the heterosexual mode of transmission accounts for the vast majority of infections worldwide (Table 1).

Pathophysiology and diagnosis

Retroviruses contain the enzyme reverse transcriptase that allows viral RNA to be transcribed into DNA, which is then incorporated into the host cell genome. The virus preferentially infects T-helper lymphocytes (CD4+ T cells) and progressively destroys them, leading to increased susceptibility to opportunistic infections (Table 2) and malignancies.

As HIV infection is associated with a broad spectrum of illness, several classification systems have been proposed. The Centers for Disease Control and Prevention classification is most commonly used in Europe. The USA definition also incorporates CD4+ T-cell counts in addition to the clinical classification. Four main groups are identified:

(i) Group I. Acute seroconversion illness. This occurs soon after infection and has high viral load. Most patients remain asymptomatic.
(ii) Group II. Asymptomatic infection. The majority of people with HIV remain asymptomatic. Some 10% progress to

Table 1: High-risk groups and modes of HIV transmission

<table>
<thead>
<tr>
<th>Modes of transmission</th>
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<tr>
<td>Sexual intercourse (vaginal and anal)</td>
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<tr>
<td>Mother to child (during pregnancy, labour and breast-feeding)</td>
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<tr>
<td>Contaminated blood, blood products and organ donations</td>
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<tr>
<td>Contaminated needles</td>
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<tr>
<td>High-risk groups</td>
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<tr>
<td>Promiscuous heterosexuals</td>
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<tr>
<td>Patients with other sexually transmitted diseases</td>
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<tr>
<td>I.V. drug users</td>
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<tr>
<td>Haemophiliacs</td>
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<tr>
<td>Haitian and Central/West African population</td>
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Table 2: Major opportunistic pathogens in HIV/AIDS

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<thead>
<tr>
<th>Pathogens</th>
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<tbody>
<tr>
<td>Protozoa</td>
</tr>
<tr>
<td>T. gondii</td>
</tr>
<tr>
<td>C. parvum</td>
</tr>
<tr>
<td>Isospora</td>
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<tr>
<td>Fungi and yeasts</td>
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<tr>
<td>C. albicans</td>
</tr>
<tr>
<td>C. neoformans</td>
</tr>
<tr>
<td>Coccidioides</td>
</tr>
<tr>
<td>Viruses</td>
</tr>
<tr>
<td>CMV</td>
</tr>
<tr>
<td>HSV</td>
</tr>
<tr>
<td>Varicella</td>
</tr>
<tr>
<td>Bacteria</td>
</tr>
<tr>
<td>M. avium</td>
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<td>M. tuberculosis</td>
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Key points

The increased prevalence of HIV infection has led to increasing exposure of healthcare workers to this patient population.

Advances in treatment have brought about delayed disease progression and improved survival.

General anaesthesia should not be withheld on the grounds of HIV infection alone.

There is increasing survival of HIV-infected patients treated in intensive care, and similar principles of ethics apply whether or not the patient is HIV-infected.

An understanding of HIV infection, testing, universal precautions and the natural history of the disease is important for all healthcare workers.
AIDS within 2–3 yr whilst the remainder develop AIDS within a median of 10 yr.

(iii) Group III. Persistent generalized lymphadenopathy.
(iv) Group IV. Symptomatic HIV infection.

Diagnosis is based on detection of anti-HIV IgG antibodies. An enzyme-linked immunosorbent assay (ELISA) is cheap and simple to perform. A western blot analysis may be used to confirm a positive result. In acute seroconversion, the antibody response may not mount for up to 12 weeks. HIV RNA measurement and detection of p24 antigen may be useful.

Treatment of HIV infection

The outlook for patients with HIV infection has improved dramatically during the last decade. New drugs have been developed; in particular, protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTI). Combination antiretroviral therapy delays disease progression and improves survival.

