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Research on AIDS

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UNITED AGAINST AIDS

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What is AIDS

Acquired immune deficiency syndrome or acquired immunodeficiency syndrome (AIDS or Aids) is a collection of symptoms and infections resulting from the specific damage to the immune system caused by the human immunodeficiency virus (HIV) in humans, and similar viruses in other species (SIV, FIV, etc.).

The late stage of the condition leaves individuals susceptible to opportunistic infections and tumors.

Although treatments for AIDS and HIV exist to decelerate the virus' progression, there is currently no known cure.

HIV, et al., are 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.

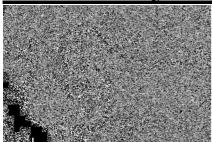
This transmission can come in the form of anal, vaginal or oral sex, blood transfusion, contaminated hypodermic needles, exchange between mother and baby during pregnancy, childbirth, or breastfeeding, or other exposure to one of the above bodily fluids. Most researchers believe that HIV originated in sub-Saharan Africa during the twentieth century; it is now a pandemic, with an estimated 33.2 million people now living with the disease worldwide.

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 June 5, 1981, making it one of the most destructive epidemics in recorded history. In 2005 alone, AIDS claimed an estimated 2.4–3.3 million lives, of which more than 570,000 were children.

A third of these deaths are occurring in sub-Saharan Africa, retarding economic growth and destroying human capital. Antiretroviral treatment reduces both the mortality and the morbidity of HIV infection, but routine access to antiretroviral medication is not available in all countries.

HIV/AIDS stigma is more severe than that associated with other life-threatening conditions and extends beyond the disease itself to providers and even volunteers involved with the care of people living with HIV.

Infection by HIV



Scanning electron micrograph of HIV-1 budding from cultured lymphocyte.

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.

CD4⁺ T cells are required for the proper functioning of the immune system. When HIV kills $CD4^+$ T cells so that there are fewer than 200 $CD4^+$ T cells per micro-liter (µL) of blood, cellular immunity is lost.

In some countries, such as the United States, this leads to a diagnosis of AIDS.

In other jurisdictions, such as in Canada, AIDS is only diagnosed when a person infected with HIV is diagnosed with one or more of several AIDS-related opportunistic infections or cancers.

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 in the blood, and/or the presence of certain infections, as noted above.

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 CCR5- Δ 32 mutation 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.

The use of highly active antiretroviral therapy prolongs both the median time of progression to AIDS and the median survival time.

Diagnosis

Since June 5, 1981, many definitions have been developed for epidemiological surveillance such as the Bangui definition and the 1994 expanded World Health Organization AIDS case definition.

However, clinical staging of patients was not an intended use for these systems as they are neither sensitive, nor specific. In developing countries, the World Health Organization staging system for HIV infection and disease, using clinical and laboratory data, is used and in developed countries, the Centers for Disease Control (CDC) Classification System is used.

WHO disease staging system for HIV infection and disease

In 1990, the World Health Organization (WHO) grouped these infections and conditions together by introducing a staging system for patients infected with HIV-1.

An update took place in September 2005.

Most of these conditions are opportunistic infections that are easily treatable in healthy people.

- Stage I: HIV infection is asymptomatic and not categorized as AIDS
- Stage II: includes minor mucocutaneous manifestations and recurrent upper respiratory tract infections
- Stage III: includes unexplained chronic diarrhea for longer than a month, severe bacterial infections and pulmonary tuberculosis
- Stage IV: includes toxoplasmosis of the brain, candidiasis of the esophagus, trachea, bronchi or lungs and Kaposi's sarcoma; these diseases are indicators of AIDS.

CDC classification system for HIV infection

In the beginning, the Centers for Disease Control and Prevention (CDC) did not have an official name for the disease, often referring to it by way of the diseases that were

associated with it, for example, lymphadenopathy, the disease after which the discoverers of HIV originally named the virus.

They also used *Kaposi's Sarcoma and Opportunistic Infections*, the name by which a task force had been set up in 1981.

In the general press, the term *GRID*, which stood for Gay-Related Immune Deficiency, had been coined.

However, after determining that AIDS was not isolated to the homosexual community, the term GRID became misleading and *AIDS* was introduced at a meeting in July 1982.

By September 1982 the CDC started using the name AIDS, and properly defined the illness.

In 1993, the CDC expanded their definition of AIDS to include all HIV positive people with a CD4⁺ T cell count below 200 per μ L of blood or 14% of all lymphocytes.

The majority of new AIDS cases in developed countries use either this definition or the pre-1993 CDC definition.

The AIDS diagnosis still stands even if, after treatment, the CD4⁺ T cell count rises to above 200 per μ L of blood or other AIDS-defining illnesses are cured.

HIV test

Many people are unaware that they are infected with HIV.

Less than 1% of the sexually active urban population in Africa has been tested, and this proportion is even lower in rural populations.

Furthermore, only 0.5% of pregnant women attending urban health facilities are counseled, tested or receive their test results.

Again, this proportion is even lower in rural health facilities.

Therefore, donor blood and blood products used in medicine and medical research are screened for HIV.

Typical HIV tests, including the HIV enzyme immunoassay and the Western blot assay, detect HIV antibodies in serum, plasma, oral fluid, dried blood spot or urine of patients.

However, the window period (the time between initial infection and the development of detectable antibodies against the infection) can vary.

This is why it can take 3–6 months to seroconvert and test positive.

Commercially available tests to detect other HIV antigens, HIV-RNA, and HIV-DNA in order to detect HIV infection prior to the development of detectable antibodies are available.

For the diagnosis of HIV infection these assays are not specifically approved, but are nonetheless routinely used in developed countries.

Symptoms and complications of HIV

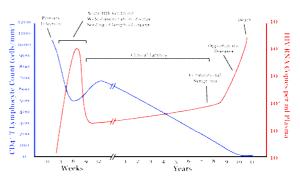
A generalized graph of the relationship between HIV copies (viral load) and CD4 counts

over the average course of untreated HIV infection; any particular individual's disease course may vary considerably.

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.

