STUDY OF GENETICALLY EVALUATION OF HIV VIRUS

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INTRODUCTION

Acquired immune deficiency syndrome or acquired immunodeficiency syndrome (AIDS) is a disease of the human immune system caused by the human immunodeficiency virus (HIV).

This condition progressively reduces the effectiveness of the immune system and leaves individuals susceptible to opportunistic infections and tumors. HIV is transmitted through direct contact of a mucous membrane or the bloodstream with a bodily fluid containing HIV, such as blood, semen, vaginal fluid, preseminal fluid, and breast milk.

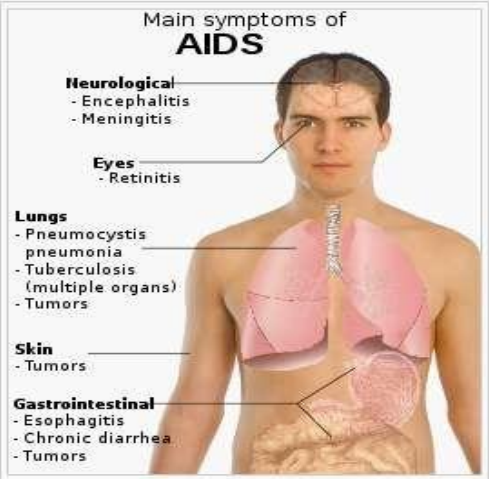
This transmission can involve anal, vaginal or oral sex, blood transfusion, contaminated hypodermic needles, exchange between mother and baby during pregnancy, childbirth, breastfeeding or other exposure to one of the above bodily fluids.

AIDS is now a pandemic. In 2007, it was estimated that 33.2 million people lived with the disease worldwide, and that AIDS had killed an estimated 2.1 million people, including 330,000 children. Over three-quarters of these deaths occurred in sub-Saharan Africa, retarding economic growth and destroying human capital.

Genetic research indicates that HIV originated in west-central Africa during the late nineteenth or early twentieth century. AIDS was first recognized by the U.S. Centers for Disease Control and Prevention in 1981 and its cause, HIV, identified in the early 1980s.

Although treatments for AIDS and HIV can slow the course of the disease, there is currently no vaccine or cure. Antiretroviral treatment reduces both the mortality and the morbidity of HIV infection, but these drugs are expensive and routine access to antiretroviral medication is not available in all countries. Due to the difficulty in treating HIV infection, preventing infection is a key aim in controlling the AIDS pandemic, with health organizations promoting safe sex and needle-exchange programmes in attempts to slow the spread of the virus.

SYMPTOMS



Main symptoms of AIDS.

The symptoms of AIDS are primarily the result of conditions that do not normally develop in individuals with healthy immune systems. Most of these conditions are infections caused by bacteria, viruses, fungi and parasites that are normally controlled by the elements of the immune system that HIV damages.

Opportunistic infections are common in people with AIDS. HIV affects nearly every organ system.

People with AIDS also have an increased risk of developing various cancers such as Kaposi's sarcoma, cervical cancer and cancers of the immune system known as lymphomas. Additionally, people with AIDS often have systemic symptoms of infection like fevers, sweats (particularly at night), swollen glands, chills, weakness, and weight loss. The specific opportunistic infections that AIDS patients develop depend in part on the prevalence of these infections in the geographic area in which the patient lives.

CAUSE

AIDS is the most severe acceleration of infection with HIV. HIV is a retrovirus that primarily infects vital organs of the human immune system such as $CD4^+$ T cells (a subset of T cells), macrophages and dendritic cells. It directly and indirectly destroys $CD4^+$ T cells.

Once HIV has killed so many $CD4^+$ T cells that there are fewer than 200 of these cells per microliter (μL) of blood, cellular immunity is lost. Acute HIV infection progresses over time to clinical latent HIV infection and then to early symptomatic HIV infection and later to AIDS, which is identified either on the basis of the amount of $CD4^+$ T cells remaining in the blood, and/or the presence of certain infections, as noted above.


Scanning electron micrograph of HIV-1, colored green, budding from a cultured lymphocyte.

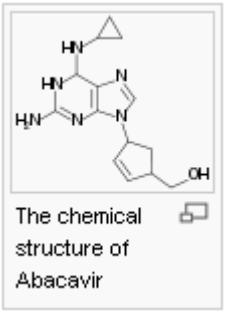
In the absence of antiretroviral therapy, the median time of progression from HIV infection to AIDS is nine to ten years, and the median survival time after developing AIDS is only 9.2 months. However, the rate of clinical disease progression varies widely between individuals, from two weeks up to 20 years.

Many factors affect the rate of progression. These include factors that influence the body's ability to defend against HIV such as the infected person's general immune function. Older people have weaker immune systems, and therefore have a greater risk of rapid disease progression than younger people.

Poor access to health care and the existence of coexisting infections such as tuberculosis also may predispose people to faster disease progression. The infected person's genetic inheritance plays an important role, and some people are resistant to certain strains of HIV. An example of this is people with the homozygous CCR5-Δ32 variation are resistant to infection with certain strains of HIV. HIV is genetically variable and exists as different strains, which cause different rates of clinical disease progression.

