STAGE 1: Primary HIV infection

This stage of infection lasts for a few weeks and is often accompanied by a short flu-like illness. In up to about 20% of people the HIV symptoms are serious enough to consult a doctor, but the diagnosis of HIV infection is frequently missed. During this stage there is a large amount of HIV in the peripheral blood and the immune system begins to respond to the virus by producing HIV antibodies and cytotoxic lymphocytes. This process is known as seroconversion. If an HIV antibody test is done before seroconversion is complete then it may not be positive.

STAGE 2: Clinically asymptomatic stage

This stage lasts for an average of ten years and, as its name suggests, is free from major symptoms, although there may be swollen glands. The level of HIV in the peripheral blood drops to very low levels but people remain infectious and HIV antibodies are detectable in the blood, so antibody tests will show a positive result. Research has shown that HIV is not dormant during this stage, but is very active in the lymph nodes. A test is available to measure the small amount of HIV that escapes the lymph nodes. This test which measures HIV RNA (HIV genetic material) is referred to as the viral load test, and it has an important role in the treatment of HIV infection.

STAGE 3: Symptomatic HIV infection

Over time the immune system becomes severely damaged by HIV. This is thought to happen for three main reasons:

- The lymph nodes and tissues become damaged or 'burnt out' because of the years of activity;
- HIV mutates and becomes more pathogenic, in other words stronger and more varied, leading to more T helper cell destruction;
- The body fails to keep up with replacing the T helper cells that are lost.

Antiretroviral treatment is usually started once an individuals CD4 count (the number of T helper cells) drops to a low level, an indication that the immune system is deteriorating. Treatment can stop HIV from damaging the immune system, therefore, HIV-infected individuals on treatment usually remain clinically asymptomatic.

However, in HIV-infected individuals not receiving treatment or on treatment that is not working, the immune system fails and symptoms develop. Initially many of the symptoms are mild, but as the immune system deteriorates the symptoms worsen.

Symptomatic HIV infection is mainly caused by the emergence of certain opportunistic infections that the immune system would normally prevent. This stage of HIV infection is often characterised by multi-system disease and infections can occur in almost all body systems.

Treatment for the specific infection is often carried out, but the underlying cause is the action of HIV as it erodes the immune system. Unless HIV itself can be slowed down the symptoms of immune suppression will continue to worsen.

STAGE 4: Progression from HIV to AIDS

As the immune system becomes more and more damaged the individual may develop increasingly severe opportunistic infections and cancers, leading eventually to an AIDS diagnosis.

A clinical criteria is used by WHO to diagnose the progression to AIDS, this differs slightly between adults and children under five. In adults and children (aged 5 or over) the progression to AIDS is diagnosed when any condition listed in clinical stage 4 is diagnosed and/or the CD4 count is less than 200 cells/mm$^3$ or a CD4 percentage less than 15. In children younger than five, an AIDS diagnosis is based on having any stage 4 condition and/or a CD4 percentage less than 20 (children aged 12-35 months) and a CD4 percentage less than 25 (children less than 12 months). The criteria for diagnosing AIDS may differ depending on individual country guidelines.

Examples of opportunistic infections and cancers

The table below shows examples of common opportunistic infections and cancers and the body systems that they occur in.

<table>
<thead>
<tr>
<th>System</th>
<th>Examples of Infection/Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory system</td>
<td>Pneumocystis jirovecii Pneumonia (PCP)</td>
</tr>
<tr>
<td></td>
<td>Tuberculosis (TB)</td>
</tr>
<tr>
<td></td>
<td>Kaposi's Sarcoma (KS)</td>
</tr>
<tr>
<td>Gastro-intestinal system</td>
<td>Cryptosporidiosis</td>
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<tr>
<td></td>
<td>Candida</td>
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<tr>
<td></td>
<td>Cytomegolavirus (CMV)</td>
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<tr>
<td></td>
<td>Isosporias</td>
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<tr>
<td>Central/peripheral Nervous system</td>
<td>Skin</td>
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<td>---------------------------------</td>
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</tr>
<tr>
<td>Kaposi's Sarcoma</td>
<td>Varicella Zoster</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Herpes simplex</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>Herpes simplex</td>
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<tr>
<td>Cryptococcosis</td>
<td>Kaposi's sarcoma</td>
</tr>
<tr>
<td>Non Hodgkin's lymphoma</td>
<td>Varicella Zoster</td>
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<tr>
<td>Varicella Zoster</td>
<td>Varicella Zoster</td>
</tr>
</tbody>
</table>

**WHO clinical staging of HIV disease in adults and adolescents (2006 revision)**

In resource-poor settings, medical facilities are sometimes poorly equipped and tests to measure CD4 count and viral load are unavailable. In this case, another method to determine whether an individual should begin treatment is used. The World Health Organisation (WHO) developed a staging system for HIV disease based on clinical symptoms, which may be used to guide medical decision making.

**Clinical Stage I:**
- Asymptomatic
- Persistent generalized lymphadenopathy

**Clinical Stage II:**
- Moderate unexplained* weight loss (under 10% of presumed or measured body weight)**
- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)
- Herpes zoster
- Angular cheilitis
- Recurrent oral ulceration
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections

**Clinical Stage III:**
- Unexplained* severe weight loss (over 10% of presumed or measured body weight)**
- Unexplained* chronic diarrhoea for longer than one month
- Unexplained* persistent fever (intermittent or constant for longer than one month)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis
- Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained* anaemia (below 8 g/dl), neutropenia (below 0.5 billion/l) and/or chronic thrombocytopenia (below 50 billion/l)

**Clinical Stage IV:**
- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month’s duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacteria infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated mycosis (extrapulmonary histoplasmosis, coccidiomyocosis)
- Recurrent septicaemia (including non-typhoidal Salmonella)
- Lymphoma (cerebral or B cell non-Hodgkin)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy