

HIV AIDS

Version 1 Final

Document control

Version history

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Changes since last version

Introduction

Human immunodeficiency virus (HIV) infection results from 1 of 2 similar retroviruses (HIV-1 and rarely HIV-2) that destroy CD4+ lymphocytes and impair cell-mediated immunity, increasing risk of certain infections and cancers. [1]
The virus also has the potential to infect various other tissues especially nervous tissue leading to functional impairment. This is most likely to occur in later stages of chronic infection, when the virus seems to expand its affinity for other tissues.

Description

HIV infection refers to infection with the human immunodeficiency virus (HIV) type 1 or type 2. Initial infection may produce non-specific febrile illness. The risk of subsequent manifestations - related to immunodeficiency - is proportional to the level of CD4+ T lymphocytes.

Asymptomatic carriage of *human immunodeficiency virus may continue for 8 to 10 years*. HIV infection is diagnosable during this time by antibody or antigen testing. Treatment aims to suppress HIV replication by combinations of drugs that inhibit HIV enzymes.

Current treatments interrupt the life cycle of the virus but without affecting a cure. In patients with inadequate adherence to the treatment regimen, mutations in the viral genome result in gradual resistance drift leading to multi-drug resistance and increasing ineffectiveness of drug treatment. [2]

Repeated episodes of illness of varying and increasing severity then occur as immune function deteriorates, resulting in acquired immune deficiency syndrome (AIDS), which manifests with serious opportunistic infections or cancers.

Epidemiology

Incidence / Prevalence

Worldwide estimates suggest that by December 2005 about 38.6 million people were living with HIV. In 2005, there were estimated to be 4.1 million new cases of HIV infection and 3.3 million deaths from AIDS.

About 95% of HIV infections occur in the developing world.

Occupationally acquired HIV infection in healthcare workers is rare and results invariably from needlestick injury. By 1999 this had been documented in at least 102 definite and 217 possible cases. [3]

Risk Factors

The major risk factor for transmission of HIV is unprotected heterosexual or homosexual intercourse. Rates of infection in the gay community will vary by locale and over time. In the UK the highest rates are in London and Brighton. Heterosexual infection rates in Britain are highest amongst African asylum seekers. High rates also occur in the sexual partners of IV drug users and residents of areas of high endemicity e.g. Africa, Spain.

Other risk factors include sharing drug injecting equipment, blood transfusion and needlestick injury. An HIV infected woman may also transmit the virus to her baby trans-placentally during birth, or through breast milk. [4]

This has been reported in 15–30% of pregnant women with HIV infection. Not everyone who is exposed to HIV will become infected [5], although risk increases if exposure is repeated, at high dose, or through blood.

There is at least a two to fivefold greater risk of HIV infection among people with other sexually transmitted diseases. [2]

Clinical Classification

AIDS is defined as HIV infection that leads to any of the disorders listed in Category C of the following table. [6]

Clinical Categories of HIV Infection	
Category A (<i>earlier stages</i>)	Asymptomatic Symptoms of acute primary HIV infection Persistent generalized adenopathy
Category B (<i>symptomatic progression</i>)	Bacillary angiomatosis Candidiasis, oropharyngeal (thrush) Candidiasis, vulvovaginal; persistent, frequent, or poorly responsive to therapy

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Category B (symptomatic progression)	Cervical dysplasia (moderate or severe)/cervical carcinoma in situ Constitutional symptoms, such as fever $\geq 38.5^{\circ}\text{C}$ or diarrhoea lasting > 1 month Hairy leukoplakia, oral Herpes zoster (shingles), involving at least 2 distinct episodes or > 1 dermatome Immune thrombocytopenic purpura Listeriosis Pelvic inflammatory disease, particularly if complicated by tubo-ovarian abscess Peripheral neuropathy
Category C (AIDS)	Candidiasis of bronchi, trachea, or lungs Candidiasis, oesophageal Cervical cancer, invasive Coccidioidomycosis, disseminated or extrapulmonary Cryptococcosis, extrapulmonary Cryptosporidiosis, chronic intestinal (> 1 mo duration) Cytomegalovirus disease (e.g. retinitis or abdominal disease) HIV related Encephalopathy, Herpes simplex: chronic ulcer(s) (> 1 mo duration); or bronchitis, pneumonitis, or oesophagitis Histoplasmosis, disseminated or extrapulmonary Isosporiasis, chronic intestinal (> 1 mo duration) Kaposi's sarcoma Lymphoma, Burkitt's (or equivalent term) Lymphoma, immunoblastic (or equivalent term) Lymphoma, primary, of brain <i>Mycobacterium avium</i> complex or <i>M. kansasii</i> , disseminated or extrapulmonary <i>M. tuberculosis</i> , any site (pulmonary or extrapulmonary) <i>Mycobacterium</i> , other species or unidentified species, disseminated or extrapulmonary <i>Pneumocystis jiroveci</i> (formerly <i>P. carinii</i>) pneumonia Pneumonia, recurrent Progressive multifocal leukoencephalopathy <i>Salmonella</i> septicemia, recurrent Toxoplasmosis of brain Wasting syndrome due to HIV

