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DST

Jornal Brasileiro de Doenças Sexualmente Transmissíveis

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Órgão Oficial da Sociedade Brasileira de Doenças Sexualmente Transmissíveis
Órgão Oficial para América Latina da União Internacional Contra as Infecções de Transmissão Sexual (IUSTI)
Órgão Oficial do Setor de Doenças Sexualmente Transmissíveis MIP / CMB / CCM / Universidade Federal Fluminense

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* J bras DST Agradece a colaboração especialmente nesse número à professora Wanda Esteves.

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Editorial

International Aids Conference in Brazil

In 1998, the National Co-ordination of STD/Aids returned to us the BID for the oficial presentation of Brazil to host the XV International Aids Conference, Rio 2004. At that time such proposal was presented to the National Committee of Aids, but unfortunately there was no echo and the papers were returned in blank.

We decided to face the challenge and make a new start.

Going to Geneva, we officially handed in the BID so that Brazil could host the Congress. The home pages www.uff/br/dst/ and www.uf.aidsrio2004 gave us the support we expected.

On the occasion we made public the following texts:

"Dear Dr. Lars Kallings, Executive Secretary of IAS,

Considering that:

- In Brazil there is a very intensive work at the Universities, Research Institutes, NGOs, and especially at the Ministry of Health – National Co-ordination of STD/Aids, which together with the Health Secretaries of States and Municipalities guarantee totally FREE OF CHARGE tests and anti-retroviral therapy to all population,
- Latin America is the thirtieth largest world population infected with Aids, and with very well organized NGOs, *we urge to make a very well organized Conference for the COMMUNITY.*
- The figures of orphan children from Aids are already 100,000 (UNAIDS),
- Life expectation has decreased by 5.3 years since Aids occurred,
- There is political and economic stability (inflation is less than 5% a year),
- A lot of international investments are turning to Brazil and other countries in Latin America, such as Argentina, Uruguay and Chile,
- In 1992, Rio de Janeiro hosted the UNCED – United National Conference Environmement and Development, receiving at the same time 147 chiefs of state and 15,000 participants at the Rio Convention Center,
- In April 1998, at the same Convention Center, the World Congress of Cardiology brought to Rio 20,000 participants from 124 countries,

Bringing Aids 2004 to Rio would be important not only for the millions of infected people, but also to the whole population, *160 million inhabitants,* by creating a forum for discussion and breaking myths and prejudices. This will bring hope for a brighter future.

With this in mind, we would like to say that our people need the most advanced international community not only to speak about our problems, but actually act on them, bringing technical, scientific and social progress to our health specialists and educators, our students and citizens.

North America has already hosted this important Conference many times, as well as Europe, Australia and Asia. In two years from now we will be in Africa and then back to Europe. Meet me in Rio 2004. WHY NOT?"

During the event in Geneva, specifically for Brazilians, we divulged the following:

"OPEN LETTER

International Aids Conference, Rio 2004

Dear Colleagues,

Since 1989 Brazil has been trying to host the International Aids Conference. We were very close to it, but unfortunately we had no chance. There were misunderstandings in communication and we did not stick to it completely.

Today our time has changed. The National Co-ordination of STD/Aids – Ministry of Health, together with Universities, Research Institutes, Secretaries of Health from States and Municipalities, NGOs, Foundations, Private and Governmental Enterprises, Medical Associations are all integrated in actions to turn our work fearless and highly productive.

When an event of such an extent and technical-scientific and social importance comes to a country, everyone profits. Researchers profit with a great interchange, professors by aquisition of knowledge, health professionals with experience and students profit, too, once they can participate more actively in academic studies.

Also the population profits with cultural exchange, but, above all, patients gain, for their problems are closely discussed, diminishing prejudices and adding knowledge to their problems as well as raising their hopes for better days.

Colleagues, no matter who breaks loose the proposal, no matter where the event will take place – Brazil deserves to be the winner.

We believe Latin America, represented by Brazil, will be able to debate the subject, and with the mediation and the guidance of the National Co-ordination of STD/Aids and the Ministry of Health we will be able to gather a group where all segments will be represented."

Unfortunately we were not united for the cause and again misunderstanding in communication and interpretation – mainly from Brazilians, weakened the project. Canada, for the third time, was proposed to hold the Conference in 2004.

However, those who have been to such Conferences know the strength of the Brazilian Delegation, both in number of participants and scientific/community activities, human rights, among others.

Recently, at the *XIII Aids International Conference,* in Durban, South Africa, there were 267 Brazilian participants. It was the 6th largest delegation, just after the United States (2,602), South Africa (2,539) the United Kingdom (622), France (444) and Spain (313); Barcelona will host the next Conference, in 2002.

Almost 100 papers and Brazilian presentations were delivered at the Conference in Durban. Several Brazilian representatives were brilliant in their oral presentations, round tables, debates and plenary sessions. Participants from other countries referred to Brazilian experiences in their speeches, always praising the work developed in Brazil.

We also want to mention the outstanding efficiency in the organization of the Conference in Durban. The South Africans were an example to the world: with determination and competence, it is possible to overcome the most difficult situations.

Today we see our Brazil firm and strong. We have learnt to join our differences. We are ready to organize a large event. The work developed by the Programs of STD/Aids (at National, State and Municipal levels) together with study centres, research, care, NGOs, enterprise councils and the whole civil society, is mentioned as an example by the UNAIDS and even by the General Secretary of UNO.

The understructure conditions of Brazil, especially in Rio de Janeiro, are prepared for such an event. As an example, we can mention Carnival in Rio, which for five days had more than 350,000 tourists. One third, at least were foreigners. Not mentioning its natural beauty, Rio de Janeiro is well organized in tourism and especialized services, which makes it capable to host national and international events and Congresses of any kind.

The International Airport of Rio de Janeiro/Galeão – Antonio Carlos Jobim - has two runways of 4.8km each, where an average of 230 flights land and take off every day. Twenty-four airlines link regularly Rio de Janeiro to the main capital cities in the world. It is possible to fly from Brazil to 80 different countries using the connections offered by well-known airlines. Rio is the most visited city in Brazil. Over 15 million passengers use the Airport every year. It is linked to down-town and the south area by an express via – Linha Vermelha – and the route to the main hotels takes no more than 20 minutes. The Airport is also linked to the West side, where the largest Convention Centre in Latin America – RioCentro - is located. It takes 20 minutes to get there by a new express route – Linha Amarela.

The city offers 23,000 hotel rooms (not including flats, youth hostels, University accommodation, lodgings) and, in a short time, this number will add 5,000 rooms in hotels which are being built, mainly in Barra da Tijuca. This wide range of hotels include the most famous international chains and excellent national hotels. Several of these hotels have Convention Centres which can hold up to 2,200 participants.

RioCentro, the largest Convention Centre in Latin America, has an area of 100,209 square meters, with 5 pavilions available for exhibition.

Versatile and with all necessary facilities, RioCentro is located in Barra da Tijuca, one of the most modern areas in Rio, with lots of good shopping-centres, restaurants, theatres and a lovely beach. Among others, RioCentro has hosted the World Congress of Cardiology in 1998, with over 19,000 participants from all over the world and the Americas Telecom (for the 3rd time in Rio) in April 2000, gathering 27,000 people.

The ICCA – International Congress & Convention Association classifies Rio de Janeiro among the ten best places in the world to host international events.

Having in mind the social extent of this Conference, we are quite sure that the State Government would support a holiday during the event. Public transport could offer more buses from all areas to RioCentro. This was done when ROCK IN RIO III took place – one million two thousand people in seven days were present at the festival in an area next to RioCentro.

The IAS admits the importance of having the Conference in South America. Brazil, obviously, is the main candidate, even for the year 2004. Canada could acknowledge our effort and struggle in fighting Aids, giving us the chance of hosting the next Congress.

South America thanks in advance.

Mauro Romero Leal Passos, MD. PhD
Chief Editor
Professor, STD Sector
Universidade Federal Fluminense

INTERNATIONAL AIDS CONFERENCES

Past & Planned International AIDS Conferences

The International AIDS Conferences are the events organized by the IAS. They were held on an annual basis until 1996 when it was decided to arrange the Conferences biennially.

PAST & PLANNED INTERNATIONAL AIDS CONFERENCES

1985: Atlanta, GA, USA
1986: Paris, France
1987: Washington DC, USA
1988: Stockholm, Sweden
1989: Montreal, Canada
1990: San Francisco, USA
1991: Florence, Italy
1992: Amsterdam, The Netherlands
1993: Berlin, Germany
1994: Yokohama, Japan
1996: Vancouver, Canada
1998: Geneva, Switzerland
2000: Durban, South Africa
2002: Barcelona, Spain
2004: Toronto, Canada

INTERNATIONAL AIDS CONFERENCE IN BRAZIL

WHY NOT

?

INTERNATIONAL AIDS CONFERENCE

Rio de Janeiro
Brazil

Candidate City

Joining the differences

SBDST

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Av. Roberto Silveira, 123 - Niterói - RJ
CEP 24230-160
Tels.: (021) 710-1549 e 711-4766

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Chefe do Setor do DST:
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Diretor da Faculdade de Medicina:
José Carlos Carraro Eduardo

Prefeito do Campus Universitário:
José Carlos Batista Xavier

MINISTÉRIO DA SAÚDE
Ministro
José Serra

COORDENAÇÃO NACIONAL DE DST/Aids
Paulo Roberto Teixeira

JB DST é o órgão oficial para a América Latina da União Internacional Contra as Infecções de Transmissão Sexual (IUSTI)

Presidente:
Ross Philpot

Secretário Geral:
Ron Ballard

Direcionamento e Distribuição:
O **Jornal Brasileiro de DST** é direcionado aos sócios da SBDST, Urologistas, Ginecologistas, Assinantes, Bibliotecas, Centros de Estudos, Centros de Referências, Bancos de Sangue e Entidades afins. Entidades que mantêm convênio.

Pede-se permuta
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Se solicita el canje
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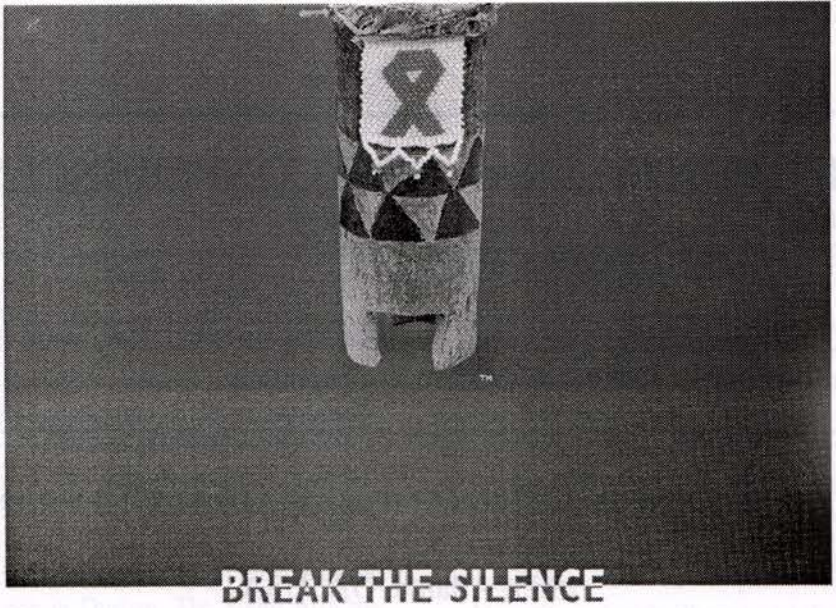

XIII INTERNATIONAL AIDS CONFERENCE

DURBAN • SOUTH AFRICA • 9-14 JULY 2000

SOME PRINCIPAL MOMENTS

Conference Statistics:

Registrants:	12.700
Delegates:	8.000
Press:	1,459
Volunteers:	700
Students:	550
Scholarships:	550
Breakdown of nationalities:	1.500
1st United States	2.602
2nd South Africa	2.539
3rd United Kingdom	622
4th France	444
5th Spain	313
6th Brazil	267
7th Thailand	243
8th Switzerland	230
9th Germany	229
10th Canada	227
Number of Participants	12.437

Regions

Africa	4.560
Europe	3.001
North America	2.829
South and Central America	815
Asia and the Pacific	1.232
Total	12.437

Note: Out of 4,560 from Africa
2.539 come from South Africa

Statistics from the scientific programme:

total abstracts received (excluding late breakers): 6.636
abstracts in oral sessions: 773
abstracts in poster presentations: 534
abstracts in exhibitions: 3.894
abstracts rejected: 1.435
rejection rate: 21,6%
total number of parallel sessions: 167
number of debates: 15
joint tract symposia: 21
roundtables: 9
total number of invited speakers: 123
number of track sessions
A – 18
B – 23
C – 23
D – 34
E – 19
late breaker abstracts submitted: 240
late breakers accepted as poster presentations: 24
late breakers accepted as poster exhibitions: 131
rejection rate: 23,8%
number of discussants invited: 7
number of chairmen: 542
number of commercial satellite meetings: 10
number of NGO satellite meetings: 56

INTERNATIONAL AIDS SOCIETY

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The current IAS President is Mark A. Wainberg whilst Stefano Vella is President-elect and David D. Cooper is Past President. Lars O. Kallings is the IAS Secretary-General.

