
INTERNATIONAL AIDS SOCIETY

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20 Years of HIV/Aids Epidemic and a prologue of 70 years ago

HIV/Aids is a disease that can summarize the distinctive features of our time: Aids if caused by HIV, a virus, that is a sequence of information. This disease is spreading to such an extent to acquire the dimension of a pandemic: that is happening in the era of information and of personal media. But the information contained in the virus *must* be communicated for the contagion to happen.

Perhaps, the HIV infection is the only one that was covered since the early beginning by the television, the radio and the newspapers which testified its diffusion and impact day by day.

It has been written that there is no epidemic – and no contagion – if there is not communication, that is spreading and sharing of information about the awareness of the existence of the disease and its transmission from person to person. In one sense is the West of the world, with its science and technology, to communicate to the South of the world that Aids is present and, metaphorically to infect it.

On the turning point of the new millennium, it can be useful running through again the 20 years of infection history, that is an area of medicine characterized by the quick piling up of so much information in so short time. The communication processes have been speeded up so intensively to actually cancel the lag time between the understanding of the disease within the scientific community and the lay opinion creation upon the HIV infection.

Prologue

In order to define the prologue of HIV infection, draw pathways and detail times, in other words to reconstruct the HIV genealogical tree, information technologies has been widely used.

1931 This if the year of the identification of the oldest ancestor of HIV-1.

A group of investigators from the Department of Energy's of the Los Alamos National Laboratory estimated that the closest ancestor of the most common HIV-1 strain (responsible for the Aids pandemic) appeared in the early 30s, that is thirty years before the oldest and available blood HIV positive sample.

The paper has been published in June 2000 on *Science* and details a research that has been carried out by the biologist Bette Korber and the physicist Tanmoy Bhattacharya who used the ultra fast supercomputer Nirvana to analyze all the data regarding the HIV-1 sequences stored in the Los Alamos Aids and Human Retroviruses database with the purpose of dating the origin of the HIV strains which caused the infection of more than 50 million people worldwide until now.

The epidemic

The virus that will be subsequently identified as responsible for the Human Acquired Immune Deficiency Syndrome, made its appearance in the western world at the early '80.

1981 At page no. two of the *Morbidity and Mortality Weekly Report* on June 5th 1981: the investigators from the Centers for Diseases Control and Prevention (CDC) of Atlanta, reported a sudden increase in the diagnosis of cases of *Pneumocystis carinii* pneumonia and of Kaposi's Sarcoma in young men who had sex with men, in the USA. Such diseases had not been previously related to any severe clinical course in immunocompetent subjects. On 3rd July 1981, the New York Times published the news. The awareness on the existence of a new syndrome in the history of medicine started to grow as a consequence of such unusual observation. The story of Aids had begun. The infection is soon linked to men

who have sex with men and 422 cases had been diagnosed by the end of the year with 159 deaths.

1982 The CDC related the HIV infection to blood transfusion. Following a number of cases of infection in haemofiliac patients, reported during an FDA meeting on blood products, Bruce Voeller, former Director of the National Gay Task Force proposed to name *Acquired Immune-Deficiency Syndrome* (Aids) the new disease. In the meantime, the number of Aids cases in the USA were 1614 with 619 deaths. The Gay Men Health Crisis, the first activists association against Aids, is established. Its foundation will foster the development of a strong and deeprooted movement against the infection.

1983 The CDC alerted against the possible risks regarding the blood banks and the shortage of usable blood packages. A virus with possible relationship to the infection is isolated by the Pasteur Institution in France. The scientific community began to understand that the infection was not limited to gay and haemofiliac but hit also other groups at risk, e.g. the intravenous drug users and was spreading not only in the USA but all over the world. It was clear that the infection is targeted towards the immune system which is quickly compromised, leading to several opportunistic infections that would be easily under control by a healthy body.