Description of Clinical Stages

Acute HIV Infection

(Primary HIV infection; HIV seroconversion syndrome; Acute retroviral syndrome)

Primary or acute HIV infection is a condition that occurs 2-4 weeks after infection with the human immunodeficiency virus (HIV).

Acute HIV infection can resemble infectious mononucleosis, flu, or other viral syndromes. Typical symptoms include fever, headache, fatigue, and swollen lymph nodes.

Those affected may also experience aching muscles and a rash that occurs anywhere on the body and may change locations.

These symptoms may last from a few days to 4 weeks, and then subside.

After an infection with HIV, antibodies to the virus can be detected in the blood. This is called HIV seroconversion (converting from HIV negative to HIV positive), and usually occurs within 3 months of exposure, but on rare occasions may take up to a year after exposure to occur.

Following the acute infection, there may be no further evidence of illness for the next decade.

Acute HIV infection can, but does not always, progress to early symptomatic HIV infection and to advanced HIV disease (AIDS).

It cannot be assumed that all people infected with HIV will inevitably progress to AIDS, but time has shown that the vast majority do.

To date there are a small number of people who have unquestionably tested positive for HIV, but have undetectable viral load for a long time without anti HIV drugs and have absolutely no signs of disease. They are known as Long Term Non Progressors (LTNPs). Their numbers are extremely small, but they provide evidence that the human body may be capable of controlling the disease long term. [7]

These people are being carefully watched and studied.

Asymptomatic HIV Infection

Asymptomatic HIV infection is a phase during chronic infection with HIV during which there are no overt symptoms of HIV infection.

The length of this phase is highly variable among individuals and correlates with the level of replication of HIV in each individual, as well as genetic differences in the way the immune system handles the virus, but there is a slow deterioration of the immune system despite the lack of clinical symptoms.

There is frequently a gradual decline in CD4 counts, an index of immune function.

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In some individuals the asymptomatic phase can last 10 years or more, while in others clinical symptoms and worsening immune function may occur within a few years from the time of the original infection.

Acquired Immune Deficiency Syndrome

Deaths in America (and Europe) from AIDS rose remorselessly year by year, peaking in 1995 when the CDC reported AIDS as being the commonest cause of death among persons between ages 25 and 44 in the United States. [8] Highly Active Anti-Retroviral Therapy (HAART) was first introduced in 1995 the year that progress was made on many fronts.

The number of deaths from AIDS has shown a marked drop between 1995 and 1998 and a slower but continuing decrease since, such that in 2004 (the last figures available) HIV/AIDS was considered responsible for 5% of deaths in the United States in the 25 to 44 range (after malignancy, heart disease, suicide and homicide) with unintentional injury the number one cause accounting for 23.4% of deaths in this age range. [9], [10]

Similarly in Europe, in contrast to HIV diagnoses, AIDS incidence has been declining since 1995, when it peaked. Similar trends are observed in most EU countries. Exceptions are Portugal and the Baltic States, where the HIV epidemic is much more recent and access to antiretroviral treatment is likely to be more limited than in other countries. [11]

The rates of AIDS cases can therefore be expected to continue to rise for the medium term, against the general trends in Europe.

About 25 million people worldwide have died from this infection since the start of the epidemic, and 40.3 million people are currently living with HIV/AIDS globally.