After the diagnosis of AIDS is made, the current average survival time with antiretroviral therapy (as of 2005) is estimated to be more than 5 years, but because 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 factors relating to the viral strain.

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.

Major pulmonary illnesses

X-ray of Pneumocystis jirovecii caused pneumonia.

There is increased white (opacity) in the lower lungs on both sides, characteristic of *Pneumocystis* pneumonia

<u>Pneumocystis pneumonia</u> (originally known as *Pneumocystis carinii* pneumonia, and still abbreviated as PCP, which now stands for **P**neumo**c**ystis **p**neumonia) is relatively rare in healthy, immunocompetent people, but common among HIV-infected individuals. It is caused by *Pneumocystis jirovecii*. Before the advent of effective diagnosis, treatment and routine prophylaxis in Western



countries, it was a common immediate cause of death. In developing countries, it is still one of the first indications of AIDS in untested individuals, although it does not generally occur unless the CD4 count is less than 200 per μ L.

Tuberculosis (TB) is unique among infections associated with HIV because it is transmissible to immunocompetent people via the respiratory route, is easily treatable once identified, may occur in early-stage HIV disease, and is preventable with drug therapy. However, multidrug resistance is a potentially serious problem. Even though its incidence has declined because of the use of directly observed therapy and other improved practices in Western countries, this is not the case in developing countries where HIV is most prevalent. In early-stage HIV infection (CD4 count >300 cells per µL), TB typically presents as a pulmonary disease. In advanced HIV infection, TB often presents atypically with extrapulmonary (systemic) disease a common feature. Symptoms are usually constitutional and are not localized to one particular site, often affecting bone marrow, bone, urinary and gastrointestinal tracts, liver, regional lymph nodes, and the central nervous system. Alternatively, symptoms may relate more to the site of extrapulmonary involvement.

Major gastro-intestinal illnesses

- <u>Esophagitis</u> is an inflammation of the lining of the lower end of the esophagus (gullet or swallowing tube leading to the stomach). In HIV infected individuals, this is normally due to fungal (candidiasis) or viral (herpes simplex-1 or cytomegalovirus) infections. In rare cases, it could be due to mycobacteria.
- <u>Unexplained chronic diarrhea</u> in HIV infection is due to many possible causes, including common bacterial (*Salmonella*, *Shigella*, *Listeria*, *Campylobacter*, or *Escherichia coli*) and parasitic infections; and uncommon opportunistic infections such

as cryptosporidiosis, microsporidiosis, *Mycobacterium avium* complex (MAC) and cytomegalovirus (CMV) colitis. In some cases, diarrhea may be a side effect of several drugs used to treat HIV, or it may simply accompany HIV infection, particularly during primary HIV infection. It may also be a side effect of antibiotics used to treat bacterial causes of diarrhea (common for *Clostridium difficile*). In the later stages of HIV infection, diarrhea is thought to be a reflection of changes in the way the intestinal tract absorbs nutrients, and may be an important component of HIV-related wasting.

Major neurological illnesses

- <u>Toxoplasmosis</u> is a disease caused by the single-celled parasite called *Toxoplasma gondii*; it usually infects the brain causing toxoplasma encephalitis but it can infect and cause disease in the eyes and lungs.
- <u>Progressive multifocal leukoencephalopathy</u> (PML) is a demyelinating disease, in which the gradual destruction of the myelin sheath covering the axons of nerve cells impairs the transmission of nerve impulses. It is caused by a virus called JC virus which occurs in 70% of the population in latent form, causing disease only when the immune system has been severely weakened, as is the case for AIDS patients. It progresses rapidly, usually causing death within months of diagnosis.
- <u>AIDS dementia complex</u> (ADC) is a metabolic encephalopathy induced by HIV infection and fueled by immune activation of HIV infected brain macrophages and microglia which secrete neurotoxins of both host and viral origin. Specific neurological impairments are manifested by cognitive, behavioral, and motor abnormalities that occur after years of HIV infection and is associated with low CD4⁺ T cell levels and high plasma viral loads. Prevalence is 10–20% in Western countries but only 1–2% of HIV infections in India. This difference is possibly due to the HIV subtype in India.
- <u>Cryptococcal meningitis</u> is an infection of the meninx (the membrane covering the brain and spinal cord) by the fungus *Cryptococcus neoformans*. It can cause fevers, headache, fatigue, nausea, and vomiting. Patients may also develop seizures and confusion; left untreated, it can be lethal.

Major HIV-associated malignancies



Kaposi's sarcoma

Patients with HIV infection have substantially increased incidence of several malignant cancers. This is primarily due to co-infection with an oncogenic DNA virus, especially Epstein-Barr virus (EBV), Kaposi's sarcoma-associated herpesvirus (KSHV), and human

papillomavirus (HPV). The following confer a diagnosis of AIDS when they occur in an HIV-infected person.

- Kaposi's sarcoma (KS) is the most common tumor in HIV-infected patients. The appearance of this tumor in young homosexual men in 1981 was one of the first signals of the AIDS epidemic. Caused by a gammaherpes virus called Kaposi's sarcoma-associated herpes virus (KSHV), it often appears as purplish nodules on the skin, but can affect other organs, especially the mouth, gastrointestinal tract, and lungs.
- High-grade B cell lymphomas such as Burkitt's lymphoma, Burkitt's-like lymphoma, diffuse large B-cell lymphoma (DLBCL), and primary central nervous system lymphoma present more often in HIV-infected patients. These particular cancers often foreshadow a poor prognosis. In some cases these lymphomas are AIDS-defining. Epstein-Barr virus (EBV) or KSHV cause many of these lymphomas.
- Cervical cancer in HIV-infected women is considered AIDS-defining. It is caused by human papillomavirus (HPV).

In addition to the AIDS-defining tumors listed above, HIV-infected patients are at increased risk of certain other tumors, such as Hodgkin's disease and anal and rectal carcinomas. However, the incidence of many common tumors, such as breast cancer or colon cancer, does not increase in HIV-infected patients. In areas where HAART is extensively used to treat AIDS, the incidence of many AIDS-related malignancies has decreased, but at the same time malignant cancers overall have become the most common cause of death of HIV-infected patients.