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 tranmission 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 pathaways 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 plantet, 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 erradicate 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: delevirdine 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 (leaded 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, throught 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.

Mark Wainberg
President

Lars O. Kallings
Secretary-General

Stefano Vella
President-elect

THE DURBAN DECLARATION

HIV CAUSES AIDS. CURBING THE SPREAD OF THIS VIRUS MUST REMAIN THE FIRST STEP TOWARDS ELIMINATING THIS DEVASTATING DISEASE

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DST – *J bras Doenças Sex Transm* 13(1): 14-15, 2001

Seventeen year after the discovery of the human immunodeficiency virus (HIV), thousands of individuals from around the world are gathering in Durban, South Africa, to attend the XIII International Aids Conference, which starts next week (9 July). At the turn of the milennium, figures released last week reveal that an estimated 34,3 million people worldwide are living with HIV or Aids, 24,5 million of them in sub-Saharan Africa[1]. Last year alone, 2,8 million people died of Aids, the highest rate since the start of the epidemic. If current trends continue, southern and Southeast Asia, South America and regions of the former Soviet Union will also bear a heavy burden in the next two decades.

Aids spreads by infection, like many other diseases, such as tuberculosis and malaria, that cause illness and death particularly in underprivileged and impoverished communities. HIV-1, which is responsible for the Aids pandemic, is a retrovirus closely related to a simian immunodeficiency virus (SIV) that infects chimpanzees. HIV-2, which is prevalent in West Africa and has spread to Europe and India, is almost indistinguishable from an SIV that infects sooty mangabey monkeys. Although HIV-1 and HIV-2 first arose as zoonoses[2] – infections transmitted from animals to humans – both now spread among humans through sexual contact; from mother to infant; and via contaminated blood.

An animal source for an infection is not unique to HIV. The plague came from rodents and influenza from birds. The new Nipah virus in Southeast Asia reached humans via pigs. Variant Creutzfeldt-Jakob disease in the United Kingdom is identical to 'mad cow' disease. Once HIV became established in humans, it soon followed human habits and movements. Like many other viruses, HIV recognizes no social, political or geographic boundaries.

The evidence that Aids is caused by HIV-1 or HIV-2 is clear-cut, exhaustive and unambiguous, meeting the highest standards of science[3-7]. The data fulfil exactly the same criteria as for other viral diseases, such as polio, measles and smallpox:

- Patients with acquired immune deficiency syndrome, regardless of where they live, are infected with HIV[3-7].
- If not treated, most people with HIV infection show signs of Aids within 5-10 years[6,7]. HIV infection is identified in blood by detecting antibodies, gene sequences or viral isolation. These tests are as reliable as any used for detecting other virus infections.
- People who receive HIV-contaminated blood or blood products develop Aids, whereas those who receive untainted or screened blood do not[6].
- Most children who develop Aids are born to HIV-infected mothers. The higher the viral load in the mother, the greater the risk of the child becoming infected.
- In the laboratory, HIV infects the exact type of white blood cell (CD4 lymphocytes) that becomes depleted in people with Aids[3-5].
- Drugs that block HIV replication in the test tube also reduce virus load in people and delay progression to Aids. Where available, treatment has reduced Aids mortality by more than 80% (ref. 9).
- Monkeys inoculated with cloned SIV DNA become infected and develop AIDS[10].

Further compelling data are available[4]. HIV causes Aids[6]. It is unfortunate that a few vocal people continue to deny the evidence. This position will cost countless lives.

In different regions of the world, HIV/Aids can show altered patterns of spread and symptoms. In Africa, for example, people infected with HIV are 11 times more likely to die within five years, and more than 100 times more likely than uninfected people to develop Kaposi's sarcoma, a cancer linked to yet another virus[11].

As with any other chronic infection, various factors have a role in determining the risk of disease. People who are malnourished, who already suffer other infections or who are older, tend to be more susceptible to the rapid development of Aids following HIV infection. However, none of these factors weakens the scientific evidence that HIV is the sole cause of the Aids epidemic.

In this global emergency, prevention of HIV infection must be our greatest world-wide public-health priority. The knowledge and tools to prevent infection are available. The sexual spread of HIV can be stopped by mutu-

al monogamy, abstinence or by using condoms. Blood transmission can be prevented by screening blood products and by not reusing needles. Mother-to-child transmission can be reduced by half or more by short courses of antiviral drugs[12,13].

Limited resources and the crushing burden of poverty in many parts of the world constitute formidable challenges to the control of HIV infection. People already infected can be helped by treatment with life-saving drugs, but the high cost of these drugs puts these treatments out of reach for most of the world. It is crucial to develop new antiviral drugs that are easier to take, have fewer side effects and are much less expensive, so that millions more can benefit from them.

There are many ways of communicating the vital information on HIV/Aids, and what works best in one country may not be appropriate in another. But to tackle the disease, everyone must first understand that HIV is the enemy. Research, not myths, will lead to the development of more effective and cheaper treatments, and, it is hoped, a vaccine. But for now, emphasis must be placed on preventing sexual transmission.

There is no end in sight to the Aids pandemic. But, by working together, we have the power to reverse its tide. Science will one day triumph over Aids, just as it did over smallpox. Curbing the spread of HIV will be the first step. Until then, reason, solidarity, political will and courage must be our partners.

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TIME TO TURN THE TIDE

OPENING STATEMENT – XIII INTERNATIONAL AIDS CONFERENCE
DURBAN, SOUTH AFRICA 9TH JULY, 2000

Peter Piot
Executive Director – UNAIDS

ISSN: 0103-0465
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Mr President, His Majesty King Zwelithini, Professor Coovadia, Nkosi, friends... good evening.

We have come to Durban to break the silence –

To break the silence, stigma, indifference and ignorance surrounding the Aids epidemic.

At the outset, I pay tribute to those who marched this afternoon, to break the silence around treatment and care for people living with HIV.

I have attended all International Aids Conferences since 1985. But *this* one feels different to me. Because this is the first international conference in the south – in Africa. Finally.

Today, there is new hope – we are seeing an unprecedented increase in political commitment and resources to fight the epidemic. And I wholeheartedly applaud President Mbeki's powerful voice here tonight.

There is new hope – because we now have strong evidence that *prevention works*. But we need to greatly expand these efforts, and to give communities the power and resources to respond to Aids.

On the eve of the G8 summit, we appeal to the international community to guarantee that no country should fail in its fight against Aids due to lack of male and female condoms and other effective tools. And of course, we urgently need a vaccine and a microbicide for women.

There is also, for the first time, new hope for access to treatment and care for people living with HIV in the developing world.

We have called on the pharmaceutical companies to put humanity ahead of the balance sheet and dramatically lower their prices... and the companies are beginning to respond.

Together with our UNAIDS Cosponsors, we will utilize existing UN procurement mechanisms for countries that are interested in purchasing HIV drugs at the lowest possible prices, for *all* legitimate sources of supply. We have called on governments and their partners to build effective systems to deliver treatment and care. We have also asked them to explore all options available under international agreements to expand access to life-saving medicines.

And we are hearing and heeding the ever louder call of people living with HIV to place the issue of access to treatment at the center of the world's moral agenda.

In tackling the issue of care, let's not wait for the *perfect* solution. Because I know what happens when we wait – the rich get care, and the poor get nothing.

We need to continue working to get antiretroviral therapy to as many people as possible – but *right now* we need a major new effort to prevent and treat opportunistic infections, for example with cotrimoxazole.

We have the tools. The political commitment has never been greater. But now we need major new *resources* to fight HIV.

Today, we need *billions* – not millions – to fight Aids. We need, at a *minimum*, US$3 billion *per year*, for Africa alone – for just the most basic prevention and care, before we even consider combination therapy. This figure is nearly *ten times* what is being spent today.

Where will this money come from? We call on governments in the south to invest more resources in Aids. And we call the governments in the north to greatly increase their contributions to fight Aids in the developing world.

But also let's not forget that each year African countries are paying US$15 billion in debt repayments – that's four times more than they spend on health or education. We call on governments in the north and the international financial institutions to cancel the debts. Now.

Friends, the time has come to turn the tide on Aids here in Africa and globally. Let this be the conference the world remembers for *solutions*, for *mobilisation* and for *breaking the silence*. Because the time has come to *turn the tide*.

Thank You.

Peter Piot

SPEECH OF THE PRESIDENT OF SOUTH AFRICA, THABO MBEKI, AT THE OPENING SESSION OT THE 13TH INTERNATIONAL AIDS CONFERENCE: DURBAN, JULY 9, 2000

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Chairperson,
Participants at the 13th International Aids Conference;
Comrades, ladies and gentlemen:

On behalf of our government and the people of South Africa, I am happy to welcome you to Durban and to our country.

You are in Africa for the first time in the history of the International Aids Conferences.

We are pleased that you are here because we count you as a critical component part of the global forces mobilised to engage in struggle against the Aids epidemic confronting our Continent.

The peoples of our Continent will therefore be closely interested in your work. They expect that out of this extraordinary gathering will come a message and a programme of action that will assist them to disperse the menacing and frightening clouds that hang over all of us as a result of the Aids epidemic.

You meet in a country to whose citizens freedom and democracy are but very new gifts. For us, freedom and democracy are only six years old.

The certainty that we will achieve a better life for all our people, whatever the difficulties, is only half-a-dozen years old.

Because the possibility to determine our own future together, both black and white, is such a fresh and vibrant realty, perhaps we often overestimate what can be achieved within each passing day.

Perhaps, in thinking that your Conference will help us to overcome our problems as Africans, we overestimate what the 13th International Aids Conference can do.

Nevertheless, that overestimation must also convey a message to you. That message is that we are a country and a Continent driven by hope, and not despair and resignation to a cruel fate.

Those who have nothing would perish if the forces that govern our universe deprived them of the capacity to hope for a better tomorrow.

Once more I welcome you all, delegates at the 13th International Aids Conference, to Durban, to South Africa and to Africa, convinced that you would not have come here, unless you were to us, messengers of hope, deployed against the spectre of the death of millions from disease.

You will spend a few days among a people that has a deep understanding of human and international solidarity.

I am certain that there are many among you who joined in the international struggle for the destruction of the anti-human apartheid system.

You are therefore as much midwives of the new, democratic, non-racial and non-sexist South Africa as are the millions of our people who fought for the emancipation of all humanity from the racist yoke or the apartheid crime against humanity.

We welcome you warmly to South Africa also for this reason.

Let me tell you a story that the World Health Organisation told the world in 1995. I will tell this story in the words used by the World Health Organisation.

This is the story.

"The world's biggest killer and the greatest cause of ill-health and suffering across the globe is listed at the end of the International Classification of Diseases. It is given the code Z59.5 – extreme poverty.

"Poverty is the main reason why babies are not vaccinated, why clean water and sanitation are not provided, why curative drugs and other treatments are unavailable and why mothers die in childbirth. It is the underlying cause of reduced life expectancy, handicap, disability and starvation. Poverty is a major contributor to mental illness, stress, suicide, family disintegration and substance abuse. Every year in the developing world 12,2 million children under 5 years die, most of them from causes which could be prevented for just a few US cents per child. They die largely because of world indifference, but most of all they die because they are poor...

"Beneath the heartening facts about decreased mortality and increasing life expectancy, and many other undoubted health advances, lie unacceptable disparities in wealth. The gaps between rich and poor, between one population group and another, between ages and between sexes, are widening. For most people in the world

today every step of life, from infancy to old age, is taken under the twin shadows of poverty and inequity, and under the double burden of suffering and disease.

"For many, the prospect of longer life may seem more like a punishment than a gift. Yet by the end the century we could be living in a world without poliomyelitis, a world without new cases of leprosy, a world without deaths from neonatal tetanus and measles. But today the money that some developing countries have to spend per person on health care over an entire year is just US$4 – less than the amount of small change carried in the pockets and purses of many people in the developed countries.

"A person in one of the least developed countries in the world has a life expectancy of 43 years according to 1993 calculations. A person in one of the most developed countries has a life expectancy of 78 – a difference of more than a third of a century. This means a rich, healthy man can live twice as long as a poor, sick man.

"That inequity alone should stir the conscience of the world – but in some of the poorest countries the life expectancy picture is getting worse. In five countries life expectancy at birth is expected to decrease by the year 2000, whereas everywhere else it is increasing. In the richest countries life expectancy in the year 2000 will reach 79 years. In some of the poorest it will go backwards to 42 years. Thus the gap continues to widen between rich and poor, and by the year 2000 at least 45 countries are expected to have a life expectancy at birth of under 60 years.