Diagnosis

Tests of Diagnostic and Prognostic Value

Initial Diagnostic Tests

Each patient initially entering care should have a complete medical history, physical examination, and laboratory evaluation. The purpose is to confirm the presence of HIV infection, determine if HIV infection is acute, determine the presence of co-infections and assess overall health condition as recommended by the primary care guidelines for the management of HIV infected patients.

The standard test is an HIV antibody test which becomes positive about 6-12 weeks after infection. If positive a quantitative polymerase chain reaction test - known as the HIV viral load - is undertaken since this has prognostic importance. Increasingly tests for HIV drug resistance are carried out before therapy is initiated to ensure that the virus is not resistant to any drugs chosen, since drug resistant virus can be transmitted, for example, between sexual partners. Tests are also undertaken to exclude other important infections such as Hepatitis B and C, Sexually transmitted diseases (STDs) and Tuberculosis

The following laboratory tests should be performed for each new patient during initial visits:

- HIV antibody testing (if laboratory confirmation is not already available)
- CD4 + T cell count
- Plasma HIV RNA
- Complete blood count, chemistry profile, transaminase levels, BUN (blood urea nitrogen) and creatinine, and urinalysis
- RPR or VDRL, tuberculin skin test (unless a history of previous tuberculosis or positive skin test)
- *Toxoplasma gondii* IgG, Hepatitis A, B, and C serologies and PAP smear in women
- Fasting blood glucose and serum lipids if considered at risk for cardiovascular disease and for baseline evaluation prior to initiation of combination antiretroviral therapy
- For patients with pre-treatment HIV RNA > 1,000 copies/mL - genotype resistance testing prior to initiation of therapy. If therapy is to be deferred resistance testing may still be considered.

In addition

- An optimal test for Chlamydia trachomatis and Neisseria gonorrhoea, Syphilis and Herpes in order to identify high risk behaviour and the need for STD therapy
- Chest X-ray to exclude Tuberculosis

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Standard Tests at Routine Clinic Visits

The two important tests are the viral load which should always be undetectable (most test at 50 viral copies/mL) and the CD4 count. In addition routine biochemistry including Glucose and Lipids may be done as well as an FBC.

AIDS and Advanced HIV Infection

AIDS may present with symptoms more specific to infections that do not normally develop in individuals with healthy immune systems. These are called opportunistic infections.

Patients with AIDS have had their immune system depleted by HIV and are very susceptible to such opportunistic infections. The signs and tests section below has further information on common opportunistic infections and major symptoms associated with them.

As HIV infection progresses towards AIDS common symptoms may include:

- fevers,
- increasing sweats (particularly at night),
- swollen glands and splenomegaly.
- oral symptoms such as thrush or ulcers
- weakness,
- weight loss.

Important AIDS –Defining Illnesses

Different AIDS illnesses tend to emerge at different degrees of CD4 cell destruction. The danger of an AIDS illness greatly increases at CD4 levels below 200cell/cms-when Co-trimoxazole prophylaxis for PCP is usually initiated-and increases thereafter. The following are some common examples of AIDS.

CD4 count below 350cells / μ L

Tuberculosis -- infection by the tuberculosis bacteria that predominately affects the lungs, but can affect other organs such as the bowel, lining of the heart or lungs, brain, or lining of the central nervous system.

Non-Hodgkin's lymphoma -- cancer of the lymph glands.

Kaposi's sarcoma -- Cancer of the skin, lungs, and bowel, associated with a herpes virus (HHV-8). Can occur at any CD4 count, but more likely at lower CD4 counts, and more common in men than women.

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CD4 count below 200 cells/ μ L

Pneumocystis carinii pneumonia, "PCP pneumonia," now called *Pneumocystis jiroveci* pneumonia.

Candida esophagitis -- painful yeast infection of the oesophagus.

Bacillary angiomatosis -- Skin lesions caused by a bacteria called *Bartonella*, which is usually acquired from cat scratches.

CD4 count below 100 cells/ μ L

Cryptococcal meningitis -- infection of the lining of the brain by a yeast.

AIDS dementia -- worsening and slowing of mental function, caused by HIV itself

Toxoplasmosis encephalitis -- infection of the brain by a parasite, which is frequently found in cat faeces; causes discrete lesions in the brain.