Other opportunistic infections

AIDS patients often develop opportunistic infections that present with non-specific symptoms, especially low-grade fevers and weight loss. These include infection with *Mycobacterium avium-intracellulare* and cytomegalovirus (CMV). CMV can cause colitis, as described above, and CMV retinitis can cause blindness. Penicilliosis due to *Penicillium marneffei* is now the third most common opportunistic infection (after extrapulmonary tuberculosis and cryptococcosis) in HIV-positive individuals within the endemic area of Southeast Asia.

Transmission and prevention of HIV

The three main transmission routes of HIV are sexual contact, exposure to infected body fluids or tissues, and from mother to fetus or child during perinatal period. It is possible to find HIV in the saliva, tears, and urine of infected individuals, but there are no recorded cases of infection by these secretions, and the risk of infection is negligible.

Sexual contact

The majority of HIV infections are acquired through unprotected sexual relations between partners, one of whom has HIV. Heterosexual intercourse is the primary mode of HIV infection worldwide.

Sexual transmission occurs with the contact between sexual secretions of one partner with the rectal, genital or oral mucous membranes of another.

Unprotected receptive sexual acts are riskier than unprotected insertive sexual acts, with the risk for transmitting HIV from an infected partner to an uninfected partner through unprotected anal intercourse greater than the risk for transmission through vaginal intercourse or oral sex. Oral sex is not without its risks as HIV is transmissible through both insertive and receptive oral sex.

The risk of HIV transmission from exposure to saliva is considerably smaller than the risk from exposure to semen; contrary to popular belief, one would have to swallow gallons of saliva from a carrier to run a significant risk of becoming infected.

Approximately 30% of women in ten countries representing "diverse cultural, geographical and urban/rural settings" report that their first sexual experience was forced or coerced, making sexual violence a key driver of the HIV/AIDS pandemic.

Sexual assault greatly increases the risk of HIV transmission as protection is rarely employed and physical trauma to the vaginal cavity frequently occurs which facilitates the transmission of HIV.

<u>Sexually transmitted infections</u> (STI) increase the risk of HIV transmission and infection because they cause the disruption of the normal epithelial barrier by genital ulceration and/or microulceration; and by accumulation of pools of HIV-susceptible or HIV-infected cells (lymphocytes and macrophages) in semen and vaginal secretions. Epidemiological studies from sub-Saharan Africa, Europe and North America have suggested that there is approximately a four times greater risk of becoming infected with HIV in the presence of a genital ulcer such as those caused by syphilis and/or chancroid. There is also a significant though lesser increased risk in the presence of STIs such as gonorrhea, Chlamydial

infection and trichomoniasis which cause local accumulations of lymphocytes and macrophages.

Transmission of HIV depends on the infectiousness of the index case and the susceptibility of the uninfected partner. Infectivity seems to vary during the course of illness and is not constant between individuals.

An undetectable plasma viral load does not necessarily indicate a low viral load in the seminal liquid or genital secretions. Each 10-fold increment of blood plasma HIV RNA is associated with an 81% increased rate of HIV transmission.

Women are more susceptible to HIV-1 infection due to hormonal changes, vaginal microbial ecology and physiology, and a higher prevalence of sexually transmitted diseases. People who are infected with HIV can still be infected by other, more virulent strains.

During a sexual act, only male or female condoms can reduce the chances of infection with HIV and other STDs and the chances of becoming pregnant.

The best evidence to date indicates that typical condom use reduces the risk of heterosexual HIV transmission by approximately 80% over the long-term, though the benefit is likely to be higher if condoms are used correctly on every occasion.

The effective use of condoms and screening of blood transfusion in North America, Western and Central Europe is credited with contributing to the low rates of AIDS in these regions. Promoting condom use, however, has often proved controversial and difficult.

Many religious groups, most noticeably the Roman Catholic Church, have opposed the use of condoms on religious grounds, and have sometimes seen condom promotion as an affront to the promotion of marriage, monogamy and sexual morality. Defenders of the Catholic Church's role in AIDS and general STD prevention state that, while they may be against the use of contraception, they are strong advocates of abstinence outside marriage.

This attitude is also found among some health care providers and policy makers in sub-Saharan African nations, where HIV and AIDS prevalence is extremely high.

They also believe that the distribution and promotion of condoms is tantamount to promoting sex amongst the youth and sending the wrong message to uninfected individuals.

However, no evidence has been produced that promotion of condom use increases sexual promiscuity, and abstinence-only programs have been unsuccessful in the United States both in changing sexual behavior and in reducing HIV transmission.

Evaluations of several abstinence-only programs in the US showed a negative impact on the willingness of youths to use contraceptives, due to the emphasis on contraceptives' failure rates.

The male latex condom, if used correctly without oil-based lubricants, is the single most effective available technology to reduce the sexual transmission of HIV and other sexually transmitted infections. Manufacturers recommend that oil-based lubricants such as petroleum jelly, butter, and lard not be used with latex condoms, because they dissolve the latex, making the condoms porous. If necessary, manufacturers recommend using water-based lubricants. Oil-based lubricants can however be used with polyurethane condoms.

Latex condoms degrade over time, making them porous, which is why condoms have expiration dates.

In Europe and the United States, condoms have to conform to European (EC 600) or American (D3492) standards to be considered protective against HIV transmission.

The female condom is an alternative to the male condom and is made from polyurethane, which allows it to be used in the presence of oil-based lubricants. They are larger than male condoms and have a stiffened ring-shaped opening, and are designed to be inserted into the vagina.

The female condom contains an inner ring, which keeps the condom in place inside the vagina — inserting the female condom requires squeezing this ring. However, at present availability of female condoms is very low and the price remains prohibitive for many women. Preliminary studies suggest that, where female condoms are available, overall protected sexual acts increase relative to unprotected sexual acts, making them an important HIV prevention strategy.

With consistent and correct use of condoms, there is a very low risk of HIV infection.

Studies on couples where one partner is infected show that with consistent condom use,

HIV infection rates for the uninfected partner are below 1% per year.