"In the space of a day passengers flying from Japan to Uganda leave the country with the world's highest life expectancy – almost 79 years – and land in one with the world's lowest – barely 42 years. A day away by plane, but half a lifetime's difference on the ground. A flight between France and Cote d'Ivoire takes only a few hours, but it spans almost 26 years of life expectancy. A short air trip between Florida in the USA and Haiti represents a life expectancy gap of over 19 years...

"...HIV and Aids are having a devastating effect on young people. In many countries in the developing world, up to two-thirds of all new infections are among people aged 15-24. Overall it is estimated that half the global HIV infections have been in people under 25 years – with 60% of infections of females occurring by the age of 20. Thus the hopes and lives of a generation, the breadwinners, providers and parents of the future, are in jeopardy. Many of the most talented and industrious citizens, who could build a better world and shape the destinies of the countries they live in, face tragically early death as a result of HIV infection."

(World Health Report 1995: Executive Summary, WHO.)

This is part of the story that the World Health Organisation told in its World Health Report in 1995.

Five years later, the essential elements of this story have not changed. In some cases, the situation will have become worse.

You will have noticed that when the WHO used air travel to ilustrate the import of the message of the story it told, it spoke of a journey from Japan to Uganda, another from France to the Cote d'Ivoire and yet another from the United States to Haiti.

From developed Asia, Europe and North America, two of these journeys were to Africa and the third to the African Diaspora.

Once again, I welcome you to Africa, recognising the fact that the majority of the delegates to the 13th International Aids Conference come from outside our Continent.

Because of your heavy programme and the limited time you will spend with us, what you will see of this city, and therefore of our country, is the more developed world of which the WHO spoke when it told the story of world health in 1995.

You will not see the South African and African world of the poverty of which the WHO spoke, in which Aids thrives – a partner with poverty, suffering, social disadvantage and inequity.

As an African, speaking at a Conference such as this, convened to discuss a grave human problem such as the acquired human deficiency syndrome, I believe that we should speak to one another honestly and frankly, with sufficient tolerance to respect everybody's point of view, with sufficient tolerance to allow all voices to be heard.

Had we, as a people, turned our backs on these basic civilised precepts, we would never have achieved the much-acclaimed South African miracle of which all humanity is justly proud.

Some in our common world consider the questions I and the rest of our government have raised around the HIV-Aids issue, the subject of the Conference you are attending, as akin to grave criminal and genocidal misconduct.

What I hear being said repeatedly, stridently, angrily, is – do not ask any questions!

The particular twists of South African history and the will of the great majority of our people, freely expressed, have placed me in the situation in which I carry the title of President of the Republic of South Africa.

As I sat in this position, I listened attentively to the story that was told by the World Health Organisation.

What I heard as that story was told, was that extreme poverty is the world's biggest killer and the greatest cause of ill health and suffering across the globe.

As I listened longer, I heard stories being told about malaria, tuberculosis, hepatitis B, HIV-Aids and other diseases.

I heard also about micronutrient malnutrition, iodine and vitamin A deficiency. I heard of syphilis, gonorrhoea, genital herpes and other sexually transmitted deseases as well as teenage pregnancies.

I also heard of cholera, respiratory infections, anaemia, bilharzia, river blindness, guinea worms and other illnesses with complicated Latin names.

As I listened even longer to this tale of human woe, I heard the name recur with frightening frequency – Africa, Africa, Africa!

And so, in the end, I came to the conclusion that as Africans we are confronted by a health crisis of enormous proportions.

One of the consequences of this crisis is the deeply disturbing phenomenon of the collapse of immune systems among millions of our people, such that their bodies have no natural defence against attack by many viruses and bacteria.

Clearly, if we, as African countries, had the level of development to enable us to gather accurate statistics about our own countries, our morbidity and mortality figures would tell a story that would truly be too frightening to contemplate.

As I listened and heard the whole story told about our own country, it seemed to me that we could not blame everything on a single virus.

It seemed to me also that every living African, whether in good or ill health, is prey to many enemies of health that would interact one upon the other in many ways, within one human body.

And thus I came to conclude that we have a desperate and pressing need to wage a war on all fronts to guarantee and realise the human right of all our people to good health.

And so, being insufficiently educated, and therefore ill prepared to answer this question, I started to ask the question, expecting an answer from others – what is to be done, particularly about HIV-Aids.!

One of the questions I have asked is – are safe sex, condoms and anti-retroviral drugs a sufficient response to the health catastrophe we face!

I am pleased to inform you that some eminent scientists decided to respond to our humble request to use their expertise to provide us with answers to certain questions.

Some of these have specialised on the issue of HIV-Aids for many years and differed bitterly among themselves about various matters. Yet, they graciously agreed to join together to help us find answers to some outstanding questions.

I thank them most sincerely for their positive response, inspired by a common resolve more effectively to confront the Aids epidemic.

They have agreed to report back by the end of this year having worked together, among other things, on the reliability of and the information communicated by our current HIV tests and the improvement of our disease surveillance system.

We look forward to the results of this important work, which will help us to ensure that we achieve better results in terms of saving the lives of our people and improving the lives of millions.

In the meantime, we will continue to intensify our own campaign against Aids, including:

- a sustained public awareness campaign encouraging safe sex and the use of condoms;
- a better focused programme targeted at the reduction and elimination of poverty and the improvement of the nutritional standards of our people;
- a concerted fight against the so-called opportunistic diseases, incluing TB and all sexually transmitted diseases;
- a humane response to people living with HIV and Aids as well as the orphans in our society;
- contributing to the international effort to develop an Aids vaccine; and,
- further research on anti-retroviral drugs.

You will find all of this in our country's Aids action plan which I hope has been or will be distributed among you.

You will see from that plan, together with the work that has been going on, that there is no substance to the allegation that there is any hesitation on the part of our government to confront the challenge of HIV-Aids.

However, we remain convinced of the need for us better to understand the essence of what would constitute a comprehensive response in a context such as ours which is characterised by the high levels of poverty and disease to which I have referred.

As I visit the areas of this city and country that most of you will not see because of your heavy programme and your time limitations, areas that are representative of the conditions of life of the overwhelming majority of the people of our common world, the story told by the World Health Organisation always forces itself back into my consciousness.

The world's biggest killer and the greatest cause of ill health and suffering across the globe, including South Africa, is extreme poverty.

Is there more that all of us should do together, assuming that in a world driven by a value system based on financial profit and individual material reward, the notion of human solidarity remains a valid precept governing human behaviour!

On behalf of our government and people, I wish the 13th International Aids Conference success, confident that you have come to these African shores as messengers of hope and hopeful that when you conclude your important work, we, as Africans, will be able to say that you who came to this city, which occupies a fond place in our hearts, came here because you care. Thank you for your attention.

Thabo Mbeki

"THE DEAFENING SILENCE OF AIDS"

PLENARY PRESENTATION

Mr Justice Edwin Cameron
High Court of South Africa, Johannesburg

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It is a great honour to be asked to deliver the first Jonathan Mann Memorial Lecture. It is fitting that this remembrance should have been created to honour Mann's memory and legacy. He more than any other individual must be credited with first conceiving and constructing a global response to the AIDS epidemic. This he did not only as founding director of the World Health Organisation's Global Programme on AIDS between 1986 and 1990, but also after he left the WHO, in his theoretical and advocacy work within the discipline of public health.

It is particularly fitting that the lecture should be initiated at the start of the first international conference on AIDS to take place on African soil. Jonathan Mann's earliest experience with the epidemic was in Africa, where from March 1984 to June 1986 he was director of the Zaire AIDS Research Programme. It was here that Mann first confronted the social complexities and the dire implications of the disease.

Mann's work in Africa included epidemiological, clinical and laboratory components. In retrospect it is clear that it was on this continent that the motive forces impelling his insights into the epidemic were formed. He published early research indicating that HIV transmission occurs only rarely in the home or healthcare setting. His work in Zaire subjected him to an arduous schooling in all aspects of HIV: surveillance and epidemiology, issues of testing in a developing country, case definition, condom usage, and exposure amongst commercial sex workers. It alerted him from the outset to the fearful twinned menace of HIV and tuberculosis. His time in Africa also attuned him to questions involving children and pediatric AIDS, and he published pioneering work on what has perhaps become the epidemic's most poignant issue in Africa-transmission of the virus from mother to child.

But it was not in only the details of the epidemiology and management of HIV that Mann's years in Africa yielded insights that later proved critical. His work amongst Africa's at-risk communities, with Africans living with HIV and with those dying from AIDS, with the healthcare personnel, mothers, sex workers and government bureaucrats in Africa formed the basis of an insight he later termed a 'very intense, emotional, and personal' discovery. This was his realisation during the 1980's that there are empirical and theoretical links between human rights abuses and vulnerability to HIV/AIDS. In each society, Mann later wrote, those people who were marginalised, stigmatized and discriminated against - before HIV/AIDS arrived - have later become over time those at highest risk of HIV infection'.

Mann's statement cannot be accepted without nuance, since in Africa it is relative mobility affluence that have placed people at risk of exposure to HIV. But Mann's analysis here had led him to a more fundamental and general insight - one that formed the focus of his future work and advocacy. This was his realisation that health and human rights are not opposing, but are complementary, approaches to what he called 'the central problem of defining and advancing human well-being'.

In relation to AIDS, Justice Michael Kirby of the High Court of Australia - one of the world's most eloquent voices for truth and fairness - has termed this "the HIV paradox": the insight that sound reasons rooted not only in respect for human rights, but in effective public health planning, necessitate a just and nondiscriminatory response to AIDS; that recognition of and respect for individual human rights does not impede prevention and containment of HIV, but actually enhances it.

In this perception Jonathan Mann located the core of his remaining life-work. And his commitment to advancing its practical realisation constitutes his most profound contribution to securing a humane world-wide response to the AIDS epidemic. Amidst the grievous facts of the epidemic, the one gleam of redemption is the fact that nowhere have the doctrines of public health overtly countenanced repression and stigma, discrimination and isolation, as legitimate governmental responses to AIDS.

That there has been discrimination and stigma against persons with AIDS and HIV, on an enormous and debilitating scale, is certain. The death by stabbing and stoning of Gugu Dhiamini, the township activist, not twenty kilometres from here, in December 1998, provides a brutal testament of such hatred and ignorance. But these practices have not been supported - at least officially, or in any large measure - by the institutional power of the world's public health systems. That public policy at national and international level have weighed against them, constitutes a significant portion of the legacy of Jonathan Mann.

But this does not exhaust his legacy. In the fourteen years since Mann left Zaire for Geneva in 1986, the epidemic has manifested momentous changes. The two most considerable are these: demographics of its spread; and the medical-scientific resources available to counter it.

In its demographics HIV has altered from an epidemic whose primary toll seemed to be within the gay white men of North America and Western Europe, to one that, overwhelmingly, burdens the heterosexual populations of Africa and the developing world. The data are so dismaying that reciting the statistics of HIV prevalence and of AIDS morbidity and mortality - the infection rates, the anticipated deaths, the numbers of orphans, the healthcare costs, the economic impact – threatens to drive off, rather than engage our sympathetic imagination. Our imagination shrinks from the thought that these figures can represent real lives, real people, and real suffering.

But amidst the welter of disheartening data, two facts stand out very clearly:

- nine-tenths of all people living with HIV/AIDS are in poor countries; and
- two-thirds of the total are in sub-Saharan Africa.

But the demography of HIV has been overlain by a shift even more momentous and one that in its nature is optimistic. It is the fact that over the last half-decade, various aggregations of drug types, some old and some new, have been shown, when taken in combination, to quell the replication of the virus within the body. The result has been exciting, life altering and near revolutionary. For most of those with access to the new drug combinations, immune decline has not only halted, but been reversed.

In most of Europe, in North America and in Australasia, illness and death from AIDS have dropped dramatically. Hundreds of thousands of people who a few years ago faced imminent and painful death have been restored to living. Opportunistic infections have diminished, and suffering, pain and bereavement from AIDS have greatly reduced.

Beneficent social effects have come with the medical breakthrough. The social meaning of the new drugs is that the equation between AIDS and death. AIDS can now be compared with other chronic conditions which on appropriate treatment, and with proper care, can in the long term be subjected to successful medical management. Amongst the public at large, the result has been that fear, prejudice and stigma associated with AIDS have lessened. And persons living with HIV/AIDS have suffered less within themselves and in their working and social environments.

In short, the new combination drug treatments are not a miracle. But in their physiological and social effects they come very close to being miraculous.

But this near-miracle has not touched the lives of most of those who most desperately need it. For Africans and others in resource-poor countries with AIDS and HIV, that near miracle is out of reach. For them, the implications of the epidemic remain as fearsome as ever. In their lives, the prospect of debility and death, and the effects of discrimination and societal prejudice, loom as huge as they did for the gay men of North America and Western Europe.