Progressive multifocal leukoencephalopathy -- a viral disease of the brain caused by a virus (called the JC virus) that results in a severe decline in cognitive and motor functions.

Wasting syndrome -- extreme weight loss and loss of appetite, caused by HIV.

Cryptosporidium diarrhoea -- Extreme diarrhoea caused by one of several related parasites

CD4 count below 50 cells/ μ L

Mycobacterium avium bacteraemia -- a blood infection by a bacterium related to tuberculosis.

Cytomegalovirus infection -- a viral infection can affect almost any organ system, especially the large bowel and the eyes.

Those with HIV infection require regular monitoring of CD4 count, HIV RNA load (viral load), as well as basic screening lab tests. It is also important regular to undertake regular vaginal Pap smears are due to the increased risk of cervical cancer in immunocompromised patients. Anal Pap smears to detect potential cancers may also be important in both HIV infected men and women.

Management

General Management

Aims of intervention

To reduce transmission of HIV, to prevent or delay the onset of AIDS, (as manifested by opportunistic infections and cancers), increase survival and minimise loss of quality of life caused by inconvenience, with minimal adverse effects. [2]

Management

Certain advice should be followed at all stages of HIV infection:

- Avoid illicit drugs particularly intravenous use.
- Avoid excess alcohol.
- Stress should be kept to a minimum.
- Avoidance of exposure to people with acute infectious illnesses.
- Adequate exercise.
- Maintain a nutritious diet with adequate caloric intake.
- Avoidance of settings and situations that could lead to depression. Maintain positive social contacts, hobbies, interests, and pets.
- The practice of safer sex. The disease is highly infectious in the first months after infection, at later stages and in those with persistently high HIV viral loads.

Support Groups

The stress of illness can often be reduced by joining a support group, where members share common experiences and problems. [12] This may help adherence, given the signal importance of strict drug adherence to prevent emergence of multi-drug resistance

Combination Antiretroviral Therapy

Infection with the human immunodeficiency virus (HIV) usually leads to 8-10 years of asymptomatic infection before immune function deteriorates and AIDS develops.

Without treatment, about 50% of infected people will die of AIDS over 10 years. With treatment, prognosis depends on age, CD4 cell count and initial viral load.

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Antiretroviral therapy is recommended for all patients with a history of HIV infection and an opportunistic illness which meets the definition of AIDS, or severe symptoms of HIV regardless of CD4+T cell count.

There are currently four classes of antiretroviral drugs in use but several new classes are in advanced development, whilst a second generation of established classes is emerging. Given the problem of toxicity and multi-drug resistance this is increasingly required.

- 1) Nucleoside analogue R.T. inhibitors (usually referred to as “nukes”) e.g. lamivudine, abacavir
- 2) Non-nucleoside R.T inhibitors (usually referred to as “non-nukes”) e.g. efavirenz, nevirapine
- 3) Protease inhibitors (PI) increasingly now used in a combination of two e.g. Kaletra (lopinavir with ritonavir) known as boosted PI
- 4) Fusion inhibitors e.g. enfuvirtide (T20)-injected and only used in multi-drug resistance.

For routine use 3 drugs (in abbreviation :HAART) are used in combination. As “backbone” two “nukes” are chosen from a total now of 5, and the 3rd choice is either one of two “non-nukes” or one/boosted combination of 6 “PIs”. Whilst there are fewer serious toxicities in newer drugs, this is a real problem being faced daily in clinics, which complicates adherence and need for drug switches. Marrow depression, painful neuropathy, hepatitis and severe skin rashes are but a few of these. However the commonest problem relates to the lipid upsets such as facial lipodystrophy, atherosclerosis, diabetes and metabolic syndrome which may lead to myocardial infarction or need for statin drugs.

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When to start HAART

The optimum time to initiate HAART balancing the benefits of suppression against the long term problems of toxicity and emergence of resistance has yet to be determined, but long term trials are ongoing. The following reflects current thinking.