The United States government and health organizations both endorse the *ABC Approach* to lower the risk of acquiring AIDS during sex:

Abstinence or delay of sexual activity, especially for youth,

Being faithful, especially for those in committed relationships,

Condom use, for those who engage in risky behavior.

This approach has been very successful in Uganda, where HIV prevalence has decreased from 15% to 5%. However, more has been done than just this.

However, criticism of the ABC approach is widespread because a faithful partner of an unfaithful partner is at risk of contracting HIV and that discrimination against women and girls is so great that they are without voice in almost every area of their lives.

Other programs and initiatives promote condom use more heavily. Condom use is an integral part of the *CNN Approach*. This is:

Condom use, for those who engage in risky behavior,

Needles, use clean ones,

Negotiating skills; negotiating safer sex with a partner and empowering women to make smart choices.

In December 2006, the last of three large, randomized trials confirmed that male circumcision lowers the risk of HIV infection among heterosexual African men by around 50%. It is expected that this intervention will be actively promoted in many of the countries worst affected by HIV, although doing so will involve confronting a number of practical, cultural and attitudinal issues. Some experts fear that a lower perception of vulnerability among circumcised men may result in more sexual risk-taking behavior, thus negating its preventive effects.

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

Exposure to infected body fluids

This transmission route is particularly relevant to intravenous drug users, hemophiliacs and recipients of blood transfusions and blood products. Sharing and reusing syringes contaminated with HIV-infected blood represents a major risk for infection with not only HIV, but also hepatitis B and hepatitis C.

Needle sharing is the cause of one third of all new HIV-infections and 50% of hepatitis C infections in North America, China, and Eastern Europe.

The risk of being infected with HIV from a single prick with a needle that has been used on an HIV-infected person is thought to be about 1 in 150.

Post-exposure prophylaxis with anti-HIV drugs can further reduce that small risk.

Health care workers (nurses, laboratory workers, doctors etc) are also concerned, although more rarely.

This route can affect people who give and receive tattoos and piercings.

Universal precautions are frequently not followed in both sub-Saharan Africa and much of Asia because of both a shortage of supplies and inadequate training.

The WHO estimates that approximately 2.5% of all HIV infections in sub-Saharan Africa are transmitted through unsafe healthcare injections.

Because of this, the United Nations General Assembly, supported by universal medical opinion on the matter, has urged the nations of the world to implement universal precautions to prevent HIV transmission in health care settings.

Drug abuse has an additional effect of an increased tendency to engage in unprotected sexual intercourse.

The risk of transmitting HIV to blood transfusion recipients is extremely low in developed countries where improved donor selection and HIV screening is performed.

However, according to the WHO, the overwhelming majority of the world's population does not have access to safe blood and "between 5% and 10% of HIV infections worldwide are transmitted through the transfusion of infected blood and blood products".

Medical workers who follow universal precautions or body-substance isolation, such as wearing latex gloves when giving injections and washing the hands frequently, can help prevent infection by HIV.

All AIDS-prevention organizations advise drug-users not to share needles and other material required to prepare and take drugs (including syringes, cotton balls, the spoons, water for diluting the drug, straws, crack pipes, etc).

It is important that people use new or properly sterilized needles for each injection. Information on cleaning needles using bleach is available from health care and addiction professionals and from needle exchanges.

In some developed countries, clean needles are available free in some cities, at needle exchanges or safe injection sites.

Additionally, many nations have decriminalized needle possession and made it possible to buy injection equipment from pharmacists without a prescription.

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 to the child during pregnancy, labor and delivery is 25%.

However, when the mother has access to antiretroviral therapy and gives birth by caesarean section, the rate of transmission is just 1%.

A number of factors influence the risk of infection, particularly the viral load of the mother at birth (the higher the viral load, the higher the risk). Breastfeeding increases the risk of transmission by 10–15%. This risk depends on clinical factors and may vary according to the pattern and duration of breast-feeding.

Studies have shown that antiretroviral drugs, caesarean delivery and formula feeding reduce the chance of transmission of HIV from mother to child.

Current recommendations state that when replacement feeding is acceptable, feasible, affordable, sustainable and safe, HIV-infected mothers should avoid breast-feeding their infant. However, if this is not the case, exclusive breast-feeding is recommended during the first months of life and discontinued as soon as possible.

In 2005, around 700,000 children under 15 contracted HIV, mainly through MTCT, with 630,000 of these infections occurring in Africa.

Of the children currently living with HIV, 2 million (almost 90%) live in sub-Saharan Africa.

Prevention strategies are well known in developed countries, however, recent epidemiological and behavioral studies in Europe and North America have suggested that a substantial minority of young people continue to engage in high-risk practices and that despite HIV/AIDS knowledge, young people underestimate their own risk of becoming infected with HIV.

However, transmission of HIV between intravenous drug users has clearly decreased, and HIV transmission by blood transfusion has become quite rare in developed countries.

Treatment



Abacavir - a nucleoside analog reverse transcriptase inhibitors (NARTIs or NRTIs)

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.

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 anti-retroviral 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.

HAART allows the stabilization of the patient's symptoms and viremia, but it neither cures the patient of HIV, nor alleviates the symptoms, and high levels of HIV-1, often HAART resistant, return once treatment is stopped.

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.

This average reflects the fact that for some patients — and in many clinical cohorts this may be more than fifty percent of patients — HAART achieves far less than optimal results. This is due to a variety of reasons such as medication intolerance/side effects, prior ineffective antiretroviral therapy and infection with a drug-resistant strain of HIV. However, non-adherence and non-persistence with antiretroviral therapy is the major reason most individuals fail to get any benefit from and develop resistance to HAART.

The reasons for non-adherence and non-persistence with HAART are varied and overlapping. Major psychosocial issues, such as poor access to medical care, inadequate social supports, psychiatric disease and drug abuse contribute to non-adherence. The complexity of these HAART regimens, whether due to pill number, dosing frequency, meal restrictions or other issues along with side effects that create intentional non-adherence also has a weighty impact.

The side effects include lipodystrophy, dyslipidaemia, insulin resistance, an increase in cardiovascular risks and birth defects.