This is not because the drugs are prohibitively expensive to produce. They are not. Recent experience in India, Thailand and Brazil has shown that most of the critical drugs can be produced at costs that puts them realistically within reach of the resource-poor world. The primary reason why the drugs are out of reach to the developing world is two-fold.

On the one hand, drug-pricing structures imposed by the manufacturers make the drugs unaffordably expensive.

On the other, the international patent and trade regime at present seeks to choke off any large-scale attempt to produce and market the drugs at affordable levels.

With characteristic prescience, Mann in his address at the Xlth International AIDS Conference in Vancouver in 1996 foresaw the significance of the treatment issue. He said that of all the walls dividing people in the AIDS epidemic, "the gap between the rich and the poor is most pervasive and pernicious".

It is this divide that, fourteen years after Mann left Africa, threatens to swallow up 25 million people in Africa.

I speak of the gap not as an observer or as a commentator, but with intimate personal knowledge. I am an African, proudly an African. I am living with AIDS. I therefore count as one amongst the forbidding statistics of AIDS in Africa. Including the fact that nearly five million South Africans who have the virus.

I speak also of the dread effects of AIDS not as an onlooker. Nearly three years ago, more than twelve years after I had seroconverted, I fell severely ill with the symptomatic effects of HIV. Fortunately for me, I had access to good medical care. After treatment for opportunistic infections that were making me feel sick unto death. Then my doctor started me on combination therapy. Since then, with relatively minor adjustments, I have been privileged to lead a vigorous, healthy, and productive life. I am able to do so because, twice a day, I take two tablets - one containing a combination of AZT [zidovudine] and 3TC, and the other Nevirapine [Viramune]. I can take these tablets because, on the salary of a judge, I am able to afford their cost.

If, without combination therapy, the mean survival time for a well-tended male in his mid-forties after onset of full AIDS is 30 - 36 months, I should be dead by approximately now. Instead, I am more healthy, more vigorous, more energetic, and more full of purposeful joy than at any stage in my life.

In this I exist as a living embodiment of the iniquity of drug availability and access in Africa. This is not because, in an epidemic in which the heaviest burden of infection and disease are borne by women, I am male; nor because, on a continent in which the virus transmission has been heterosexual, I am proudly gay; nor even because, in a history fraught with racial injustice, I was born white. My presence here embodies the injustices of AIDS in Africa because, on a continent in which 290 million Africans survive on less than one US dollar a day, I can afford monthly medication costs of approximately US$400 per month.

Amidst the poverty of Africa, I stand before you because I am able to purchase health and vigour. I am here because I can pay for life itself.

To me this seems a shocking and monstrous iniquity of very considerable proportions - that, simply because of relative affluence, I should be living when others have died; that I should remain fit and healthy when illness and death beset millions of others.

Given the epidemic's two most signal changes, in demographics and in medical science, it must surely be that the most urgent challenge it offers us is to find constructive ways of

bringing these life-saving drugs to the millions of people whose lives and well-being can be spared by them.

Instead of continuing to accept what has become a palpable untruth (that AIDS is of necessity a disease of debility and death), our overriding and immediate commitment should be to find ways to make accessible for the poor what is within reach of the affluent.

If this is the imperative that our circumstances impose upon us, one would have expected the four years since Vancouver to have been filled with actions directed to its attainment by those with power to change the course of history and the force of the epidemic.

Instead, from every side, those millions living with AIDS in resource-poor countries have been disappointed. International agencies, national governments, and especially those who have primary power to remedy the iniquity - the international drug companies - have failed us in the quest for accessible treatment.

In my own country, a government that in its commitment to human rights and democracy has been a shining example to Africa and the world has at almost every conceivable turn mismanaged the epidemic. So grievous has governmental ineptitude been that South Africa has since 1998 had the fastest-growing HIV epidemic in the world. It currently has one of the world's highest prevalences. Nor has there been silence, as the title of my lecture suggests. Indeed, there has been a cacophony of task groups, workshops, committees, councils, policies, drafts, proposals, statements, and pledges. But all have thus far signified piteously little.

A basic and affordable humane intervention would be a national programme to limit mother-to-child transmission of HIV through administration of short courses of anti-retroviral medication. Research has shown this will be cost-effective in South Africa. Such a programme, if implemented, would have signaled our government's appreciation of the larger problem, and its resolve to address it. To the millions of South Africans living with HIV, it would have created a ray of light. It would have promised the possibility of increasingly constructive interventions for all with HIV, including enhanced access to drug therapies.

To our shame, our country has not yet come so far as even to commit itself to implementing such a programme. The result, every month, is that 5,000 babies are born, unnecessarily and avoidably, with HIV. Their lives involve preventable infections, preventable suffering, and preventable death. And if none of that is persuasive, then from the point of view of the nation's economic self-interest, their HIV infections entail preventable expense. Yet we have done nothing.

In our national struggle to come to grips with the epidemic, perhaps the most intractably puzzling episode has been our President's flirtation with those who in the face of all reason and evidence have sought to dispute the aetiology of AIDS. This has shaken almost everyone responsible for engaging the epidemic. It has created an air of unbelief amongst scientists, confusion among those at risk of HIV, and consternation amongst AIDS workers.

One of the continent's foremost intellectuals, Dr Mamphela Rampele, has described the official sanction given to scepticism about the cause of AIDS as 'irresponsibility that borders on criminality'. If this aberrant and distressing interlude has delayed the implementation of life-saving measures to halt the spread of HIV and to curtail its effects, then history will not judge this pronouncement too harsh. I cannot believe that our President's address at the opening last night has done enough to alleviate the concerns.

At the international level also, there have been largely frustration and disappointment. At the launch of the International Partnership Against AIDS in Africa in December 1999, UN Secretary General Kofi Annan made an important acknowledgement. He stated: 'Our response so far has failed Africa.' The scale of the crisis, he said, required 'a comprehensive and coordinated strategy' between governments, inter-governmental bodies, community groups, science and private corporations.

That was seven long months ago. In seven months, there are more than 200 days: days in which people have fallen sick and others have died; days on each of which, in my country alone, approximately 1.700 people have become newly infected with HIV.

In that time, the World Bank, to its credit, has made the search for an AIDS vaccine one of its priorities. President Clinton, to his credit, in an effort 'to promote access to essential medicines', has issued an executive order that somewhat loosens the patent and trade throttles around the necks of African governments. And UNAIDS, to its credit, 'has begun' what it describes as 'a new dialogue' with five of the biggest pharmaceutical companies. The purpose is "to find ways to broaden access to care and treatment, while ensuring rational, affordable, safe and effective use of drugs for HIV/AIDS-related illnesses".

All these efforts are indisputably commendable. But, whether taken individually or together, they fail to command the urgency and sense of purpose appropriate to an emergency room where a patient is dying. The analogy is under-stated - for the patients who are dying number in their tens of millions. For each of them, and for all their families and loved ones, the emergency is dire and immediate. What is more, the treatment that can save them exists. What is needed is only that it be made accessible to them.

Amidst all these initiatives, the critical question remains drug pricing. No one denies that drug prices are 'only one among many obstacles to access' in poor countries. But there are many, many persons in the resource poor world for whom prices on their own are, right now, the sole impediment to health and well-being. A significant number of Africans with access to healthcare could pay modest amounts for the drugs now. On any scenario, therefore, lowering drug prices immediately is necessary. It should therefore be an immediate and overriding priority.

In fact, lower drug prices are an indispensable precondition to creating just and practicable access to care and treatment. This is so for a number of reasons. First, the debate about drug pricing diverts attention and energy from the other vital issues, such as creating the institutional infrastructure for delivery and monitoring in poor countries. Second, it has sadly provided some governments with a make-weight for delaying implementation of programmes to prevent mother-to-child transmission of the

virus. It has delayed also consideration of more ambitious alternatives in anti-retroviral therapy.

Amidst all of this, it is hard to avoid the impression that the drug companies are shadow-boxing with the issues. There is some evidence that they, in turn, are using lack of governmental commitment on drug provision as a pretext for not lowering drug prices immediately. There certainly has been no immediate follow-through to the announcement eight weeks ago that five of the largest drug companies had undertaken to "explore" ways to reduce their prices. This has devastated the hopes of many poor people who need lower prices, now, to stay alive and healthy.

It is in this context that it is also hard to avoid the conclusion that UNAIDS - whose programme leader, Dr Peter Piot, is a perceptive man of principle who worked with Jonathan Mann in Africa ~ has failed to muster its institutional power with sufficient resourcefulness, sufficient creativity and sufficient force.

Amidst this disappointment, it is quite wrong to speak, as the title of my lecture does, of "the deafening silence of AIDS'. There has not been a silence. Gugu Dhlamini was not silent. She paid with her life for speaking out about her HIV status. But she was not silent. And her death has not silenced many other South Africans living with AIDS, black and white, male and female - most who are less privileged than I - who have spoken out for dignity and justice in the epidemic.

There has also been the principled trumpet of treatment activism. In America, brave activists changed the course of presidential politics by challenging Vice-President Gore's stand on drug pricing and trade protection. Their actions paved the way for subsequent revisions of President Clinton's approach to the drug pricing issue.

In my own country, a small and under-resourced group of activists in the Treatment Action Campaign, under the leadership of Zackie Achmat, has emerged. In the face of considerable isolation and hostility, they have succeeded in re-ordering our national debate about AIDS. And they have focussed national attention on the imperative issues of poverty, collective action and drug access. In doing so they have energised a dispirited PWA movement with the dignity of self-assertion, and renewed within it the faith that by action we can secure justice.

In the last years of his life Jonathan Mann began speaking with increasing passion about the moral imperatives to action that challenge us all. He well understood that this involves what he called: 'A challenge to the political and societal status quo.'

He also understood, in his last writing, the fundamental significance of human dignity in the debate about health and human rights. His work foreshadowed the transition of health and human rights and the 'HIV paradox' to a full human entitlement to health care, where the means for it are available.

Ten months before his death, in November 1997, he called on an audience to place themselves 'squarely on the side of those who intervene in the present, because they believe that the future can be different'.

That is the true challenge to this Conference: to make the future different. Drugs are available to make AIDS, for most people with the virus, a chronically manageable disease. But for most people with the virus, unless we intervene in the present with immediate urgency, that will not happen.

We gather here in Durban as an international grouping of influential and knowledgeable people concerned about alleviating the effects of this epidemic. By our mere presence here, we identify ourselves as the 12,000 best-resourced and most powerful people in the epidemic. By our action and resolutions and collective will, we can make the future different for many millions of people with AIDS and HIV for whom the present offers only illness and death.

This gathering can address the drug companies. It can demand not dialogue, but urgent and immediate price reductions for resource-poor countries. It can challenge the companies to permit without delay parallel imports and the manufacture under license of drugs for which they hold the patents.

Corporately and individually we can address the governments and inter-governmental organisations of the world, demanding a plan of crisis intervention that will see treatments provided under managed conditions to those who most need them.

Vancouver four years ago was a turning point in the announcement of the existence of these therapies. This Conference can be a turning point in the creation of an international impetus to secure equitable access to these drugs for all persons with AIDS in the world.

Moral dilemmas are all too easy to analyse in retrospect. Many books have been written about how ordinary Germans could have tolerated the moral iniquity that was Nazism; or how white South Africans could have countenanced the evils that apartheid inflicted, to their benefit, on the majority of their fellows.

Yet the position of people living with AIDS or HIV in Africa and other resource-poor countries poses a comparable moral dilemma for the developed world today. The inequities of drug access, pricing and distribution mirror the inequities of a world trade system that weighs the poor with debt while privileging the wealthy with inexpensive raw materials and labour.

Those of us who live affluent lives, well-attended by medical care and treatment, should not ask how Germans or white South Africans could tolerate living in proximity to moral evil. We do so ourselves today, in proximity to the impending illness and death of many millions of people with AIDS. This will happen, unless we change the present government ineptitude and corporate blocking. Available treatments are denied to those who need them for the sake of aggregating corporate wealth for shareholders who by African standards are already unimaginably affluent.

That cannot be right, and it cannot be allowed to happen. No more than Germans in the Nazi era, nor more than white South Africans during apartheid, can we at this Conference say that we bear no responsibility for 30 million people in resource-poor countries who face death from AIDS unless medical care and treatment is made accessible to them.

The world has become a single sphere, in which communication, finance, trade and travel occur within a single entity. How we live our lives affects how others live theirs. We cannot wall off the plight of those whose lives are proximate to our own.

That is Mann's call - the clarity of his call - his legacy to the world of AIDS policy; and it is the challenge of his memory to this Conference today.