1984 The virus responsible for Aids is identified: it is called HIV, a virus which can be transmitted through blood and sexual exposure. There were 11,055 cases of Aids in the USA and 5,620 deaths.

1985 The first tests to detect antibodies against HIV are developed and blood products are starting to be tested in the USA and Japan. The CDC arranged the first International Conference on Aids in Atlanta. The WHO sponsored such a congress: about 2000 investigators from 30 countries realized the presence of an African focus of the infection. There were 22,996 cases of Aids in the USA and 12,592 deaths: among those who died there was also Rock Hudson. The global world Aids cases were estimated around 20,008 but data from Africa were missing. 1,617 Aids cases were reported in Europe. The eterosexual transmission of the virus was shown.

1986 The first American report on Aids was issued, highlighting the importance of providing information on sexual behaviors to prevent the infection. The II International Conference on Aids was held in Paris and the first estimate regarding Africa countries was available. The WHO estimated that there were about 5 to 10 million people living with HIV infection in the world. Testing of blood products started in Europe as well. It was now clear that the infection could hit both men and women, regardless of their sexual behavior, at any age. The importance of preventive campaign is recognized and preliminary data on promising drugs against the virus are produced.

1987 The III International Conference on Aids was held in Washington with more than 12,000 delegates from 110 countries. The USA Administration is attending the congress through its federal agencies: CDC, NIH and PHS. Ronald Regan mentioned the word Aids in an official speech for the first time. The Conference highlighted the importance of the use of condoms and the high risk of transmission of the infection following intravenous drug use. The USA established rules which did not allow the admittance of HIV positive people in the states, in spite of several appeals against discrimination of people with Aids. The WHO set up its Global Program on Aids, and the World Health Assembly approved a global strategy for coping with the epidemic. The FDA, following a previous non experienced pressure from the activists, reduced the time for approval of drugs against Aids. The first approved antiretroviral drug was AZT. There were more than 50,000 cases of Aids in the world.

1988 The IV International Conference on Aids was held in Stockholm. For the first time there was a substantial number of delegates from developing countries. 96,443 Aids cases were reported worldwide. 1st December is chosen as the world Aids day.

1989 The V International Conference on Aids was held in Montreal. The voice of activism reached the delegates: activists occupied the podium and cried their claims. The cases of Aids peaked to 160,000 worldwide. In the USA, the Burroughs Wellcome is obliged to lower the price of AZT because of the activists protests. John Holmes, the most famous and well-paid pornstar in the world, died due to Aids.

1990 Ronald Regan admitted not to have properly considered the Aids epidemic. That was not enough for thousands of activists who, during the VI International Conference on Aids held in San Francisco, protested against the discriminating rules issued by the George Bush's Government and to raise awareness on the infection. There were 254,000 reported cases of Aids in the world, more than 12,000 just in Uganda.

1991 ddI, a new drug against HIV, is approved. Like AZT, it inhibits a virus enzyme called reverse transcriptase. Magic Johnson declared to be seropositive. The VII International Conference on Aids was held in Florence: 9,053 Aids cases are reported in Italy, 47,594 in Europe and 380,000 worldwide. There were about 10 million HIV positive people in the world.

1992 The FDA set up a specific accelerated process of approval for antiretroviral drugs, aimed to speed up the availability of new molecules for the fight against Aids. ddC, another inhibitor of the reverse transcriptase, is approved. The first clinical trial on combination therapy started to enroll patients. Because of the restrictive rules regarding admittance of people living with HIV/Aids in the USA, the VIII International Conference on Aids was shifted from Boston to

Amsterdam. There were more than 213,000 cases of Aids in the USA, 71,568 in Europe and more than 30,000 in Uganda.