Daily multivitamin and mineral supplements have been found to reduce HIV disease progression among men and women. This could become an important low-cost intervention provided during early HIV disease to prolong the time before antiretroviral therapy is required. Some individual nutrients have also been tried.

Anti-retroviral drugs are expensive, and the majority of the world's infected individuals do not have access to medications and treatments for HIV and AIDS.

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, after over 20 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.

Various forms of alternative medicine have been tried to treat symptoms or alter the course of the disease.

In the first decade of the epidemic when no useful conventional treatment was available, a large number of people with AIDS experimented with alternative therapies. The definition of "alternative therapies" in AIDS has changed since that time. Then, the phrase often referred to community-driven treatments, untested by government or pharmaceutical company research, that some hoped would directly suppress the virus or stimulate immunity against it. Examples of alternative medicine that people hoped would improve their symptoms or their quality of life include massage, stress management, herbal and flower remedies such as boxwood, and acupuncture; when used with conventional treatment, many now refer to these as "complementary" approaches. Despite the widespread use of complementary and alternative medicine by people living with HIV/AIDS, the effectiveness of these therapies has not been established.

Epidemiology

 Prevalence of HIV among adults per country at the end of 2005.

 15-50%
 5-15%

 1-5%
 0.5-1.0%

 0.1-0.5%
 <0.1%</td>

UNAIDS and the WHO estimate that AIDS has killed more than 25 million people since it was first recognized in 1981, making it one of the most destructive epidemics in recorded history. Despite recent, improved access to antiretroviral treatment and care in many regions of the world, the AIDS epidemic claimed an estimated 2.8 million (between 2.4 and 3.3 million) lives in 2005 of which more than half a million (570,000) were children. Globally, between 33.4 and 46 million people currently live with HIV.

In 2005, between 3.4 and 6.2 million people were newly infected and between 2.4 and 3.3 million people with AIDS died, an increase from 2003 and the highest number since 1981.

Sub-Saharan Africa remains by far the worst affected region, with an estimated 21.6 to 27.4 million people currently living with HIV. Two million [1.5–3.0 million] of them are children younger than 15 years of age. More than 64% of all people living with HIV are in sub-Saharan Africa, as are more than three quarters (76%) of all women living with HIV. In 2005, there were 12.0 million [10.6–13.6 million] AIDS orphans living in sub-Saharan Africa 2005.

South Africa has the largest population of HIV patients in the world, followed by Nigeria.

South & South East Asia are second worst affected with 15%. AIDS accounts for the deaths of 500,000 children in this region. Two-thirds of HIV/AIDS infections in Asia occur in India, with an estimated 2.5 million infections (0.02% of population) making it the country with the third highest number of HIV infections in the world. In the 35 African nations with the highest prevalence, average life expectancy is 48.3 years— 6.5 years less than it would be without the disease.

The latest evaluation report of the World Bank's Operations Evaluation Department assesses the effectiveness of the World Bank's country-level HIV/AIDS assistance, defined as policy dialogue, analytic work, and lending, with the explicit objective of reducing the scope or impact of the AIDS epidemic.

This is the first comprehensive evaluation of the World Bank's HIV/AIDS support to countries, from the beginning of the epidemic through mid-2004. Because the Bank's assistance is for implementation of government programs by government, it provides important insights on how national AIDS programs can be made more effective.

The development of HAART as effective therapy for HIV infection and AIDS has substantially reduced the death rate from this disease in those areas where it is widely available. This has created the misperception that the disease has gone away. In fact, as the life expectancy of persons with AIDS has increased in countries where HAART is widely used, the number of persons living with AIDS has increased substantially. In the United States, the number of persons with AIDS increased from about 35,000 in 1988 to over 220,000 in 1996.

In Africa, the number of MTCT and the prevalence of AIDS is beginning to reverse decades of steady progress in child survival. Countries such as Uganda are attempting to curb the MTCT epidemic by offering VCT (voluntary counseling and testing), PMTCT (prevention of mother-to-child transmission) and ANC (ante-natal care) services, which include the distribution of antiretroviral therapy.

<u>Stigma</u>

AIDS stigma exists around the world in a variety of ways, including ostracism, rejection, discrimination and avoidance of HIV infected people; compulsory HIV testing without prior consent or protection of confidentiality; violence against HIV infected individuals or people who are perceived to be infected with HIV; and the quarantine of HIV infected individuals. Stigma-related violence or the fear of violence prevents many people from seeking HIV testing, returning for their results, or securing treatment, possibly turning what could be a manageable chronic illness into a death sentence and perpetuating the spread of HIV. AIDS stigma has been further divided into the following three categories:

- 1. Instrumental AIDS stigma—a reflection of the fear and apprehension that are likely to be associated with any deadly and transmissible illness.
- 2. Symbolic AIDS stigma—the use of HIV/AIDS to express attitudes toward the social groups or lifestyles perceived to be associated with the disease.

3. Courtesy AIDS stigma—stigmatization of people connected to the issue of HIV/AIDS or HIV- positive people.

Often, AIDS stigma is expressed in conjunction with one or more other stigmas, particularly those associated with homosexuality, bisexuality, promiscuity, and intravenous drug use.

In many developed countries, there is an association between AIDS and homosexuality or bisexuality, and this association is correlated with higher levels of sexual prejudice such as anti-homosexual attitudes.

There is also a perceived association between AIDS and all male-male sexual behavior, including sex between uninfected men.

Those most likely to hold misconceptions about HIV transmission and to harbor HIV/AIDS stigma are less educated people and people with high levels of religiosity or conservative political ideology.

Origin of HIV

AIDS was first reported June 5, 1981, when the U.S. Centers for Disease Control and Prevention recorded a cluster of *Pneumocystis carinii* pneumonia (now still classified as PCP but known to be caused by *Pneumocystis jirovecii*) in five homosexual men in Los Angeles.

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

HIV-1 is more virulent and more easily transmitted. HIV-1 is the source of the majority of HIV infections throughout the world, while HIV-2 is not as easily transmitted and is largely confined to West Africa.

Both HIV-1 and HIV-2 are of primate origin.