TREATMENT

Abacavir—a nucleoside analog reverse transcriptase inhibitor (NARTI or NRTI)



The chemical structure of Abacavir

There is currently no vaccine or cure for HIV or AIDS. The only known methods of prevention are based on avoiding exposure to the virus or, failing that, an antiretroviral treatment directly after a highly significant exposure, called post-exposure prophylaxis (PEP). PEP has a very demanding four-week schedule of dosage. It also has very unpleasant side effects including diarrhea, malaise, nausea and fatigue.

Antiviral therapy

Current treatment for HIV infection consists of highly active antiretroviral therapy, or HAART. This has been highly beneficial to many HIV-infected individuals since its introduction in 1996 when the protease inhibitor-based HAART initially became available. Current optimal HAART options consist of combinations (or "cocktails") consisting of at least three drugs belonging to at least two types, or "classes," of antiretroviral agents. Typical regimens consist of two nucleoside analogue reverse transcriptase inhibitors (NARTIs or NRTIs) plus either a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor (NNRTI). Because HIV disease progression in children is more rapid than in adults, and laboratory parameters are less predictive of risk for disease progression, particularly for young infants, treatment recommendations are more aggressive for children than for adults. In developed countries where HAART is available, doctors assess the viral load, rapidity in CD4 decline, and patient readiness while deciding when to recommend initiating treatment.

Standard goals of HAART include improvement in the patient's quality of life, reduction in complications, and reduction of HIV viremia below the limit of detection, but it does not cure the patient of HIV nor does it prevent the return, once treatment is stopped, of high blood

levels of HIV, often HAART resistant. Moreover, it would take more than the lifetime of an individual to be cleared of HIV infection using HAART. Despite this, many HIV-infected individuals have experienced remarkable improvements in their general health and quality of life, which has led to the plummeting of HIV-associated morbidity and mortality. In the absence of HAART, progression from HIV infection to AIDS occurs at a median of between nine to ten years and the median survival time after developing AIDS is only 9.2 months. HAART is thought to increase survival time by between 4 and 12 years.

Experimental and proposed treatments

It has been postulated that only a vaccine can halt the pandemic because a vaccine would possibly cost less, thus being affordable for developing countries, and would not require daily treatments. However, even after almost 30 years of research, HIV-1 remains a difficult target for a vaccine.

Research to improve current treatments includes decreasing side effects of current drugs, further simplifying drug regimens to improve adherence, and determining the best sequence of regimens to manage drug resistance. A number of studies have shown that measures to prevent opportunistic infections can be beneficial when treating patients with HIV infection or AIDS. Vaccination against hepatitis A and B is advised for patients who are not infected with these viruses and are at risk of becoming infected. Patients with substantial immunosuppression are also advised to receive prophylactic therapy for Pneumocystis jiroveci pneumonia (PCP), and many patients may benefit from prophylactic therapy for toxoplasmosis and Cryptococcus meningitis as well.

Researchers have discovered an abzyme that can destroy the protein gp120 CD4 binding site. This protein is common to all HIV variants as it is the attachment point for B lymphocytes and subsequent compromising of the immune system.

Alternative medicine

Various forms of alternative medicine have been used to treat symptoms or alter the course of the disease. Current studies indicate that alternative medicine therapies have little effect on the mortality or morbidity of the disease but may improve the quality of life of individuals with AIDS. The psychological benefits of these therapies are the most important use. Acupuncture has been used to alleviate some symptoms with no success and cannot cure the HIV infection. Several randomized clinical trials testing the effect of herbal medicines have shown that there is no evidence that these herbs have any effect on the progression of the disease but may instead produce serious side-effects.

Prognosis

Without treatment, the net median survival time after infection with HIV is estimated to be 9 to 11 years, depending on the HIV subtype, and the median survival rate after diagnosis of AIDS in resource-limited settings where treatment is not available ranges between 6 and 19 months, depending on the study. In areas where it is widely available, the development of HAART as effective therapy for HIV infection and AIDS reduced the death rate from this disease by 80% and raised the life expectancy for a newly diagnosed HIV-infected person to about 20 years.

As new treatments continue to be developed and because HIV continues to evolve resistance to treatments, estimates of survival time are likely to continue to change. Without antiretroviral therapy, death normally occurs within a year. Most patients die from opportunistic infections or malignancies associated with the progressive failure of the immune system. The rate of clinical disease progression varies widely between individuals and has been shown to be affected by many factors such as host susceptibility and immune function health care and co-infections, as well as which particular strain of the virus is involved.

Epidemiology

Estimated prevalence of HIV among young adults (15-49) per country at the end of 2005

The AIDS pandemic can also be seen as several epidemics of separate subtypes; the major factors in its spread are sexual transmission and vertical transmission from mother to child at birth and through breast milk. Despite recent, improved access to antiretroviral treatment and care in many regions of the world, the AIDS pandemic claimed an estimated 2.1 million (range 1.9–2.4 million) lives in 2007 of which an estimated 330,000 were children under 15 years. Globally, an estimated 33.2 million people lived with HIV in 2007, including 2.5 million children. An estimated 2.5 million (range 1.8–4.1 million) people were newly infected in 2007, including 420,000 children.

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