MARCH FOR HIV/AIDS TREATMENT

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Memorandum

Global Manifesto to Save 34 Million Lives: Measures Needed to Rapidly Expand Access to Essential Treatments for HIV/Aids

Health before profits!
Sunday July 9th 2000

To:

The Honourable Deputy President of South Africa and Chairperson of the South African National Aids Council, Mr. Jacob Zuma

The Honourable South African Minister of Health, Dr. Manto Tshabalala-Msimang

The Honourable South African Minister of Foreign Affairs, Dr. Nkosazana Dlamini-Zuma

Ms. Sandra Thurman, Coordinator, Director of the United States Office of National Aids Policy on behalf of United States President, Mr. Bill Clinton

Mr. Michael Laidler, Ambassador of the European Union in South Africa

Dr. Harvey Bale, Director General of the International Federation of Pharmaceutical Manufacturers Associations

Dr. Peter Piot, Executive Director of UNAIDS

Prof. Jerry Coovadia, Chairperson of the International Aids Conference

Dr. Stefano Vella, President elect of the International Aids Society

The Treatment Action Campaign and Health Global Access Project Coalition (Health GAP) have mobilized the largest coalition of concerned citizens ever assembled to insist on the right to health care and access to life-sustaining medicines.

Our march today demanding access to treatment is the most broad-based in the twenty-year history of the HIV epidemic. We bring before you thousands of people from many different countries and perspectives. On our march today are thousands of people living with HIV and Aids, our friends and families, as well as trade unionists, representatives of political parties, and a wide range of non-governmental organizations. We represent organizations and movements in over 34 countries, many of which cannot be physically present with us today.

We are all united with a single purpose, to ensure that everyone – including people with HIV and Aids – has access to their fundamental right to health.

Underpinning our demands are several issues, which we ask you to recognize publicly:

- Aids has become a catastrophe that threatens the very future of this planet.
- Terrible high levels of HIV infection and death due to Aids are now a reality (rather than merely a projection) in poor communities worldwide. More than half of all these infections occur among women. Aids is causing widespread devastation in Africa and Asia especially. This was avoidable. It is the consequence of negligence, particularly on the part of 'First World' governments whose resources could have been mobilized to come to the practical assistance of poor nations many years ago.
- Scientific research has blessed us with breakthroughs in treatment and care. These advances have resulted in a major drop in Aids-related mortality in rich countries, and have turned HIV infection from a certain death sentence into a chronic disease. With few exceptions, these benefits have not been extended to developing countries, despite the fact that more than 95% of all people with HIV live in these nations.
- These breakthroughs could be brought *very quickly* to benefit many millions of lives – if only the drive for profit by pharmaceutical companies could be tempered. Profiteering from essential goods contributes to what Gro Harlem Brundtland, Director General of the World Health Organization, recently described as the "scandalous inequity" in access to health care. In this regard, we note that in 1999 the combined profits of the 12 largest pharmaceutical companies was US$27,3 billion. This amounts to a horrendous exploitation of the needs of the poor, the sick and the vulnerable.
- Access to medical treatment is essential to effective HIV prevention. People with HIV have the right to expect access to the best treatment. To expect anything less is to surrender.

Recognizing these truths has implications for governments of the North and South, pharmaceutical companies, UNAIDS,

and civil society. We will ensure that history measures your response from this day onward.

We would like to address specific proposals to each of the parties we have called here today:

1. To the South African Government

The South African Government has a unique potential to right the wrongs and inequalities that exist around Aids. Not only is South Africa the worst affected country in the world, but you have the moral legitimacy that has accrued to a nation that has risen peacefully from apartheid, under the leardership of former President Nelson Mandela. In your own words, Aids is a "new struggle". In the words of the Organisation of African Unity's recently signed Ouagadougou Commitment (May 2000) "health constitutes a right and a foundation for socio-economic development," whereas the Aids epidemic is a major "public health, development and security problem for Africa."

We call on the SA Government to:

- Immediately implement a country-wide program to reduce the risk of mother-to-child transmission of HIV using AZT or nevirapine.
- Immediately accept and implement currently offered drug donation programs provided there are no strings attached.
- Immediately issue a compulsory license for fluconazole. This drug could be immediately imported from the lowest-priced producers to extend the lives and improve the quality of life of people with HIV.
- Call on other developing countries to do likewise.
- Demonstrate leadership and integrity in the governance of its HIV/Aids programs as a model for developing countries.
- Compaign for the appropriate and transparent use of public funds for public need, and especially for the development of health infrastructure.

2. To the Governments of the USA and European Union

People from poor countries cannot help but believe that whilst your governments will draw massively from public funds when your own security is threatened, the lives of poor and black people in the emerging 'global village' are considered dispensable and unworthy of protection.

The policies of trade liberalization that you endorse and have pursued through bodies such as the World Bank, IMF and World Trade Organization have had a devastating impact on social services, and particularly health services.

We demand that you:

- Immediately and publicly renounce all trade sanctions or other punitive measures against governments exercising their right to protect the health and well-being of their populations through mechanisms such as compulsory licensing and parallel importing.
- Renounce all threats of bilateral trade sanctions against any country and adhere to the multilateral procedures for dispute resolution to which you are committed by treaty and international law. Least-developed countries should not be pressured to develop intellectual property laws until the established deadline of 2006.
- Immediately offer financing to developing countries, to improve and expand the health infrastructure, both human and capital, needed to treat HIV, Aids and many other causes of illness and disease. This will benefit all people, not just those affected by HIV/Aids.

We call on the US government to extend the scope of the recently issued US Executive Order acknowledging countries' rights to employ compulsory licensing and parallel importing to protect public health to *all* developing countries, not just Africa.

We call on the European Union to adopt similar measures. All these measures should be represented not as charitable "exceptions," but as recognition of countries' legitimate rights under international law.

We also demand that you provide substantial public funding for independent scientific research to develop new therapies and find a cure. This research should be free from the grip of pharmaceutical companies who will exploit it for private interest. Resulting products should remain a public trust, and be made available to the international community. In addition to relevant vaccine research, we consider particularly important the urgent development of effective spermicidal and non-spermicidal microbicides. These will reduce gender inequality and increase women's ability to protect themselves. In addition we call for anti-retroviral therapies that are easier to use by children and adults in countries where there is a shortage of food, water and electricity.

Immediately grant licenses to international agencies to produce all HIV medications for which governments maintain licensing rights, and provide funding to produce these medications in quantity for developing nations.

3. To the International Federation of Pharmaceutical Manufactures' Association (IFPMA)

The pricing policy defended by the IFPMA, where patent monopolies allow your members to place essential drugs beyond the influence of market competition, has become the cause of an unprecedented burden of illness and death. We do not dispute your need to recover investments in research and development, or to profit from these investments. But, in your hands, the profit motive has led to the development of new medicines that are far out of reach of the people who need them.

We call on all members of the IFPMA to:

- Immediately reduce the price of essential anti-HIV/Aids medications to a level affordable to the populations of developing countries.
- Publish on a drug-by-drug basis the actual costs of research and development, active ingredients, manufacturing costs, and all other relevant information necessary for an objective evaluation of the pricing structure for all essential HIV/Aids medications.
- Direct the South African Pharmaceutical Manufactures' Association to withdraw its Court action against the South African Government aimed at preventing health service transformation.
- Cease all actions, whether through litigation or through pressure exerted by other governments, aimed at preventing states from exercising their rights to use compulsory licensing and parallel importing to protect the health of their populations.
- Negotiate with government of developing countries in good faith, toward serious action aimed at addressing a global health-care crisis – not with the media, in public statements aimed at confusing cosmetic gestures with real solutions.

We specifically demand that Pfizer, Inc.:

- Reduce the price of fluconazole internationally to the lowest currently available price per 200 mg tablet by 1 October 2000, e.g. US$0,29.
- Eliminate all conditions from your drug donations. Donations should apply to all developing countries and to all relevant medical conditions, without restriction; should be implemented without delay; and should entail no arbitrary time limitations.
- Not require any conditions that would adversely affect governments' efforts to employ compulsory licensing, parallel importing, or other legal mechanisms to protect public health.

We specifically demand that Boehringer Ingelheim, Inc.:

- Expand your proposed donation of nevirapine for pregnant women to all developing countries and relevant medical conditions; implement the program without delay without arbitrary time limitations. All Boehringer Ingelheim's available resources should be devoted to making this donation a meaningful act, not a publicity stunt.
- Not require any conditions that would adversely affect government's efforts to employ compulsory licensing, parallel importing, or other legal mechanisms to protect public health.
- Include countries manufacturing generic versions of nevirapine in this offer.
- Reduce the price of nevirapine for users other than pregnant women.

4. To UNAIDS

We salute the efforts made by UNAIDS and its predecessor the Global Programme on Aids (GPA). But they have been insufficient. In your own words "18,8 million people around the world have died of Aids, 3,8 million of them children."

But we reject the manner in which you already appear to have given up on the lives of those who today live with HIV. You say, "34,3 million are now living with HIV, the virus that causes Aids. Barring a miracle, most of these will die over the next decade or so."

We do not need a miracle. We need political leardership, resolve and action on the recognition that health is a human right. UNAIDS is vested with this responsibility. We therefore call on UNAIDS to:

- Support national governments by beginning international procurement of Aids drugs, and by December 1, 2000 put out tenders to the proprietary and generic industry for mass procurement of opportunistic infection and HIV medicines. Consider previous vaccine and contraception procurement projects as a guide.
- In all negotiations with drug companies, consult with and ensure the participation of states, particularly developing countries, most affected by the Aids pandemic. All "partnerships" should be accountable to the populations whose lives are at stake.
- With the World Bank, ensure that countries have sufficient financing (offered without restrictive or repressive conditions) to develop a health infrastructure appropriate to administering Aids therapies.

5. To the International Aids Society (IAS), Clinicians and Researchers

We salute your commitment to understanding HIV and to research into treatments and vaccines. We call on you to

- Step up this research. Also, we request that you make your voices heard side-by-side with us in demanding additional public funding and the best use of medicines for the greatest number of people. Silence equals complicity when institutions that use your intellectual ability to produce medicines that are then withheld from the people who most need them.
- Publicly quantify and demand the funds you consider necessary for urgent and relevant vaccine research, effective microbicides and anti-retroviral therapies that are easier to use by children and adults in countries where there is a shortage of food, water and electricity. We will actively campaign for the necessary funding if you announce the sums needed.
- Initiate and coordinate an international scientific collaboration on a plan and timeframe for research. The alliance you have constructed behind the Durban Declaration, which we

welcome without reservation, must now be turned to research.

In conclusion we request:

- An initial response from each of the parties we have addressed at the close of the International Aids Conference on July 14th 2000.
- A detailed response to the proposals made in this Memorandum by August 8th, 2000.

Failure to satisfy us on these proposals will result in an international day of action on December 10th, International Human Rights Day.

We conclude with the words of the Gro Harlem Brundtland, Director General of the World Health Organization, who stated in an address to the Parliament of Brazil earlier this year, "investing in health is a measurable, results-oriented and effective way to reduce poverty... access for all to essential drugs and vaccines is also a short cut to lower mortality and better health for the entire population. Improving such access is among the most effective health interventions any country can make. Health is not a peripheral issue that only more affluent economies can afford to spend money on. It is a central element of development. And access to drugs is an essential element of any health policy."

The millions of people who stand behind our call are awaiting a meaninful response to these demands. We will not go away.

Promise Mthembu
On behalf of the TAC

Mark Heywood
On behalf of the TAC

Julie Davids
On behalf of Health GAP

Eric Sawyer
On behalf of Health GAP

ETHICS OF AIDS RESEARCH IN A DEVELOPING COUNTRY – BALANCING POWER IN DISGUISE

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Chairperson, Honourable Ministers of Health, distinguished colleagues, ladies and gentlemen. It is indeed a great honour for me and the organisation I represent, the MRC, to be given an opportunity to share some thoughts and experiences on the issue of "Ethics of Aids Research in Developing Countries on this prestigious plenary. I thank the organisers of the 13th International Aids Conference for this opportunity. For the purpose of this talk, I have modified the title to "Ethics of Aids Research in a Developing Country – Balancing Power in Disguise".

Breaking my Silence: Twenty years into the HIV/Aids epidemic research continue to focus on women, children, orphans and newborns – many aspects of these have been presented at this conference. We have yet to focus research on boys and men in HIV/Aids. *Let's* remember Aids was first described in men, continues to be spread by men who occasionally infect and affect their female partners. Perhaps one needs to compare research in Aids with research into contraception – 50 years after the female contraceptive pill, we still have to a male equivalent that is universally used.