The origin of HIV-1 is the Central Common Chimpanzee (*Pan troglodytes troglodytes*) found in southern Cameroon.

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

Most experts believe that HIV probably transferred to humans as a result of direct contact with primates, for instance during hunting or butchery.

A more controversial theory known as the OPV AIDS hypothesis suggests that the AIDS epidemic was inadvertently started in the late 1950s in the Belgian Congo by Hilary Koprowski's research into a polio vaccine.

According to scientific consensus, this scenario is not supported by the available evidence.

A 2007 study published in the Proceedings of the National Academy of Sciences by Michael Worobey and Dr. Arthur Pitchenik claimed that, based on the results of genetic analysis, HIV probably moved from Africa to Haiti and then entered the United States around 1969.

Alternative hypotheses

A small minority of scientists and activists question the connection between HIV and AIDS, the existence of HIV itself, or the validity of current testing and treatment methods. Though these claims have been examined and widely rejected by the scientific community, they have had a significant political impact, particularly in South Africa, where governmental acceptance of AIDS denialism has been blamed for an ineffective response to that country's AIDS epidemic.

HIV and AIDS misconceptions

A number of misconceptions have arisen surrounding HIV/AIDS. Three of the most common are that AIDS can spread through casual contact, that sexual intercourse with a virgin will cure AIDS, and that HIV can infect only homosexual men and drug users. Other misconceptions are that any act of anal intercourse between gay men can lead to AIDS

infection, and that open discussion of homosexuality and HIV in schools will lead to increased rates of homosexuality and AIDS.

European Action to confront HIV/AIDS

In response to the rapid worldwide spreading of the three main communicable diseases linked to poverty, and in particular HIV/AIDS, the European Commission has developed a coherent policy framework to confront HIV/AIDS, Malaria and Tuberculosis through external action.

This led in April 2005 to the adoption of a European Programme for Action covering all developing countries for the period 2007-2011.

The Programme for Action proposes the European Union (EC and EU Member States) to support country-lead programmes confronting the three diseases as well as action at global level in areas where the EU can add value.

It also argues for an increasing EU contribution to help fill the financial gap, thus reflecting Europe's weight as international partner in development.

- <u>At country level</u>, the Programme for Action focuses on improving political and policy dialogue on human rights-related issues, needs of vulnerable groups and issues around stigma and discrimination. It puts emphasis on monitoring and data collection, on capacity building in the areas of human resources, clinical research and procurement policy, as well as on the need to create synergies with programmes promoting sexual and reproductive health and rights.
- <u>At global level</u>, the Programme for Action proposes to strengthen regional networks and cooperation, to promote affordable and safe pharmaceutical products, to reinforce the regulatory capacity of partner countries, to address the human resource crisis in health and to support research and development of new preventive and therapeutic tools.

The Programme for Action calls for a strong partnership with key players and initiatives such as the Global Fund to Fight HIV/AIDS, TB and Malaria (GFATM) and highlights the need to promote and defend internationally the European voice on issues related to these areas of intervention.

Programming decisions and budget allocations with respect to both global and country action proposed in the Programme for Action will be made in accordance with the new financial instruments (2007-2013).

HIV/AIDS research: a priority for the EU

The Sixth Framework Programme for Research and Development (FP6, 2002-2006) allocates a total of 400 million Euro to the three main poverty-related diseases, a four-fold budget increase in comparison with the previous Framework Programme (FP5, 1998-2002).

Research on HIV/AIDS will continue being a priority under FP7 (2007-2013).

Projects financed by the European Commission on HIV/AIDS cover both prevention and treatment aspects, including research on new drugs, microbicides and vaccines. EC-funded research projects:

- <u>Highly innovative approaches</u>. Proposals have an average of 5-6 partners and receive about 1 million of Euro during 2-3 years. Both basic and preclinical research on prevention and treatment are financed.
- <u>Integrated projects</u>, covering research up to early human testing. Funded with an average of 10 million of Euro, these projects usually include 10-30 partners for a period of 5 years.

 <u>Networks of excellence</u>. Under the 6th Framework Programme, the European Commission will finance three broad networks of European researchers on HIV preventive technologies (vaccines and microbicides), therapeutic clinical trials, and cohort studies. Each of these networks receives funding in the range of 8-15 million of Euro for a period of 4-5 years, and includes more than 100 researchers.

EDCTP

In addition to basic, preclinical and early clinical research, the European Union is also financing capacity building and advanced clinical trials in Sub-Saharan Africa through the European and Developing Countries Clinical Trials Partnership.

The EDCTP is an independent organisation based in The Netherlands, partnering with 14 European Member States plus Norway and Switzerland.

Combating HIV/AIDS

The re-emerging of HIV/AIDS in Europe and its neighbouring countries highlighted the need for immediate European action through the adoption of a specific strategy in these regions.

This led to the adoption of a policy document on "Combating HIV/AIDS within the European Union and in the neighbouring countries, 2006-2009" which firmly puts HIV/AIDS on the EU policy agenda.

The Communication sets out objectives and priorities for action and identifies areas where work at European level should be intensified, building on the orientations set out in the Commission's working paper 'Coordinated and integrated approach to combat HIV/AIDS within the EU and in its Neighbourhood'.

Work is being taken forward in close coordination with stakeholders, international organisations and Member States.

Key areas for action:

- Combating stigma and discrimination through capacity building among health care workers and NGOs, promotion of voluntary counselling and testing, and awareness raising;
- Prevention of new infections through education, awareness raising, and facilitating the implementation of comprehensive prevention programmes reaching also the most vulnerable populations;
- Improving HIV/AIDS surveillance in close collaboration with the ECDC and the EuroHIV network, Member States, neighbouring countries and other partners;
- Involving civil society through the HIV/AIDS Civil Society Forum and other relevant structures in the development, implementation and monitoring of HIV/AIDS policies at all levels;
- Working with neighbouring countries includes continuous political dialogue with the Russian Federation and other partners under the European Neighbourhood Policy (ENP) to facilitate the development of leadership and crucial collaboration between different authorities.

EC programmes in the area of HIV/AIDS

The European Commission supports HIV/AIDS related interventions in developing countries through several geographical and thematic instruments mainly at country or regional level (through national and regional indicative programmes).