CD4+T count (cells/ μ L)	Plasma HIV RNA (copies/mL)	Treatment
< 200		Recommended
201 - 350		Offer
> 350	> 100,000	Usually defer
> 350	< 100,000	Defer

{reduction in CD4+ T lymphocytes leads to reduction in immunity}
{increase in HIV RNA copies increases risk of progression to AIDS}

Antiretroviral treatment - Which Drugs to Choose

- Boosted protease inhibitor based regimens may be more effective than standard protease based triple regimens at reducing viral load and preventing HIV progression and death.
- Non-nucleoside reverse transcriptase inhibitor (NNRTI: efavirenz or nevirapine) based triple regimens increase viral suppression compared with protease inhibitor based triple regimens, although HIV progression rates may not be reduced.
- Protease inhibitor based triple regimens are at least as good as NNRTI based triple regimens at reducing viral load, however, Protease based regimens may increase cholesterol and triglyceride levels.
- Highly Active Anti-Retroviral Therapy (HAART) consists of 3 or more highly potent anti-HIV drugs, commonly reverse transcriptase inhibitors and protease inhibitors. (The principle that lies behind HAART is that a single drug therapy may be successful for a while, but because HIV changes to avoid detection, drug-resistant strains will often arise in the patient. (This happens through a kind of evolution by natural selection - any new viruses which happen to be resistant to the drug will go on to multiply, while the others are stopped.)

The chances of a HIV genome mutating such that it can resist three separate drug treatments at once, however, is so small-except when adherence is poor, that the pressure of this therapy prevents the emergence of resistant strains.)

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It is yet unclear whether early initiation of antiretroviral treatment using triple regimens improves long term survival compared with delayed treatment. The decision about when to start treatment currently depends on severity of symptoms and CD4 lymphocyte count, so that likely benefits can be balanced against risks of adverse effects of treatment. [2]

Limitations to Treatment

Safety and Efficacy

A number of factors may influence the safety and efficacy of antiretroviral therapy in individual patients. Examples include, but are not limited to:

- Non adherence to therapy
- Adverse drug reactions
- Drug/drug interactions
- Development of drug resistance.

Adherence

Adherence to Antiretroviral Therapy

HIV viral suppression, reduced rates of resistance and improved survival have been correlated with high rates of adherence to antiretroviral therapy. Many patients will be initiating, or have initiated treatment when asymptomatic. Strict adherence must be maintained for a life time, which is an even greater challenge, given that the efficacy of therapy has increased life expectancy for people living with HIV. A commitment to lifelong therapy requires a commitment both patient and the health care team.

Adverse Effects

Serious side effects of antiretroviral drugs do occur. Some of them, notably anaemia, pancreatitis, hepatitis and glucose intolerance, can be detected by blood tests before they cause symptoms. Patients should be screened regularly, both clinically and with appropriate laboratory testing especially when starting new drugs or if unexpected symptoms develop.

Metabolic effects consist of interrelated syndromes of fat redistribution, hyperlipidaemia and insulin resistance. A common development is redistribution of subcutaneous fat from the face and distal extremities to the trunk and abdomen. The cosmetic effect can stigmatise and distress patients. Facial treatments with injected collagen or polylactic acid can be beneficial.

Hyperlipidaemia and hyperglycaemia due to insulin resistance and non-alcoholic steatohepatitis may occur with lipodystrophy. Drugs from all classes appear to contribute to these metabolic effects. Ritonavir or d4T does so commonly while others such as atazanavir appear to have minimal effects on lipid levels.

Mechanisms accounting for metabolic effects appear to be multiple of which one is mitochondrial activity.

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The risk of mitochondrial toxicity and metabolic effects varies by drug class (highest with NRTIs and **PIs**) and within drug classes e.g., among NRTIs the highest with d4T. Effects are dose dependent and often begin in the first one to two years of treatment. The long term effects and long term management of metabolic effects are unclear. Lipid lowering statins and insulin sensitizing drugs (glitazones) may be helpful.