I shall focus only on two areas: *Power and Informed Consent*. I shall use the South African experience and examples to support my story and draw the following lessons:

i) Ethics of research in a developing country poses exciting challenges for scholars, practitioners and communities that are driven by the principles of equity, human rights and the genuine protection of both the powerful and powerless.

ii) Ethics in developing, continues to demystify and destroy the male liberal racial theory that emerged in the last century.

iii) Informed Consent that is based on the language, idiom and culture of the participant is empowering, not only to the subject but also to the investigator.

iv) Ethics in developing countries remains an important beacon of hope and an integral component and an instrument of transforming society, consolidating young democracies, defining national identities, reclaiming lost cultures and contributing to the global village.

v) Ethics allow us to understand the intricate, the multifaceted nature of and the subtle relationship between power and equality.

vi) Research focusing on men should receive specific attention and resources as part of the greater understanding of the epidemic.

Chaiperson, Homo sapiens-cum-Homo modificans – we are wise, but importantly we continue to modify our environment, ourselves through organ transplants, genetic manipulation and medications – and drive our own evolution – has the following interesting characteristics: the formation of *hierachies*; the expectation to be *imitated within the hierarchy*; a *culture and language/music* as a means of communication which are determined by the dominant group. It is within the characteristics of hierarchy and imitation that dominance and power are located. You may ask – what has power to do with ethics or why is power so crucial in the ethics of Aids or research in a developing country?

Power organises societies, **power** determines relationship; **power** determines norms and behaviour, **power** determines authority and trust; **power** determines what is right or wrong, **power** determines and appropriates knowledge, information in society – in short **power** is powerful. It is within the context of hierarchies, imitation, culture and language that we should locate and contextualise the ethics of research in developing countries.

The practice of ethics in Health Research has been premised on the notion that it ensures good clinical practice and protects the subject, the weak and the powerless. In short,

the practice of ethics has been based on a clear understanding and recognition of the power balance between the practitioner and the subject. It is in the protection of the abuse of this power that ethics has played a central role and emerged as a critical discipline in the development of medical practice and health research.

Because research is to a large extent motivated by scientific objectives such as developing or testing new knowledge, temptations may remain to subordinate the welfare of the volunteers of these objectives and treat human beings as a means to an end. Research may also be motivated by financial gains where expediency obscures ethics to the detriment of volunteers and the integrity of science. Particularly the history of health research in Africa has gone through three phases – the phase of Federal Express Research up to the late 60s, followed by Safari/Sunshine Research in the 70s and 80s and now we have entered the exciting phase of partnerships. The ethics underlying each of these phases leaves much to be desired. Those that have resources choose African partners that are weak, countries that are so poor that the research priorities are not those of the country but those of the foreign partner. The ethics are really guided by the idiom of "He who plays the pipers calls the tune". This is power disguised under good intentions.

It is widely acknowledged that science and ethics are closely connected; poor science is unethical. The scientific integrity of research proposal is an important criterion for ethical approval. However, it is not often stated how sound ethics are a necessary component of good science.

The ethical principles of autonomy – personal liberty of thought and action –, beneficence – the moral obligation to minimize possible harm and actively maximise possible benefits; and justice – fairness in distribution, ensuring that benefits and burdens of research are fairly and equitably distributed – are inscribed in research practices such as Informed Consent and the protection of confidentiality. These inscriptions tend to be treated as "add-ons" rather than intrinsic.

What has not been often emphasised is that the intended and unintended consequences of science, medical practice and health research have their greatest impact on patients, subjects and society. These are usually the weak, inappropriately informed and the powerless in society.

However, there is no doubt that medical practice and medical research over time and through out the world has benefited and improved enormously through the application of ethical guidelines; since the first code of ethics in 1947, the Declaration of Helsinki in 1964 and the later modification by the World Medical Association. Later, the WHO and CIOMS guidelines attempted to deal with transcultural and inequalities issues. The recent UNAIDS codes of ethics specifically deal with international vaccine trials for HIV/Aids. These guidelines require operational elaboration and implementation by investigators, sponsors, host governments and community representative – *they require contextualisation and a transdisciplinary approach.*

Equally the development of ethics as discipline has benefited from this constructive tension between power and the abuse of power.

In a simple, monolithic society – the tension has been the power between the "haves and have-nots" and also the power between the genders – that culture-specific construct between *males and females* that has dominated society in a variety of ways including ethical principles and philosophy. Men in their hunger and quest for more power have formulated most ethical codes – of course for all of humanity and "with good intentions".

In a complex society such as South Africa and some developing countries, in addition to the above, it has been the tension of power between the former oppressors and the oppressed and dealing with the legacy thereof, the tension of power between whites and blacks and the tension of power between the educated and the uneducated.

It has been the tensions between the African perspective and the other perspectives – a world-view tension; a tension between the cultures – African, European and Oriental; a tension between the identities (African, European and Oriental) and a tension between the languages (African and non-African). Thus the definition, the evolution and understandings of ethics in our country and other developing countries are both simple but complex.

It is simple in the sense that there are international norms and principles but complex in the sense that firstly we were not part of the developments of these norms and at times their applications often appear to represent and remind us of an era we are crossing i.e. the era of *legalised inequality and unequal power relationships.*

They have also become complex because of the multifaceted and multilayeredness that disguises power in subtleties.

As ethics are loaded with value, power, a world-view, a perspective, and a culture one often has to question the relevance of concept of international ethics – is this a reality or simply an ideal to aspire towards. Common sense, which is not often common, indicates that no nation practices ideal ethics. Every nation is constrained by its institutions, its legal framework, its level of development and democracy and its commitment to the principle of equality. However, every nation should practice the best ethics that is attainable within its own constraints. This is the context in which ethics of research in developing country are taking place.

The challenge for us all in South Africa is the management of these complex and multi-layered tensions in a constructive manner such that we as a society nuance our ethical guidelines and principles in manners that allow us to improve our science, clinical practice and research but also protect and empower the weak, the powerless in our society. The develpments of our ethics mirror the development of our societal transformation, our constitution and our democracy – they are informed by broad consultations and parcipation from different sectors of our society. No longer can academics or researchers – despite their good intentions – sit in the ivory towers to construct guidelines without engaging civil society in an open and transparent process. The history of our past is riddled with mistakes that are too ghastly to list or repeat.

Ethics of research are not only an instrument of liberating ourselves from the legacy of apartheid but also a crucial instrument in liberating our former oppressors and setting a blueprint for the future.

If we were today to honestly interrogate our ethics in South Africa as the Truth and Reconciliation Commission did, there is no doubt that we would find many shortcomings. These shortcomings provides lessons and demand that we take a new path and trajectory in the development of ethics for research, science and clinical practice.

We would find that health professionals just like all human beings are by and large products of their environments and the political systems under which they live and operate. There is no doubt that ethics in South Africa evolved from the male superiority race model of apartheid in which blacks and women were inferior. This white androgenic ethical model whilst couched in reasonable language and principles, it was in reality a mere facade for and an extension of the powers and political systems that be. Theory and practise of ethics in science and research were at times like day and night.

As a result several research projects were approved that with hindsight would not be e.g. the approval of the biological warfare programme under the leadership of Dr. Wouter Basson to develop substances that would either render most blacks infertile or selectively poison or maim black people; the suppression to publish results of asbestosis in our mines that would lead to litigation of white mining officials and finally the failure to publish results that would indicate that whites our country "had thick skulls" or that some alleged pure Afrikaners were the products of mixed sexual liaisons. Of course some of these today occasionally feel entitled to affirmative action programmes – thanks to the new dispensation. There are also cases were ethics were simply ignored such as the Professor Bezwoda case at the University of the Witwatersrand where patients were subjected to inappropriate treatment trial protocols, the results of which were also "doctored". While these were suppressed to protect the powerful – the white community; there are numerous examples both in clinical practice and research that would certainly count as examples of the abuse of the weak and the powerless in our society.

Perhaps examples in this arena fall within the area *of Informed Consent* for research and generally for operations. There are many understandings of the notion of Informed Consent. The moral, legal and ethical aspects of informed consent and the practical implications of each of these factors must be carefully considered in the design of Informed Consent procedures for HIV/Aids vaccine trials.

While informed consent has been the cornerstone of clinical practice and trials and is a critical requirement for participation in studies, Informed Consent has also become one of the major ethical transgressions of our time – particularly in developing countries. Informed Consent has four essential components: disclosure of all relevant information about the research; comprehension by the prospective participant of this information to make informed decision; freedom from all coercion of the prospective participants; explicit and formal consent by the participant, usually in written form.

However, codes and requirements alone do not guarantee protection as exemplified by the Tuskegee case. In South African and most developing countries, most of our subjects speak and live for the rest of their lives in a different language from the languages of the researchers and practitioners; secondly most subjects in our countries are poorly informed with substandard education. Thirdly the power and magic of the investigators or doctors continue to give disproportionate trust and power by patients and subjects to the practitioner or researcher. "The doctors know it all and have my interest at heart" – this is how our societies have operated and that is also how Africans have been so well colonised and exploited through out history.

As we globalise the language and tactics have changed but the effect remains the same. The weak and powerless in our society require a different form of approach, education and communication in order to fully understand the magnitude and implications of signing an informed consent form. This is an area that the HIV/Aids epidemic has begun to interrogate into with telling lessons. The SAAVI Group led by Dr. Graham Lindegger and Professor Linda Richter funded by the South African government, has made seminal contribution into the whole area of designing Informed Consent within the South African settings – language and culture-sensitive.

How does one sign a consent form when one hardly understands the concepts in the projects and their roles in it? **In such instances the tendency is for power to prevail above protection.**

This is also partly the major reason why trials are always done more easily in the developing countries rather than the developed ones – because the subjects in the developed countries understand Informed Consent, demand higher standards of protection than ours in the developing countries. Perhaps for me a telling example was of a patient in 1975 who had a carcinoma of the vulva and consented to undergoing a total vulvectomy without telling her husband, her family because she did not fully appreciate what the operation would do. Clearly the surgeon and the patient could not have fully understood each other but at what and whose cost? When she woke from theatre she required psychiatric treatment rather than surgical or medical treatment – the rest of her life was totally ruined and her whole world had completely changed. The second classic example documented in the TRC's health section is how the medical profession, the state and the security system colluded in the murder of Steve Biko in 1977.

Perhaps no disease has challenged the ethical and moral principles of a society such as HIV/Aids. The areas that are of most concern here are the ethics of vaccine development and clinical trials; the areas of anti-retrovirals for HIV/Aids patients and the prevention of mother to child transmissions. These areas have posed serious moral and ethical dilemmas in our society. The affordability, sustainability of these treatments within a society that prides itself in human rights and the promotion of equity and development have posed great ethical dilemmas.

The clinical trials for our vaccines (the VEE-based clade C vaccine) are due to start early next year. Much of this vaccine

work will take place in under-resourced communities, where people are at high risk of HIV infection, so human rights implications for participants and other members of the community need careful consideration in issues of resource allocation to HIV vaccine development, the protection of trial volunteers from the risks of participation, and access to a successful vaccine.

In preparations for these Community Advisory Boards, researchers, counsellors and educators have mounted a massive education, counselling, information campagin to ensure that communities do fully understand the nature, extent and implications of these trials. These campaigns are to ensure that individuals and communities are fully empowered to know and exercise their rights as they participate in the trials. These are done in the languages, idioms and within the culture of the participant – i.e. language and culture-sensitive.

It is vitally important to recognise that empowering the participants also empowers the researcher and improve substantially the integrity of the research and the science.

Potencial participants often ask whether they are simply guinea pigs-we have heard these statements from Uganda, Kenya, South Africa and many parts of the developing world – and what it is in it for them, how will they benefit themselves and society at large, what happens to them if they should get breakthrough HIV infections and what happens to them in terms of access to ART treatment – all sensible and germane questions.

Perhaps a crucial issue for ethics in developing countries is to tease the underlying assumptions from the perspective of the participants. Too often communities are researched upon ad nauseum without any benefits accruing or flowing back to that community. **Simply stated the researcher gets the publications, the glory amongst his/her peers while the community or the participant remains dis-empowered and underdeveloped. This is the story of many African participants and many African communities.**

As part of our own ethical dilemmas in relation to HIV treatment, the government continues to seek advice and information from best practice and the results of anti-retroviral treatment regimens in order to formulate its own – equitable, affordable, accessible and sustainable – strategy for anti-retroviral treatment. The emerging consensuses are: the treatment of STDs and opportunistic infections; the treatment of advanced symptomatic HIV/Aids and the prevention for mother to child transmission in the context of a basic infrastructure are critical. These are programmes that should be prioritised for implementation within our country. We have every faith and confidence that our government will negotiate these dilemmas with success.

In conclusion, i) ethics of research in a developing country poses exciting challenges for scholars, practitioners and communities that are driven by the principles of equity, human rights and the genuine protection of both the powerful and powerless.

ii) Ethics in developing countries continues to demystify and destroy the male liberal racial theory that emerged in the last century.

iii) Informed Consent that is based on the language, idiom and culture of the participant is empowering, not only to the subject but also to the investigator.

iv) Ethics in developing countries remains an important beacon of hope and an integral component and an instrument of transforming society, consolidating young democracies, defining national indentities, reclaiming lost cultures and contributing to the global village.

v) research that specifically focus on men, their socialisation, their biology should be identified and allocated resources.

vi) Finally, ethics allow us to understand the intricate, the multifaceted nature of and the subtle relationship between power and equality.