Antiretroviral drugs in current use fall into three categories: (i) nucleoside analogue reverse transcriptase inhibitors (NRTI), e.g. Zidovudine — inhibit the synthesis of DNA by reverse transcriptase by acting as false nucleotide. (ii) nonnucleoside reverse transcriptase inhibitors (NNRTI) e.g. Nevirapine — bind to reverse transcriptase in a way that inhibits enzyme activity, and (iii) protease inhibitors (PIs) e.g. Saquinavir — prevent the processing of viral proteins into functional forms. A typical therapeutic regimen will comprise three agents (i.e. two nucleoside analogues combined with a PI or NNRTI); this has been termed highly active antiretroviral therapy (HAART). The aim of therapy is to achieve an undetectable viral load and to improve both duration and quality of life. However, side-effects and complicated dosing regimens lead to poor drug compliance.

Anaesthesia

Approximately 20% of all patients with HIV infection undergo surgery at some time during the course of their illness. Most of the procedures are for HIV-related problems; however, sometimes they are unrelated (e.g. trauma). Common procedures in adults include lymph node biopsy, splenectomy and partial colectomy. In children, placement of central venous lines and gastrostomy tubes, and diagnostic procedures are common.

There is no justification to withhold surgical intervention on the grounds of HIV infection alone as it is not associated with an increased postoperative risk of death or complications up to 30 days after the procedure. Concern has been expressed over the depression of cell-mediated immunity and alterations in immune function such as depression of natural killer cell, T-lymphocyte, monocyte and neutrophil activity after general anaesthesia. However, the changes seem to be transient and do not lead to increased likelihood of postoperative infection. It has been suggested that immune changes do not occur after regional techniques but there is insufficient evidence to recommend regional over general anaesthesia in HIV infection on immunological grounds alone.

Preoperative assessment

Preoperative assessment should take account of the potential effects of HIV infection on every organ system.

Respiratory system

The dominant respiratory complications in HIV/AIDS are as a result of opportunistic infections (Table 2) including Pneumocystis carinii pneumonia (PCP), aspergillosis, herpetic infections, oral and pharyngeal candidiasis and cytomegaloviral (CMV) pneumonia. Mycobacterial infections (Mycobacterium tuberculosis and atypical organisms, e.g. M. avium intracellulare) may progress to acute respiratory failure. Cavitatory lung disease may be due to pyogenic lung abscess, pulmonary tuberculosis, fungal and Nocardial infection. Kaposi’s sarcoma and lymphoma can also affect the lung. The diagnosis is important as some of these conditions may respond to therapy. Appropriate preoperative assessment should include careful evaluation of pulmonary function, which may include arterial blood gas analysis and spirometry. If general anaesthesia is planned, the availability of postoperative ventilatory support is a consideration.

Cardiovascular system

Opportunistic bacterial infections may cause endocarditis and/or congestive cardiac failure; vegetables are particularly associated with IVDUs. Central nervous system pathology affecting brainstem function may provoke arrhythmias. Up to 50% of patients with HIV infection have abnormal findings on echocardiography. Myocarditis, progressing to dilated cardiomyopathy, is common and may be caused by infection with Cryptococcus, coxsackie B virus, CMV, Aspergillus species as well as lymphoma and HIV itself. Thus, a preoperative ECG and echocardiogram are useful to delineate cardiac dysfunction (which may be clinically silent).

Gastrointestinal system

Diarrhoea, vomiting and loss of appetite may complicate HIV/AIDS and its treatment. Oral candidiasis causes painful eating and swallowing, and infections with CMV and cryptosporidium cause debilitating diarrhoea. Therefore, fluid and electrolyte imbalance is common and preoperative correction is important. Kaposi’s sarcoma in the mouth and upper airway may pose a hazard to endotracheal intubation.

