

HIV / AIDS

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Fosfolipid membrane

gp120 surface glykoprotein

gp 41 transmembrane glykoprotein

p 17M protein - matrix

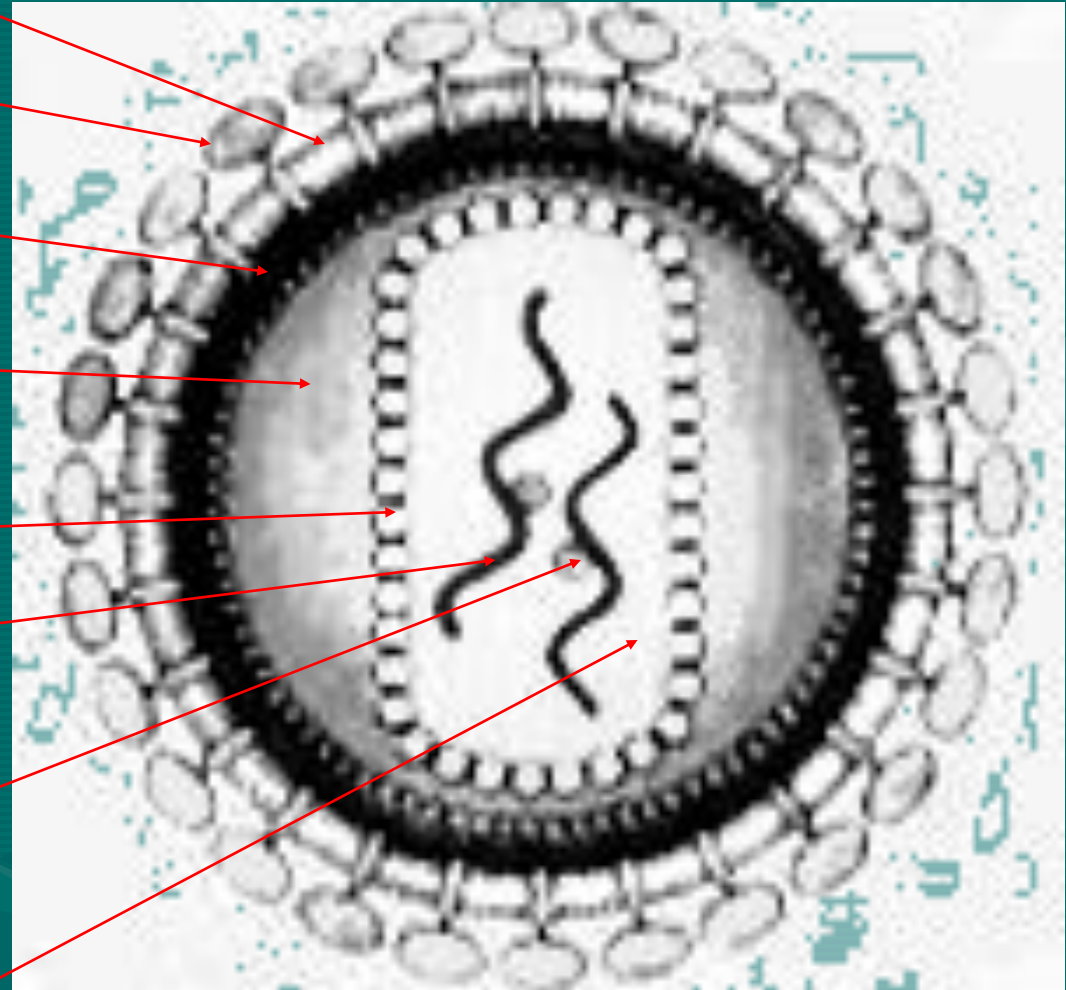
p 24 protein – nucleocapsid core

RNA genome

reverzní transkriptáza

p 7, p 9

proteiny on the nucleic acide



HIV/AIDS

Etiology:

HIV - Human Immunodeficiency Virus is classed with the **Retroviridae family, Lentivirus genus**. HIV occurs in two types: HIV - 1 and HIV - 2. Both types have similar epidemiological features, but different serological response and geographic distribution. .