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ADVANCES IN HIV/AIDS TREATMENT

PLENARY PRESENTATION, JULY, 11, 2000

Mauro Schechter, MD PhD
UFRJ – Brazil

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I would like to thank the Conference Organizers for giving me the honor and privilege of presenting this talk to such a distinguished audience.

Slide

Since the Geneva Conference, data have accumulated to indicate that eradication is unlikely with presently available drugs; virologic failures are more common in practice than in trials; the CD4 cell counts at which opportunistic infections occur in patients on therapy and patients who are not on therapy are similar; that, although many patients do not achieve full immune recovery, a large proportion achieve a "safe" level of immune competence; and that antiretroviral therapy is associated with potencially serious side effects, some of which may be time-dependent.

Slide

These newly accumulated data, in turn have led to a renewed debate on: the optimum time to treat; the choice of initial drug regimen; when to change and how to sequence regimens; how to simplify existing regimens; the role of new drugs and of pharmacologic enhancement in extending treatment benefits; and on the management and prevention of opportunistic infections.

During my presentation I will review recent data on each of these topics. I will finish by trying to predict, in light of the data reviewed, how the history of HIV treatment may unfold in the coming years.

Slide

Over the past several months, the optimal time to iniciate therapy has been hotly debated, particularly in reference to the threshold values of viral load and CD4. With regards to viral load, two separate reports published in JID have demonstrated a direct association between the slope of the increase of plasma viral load in the first few years after seroconversion and the probability of progressing to Aids. In the MACS study, as shown in these four panels, the rapidity of progression was found to be proportional to the slope of the increase of viral load. On the upper leftpanel are represented those who progressed in less than 3 years, on the upper right in 3 to 7 years, on the bottom left in more than seven and on the bottom right those who remained Aids-free for at least nine years.

Slide

It was also shown that, for those who progressed to Aids, the slope of viral load increase in the three years preceding progression to Aids was similar, regardless of prior Aids-free time. On the upper leftpanel are represented those who progressed in less than 3 years, on the upper right in 3 to 7 years, on the bottom left in more than seven and on the bottom right those who remained Aids-free for at least nine years. These observations argue against a blanket concept of a fixed set point. They also suggest that it may be more appropriate to measure viral load in a serial fashion, rather than relying on one or two measurements in order to make therapeutic decisions.

Slide

Julio Montaner will report in a late breaker session on a population based cohort analysis of antiretroviral naïve adult patients who started HAART between 08/96 and 09/00 in British Columbia. There were over 1,200 eligible participants and data were censored on January 31, 2000. Results showed that the effectiveness of therapy was dependent on baseline CD4 count, but not on age, gender, viral load, prior Aids diag-

nosis, or PI use. Furthermore, few patients with baseline CD4 > 200 cells/mm³ experienced clinical progression and progression rates were similar for patients with CD4 counts 200-350 or 350-500 cells/mm³.

Slide

These results suggest that it is probably OK to postpone treatment initiation, provided therapy is started while immune recovery to "safe" levels is still possible. The question of how to precisely define this moment remains unanswered.

Slide

Once the decision has been made to start therapy, the optimal initial regimen has also been a matter of debate. At the recent Retrovirus meeting, John Bartlett presented data on a re-analyzes of 22 different trials of triple drug therapy in naïve patients. These authors showed that when the same methodology and definitions are used virologic success rates are quite similar, regardless of the regimen used, as shown in the slide.

Slide

In the same study, these authors have also shown that, at 48 weeks, the proportion of participants with plasma viral load below 50 copies/ml or the median CD4 increase (as shown in the two columns in the far right) were very similar for patients who started triple regimens containing a protease inhibitor, a non-nuke or triple nukes.

Slide

In fact, as represented in this graph, they also showed that, regardless of the regimen, i.e, PI-containing, NNRTI-containing or triple nukes, there was a significant association between pill burden and virologic success, further reinforcing existing data on the relationship between adherence and virologic success.

Slide

Once treatmen is instituted, several groups have reported that virologic failure rates are much higher in clinical practice than in clinical trials. For example, at the Johns Hopkins HIV clinic, fewer than 40% of patients had a viral load below 500 copies/ml after 7-14 months on therapy, as shown on the right hand side of this slide.

Slide

On the other hand, immunologic failure may be less common. Several groups have reported on the so-called "discordant response". For example: Steve Deeks has recently reported in JID results on 380 patients on HAART. It was shown that, after 96 weeks of follow-up, gains in CD4 counts (shown in the upper panel) were almost identical for patients who experienced complete virologic success (i.e, remained undetectable throughout the follow-up period, represented in green in the graph) or who experienced a transient response (those who reached an undetectable level followed by viral rebound, represented in white in the graph). In addition, even patients with a partial response (those whose viral load fell but never became undetectable, purple in the graph), also experienced sustained increases in CD4 counts. These authors showed that the degree of viral suppression (the difference between the pre-treatment levels and the level achieved 12 weeks after virologic failure, termed "delta viral load" by the authors) is a stronger predictor of immunologic success than the absolute viral load achieved.

Slide

The relationship between sustained immunologic and clinical benefit despite virologic failure was demonstrated in a large prospective observational study (the Swiss Cohort Study). In this study, after 30 months of follow-up, after controlling for baseline CD4 and age, patients with transient virologic responses (the red curve in the middle panel) had clinical progression rates that were similar to that seen in patients who maintained an undetectable viral load (the red curve on the left panel).

Slide

It is worth mentioning that this phenomenon (immunologic and clinical benefit despite virologic failure) also occurs in patients receiving dual RT-therapy. For instance, this slide shows the results of a study conducted in Rio de Janeiro, involving 80 patients sequentially seen in an outpatient clinic and who started dual RT therapy in 1996/97 according to the guidelines of that time (being asymptomatic and having a CD4 > 200). After 2 years of follow-up, despite virologic failure in almost all (shown in the bottom panel), none had experienced disease progression and CD4 counts had risen on average by almost 200 cells (shown in the upper panel). This observation may be of particular importance for resource-limited settings, especially after the recently announced initiative by several pharmaceutical companies that may greatly reduce the cost of antiretrovirals, RTs in particular.

Slide

As previously discussed, regardless of the regimen chosen, a considerable proportion of patients eventually fail on their initial therapy. Thus, many patients will eventually use several antiretroviral regimens. For instance, according to Mike Saag, in the period 1996-99, at the University of Alabama, the median time on a single regimen was 4 months. Thus, for many (if not most) patients, the ultimate success of antiretroviral therapy will likely depend on the aggregate effectiveness of

sequential therapies, not solely on the potency of a particular regimen used as initial therapy. Nonetheless, there are limited data on the clinical impact of sequential therapies, particularly for patients at the earlier stages of HIV disease.

Slide

For this reason, we have developed a mathematical model which was published in AIDS last year. This model, to which we applied data from published studies, was used to compare expected clinical outcomes using three different therapeutic strategies, using PI and non-PI containing regimens as initial therapy and PI or dual PI-containing regimens after the first virologic failure. Two different scenarios (optimistic and pessimistic, according to the proportion of patients who maintained virologic control) were also used. After 5 years of follow-up, predicted clinical outcomes were virtually identical regardless of the initial regimen used, as can be seen by the almost overlapping lines in the graph. These results suggest that, with presently available data, it is not possible to predict which strategy for inicial therapy is best. Thus, it is likely that we will only be able to make firm recommendations after the results of trials that compare treatment strategies, such as INITIO and ACTG 384, are in, which may take a few years.

Slide

In the meantime, and since virologic failures are common, strategies to enhance compliance, reduce toxicity and prevent resistance are being developed, and include: the development of more user-friendly regimens; pharmacologic enhancement ("PI-boost"); development of new drugs in existing classes that are designed to select for novel mutation sites; development of new classes of drugs; and the evaluation of structured treatment interruptions.

Slide

The use of the combination of abacavir, AZT, and 3TC, which in the near future will involve only two pills a day, is an example of a simple regimen using existing drugs. In clinical trials, such as the one shown on this slide, results obtained with this regimen are comparable, in terms of viral load and CD4 response, to those obtained with a standard PI containing regimen, in this case AZT, 3TC, and Indinavir.

Slide

Regimens with single daily doses, which may even allow for directly observed therapy in some settings, are also being developed. For instance, ddI and efavirenz are already licensed for once-daily use. Studies are in progress involving other drugs, including lamivudine, FTC, nevirapine, tenofovir and combinations of PIs. In addition, a PI for once daily dosing (BMS-232632) is at an advanced stage of development.

Slide

The soon-to-be licensed drug formerly known as ABT-378 is an example of a new drug in an existing class that requires a higher genetic barrier for resistance to develop (ie, a larger number of mutations is necessary for the development of high level resistance). It is also an example of the pharmacologic boost that can be obtained with the concomitant use of small doses of ritonavir, often called "PI boost", as illustrated in this slide.

Slide

Additionally, several drugs in the existing classes are in advanced stages of development and can be expected to be licensed in the coming years. T-20 deserves special mention, since it is the first drug of a new class (fusion inhibitors) that should be entering phase III trials in the near future. In addition, T-1249 is another drug of this class entering clinical trials.

Slide

Another subject being hotly debated is the so-called "Strategic treatment interruptions". Here, two situations must be differentiated. The first involves patients failing therapy with multiply resistant HIV, which I prefer to call a "drug holiday". The second involves patients on therapy with full viral suppression, for whom temporary interruptions of treatment are being evaluated.

Slide

At the Retrovirus Conference early this year, Steve Deeks presented data to show that for patients failing therapy with multiply resistant HIV, the interruption of therapy is associated with an abrupt switch to a sensitive phenotype, which is simultaneous for all drugs, as shown for three different patients in this slide. Some cautionary notes, however, should be made. In that same presentation, convincing data was shown to indicate that this phenotypic change is associated with an abrupt drop in CD4 counts and a steep increase in viral load. In addition, once therapy is re-introduced, viruses with resistant phenotypes promptly re-emerge. These data suggest that, until more data are available, drug holidays as a therapeutic strategy should be viewed with extreme caution.

Slide

For patients on therapy and with full viral suppression, the rational for temporarily interrupting therapy is the hope that viral rebound may restore some HIV specific response (an "endogenous vaccination"), which, in turn, could lead to immunologic and clinical benefit. Studies involving such patients are being conduced by several groups. In general, as Dr. Fauci showed, it has so far been shown that decreases in CD4 counts precede

increases in viral load and that, upon resumption of HAART, viral load returns to < 50 copies/ml in nearly all individuals and the CD4 count returns to the levels prior to interrupting therapy. Notably, it has been reported that no genotypic or phenotypic resistance develops. Given these preliminary results, studies are under way to evaluate intermitent HAART as a means of controlling HIV replication while sparing patients the toxicity, inconvenience and cost of continuous HAART.

Slide

As has been reported from all countries that can afford the high price of antiretrovirals, the introduction of PIs into clinical practice was soon followed by a steep decline in mortality rates among patients with advanced HIV disease, as shown in this slide that most if not all of you have seen countless times. Nonetheless, several published reports have documented that impressive declines in mortality, rates actually preceded the availability of HAART by several years.

Slide

For instance, in British Columbia, mortality rates among patients with < 100 CD4 (in yellow in the graph) fell by approximately 70% between 1994 and 1996.

Slide

Similary, in Chicago, despite the continuous increase in the number of prevalent Aids cases (as shown in white in the larger graph), HIV-related deaths (as shown in the insert), decreased by over 60% in the same period.

Slide

In Europe, mortality rates among patients with CD4 counts below 200 and who were not on antiretroviral therapy (shown in the second column on the left) fell by 45% between 1995 and 1997. Clearly, other factors, besides HAART have influenced these declines in mortality rates.

Slide

According to data recently published in the NEJM, the incidence of opportunistic infections in the US declined markedly in the years that preceded the availability of HAART. It is thus quite possible that, in addition to the availability of potent antiretrovirals, better treatment and prophylaxis of opportunistic infections may have played an important role in the decline of mortality.

Slide

If this is the case, then the adequate use of available interventions to prevent opportunistic infections may remain very important. I would like to single out two infections, tuberculosis and pneumococcal infections, since both can cause significant morbidity and mortality in developing as well as developed countries and both may occur in patients with a relatively preserved immune system. In addition, both are potentially preventable with relatively cheap interventions.

Slide

A paper by Jones and collaborators that will be published in the next few months in the International Journal of Tuberculosis and Lung Diseases demonstrates that among patients with < 500 CD4 cells, TB incidence in the US has been steadily falling since the early 90's, irrespective of antiretroviral therapy in use, this fall being more marked amongst patients on HAART.