Support to HIV/AIDS interventions at country level has to fit into the national or regional indicative programme which strategically delineates the scope and priorities of the EC development assistance with a partner country/region for a given period.

Bilateral country support is the main approach towards improved health outcomes in developing countries; the EC supports health sector reforms and health care delivery approaches ensuring improved access to and sustainability of basic services, including AIDS related services.

Due to the consequences of the HIV epidemic on people, control of HIV/AIDS is also a priority of the health system dialogue. As a result, HIV/AIDS is mainstreamed into other sector interventions of the EC, for instance, education, infrastructure and transport.

For the delivery of thematic support in the area of HIV/AIDS, the Commission has established procedures for the selection of projects through calls for proposals rather than supporting project proposals on an adhoc basis.

Through the definition of political priorities, the European Commission sets its targets while respecting the principle of the right of initiative of NGOs and international organisations.

While the number of newly diagnosed AIDS cases continues to decrease in the EU, an upwards trend can be observed in the number of newly reported HIV infections according to data made available by EuroHIV.

For the 17 EU countries with data available for 1996 and 2003 for both HIV infections and AIDS cases, the number of newly reported HIV infections increased by almost 75% from 1996 (7 641 new infections reported) to 2003 (13 257 infections), with the most drastic increases in the number of new HIV diagnoses observed in the Baltic countries (Estonia, Latvia, Lithuania). In the same period the number of newly diagnosed AIDS cases fell by over 55% (1996: 4 085 cases, 2003: 1 772 cases).

This reduction in AIDS cases is to a large extent explained by highly active antiretroviral treatment (HAART).

Population and social conditions

According to EuroHIV the cumulative number of all diagnosed HIV infections *reported* by the end of 2003 in the EU is almost 180 000 - a figure, however, which considerably underestimates the real number of infections which have occurred.

Reporting on HIV infections is still incomplete: some of the countries with the largest HIV/AIDS epidemics (France, Italy and Spain) do not yet have a national reporting system, and even where a reporting system exists, not all prevalent HIV infections have been diagnosed and reported.

Furthermore, countries implemented HIV reporting at different dates and retrospective reporting is not systematically included. Therefore, existing data on HIV reporting still considerably underestimate the real situation.

AIDS, the acquired immunodeficiency syndrome was first recognised in 1981 while the human immunodeficiency virus (HIV) was only discovered in 1983. By then, it was also recognised that AIDS was the result of an advanced HIV infection.

During the first 15 years of reporting the number of new AIDS cases continuously grew. The reversal of this trend in the mid-90s coincides with the increased use of highly active antiretroviral treatment (HAART), a treatment to aggressively suppress viral replication and progress of the HIV disease and which has extended the AIDS-free survival time.

The introduction of HAART has had a major impact on AIDS incidence.

However, data on HIV reporting depend on national testing and reporting patterns and are not yet widely comparable between countries.

Therefore, the following analyses refer to the more comparable data on newly diagnosed AIDS cases.

However, it needs to be kept in mind that trends in AIDS incidence reflect both the underlying HIV incidence and the use of HAART.

50% in Italy and Spain in 2003

In 2003, 6441 newly diagnosed AIDS cases were reported for the EU252 according to data made available by EuroHIV.

The number of cases has continuously fallen since its peak in 19943 when more than 25000 new AIDS cases were diagnosed in the 25 countries which are now part of the EU.

For the year 2003, Italy (27%) and Spain (21%) account for around 50% of all newly diagnosed cases in EU25.

At the same time these two countries only represent 22% of the EU25 population.

Since the mid-90s, a pattern can be observed where these two countries continue to report about half of all new AIDS cases in the EU25. At the same time, both countries have followed the EU trend of falling numbers of AIDS cases since the mid-90s.

Some differences in developments can be noted between EU15 and the new Member States. For almost all EU15 countries, the high point of newly diagnosed cases can be seen around 1994, and since then substantial declines are reported.

While in Luxembourg and Finland the number of new cases only fell by around 40% between 1994 and 2003, six EU15 countries report significant decreases of over 80%: Spain. Only Portugal, due to a later HIV epidemic, deviates from this trend with the number of newly diagnosed cases showing an overall increase of around 20% from 1994 to 2003, then figures remaining stable at a high level since the late-90s.

The new Member States5 accounted for less than 5% of newly diagnosed AIDS cases in 2003 while at the same time they represented around 16% of the EU25 population. However, in a number of these countries, the number of newly diagnosed AIDS cases has continued to grow, with high rates in the Baltic Countries and in Poland, mainly due to a later onset of the epidemic.

The estimated incidence rate in EU25

For EU25, the estimated incidence rate for 2003 was 14.2 cases per 1 million population, a relatively low rate compared to 1994 with 56.3 cases.

The highest incidence in 2003 by far was reported for Portugal with 78.6 cases per 1 million population, followed by Spain (32.8) and Italy (30.6). Throughout the reporting period, the following peak incidence rates were reported: Spain (188.4 in 1994), Switzerland (104.5 in 1992), Portugal (100.7 in 1999), France (100.1 in 1994) and Italy (98.7 in 1995).

Due to the significantly lower number of newly diagnosed AIDS cases for women, incidence rates for women are below 8 cases per million in 16 EU countries in 2003. Outstanding is the high rate for women in Portugal with 31.9 cases per 1 million women.

Men show higher incidence rates by far, with the highest figures reported for Portugal (128.5), Spain (53.4), Latvia (38.2), and Switzerland (39.5).

UK – largest increase in women's share of new AIDS cases

With a share of 73.4% of all new cases diagnosed, men are still more affected by far than women. However, the share of women in new AIDS cases has constantly increased over the whole reporting period (1985-2003).

In 1985, only around 10% of new cases diagnosed were in women.

In 1995, the share of women amounted to 20%, and in 2003, 26.6% of all newly diagnosed AIDS cases are women. While throughout all European countries men are more affected than women, considerable differences exist between countries. In 2003, the share of men

in new cases ranged from below 60% in Belgium, Austria, the United Kingdom and Romania to more than 85% in the Czech Republic, Germany, Lithuania, Hungary and Slovakia.