Bone complications of HAART (highly active antiretroviral therapy) include asymptomatic osteopenia and osteoporosis which are common among patients with metabolic effects. Uncommonly avascular necrosis of large joints such as the hip and shoulder produces severe joint pain and dysfunction. Mechanisms of bone complications are poorly understood. [16]

Interruption of HAART is generally safe if all drugs are stopped simultaneously. Interruption may be necessary for treatment of intervening illness or if drug toxicity becomes intolerable or requires to be evaluated. After interruption to determine which drug is responsible for toxicity restarting most drugs as monotherapy is safe for most drugs. The most important exception is abacavir. Patients who had fever or rash during previous exposure to abacavir may develop severe and potentially fatal hypersensitivity reactions with re-exposure. [17]

1 Special Situations

Post Exposure Prophylaxis

Preventative treatment is indicated after penetrating injuries involving HIV infected blood (usually needlesticks) or heavy mucous membrane (eye or mouth) exposure. Risk of infection after percutaneous exposure is overall about 0.3% and about 0.09% after mucous membrane exposure. Risk appears proportional to the amount of inoculum, depth of injury and viral load of the source blood.

Combination of 2 NRTIs or 3 drugs (2 NRTIs plus a PI or NNRTI, Nevirapine is avoided because of rare but severe hepatitis) for one month is currently recommended. Although evidence is not conclusive Zidovudine - AZT (Retrovir, an NRTI) alone probably reduces risk of transmission after needlestick injuries by about 80%. [1]

HIV and Hepatitis

In patients with a high CD4 count not requiring HIV therapy, but requiring HBV therapy, HBV therapy should be with agents that have no anti-HIV activity at the doses used. Interferon alpha for 4-6 months is suitable in non-cirrhotic doses used. Interferon alpha for 4-6 months is suitable in non-cirrhotic HBeAg positive patients and an abnormal LFT or alternatively, long term adefovir in any patient. Pegylated interferon may replace interferon in the future. It is invariably used in HCV cases with ribavarin where it may cure 15-50% of cases depending on the serotype.

In patients requiring HIV therapy who are HBsAg-positive, therapy would normally include tenovir or a combination of tenovir with either lamivudine or FTC (emtricitabine, an NRTI antiviral drug that reduces the amount of HIV in the body) as part of, or in addition to, their antiretroviral regimen. [15]

HIV and Tuberculosis

Tuberculosis is a major opportunistic infection and cause of death in people with HIV, and often presents as non-pulmonary disease.

- In people infected with both HIV and *Mycobacterium tuberculosis*, the annual risk of developing active tuberculosis is 5-10%, more than ten times the rate for people with *M tuberculosis* infection but without HIV.
- Untreated, mortality from tuberculosis in people with HIV is likely to be very high and over 5% of people relapse after successful treatment.

Conventional anti-tuberculous treatment (2 months of rifampicin, isoniazid and pyrazinamide, with or without ethambutol, followed by 4-7 months of rifampicin plus isoniazid) is considered beneficial in people with HIV and is standard treatment. Placebo controlled RCTs of active tuberculosis would therefore be considered unethical and are unlikely to be performed. Anti-tuberculous treatment regimens containing rifabutin or quinolones are less effective, compared with

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conventional regimens but may be used in cases where rifampicin has caused problems with drug interaction.

Regimens containing thiacetazone may be less effective at producing negative sputum cultures compared with conventional regimens and may have more adverse effects, including fatal mucocutaneous reactions. [2], [14]

Mother to Child Transmission

“Over 2 million children are thought to be living with HIV/AIDS worldwide, of whom over 80% live in sub-Saharan Africa.”

- Without antiviral treatment, the risk of transmission of HIV from infected mothers to their children is 15-30% during gestation or labour, and 15-20% during breast feeding.
- HIV-1 infection accounts for most infections as HIV-2 is rarely transmitted from mother to child.
- Transmission is more likely in young mothers and those with a high viral load or advanced disease, other sexually transmitted diseases, or obstetric events increasing the risk of bleeding.
- Between 15-25% of infected infants develop AIDS or die in the first year of life. [2]
- Antiretroviral drugs (zidovudine, nevirapine and lamivudine) reduce the risk of transmission if given to the mother during pregnancy or labour, or to the baby immediately after birth.
- Longer courses of antiretroviral treatment may be more effective than shorter courses but studies have contradicted each other.
- It is not yet clear which antiretroviral drug regimen is the best at reducing transmission rates.
- Avoiding breast feeding reduces transmission of HIV where there is access to clean water and health education.
- The risks of spreading infection through breastfeeding have to be balanced against the benefits of breastfeeding, in reducing risks of infant morbidity and improving survival, in countries with high infant mortality.