The source of infection

Only infected man is the source of infection, in either the sick with manifestations of AIDS or a latent infection, (ARC - AIDS-Related Complex, PGL - Persistent Generalised Lymphadenopathy) or a symptomless carrier.

Route of transmission

Blood - borne By blood derivatives and HIV- contaminated blood.

Use of **contaminated** needles and syringes in drug administration.

Sexually-transmitted, when injury of the mucosa and bleeding occur.

Sexually transmitted Through sperma, vaginal secreta in homo and heterosexual intercourse.

From mother to child (15 to 30 %) Vertical transmission - prenatally, perinatally or possibly through the mother's milk.

Susceptibility

General.

Preventive measures:

Health education promoting a responsible approach to sex - use of condoms.

- To prevent contamination of blood tins and derivatives.
- Supporting the programme of taking/giving needles and syringes from/to intravenous drug addicts.

Virus classification

Group: Group VI (ssRNART)

Family: *Retroviridae*

Genus: *Lentivirus*

Species: *Human immunodeficiency virus 1*

Species: *Human immunodeficiency virus 2*

Diagram of HIV is different in structure from other retroviruses.

It is about 120 nm in diameter (120 billionths of a meter; around 60 times smaller than a red blood cell) and roughly spherical.

It is composed:

of **two copies** of positive single-stranded RNA that codes for the virus's nine genes enclosed by a conical capsid composed of 2,000 copies of the viral protein p24.

The single-stranded RNA is tightly bound to nucleocapsid proteins, p7 and enzymes needed for the development of the virion such as:

- **reverse transcriptase**, * **proteases**, * **ribonuclease** and * **integrase**.

A matrix composed of the viral protein p17 surrounds the capsid ensuring the integrity of the virion particle.

This is, in turn, surrounded by the viral envelope which is composed of two layers of fatty molecules called phospholipids taken from the membrane of a human cell when a newly formed virus particle buds from the cell.

Embedded in the viral envelope are proteins from the host cell and about 70 copies of a complex HIV protein that protrudes through the surface of the virus particle.

This protein, known as Env, consists of a cap made of three molecules called glycoprotein (gp) 120, and a stem consisting of three gp41 molecules that anchor the structure into the viral envelope.

This glycoprotein complex enables the virus to **attach to and fuse with target cells to initiate the infectious cycle.**

Both these surface proteins, especially gp120, have been considered as targets of future treatments or vaccines against HIV.

Of the nine genes that are encoded within the RNA genome, three of these genes, gag, pol, and env, contain information needed to make the structural proteins for new virus particles. env, for example, codes for a protein called gp160 that is broken down by a viral enzyme to form gp120 and gp41.

The six remaining genes, **tat**, **rev**, **nef**, **vif**, **vpr**, and **vpu** (or **vpx** in the case of HIV-2), are regulatory genes for proteins that control the ability of HIV to infect cells, **produce new copies of virus (replicate)**, or **cause disease**.

HIV primarily infects vital cells in the human immune system such as helper T cells (specifically CD4+ T cells), macrophages and dendritic cells.

HIV infection leads to low levels of CD4+ T cells through three main mechanisms:

- **firstly**, direct viral killing of infected cells;
- **secondly**, increased rates of apoptosis in infected cells;
- **and thirdly**, killing of infected CD4+ T cells by CD8 cytotoxic lymphocytes that recognize infected cells.

When CD4+ T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections.

The AIDS epidemic was discovered June 5, 1981, when the U.S. Centers for Disease Control and Prevention (CDC) reported a cluster of *Pneumocystis carinii pneumonia* (now classified as *Pneumocystis jiroveci pneumonia*) in five homosexual men in Los Angeles.

The disease was originally dubbed **GRID**, or Gay-Related Immune Deficiency, but health authorities soon realized that nearly half of the people identified with the syndrome were not homosexual men.

In 1982, the CDC introduced the term AIDS to describe the newly recognized syndrome, though it was still casually referred to as GRID.

In 1983, scientists led by Luc Montagnier at the Pasteur Institute in France first discovered the virus that causes AIDS. They called it lymphadenopathy-associated virus (LAV).