Nervous system

Approximately 90% of patients with HIV infection develop neurological complications. These include:

(i) Non-viral infections, for example toxoplasmosis, Cryptococcus, Candida, mycobacteria, Treponema and Aspergillus;
(ii) Subacute encephalitis;
(iii) Aseptic meningitis;
Anaesthesia and critical care for patients with HIV infection

(iv) Herpes simplex encephalitis;
(v) Multifocal leukoencephalopathy;
(vi) Neoplasia (e.g. primary cerebral lymphoma);
(vii) Polyneuropathy; and
(viii) HIV-related dementia.

It has been suggested that preoperative focal neurological deficits constitute a relative contraindication to regional anaesthesia.4

Other considerations
Anaemia, thrombocytopenia and leucopenia are common. Chemotherapeutic agents and radiotherapy may aggravate these abnormalities necessitating blood and blood product transfusions. CMV adrenalitis and/or exogenous corticosteroid administration in the treatment of peripheral neuropathy may cause adrenal suppression requiring perioperative steroid supplementation.

Other problems include anaesthesia in the IVDU group (multisystem disease, poor venous access) and problems related to drug interactions (e.g. PIs may decrease metabolism of benzodiazepines and opioids).

Reducing the risk of cross infection
In-hospital transmission of HIV in anaesthetic practice may occur from patient to anaesthetist, from patient to patient, or from anaesthetist to patient. HIV can be transmitted to the anaesthetist through a sharps injury or from splashing of a mucosal surface or broken skin by body fluid. Most injuries occur during unsafe disposal of sharps or when resheathing needles. The average risks of HIV transmission following needlestick injury and mucocutaneous transmission are 0.3% and 0.03%, respectively. Factors increasing the risk of transmission following needlestick injury are the volume of blood inoculated (e.g. hollow needle injuries) and deep punctures. The cumulative risk over an anaesthetic career may be as high as 4.5%. This calls for constant vigilance in the use of universal precautions. However, studies indicate that transmission rates among healthcare workers may be multidisciplinary and applied along the same principles used to drug interactions (e.g. PIs may decrease metabolism of benzodiazepines and opioids).

The risk of transmission from anaesthetist to patient appears to be low. It has been estimated at 2.4–24 per million procedures.7

Post-exposure prophylaxis
Post-exposure prophylaxis (PEP) is recommended for healthcare workers and should commence as soon as possible after the injury, ideally within 1–2 h. However, it can be considered up to 1–2 weeks after the injury. All hospitals should have a well-developed protocol to facilitate the process.

Obstetric anaesthesia
Approximately 2.1 million children under 15 are infected with HIV/AIDS worldwide as a result of mother-to-child transmission (MTCT). In the absence of any intervention, an estimated 15–30% of mothers with HIV infection will transmit the infection during pregnancy and delivery and 10–20% through breast milk. Vertical transmission is dramatically reduced by antiretroviral therapy. Current evidence supports the use of Nevirapine given to mother at delivery and the neonate within 72 h of delivery to prevent MTCT. Caesarean section appears independently to reduce the incidence of vertical transmission and, when combined with antiretroviral therapy (ART), the rate of transmission falls to 2%. Regional anaesthesia is not contraindicated. Epidural blood patch for post-dural puncture headache appears to be safe, but other analgesic techniques should be tried first.

Pain
Pain is particularly common in advanced disease and has numerous aetiologies including opportunistic infection (e.g. herpes simplex), HIV-related arthralgia, peripheral neuropathy and drug-related pain. The treatment of pain in HIV infection should be multidisciplinary and applied along the same principles used to manage cancer-related pain.

Intensive care
HIV-infected patients may require intensive care for a number of reasons. However, with the advent of effective ART, the spectrum and outcome of critical illness is changing. Increasing numbers of patients are presenting to the intensive care unit (ICU) with medical and surgical conditions unrelated to HIV infection. Overall mortality rates for HIV-infected patients requiring intensive care have improved during the course of the AIDS epidemic, from ~70% in the early 1980s to 30–40% presently.2