Elective caesarean section at 38 weeks may reduce HIV transmission to infants compared with vaginal delivery, but increases the risks of postpartum morbidity due to surgery.

It is not yet known whether immunotherapy with HIV hyperimmune globulin or immunoglobulin without HIV antibody, or vaginal microbicides, can reduce HIV transmission.

Vitamin A has not been shown to reduce HIV transmission or infant mortality when given as supplements to infected mothers during pregnancy or labour,

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but more research is being done to clarify this. [2], [13]

Specialist Care

HIV Units Providing Specialist Care

Ongoing clinical care for adults with diagnosed HIV infection should be under the direction of a consultant qualified to provide such care.

Services for ongoing HIV care should include the following required provisions:-

Case management for HIV as a long-term medical condition, with a focus on self-management and enabling adherence.

Assessment and routine monitoring of HIV patients and initiation and monitoring of HAART in accordance with BHIVA guidelines and other relevant local guidelines.

Appropriate laboratory services to support access to all relevant tests recommended in BHIVA guidelines for monitoring patients on and off of HAART.

Access to health advisor/counsellor as required.

Access to peer support.

Treatment support including patient education, delivered in partnership with community or voluntary providers.

Personalised information and discussion to support and enable patients in sharing in decisions about their individual care.

Facilities for partner notification.

GU/sexual health screening and services.

Access to contraception and pre-conception care.

Clearly defined arrangements for network access to all HIV centre services including 24-hour advice.

Health promotion services.

Good links with mental health services.

Access to specialist nursing within the local area.

Specialist pharmacist support, either through local staff or via outreach from the HIV centre.

Non-clinical aspects of these services may be delivered outside clinical settings and in partnership with a range of NHS and non-NHS providers, but there must be effective overseeing and co-ordination of multi-agency work to deliver the

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various service components including clearly defined arrangements for liaison with generic and voluntary services.

HIV centres

More specialised aspects of HIV should be provided through an HIV centre, which may be on a single site or may take the form of a “virtual HIV centre” comprising of an interlinked cluster of a small number(2-4) of providers within a network. In the case of such a virtual HIV centre, the role of each individual provider should be clearly defined, in particular whether it includes:

Acute medical HIV inpatient care.

Other specialised services excluding acute medical HIV inpatient care only. The medical staff of the HIV centre (whether virtual or single-site) should include a substantive body of consultant expertise covering a range of clinical aspects of HIV, able to provide care directly and to advise and support colleagues at HIV units and other clinical services within the area. Other staff should include one or more dedicated HIV specialist pharmacists and one or more consultant or equivalent senior clinical nurses able to work across organisational boundaries and support colleagues elsewhere in the area.

Each provider of acute medical HIV inpatient care must be staffed by enough consultants qualified to provide HIV inpatient care to enable a sustainable rota for 24 hour cover. Each such provider must be located at a hospital with a full range of general medical services including Intensive Care on site.

The HIV centre consultants must have direct access to inpatient beds. Day case ambulatory facilities should also be available within the centre.

When planning HIV centres, consideration should be given to co-location with other specialised units who may be involved in ongoing management.

General practice and primary care

GPs should coordinate care for non-HIV-related conditions affecting people with HIV as for other patients, in accordance with relevant national service frameworks, standards and guidelines and wherever possible in liaison with HIV services.

HIV services should strongly advise patients to register with a GP and to inform their GP of their HIV diagnosis. Unless patients refuse consent, HIV services should keep GPs updated regarding their patient’s clinical status and medication.

2 Prognosis

Direct HIV Related Prognosis

At the present time, there is no cure for AIDS. It is usually fatal if no anti HIV treatment is provided. There are a small number of individuals who are non-progressors perhaps 2 - 3% and also slow progressors. In the U.S. most patients survive many years following diagnosis because of the availability of HAART (highly active antiretroviral therapy). HAART has dramatically increased the time from diagnosis to death, and research continues in the areas of drug treatments and vaccine development.

Unfortunately, HIV medications are not always available in the developing world, where the bulk of the epidemic is raging, due to socioeconomic reasons. Without treatment, about 50% of people infected with HIV will become ill and die from AIDS over about 10 years. A meta-analysis of 13 cohort studies from Europe and the USA looked at 12,574 treatment naive people starting HAART with a combination of at least three drugs. A lower baseline CD4 cell count and higher baseline HIV-1 viral load were associated with an increased probability of progression to AIDS or death.