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1993 The CDC introduced a new classification of the Aids cases including additional opportunistic infections defining Aids. The new classification highlighted the importance of the CD4+ cell count for the definition of Aids did not offer advantages in terms of disease progression and survival. A scandal regarding infected blood burst out in France: four officers of the blood bank are jailed. Tennis player Artur Ashe and the dancer Rudolf Nureyev died due to Aids. The IX International Conference was held in Berlin in a depressed atmosphere. More than 600,000 Aids cases are reported world wide and for the first time is reported a very quick diffusion of the infection in South East Asia.

1994 FDA approved another reverse transcriptase inhibitor: d4T. Benetton launched an Ad campaign with a Ronald Regan picture showing the sign of Kaposi's Sarcoma. The X International Conference on Aids was held in Yokohama: it was the last annual conference. The number of Aids cases were globally 985,119, with a 37% increase from the previous year, however, the WHO estimated a significantly higher number of cases: about 4 million. The distribution of reported Aids cases was: 42% in the USA, 33,5% in Africa, 11,5% in Europe, 11,5% in Latin America and 1% in Asia. According to the estimated cases of Aids the distribution was quite different: more than 67% in Africa, 12% in Latin America, 10% in USA, 6% in Asia and more than 4% in Europe. The estimated number of people infected with HIV worldwide was 16 million with 1 million of infected children (mostly in Africa). The sensation of defeat produced by the results of the Concorde trial speeded up the research on combination therapy. Two studies showed tha AZT was effective in reducing the transmission of HIV infection from mother to child. The health authorities recognized that the adoption of proper preventive measures could significantly reduce the new cases of infection, particularly in the developing world. To meet such a goal 2,5 billion of \$US would be needed: the amount produced by the purchase of a single can of Coca Cola by each inhabitant of the planet, if assigned to prevention.

1995 For the first time in ten years there was not an International Aids Conference. The WHO estimated 15 million of people with HIV infection worldwide as to June with more than 30 million positive people by year 2000. The WHO

estimated 10 million deaths due to Aids by the year 2000 with 5 million of infected children and 10 million orphaned by Aids below ten years of age. The Delta and ACTG 175 trials showed that combination therapy was the way to follow for the management of HIV infection. The first marketed protease inhibitor, saquinavir, was registered together with 3TC (another inhibitor of reverse transcriptase). Greg Luganis, Olympic champion, announced to have Aids.

1996 It is the year of the turning point. Monotherapy and even double therapy are not to use any longer. In January, results from clinical trials showed the efficacy of the Highly Active Anti-Retroviral Therapy (HAART), the combination of two inhibitors of reverse transcriptase and one protease inhibitor, which will soon become the gold standard of the therapy of HIV infection. At the same time, a kit to monitor the viral load is developed. Clinical trials showed that the viral load assessment significantly predicts the progression of the disease but allows the monitoring of therapy in the individual patient as well. The goal of therapy is now to lower the viral load as much as possible: below the level of detection but with the final aim to have no circulating HIV-RNA in the plasma. David Ho presented the results of his mathematical models, suggesting that there is a chance to eradicate the infection and was appointed man of the year by Time magazine. During this year, many new antiretroviral drugs entered the market including nevirapine, the first non nucleoside inhibitor of the reverse transcriptase, and two new protease inhibitors: indinavir and ritonavir. The IX International Conference on Aids was held in Vancouver and closed providing delegates with the hope to see a light at the end of the tunnel.

1997 The benefits of new therapeutic approaches were soon clear: quick and firm decrease of mortality due to Aids, dramatic reduction of hospitalization. Enthusiasm and trust were spreading among physicians and people living with HIV. The game was shifted on the absolute need to facilitate the access to therapy and drugs to anybody. But that is a problem even for the industrialized world; people kept dying for Aids in the south, in spite of the new therapeutic tools. There were more than 22 million people with HIV/Aids worldwide. The research was moving fast and new possible combinations of antiretroviral drugs were tested, producing promising results.