A year later a team led by Robert Gallo of the United States confirmed the discovery of the virus, but they renamed it human T lymphotropic virus type III (HTLV-III).

The dual discovery led to considerable scientific disagreement, and it was not until President Mitterrand of France and President Reagan of the USA met that the major issues were resolved.

In 1986, both the French and the U.S. names for the virus itself were dropped in favour of the new term, human immunodeficiency virus (HIV).

In 2005 alone, AIDS claimed an estimated 2.4–3.3 million lives, of which more than 570,000 were children.

It is estimated that about 0.6% of the world's living population is infected with HIV.

A third of these deaths are occurring in sub-Saharan Africa, retarding economic growth and increasing poverty.

According to current estimates, HIV is set to infect 90 million people in Africa, resulting in a minimum estimate of 18 million orphans.

Subtypes:

HIV 1 - group "M" (major) – subtypes A, B, C, D, E, F, G, H, I, ...
(expected other)

Subtypes:

A – West and Middle Africa

B – Europe, North and sud America, Thailand

C – Sud Africa, Indie

D – Middle Africa

E – Middle Africa, Thailand, Indie

F – Brazilie, Romania, Zair

G – Middle Africa

H – Gabun, Zair

I – Africa

Subtypes:

- group „O“ (outlier) – subtyp O, ...
 - (expected other)
 - O – Gabun,
- group „N“ (novel)
 - N – Africa

AIDS – Acquired ImmunoDeficiency Syndrome

SIDA – Syndrome d'ImmunoDeficiencie Acquise

SPID – Syndrom Priobretěného ImunoDeficita

HIV - Human Immunodeficiency Virus

Human immunodeficiency virus (HIV) is a retrovirus that causes acquired immunodeficiency syndrome (AIDS) = a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections.

Previous names for the virus include

human T-lymphotropic virus-III (HTLV-III),
lymphadenopathy-associated virus (LAV),
and AIDS-associated retrovirus (ARV)

HIV infection in humans is now pandemic.

As of January 2006, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) estimate that

AIDS has killed more than 25 million people since it was first recognized on December 1, 1981, making it one of the most destructive pandemics in recorded history.

Antiretroviral treatment reduces both the mortality and the morbidity of HIV infection, but routine access to antiretroviral medication is not available in all countries.

If untreated, eventually most HIV-infected individuals develop AIDS (Acquired Immunodeficiency Syndrome) and die; however about one in ten remain healthy for many years, with no noticeable symptoms.

Treatment with anti-retrovirals, where available, increases the life expectancy of people infected with HIV. It is hoped that current and future treatments may allow HIV-infected individuals to achieve a life expectancy approaching that of the general public

- Upon entry of the target cell, the viral RNA genome is converted to double-stranded DNA by a virally encoded reverse transcriptase that is present in the virus particle.
- This viral DNA is then integrated into the cellular DNA by a virally encoded integrase so that the genome can be transcribed.
- Once the virus has infected the cell, two pathways are possible:
 - either the virus becomes latent and the infected cell continues to function,
 - or the virus becomes active and replicates, and a large number of virus particles are liberated that can then infect other cells.

Two species of HIV infect humans: HIV-1 and HIV-2.

HIV-1 is thought to have originated in southern Cameroon after jumping from wild chimpanzees (*Pan troglodytes troglodytes*) to humans during the twentieth century.

HIV-2 may have originated from the Sooty Mangabey (*Cercocebus atys*), an Old World monkey of Guinea-Bissau, Gabon, and Cameroon.

HIV-1 is more virulent. It is easily transmitted and is the cause of the majority of HIV infections globally.

HIV-2 is less transmittable and is largely confined to West Africa. HIV-1 is the virus that was initially discovered and termed LAV.

- Three of the earliest known instances of HIV-1 infection are as follows:
- A plasma sample taken in 1959 from an adult male living in what is now the Democratic Republic of Congo.
- HIV found in tissue samples from a 15-year-old African-American teenager who died in St. Louis in 1969.
- HIV found in tissue samples from a Norwegian sailor who died around 1976.