Acute respiratory failure is the most common reason for ICU admission in HIV-infected patients and Pneumocystis is identified as the responsible pathogen in 25–50% of these cases.2 There have been significant changes in the mortality of PCP-associated acute respiratory failure, and both patients and clinicians have changed their expectations and their approach to its management. Initial data from the 1980s showed very poor results, with survival rates of 0–13% raising questions regarding the appropriateness of ICU admission. From 1987 into the 1990s, reports emerged...
describing improved survival rates of up to 30–45%. Possible explanations include change in patient selection, increased use of PCP prophylaxis and antiretroviral medication, and increased use of adjunctive corticosteroid therapy in moderate to severe PCP. More recently, improved survival of 75% compared with 37% has been reported in patients receiving combination ART. Nevertheless, the mortality of severe PCP remains high.

Severe PCP usually manifests on the chest x-ray as bilateral diffuse granular opacities resembling acute lung injury. Thin-walled air-containing cysts, or pneumatoceles, may be seen; these predispose to pneumothorax. Pneumatoceles and pneumothoraces are more common in patients receiving nebulised pentamidine as prophylaxis. Pneumothorax may also develop spontaneously; it carries an extremely poor prognosis in patients receiving mechanical ventilation for severe PCP. Bronchoalveolar lavage cytology is the gold standard in diagnosing PCP pneumonia. Open lung biopsy is seldom used and should be reserved for selected cases.

Trimethoprim–sulfamethoxazole and i.v. pentamidine remain the most effective therapy in acute disease. Other alternatives include Dapsone, clindamycin, primaquine and atovaquone. Patients with moderate to severe PCP should receive adjuvant corticosteroids commenced within 24–72 h of PCP therapy; this has been shown to reduce the rate of respiratory failure and death. Non-invasive ventilation techniques may be associated with a reduced requirement for intubation and therefore less risk of pneumothorax; however, they require an awake and cooperative patient. For patients requiring full ventilation, PCP should probably be managed according to the current criteria for acute lung injury.

Bacterial pneumonia is the second most common cause of respiratory failure requiring ICU admission in HIV-infected patients. Empirical therapy to cover Pseudomonas aeruginosa and Staphylococcus aureus should be considered.

Patients with neurological complications of HIV infection may require intensive care for the control of intractable seizures or for depressed levels of consciousness. The underlying condition may be a mass lesion (e.g. toxoplasmosis, primary cerebral lymphoma) or meningitis (commonly Cryptococcus). Progressive multifocal leukoencephalopathy and herpes simplex virus encephalitis may also precipitate ICU admission. In a case series of patients with HIV infection admitted to ICU, neurological dysfunction accounted for 17% of admissions, with a mortality of 68%; toxoplasmosis was the most frequent diagnosis.

A Glasgow Coma Score of <7 and clinical signs of brainstem involvement were independent predictors of death. In patients with AIDS dementia, an advance directive to avoid prolongation of life in this setting may be useful.

Bleeding is the most common gastrointestinal complication requiring ICU admission. This may result from HIV-related complications (e.g. infectious ulceration, Kaposi’s sarcoma, lymphoma) or non-HIV-associated causes (e.g. gastric or duodenal ulcers, variceal bleeding, erosive gastritis). Bleeding may be complicated by HIV-associated thrombocytopenia. Bowel perforation secondary to CMV enteritis, Kaposi’s sarcoma, lymphoma and mycobacterial infection, AIDS cholangiopathy and pancreatitis are other causes of ICU admission in this population.

Predictors of mortality and impact of therapy

Sepsis and respiratory failure (particularly if associated with PCP) are associated with poorer survival in HIV-infected patients requiring ICU admission. The need for mechanical ventilation and the disease severity as assessed by the Acute Physiology and Chronic Health Evaluation II (APACHE II) is associated with increased hospital mortality. Low serum albumin and a history of weight loss are further predictors of a higher mortality.

ART may improve outcome in critically ill HIV patients, although randomized studies are awaited. The decision to initiate ART in this setting requires careful consideration in view of the potential for adverse effects and drug interactions.

References


See multiple choice questions 115–118