1998 Several results from clinical trials on combination therapies were showed during the XII International Conference on Aids in Geneva. However, investigators started to observe the first therapeutic failures in patients receiving HAART. Two issues, that still represent a challenge to meet, emerged from the conference: if therapy does not swiftly block the viral replication, HIV is able to develop resistance to drugs and even if there were more available molecules, because of cross-resistance within the different antiretroviral classes, the chance that the therapy fails are high, hence the need for salvage strategies; moreover, adherence to therapy was identified as an issue of paramount importance to the successful management of the HIV infection. Antiretroviral drugs

must be taken by patients at specific time intervals, some of them must be taken together with a large amount of water and low fat meals while other ones must be taken after a rich fat meal. Adherence was defined as the Achilles heel of therapy. There was a clear need for new drugs: more potent, more easily taken, better tolerated. The unquestionable progresses of the science in the fight of HIV (mortality was halved in the USA) produced a feeling of Aids defeat and that the epidemic is blocked but at the same time increased the sensation of a greater gap between the North and the South of the world. At least in some countries a certain confusion developed regarding cases of Aids, which were decreasing, and number of new infections, that showed no variation: 5,8 million of new infections were estimated worldwide just in 1998. The International community was plunged into mourning: Jonathan Mann died due to a plane crash.

1999 Further new antiretrovirals are added to the therapeutic armamentarium: abacavir (an inhibitor of reverse transcriptase), nelfinavir (a protease inhibitor) and two non nucleoside inhibitors of reverse transcriptase: delavirdine and efavirenz. The FDA granted the accelerated approval process to amprenavir, a new protease inhibitor, and several new drugs were under development. There were 10 new HIV infections any minute worldwide. The HIVNET 012 trial showed the efficacy of nevirapine in the prevention of mother to child transmission of the infection: the transmission rates were halved in spite of all the patients enrolled in the study breast fed their babies; such results were obtained giving the mother a single pill during labor and one dose of syrup to the newborn: the cost of such a treatment is just 4 \$US. For the first time, an affordable therapy is developed and could be used in the worst affected countries.

In September, the International Aids Society (IAS) organized the first Rome State-of-the Art Conference on Treatment of HIV Infection and launched the continuing medical education project named Share: everyone is called to concentrate the efforts on reducing the gap between North and South of the world, to start the Aids defeat.

In November, Thabo Mbeki, President of South Africa, the country that will host the next International Conference on Aids, claimed the African right to articulate its own response to Aids in various official occasions; he joined the thesis of the so called "dissidents", a group of scientists headed by Peter Duesberg, who thought that HIV is not the cause of Aids which would be due to antiretroviral drugs (led by AZT) that are considered toxic and dangerous. It should be underlined that the pregnant women in South Africa are not offered antiretroviral drugs to prevent the mother to child transmission of the infection. During the same period of time, it was announced that about 8% of South African population is HIV seropositive and 3,6 million people are living with Aids. Such figures put South Africa at the top of the worst affected countries in the world by the HIV infection. Mbeki's attitude had been poorly considered by the public opinion worldwide but fueled again the "dissident" hypothesis and run the risk to

slow down the needed interventions to face the Aids pandemic in Africa.

At the end of December, the UNAIDS reported its update of the epidemic: 5,6 million of new infections in 1999 with 33,6 million people living with HIV/Aids worldwide. Since the beginning of the epidemic there had been 16,3 million deaths.

2000 The debate on Aids concentrates on the geo-political dimension of the pandemic, as a sort of preparation to the Internal Conference on Aids. South Africa is so insisting on its dissident attitude towards worldwide shared scientific opinions to gather a panel of experts that includes different kind of researchers. Scientists who clearly showed, through their own work, that HIV is the cause of Aids and that the combination therapy is able to control the viral replication to such an extent that the natural history of the disease is modified, are seating at the same table with the "dissidents". The panel works ended with the impossibility to reach a consensus among those who refuted and those who agreed on the role of HIV in determining the disease. That following a first plenary session in a blinded Pretoria in May and subsequent discussions on an encrypted Web site.