- Although a variety of theories exist explaining the transfer of HIV to humans, no single hypothesis is unanimously accepted, and the topic remains controversial.
- The most widely accepted theory is so called 'Hunter' Theory according to which transference **from chimp to human most likely occurred when a human was bitten by a chimp or was cut while butchering one, and the human became infected.**
- The London Times published an article in 1987 stating that WHO suspected some kind of connection with its vaccine program and AIDS-epidemic. The story was almost entirely based on statements given by one unnamed WHO advisor. The theory was supported only by weak circumstantial evidence and is now disproven by unraveling the genetic code of the virus and finding out that the virus dates back to the 1930s.

- Transmission

Exposure Route Estimated infections per 10,000 exposures to an infected source:

- Blood Transfusion 9,000
- Childbirth 2,500
- Needle-sharing injection drug use 67
- Receptive anal intercourse* 50
- Percutaneous needle stick 30
- Receptive penile-vaginal intercourse* 10
- Insertive anal intercourse* 6.5
- Insertive penile-vaginal intercourse* 5
- Receptive fellatio* 1
- Insertive fellatio* 0.5

* assuming no condom use

- Since the beginning of the pandemic, three main transmission routes for HIV have been identified:
- Sexual route. The majority of HIV infections are acquired through unprotected sexual relations. Sexual transmission can occur when infected sexual secretions of one partner come into contact with the rectal, genital or oral mucous membranes of another.

Blood or blood product route. This transmission route can account for infections in intravenous drug users, hemophiliacs and recipients of blood transfusions (though most transfusions are checked for HIV in the developed world) and blood products. It is also of concern for persons receiving medical care in regions where there is prevalent substandard hygiene in the use of injection equipment, such as the reuse of needles in Third World countries. HIV can also be spread through the sharing of leaches.

Health care workers such as nurses, laboratory workers, and doctors, have also been infected, although this occurs more rarely.

People who give and receive tattoos, piercings and scarification procedures can also be at risk of infection.

Mother-to-child transmission (MTCT). The transmission of the virus from the mother to the child can occur in utero during the last weeks of pregnancy and at childbirth. In the absence of treatment, the transmission rate between the mother and child is 25%. However, where drug treatment and Caesarian section are available, this can be reduced to 1%. Breast feeding also presents a risk of infection for the baby.

- HIV-2 is transmitted much less frequently by the MTCT and sexual route than HIV-1.

HIV has been found at low concentrations in the:
saliva,
tears and
urine of infected individuals,
but there are no recorded cases of infection by
these secretions and the potential risk of
transmission is negligible.

The use of physical barriers such as the latex condom is widely advocated to reduce the sexual transmission of HIV.

Spermicide, when used alone or with vaginal contraceptives like a diaphragm, actually increases the male to female transmission rate due to inflammation of the vagina;

it should not be considered a barrier to infection.

Research is clarifying the relationship between male circumcision and HIV in differing social and cultural contexts, however critics point out that any correlation between circumcision and HIV is likely to come from cultural factors (which govern not only whether someone is circumcised, but also their sexual practices and beliefs)

Even though male circumcision may lead to a reduction of infection risk in heterosexual men by up to 60%, UNAIDS believes that it is premature to recommend male circumcision as part of HIV prevention programs.

Trials, in which some uncircumcised men were randomly assigned to be circumcised in presumably sterile conditions and others were not circumcised, conducted in Kenya and Uganda found that men who were uncircumcised were twice as likely to contract the human immunodeficiency virus (HIV) compared with circumcised counterparts.

South African medical experts are concerned that the repeated use of unsterilized blades in the ritual circumcision of adolescent boys may be spreading HIV.

Kaposi's sarcoma in a 20-year old man who had AIDS.



New“ strategy under N. Ramjee, 2006

A, B, C, D, E, F, G, H, (I)

A – abstinence

B – be faithful – být si vzájemně věrný, buď věrný

C – kondom (mužský kondom)

C = také femidom neboli kondom

D – diafragma (poševní) with spermicid

D – dental dam – dentální rouška

E – exposure prophylaxis

F – **female initiated microbicides**

G – **genital tract infections** – therapy

H – **HSV 2 suppression** Herpes simplex 2

I – „**imunity induced by vaccine**“ ?????