The largest change is seen in the United Kingdom where in 1994 88% of all new diagnosed cases were men while in 2003 this share was as low as 56%.

This sharp decrease of men and the corresponding increase of women in new AIDS cases in the United Kingdom is different from the more moderate trend which can be seen in Italy, Spain, Portugal and France.

These four countries represent more than two thirds of all newly diagnosed cases in EU25 and thus strongly influence the EU25 average where the share of men only decreased from 81% in 1994 to 73% in 2003.

Transmission categories for AIDS

Transmission through heterosexual contacts in EU25

In 2003, just over 40% of all newly diagnosed AIDS cases in EU25 were attributable to heterosexual contact.

About 30% of new cases resulted from injecting drug use (IDU), and a bit less than 20% of all cases from homo/bisexual contacts. These three transmission categories thus accounted for more than 90% of all new cases.

However, the relative share of these three main transmission categories changed substantially between 1985 and 2003 in EU25. In 1985, with around 60% of all new cases, transmission due to contacts between homosexual or bisexual males was by far the most frequent route of transmission. The share of this transmission category in all new cases dropped sharply from 1985 to 1997.

Since the late 90s, its share has remained relatively stable at around 20%. At the same time, transmission through heterosexual contact continuously grew from its lowest point in 1986 when only 7.6% of all new cases fell into this category to almost 42% in 2003. This growth of transmission through heterosexual contact is also reflected in the growing share of women in newly diagnosed cases.

The share of new cases attributable to injecting drug use shows a different pattern which is very alike both for women and men. In the second half of the 80s, a sharp increase of this transmission category can be seen.

Then, all through the 90s this share remained relatively stable at around 40%. The most recent data reveal a downward trend. However, only future data will show if this trend persists.

Transmission through heterosexual contacts

It was only in 2001 that heterosexual contacts became the most frequent transmission category among AIDS cases for EU25 (women and men together).

In 2003, the share of heterosexual transmission ranged from more than 65% in the United Kingdom, Belgium and Sweden, while Germany, Latvia and Poland reported less than 16% attributable to this category.

Transmission categories related to sexual contacts obviously differ for women and men.

For women in EU25, heterosexual contacts are the most likely route of transmission, accounting for about 70% of all new cases in 2003.

For men, this share was only 32% while another 26% of new cases are attributable to homo- and bisexual contacts.

However, for both women and men, transmission through heterosexual contacts continuously became more important: in 1985, only 6% of new cases for men and 34% for women were assigned to this category.

Almost all countries show an increase of the importance of this transmission category for women. In 2003, the highest shares, of more than 90%, were observed in Belgium and the United Kingdom, while heterosexual contacts played a less significant role for transmission in Poland, Latvia, Germany and Spain, with less than 50% of cases assigned to this group for women.

For men, the weight of transmission through heterosexual contacts increased as well. Homo- and bi-sexual contacts clearly dominated the overall transmission through sexual contacts up to the early 90s, with more than 80% of transmission through sexual contacts assigned to homo- or bisexual contacts in 11 out of the 15 countries considered.

However, in 2003, in 12 out of the 15 countries, the share of transmission attributable to homo- or bisexual contacts out of all sexual contacts was less than 50%.

Only in Germany did homo- or bisexual contacts continue to account for more than 80% of overall sexually transmitted cases for the whole reporting period.

At the same time, Germany is the only country where homo- or bisexual contacts remained the most important transmission category for all newly diagnosed cases through all years with data available.

Mortality due to AIDS

According to causes of deaths statistics collected by Eurostat, at least 6017 persons died from AIDS in the EU25 in 1999 (4850 men and 1167 women).

The overall number of deaths (all causes) was around 4.5 million.

Consequently, the share of AIDS caused deaths was low: 0.14% (0.22% for men and 0.05% for women).

In terms of absolute numbers, Spain, Italy, Portugal and France report the highest values for most recent years.

Time series in Eurostat for causes of death statistics are only available since 1994 (1999 for the new Member States). However, compared to the high absolute number of deaths caused by AIDS in the mid-90s, around 20 000 deaths (or 0.53% of all deaths), a considerable reduction can be observed. Only Portugal shows an increase in the number of AIDS caused deaths.

In 1999, the highest standardised death rates (per 100 000 standard population, see methodological notes) for men were seen in Portugal (15.3) and Spain (7.1).

While Spain saw a significant decrease in its standardised death rates since 1995 when a value of 21.9 was reached, the rates for Portugal remained roughly stable over the reporting period. Standardised death rates for women show approximately the same pattern but at a lower level (Portugal: 3.4, Spain: 1.5).

AIDS cases

The data on AIDS cases are provided to Eurostat by the European Centre for the Epidemiological Monitoring of AIDS – EuroHIV. This centre coordinates the surveillance of HIV/AIDS in the 52 countries of the World Health Organisation (WHO) European Region since 1984.

The HIV/AIDS surveillance network is supported by the European Commission.

EuroHIV is also a WHO and UNAIDS Collaborating Centre.

For each country, a single institution reports national data to EuroHIV and is responsible for the quality of the reported data. Since data are reported to EuroHIV without personal identifiers, it is not possible to eliminate double counting at European level.

The time between diagnosis of AIDS and reporting at national level causes reporting delays. These reporting delays vary widely between countries and transmission groups, and may be as long as several years in some cases.

EuroHIV suggests that the incidence trends are best assessed by examining data by year of diagnosis with adjustments for reporting delays rather than by year of reporting. EuroHIV adjusts the data only for countries with at least 50 cumulative AIDS cases,

assuming a maximum delay of 3 years (Switzerland: 5 years since cases might be reported through death certificates leading to longer delays). The latest data for Belgium and Spain were not adjusted due to irregular reporting.

For surveillance purposes, cases attributable to more than one mode of transmission are counted only once, according to the most likely route of transmission.

However, the most likely route of transmission varies between countries. The definition for heterosexual transmission also varies slightly between countries. This group includes persons in whom major risk factors for HIV infection other than heterosexual contact have not been recognised.