At the same time, rumors on the boycott of the International Conference are spreading. Nerves are so overstrung that several Pharmaceutical Companies decide to cancel their delegations to the congress and the relevant satellite symposia. In the reality, the IAS choice to organize the conference at the very epicenter of the epidemic, to underline the dimension of the catastrophe, renewed the attention of the media and of the powerful people of the world to the problem Aids.

What happened in South Africa is the basis to realize that Aids represents a concern to everyone. President Clinton defines Aids "a problem that is menacing the National security of the USA" and adopts a Marshall plan for coping with Aids in Africa. Some Pharmaceutical Companies accept to reduce problems regarding the access to drugs. This is the first time in the history of Aids and of Medicine that a scientific congress (just because of the International Aids Society to organize it in Africa) is producing so many effects and positive interventions in the fight against Aids before being actually held.

Among the various announces of possible vaccine candidates, the attention of the researchers is shifting from the research on new drugs to the identification of more effective therapeutic strategies in order to improve the use of such drugs: some trials are starting to enroll patients to see whether the so called structured therapy interruptions show the same efficacy of the continuous treatment, with potential decrease of side effects and patient's adherence improvement.

AN OPEN LETTER FROM THE INTERNATIONAL AIDS SOCIETY (IAS) TO ALL PEOPLE INVOLVED WORLDWIDE IN THE FIGHT AGAINST HIV/AIDS

On behalf of over 10,000 IAS members from more than 132 countries and as custodian of the series of biennial International Aids Conferences, we reaffirm that we stand firmly behind the XIII International Aids Conference to be held in Durban, South Africa on July 9-14, 2000.

This is the first International Aids Conference to be held in a developing country and in the very epicentre of the pandemic. The IAS selected Durban as a venue intentionally to raise the world's awareness of the catastrophic development of HIV/Aids in sub-Saharan Africa and particularly in Southern Africa. The African continent, where the incidence of HIV/Aids keeps increasing, is facing an unprecedented demographic upheaval caused by the disease. (Recent estimates project that several sub-Saharan nations, including South Africa, will lose one quarter of their population to Aids by 2010 and that an estimated 4,2 million South Africans – 10 percent of the population – are infected with HIV, with 1,700 people newly infected every day).

Any government has the right to gather data and information on HIV/Aids directly from whatever source may be considered useful in helping them to understand the problem. However, since the Durban Conference will deal with scientific and public health policies from an international perspective, its aims must not be impeded by political considerations.

The ethical imperative is the design and implementation of interventions tailored to each country's needs, in order to address the drama represented by 23,3 million people living with HIV/Aids in Africa, 2,6 million deaths due to Aids in 1999, and 16,000 new infections every day. This requires the immediate adoption of appropriate strategies already documented to be effective in Africa to stop the epidemic of HIV – the deadly virus that causes Aids.

One of the stated purposes of the IAS is to be a "Voice of Reason" in controversies: our mission is to unite all parties in order to address the problems pertaining to the HIV/Aids situation worldwide. The Conference serves as the multidisciplinary

forum at which issues can be discussed by all those affected by the HIV epidemic: scientists, international agencies, NGOs, governments, and people living with HIV/Aids.

When we chose Durban, we anticipated that there might be a number of problems related to the site, especially among Conference delegates not accustomed to Africa – even though Durban is a modern city similar to cities in Western countries. The IAS wishes to assure everyone that the Conference Organisers have established an action plan to take care of any reasonable security concern. In general, travel to Durban does not involve security considerations different than those associated with other international travel.

HIV/Aids concerns the whole world. If we do not globally address the catastrophe then the spread of HIV during the next decade might be even more rampant in Asia and the Pacific than what has happened to date in sub-Saharan Africa. Let us use this opportunity to raise awareness of the plight of HIV/Aids in developing countries and go to Durban as an act of international solidarity, as a demonstration of the joint efforts of the North and South of the world in fighting HIV/Aids.

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