Poor adherence is becoming a major factor in the survival of patients. Forgetting doses or arbitrary interruption of treatment is all too often leading to multi-drug resistance. The latter will increasingly limit the choice of available drugs leading to increasingly strange and toxic mega drug combinations.

Other independent predictors of poorer outcome were advanced age, infection through injection drug use, and a previous diagnosis of AIDS. The CD4 cell count at initiation was the dominant prognostic factor in people starting HAART. People with the most favourable prognostic factors (aged < 50 years old, not infected through injection drug use, viral load < 100,000 copies/mL, and CD4 cell count > 350 cells/ μ L on initiation of HAART) were estimated to have a 3.5% chance of progression to AIDS or death within 3 years.

People with the most unfavourable prognostic factors (aged \geq 50 years old, infected through intravenous drug use, viral load \geq 100 000 copies/mL, and CD4 cell count < 50 cells/ μ L on initiation of HAART) had an estimated 50% chance of progression to AIDS or death within 3 years.

Genetic factors have been shown to affect response to antiretroviral treatment, but were not considered in the meta-analysis. One non-systematic review was found which assessed prognosis in people in Africa.

It identified one study conducted in rural Uganda, which found similar survival rates (a median 9.8 years from the time of HIV-1 seroconversion) but found that progression to symptomatic disease was faster in Uganda than in developed countries, owing largely to the high background level of morbidity.

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The review reported that most people in hospital in Africa with HIV have the clinical features of AIDS just before they die, and many are severely immunosuppressed. The review also suggested that morbidity was similar to that in developed countries before the introduction of HAART. [2]

Liver Disease

This is becoming an increasingly important factor in prognosis and survival, and is due to various factors. HCV co-infection is the most important and is leading to an increasing number of deaths and cases of cirrhosis. HCV treatment is increasingly being employed in HIV positive individuals. Whilst occurring most commonly in drug users, HCV outbreaks are occurring through sexual transmission in HIV positive homosexual males. HBV infection also remains an important risk in unvaccinated drug users and homosexual males. Alcohol abuse is also clearly a risk for liver disease. HIV infection and its drug therapy probably also plays a part in enhancing liver damage.

Other Factors

The importance of cardiovascular disease is increasingly being recognised due to the hyperlipidaemic effects of antiretroviral drugs and the enhanced risk of Diabetes. Myocardial infarction, angina and peripheral vascular disease are occurring in unusually young age groups who all too often have a heavy smoking habit.

Patients appear also to be experiencing an increased rate of non AIDS related cancers such as lung or pancreatic cancer especially, though not invariably, if they were diagnosed late perhaps after an AIDS illness.

3 Main Disabling Effects

Care Needs

HIV infected individuals under care can typically be expected to remain generally well for a long number of years after infection. Early symptoms such as those due to minor skin conditions will not give rise to a need for attention.

Minor side effects from medication are likely to be transient or controllable. Those, who have developed one or indeed several severe AIDS illnesses, may be left with general or neurological damage, including cognitive impairment. This group is likely to require special support.

Disability furthermore may be exacerbated by more severe side effects such as cardiovascular disease, diabetes, neurological problems or lipodystrophy. Care needs may arise from features such as

- Dementia
- Neurological damage including neuropathy
- Endocrine upset:
- General debility
- Night sweats (severe)
- Altered bowel habit (severe diarrhoea)
- Muscle weakness
- Poor balance
- Psychological sequelae such as depression ,anxiety, substance abuse and alcoholism

Severe manifestations of AIDS

The need for attention and supervision will increase and may become substantial if severe manifestations ensue such as:

- Infection with opportunistic infections such as cytomegalovirus or toxoplasmosis
- Dementia
- Malignant disease

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Mobility Considerations

In advanced HIV or AIDS the ability to walk can be severely affected by a number of factors:

- Dyspnoea due to respiratory infection (PJP or TB) - though this has the potential to improve with appropriate treatment.
- Peripheral neuropathy or muscle weakness
- Severe debility
- Visual impairment can arise as a result of especially cytomegaloviral infection or brain involvement.

If significant, then this can affect the ability to get around independently.

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