Slide

Several years ago, Bill Pappe showed in Haiti that, in a population without access to antiretroviral therapy, primary prophylaxis with INH was capable of reducing mortality. In a poster presented at this conference, Dr. Santoro-Lopes in my group reports the results of a prospective study involving 306 HIV+, PPD+ patients, with a median follow-up of 4 years. In Brazil, antiretroviral therapy, including protease inhibitors, is available free of charge to all HIV infected individuals. In this study, after adjustment for antiretroviral therapy, prophylaxis was shown not only to reduce the risk of TB by 84%, but also, as shown in the graph, to reduce the risk of death by almost 60% (patients who did not receive prophylasis shown in yellow, whereas those who received prophylaxis are represented in white in these survival curves). These results firmly indicate that even in areas or for populations with high prevalence rates of *M. tuberculosis infection,* primary prophylaxis remains very important even when HAART is available.

Slide

In 1999 Osmond reported in CID the results of a large observational study conducted in the US to evaluate pulmonary complications associated with HIV infection. In that study it was shown that the development of bacterial pneumonia (in white in the graph) was associated with significantly worse subsequent HIV disease course, when compared to CD4 matched controls (yellow in the graph). These data seem to reinforce the recommendation that pneumococcal vaccination should be considered as standard of care.

Slide

Nevertheless, in a recent issue of the Lancet, a team of investigators led by Charles Gilks reported the results of the first large trial to evaluate the efficacy of pneumococcal vacci-

nation. This study, conducted in Uganda, involved approximately 1,400 participants randomized to receive a 23-valent pneumococcal vaccine or placebo. Surprisingly, it was shown that both invasive pneumococcal disease and all cause pneumonia were more common in vaccinees (white in the graph) than in placebo recipients (represented in yellow in the graph). These unexpected findings raise several questions, including that recommendations from industrialised countries need to be evaluated in resource-poor settings and that policy should be evidence based, before any intervention becomes standard of care.

Slide

In summary, considering all the data that I have just reviewed, as well as other pieces of information that time constraints did not permit me to present, I will take the liberty of making some predictions as to what I think may happen between now and when we reconvene in Barcelona in two years: The pendulum will swing back towards later treatment; the definition of failure in clinical trials will be revisited; greater emphasis will be placed on "delta viral load"; CD4 count as a guide to therapy will undergo a renaissance; and simpler drug regimens will become available.

Slide

I also predict that there will be renewed interest in the prevention of opportunistic infections, which, in turn, will take into consideration local epidemiologic conditions; there will be a re-evaluation of the role of "less potent" regimens, particularly their cost-effectiveness in resource-limited settings; STI will be discussed as a means of making treatment less toxic and more affordable; and pressure on industry and Governments will increase to ensure equal and universal access to antiretroviral therapy.

These are only predictions. If they will pan out, only time will tell, since, as one American philosopher once said...

Slide

"All predictions are difficult, particularly when they involve the future".

Slide

Finally, I would like to sincerely thank all my friends and colleagues who shared with me their data, slides and wisdom in order to make this presentation possible.

Thank you.

RESEARCH SUBJECTS IN DEVELOPING AND DEVELOPED COUNTRIES SHOULD HAVE THE SAME STANDARD OF CARE

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Thank you Mr. Chairman.

Initially let me state that I am grateful to the organizers for the invitation to take part in this session, and I am highly honoured to share this debate with Prof. Benattar.

This talk is from the perspective of an NGO activist, a person living with HIV in Brazil, a Latin American and a Math PHD. Since we are more familiar with AIDS, this talk restricts itself to a discussion of this area.

During the next minutes I shall offer some arguments supporting that participants in clinical trials in developing and developed countries should receive the same standard of care. Many national Physicians Associations, such as the Brazilian, Dutch, German, Norwegian and Thai Associations currently support this position.

Distributive Justice and the Global AIDS Pandemic

A first argument against different standards of care refers to distributive justice and the globality of the AIDS pandemic. The principle of distributive justice could be stated as: those who bear the highest burdens should receive the highest benefits.

This means that if we have a trial which could be developed in two communities, one of them more vulnerable than the other, we should conduct the trial on the more vulnerable community ONLY IF it would receive a higher benefit than the less vulnerable community. For example, we should not develop a trial in a community of poor people when the main beneficiaries will be rich people.

This is clearly stated in some CIOMS guidelines (International Ethical Guidelines for Biomedical Research Involving Human Subjects, Geneva 1993.)

Guideline 8 (CIOMS): Research involving subjects in underdeveloped communities. Persons in underdeveloped communities will not ordinarily be involved in research that could be carried out reasonably well in developed communities.

Guideline 10 (CIOMS): individuals or communities to be invited to be subjects of research should be selected in such a way that the burdens and benefits of the research will be equitably distributed.

On the other hand, AIDS is a **global epidemic**. And certainly the result of many trials conducted in developing countries will benefit developed countries. This is not the case for all diseases, like dengue for example.

Therefore, a trial whose results would benefit mostly developed countries and which is conducted in a developing country should offer, among other things, **exactly** what would be offered if the trial were conducted in the community which benefits the most from it.

Let us give an example.

A recent trial on infectivity and viral load published recently in the NEJM 2000 (342): 13; 921-929 was carried out on persons in rural Africa and proved, in a secondary analysis, that infectivity was proportional to viral load. These persons were not provided ARVs, among other things. The people who take most benefit from the result of the secondary analysis are those who can control viral load, eg, people in developed countries in general. Those who bore the heaviest burdens will have the least benefits. "The very condition that justified doing the study in Africa in the first place - the lack of availability of antiretroviral treatment - will greatly limit the relevance of the results there. As is so often the case, the results will probably find their greater application in the developed world" Angell, M. Investigators' responsibilities for human subjects in developing countries. NEJM (2000) 342 (13): 967-969

In our opinion if the aim of this trial had been to prove the relationship between viral load and infectivity, it would not fulfill the principle of distributive justice.

One of the authors, when the ethics of this trial was questioned in an internet discussion [Treatment Access list, messages #791 and #792 argued that this trial "... provides a strong rationale for the development of affordable ARV treatments or therapeutic HIV vaccines, both to benefit HIV-

infected persons and to control HIV transmission..." We think that this assertion just confirms our thought.

The following questions might be interesting for the debate: Could an identical trial be conducted in a developed country? Could a trial designed to evaluate the same relation between infectivity and viral load be conducted in a developed country?

We think so, under certain more complex conditions. The complexity is due to the fact that we would have to satisfy optimal ethics and optimal scientific methodology.

Ethics and scientific methodology have different sources and in order to respect both, the research will often have to be more complex than if we only respected science. This is a common challenge, but we are confident enough that researchers can surpass it. "...In appearance, moral demands are a brake. In fact, they contribute to the best and most beautiful of what man has produced for science, the individual and the community..." Moral limits of Medical Research and Treatment, read before the First International Congress on Histopathology of Nervous systems, Pope Pius XII. (1952) apud Beecher, H JAMA (1 959), 466-478

Researcher-volunteer versus Doctor-patient

For our next argument let us initially quote parts of the Helsinki Declaration (1996, currently under review) which is important for our discussion:

The Declaration of Geneva of the WMA (1983) binds the physician with the words, "The health of my patient will be my first consideration"

Paragraph II.3 "In any medical study, every patient - including those of a control group, if any - should be assured of the best proven diagnostic and therapeutic method".

From here on, we shall refer to the best proven treatment as optimal treatment and any other inferior therapy will be called suboptimal.

One of the ways differences in standards of care in clinical trials occur is by the provision of suboptimal treatment to people in developing countries.

As some authors have observed, offering suboptimal treatment in clinical trials yields a conflict of interests between the relations "doctor-patient" and "researcher-volunteer". The doctor-patient commitment "...is governed by justice, altruism and virtue, not by efficiency neither marketplace values..." Brennan, Troyen. Proposed revisions to the Declaration of Helsinki: will they weaken the ethical principles underlying human research. **In Bull Med. Eth**. 1999; 150 :24-28. This relationship is based on "solidarity" (Weizsaecker apud Beecher 1959)

Physician researchers engaged in trials testing the efficacy of suboptimal treatments may find themselves in conflict of interests. This would be due to the fact that researchers-physicians may often have access through various sources, to medication that could be used to supplement the suboptimal treatment their trial patients are being subjected to.

But in this case the patient would have to be withdrawn from the research sample since he would have received different treatment from those being tested. To make matters more complicated, if the patient were excluded from the suboptimal treatment he might be reduced to the supplementary doses obtained by the reseacher-physician (which in themselves might be inferior to the original suboptimal treatment).

Moreover, let us observe that the research itself can get inadequate results from its volunteers.

This happens because the physician should inform his patient that there is an optimal treatment and that he will receive a suboptimal treatment. But, for the success of the trial, the physician must also ensure that the patient - even though accurately informed - does not, procure for himself a supplement to the trial medication.

Therefore for the success of the trial, not surprisingly participants should be chosen among those who do not have the personal possibility of getting supplements, that is, the more vulnerable the better for the rigour of the research and (allegedly) for the future benefit of the society.

An example is the case of the trials comparing short course AZT versus placebo. A researcher getting some extra bottles of AZT could provide them to some people in the trial. Or a participant if adequately informed by the physician and by the Term of Informed Consent about the existence of a better regime like the one offered by PACTG076, could get some extra bottles of AZT for herself or her baby.

Multicentre studies and differentiated standards of care

Does this mean that we are only allowing multicentric studies between countries which provide exactly the same standard of care?

The conflict between the interests of "the health of my patient" and "the rigour of my research" is clearly established, unless the trial provides the optimal intervention.

AIDS Vaccines Area

In the area of HIV vaccines, efficacy trials were planned since 1994, before the last revision of the Helsinki Declaration (1996). Why is it that nobody questioned paragraph II.3 in those days? Why is it that when those efficacy trials were planned no one thought about different standards of care, while nowadays an UNAIDS document suggests this possibility-UNAIDS Ethics Guidelines (16)? Why is it that these different standards of care appear in the AIDS vaccines area EXACTLY IN THE SAME MOMENT in which the US government invests more money on HIV vaccines, the G7 group commits itself to doing the same and when the World Bank seeks funds for these purposes? Multimillionary agencies and the richest countries in the world can offer the optimal therapy to infected participants - whose number need not be great for a vaccine to show some efficacy. For these reasons, the best known standard of treatment can be provided for people infected during the trial of HIV vaccines, either in developing or developed countries.

Tell me WHY

Why are we trying to establish different standards for participants in clinical trials according to the place in which the trial is conducted?

Why is this question posed now? And why does it specially derive from the AIDS area? Why does this question appear after a Conference was held in Geneva with the motto "Bridging the Gap", obviously addressing the treatment gap? Why are we now trying to widen the treatment gap by including a population which until now clearly had access to treatment, ie, volunteers in a clinical trial? Why is it that in the Vancouver Conference we had as a motto "One world, one hope" (Vancouver, 1996) and now we propose two or much more worlds?

I think that many authors have already addressed this subject:

"It is the rapid march of science itself that is largely responsible for the pressures to weaken subject protections. Capability tends to be at odds with restraint... These increased capabilities are generating demands for ever-larger numbers of human subjects in research, for easier recruitment and conscription of research subjects", Challenges to Human Subject Protections in US Medical Research. Woodward, W. JAMA (1999) 282 (20): 1947-1952

(*)"We feel that one of the main issues we all have to face is the increasing, almost dominant role that pharmaceutical company sponsorship is now playing in the conduct of clinical studies. ...How does one make sure that such commercially funded research, involving secondary gain on the part of the sponsor and partner-researcher is ethically and scientifically sound?"A comment from Thailand (SP, HW, CP and YT) In **Bull Med. Eth**. 1999; 150: 37 (*)

In the US, "... recent, widely reported problems in clinical research have shaken public trust..." which led to a "Reaffirmation of Trust Between Medical Science and the Public" (June 7th, 2000) undersigned by more than 300 Universities and organizations in the US. This Reaffirmation states, among other things, that "... the health and welfare of patients must always be placed above all other concerns,..."

The reasons quoted for conducting research in developing countries rather than in developed ones are: "... **lower costs, lower risk of litigation, less stringent ethical review, the availability of populations prepared to give unquestioning consent**, antecipated underreporting of side effects because of lower consumer awareness, the desire for personal advancement by participants, **and the desire to create new markets for drugs**." (emphasis added) Research and Informed Consent in Africa - another look. Ijsselmuiden, Carel B. NEJM (1992) 326 (12): 830-834 and Temmerman M. Informed Consent in Africa. NEJM 1992; 327: 1102-3 apud Peter Wilmhurst. Scientific Imperialism BMJ 1997; 314: 840-841

But another source of arguments to provide suboptimal treatment in clinical trials is also that there is a need to test cheaper treatments affordable in developing countries. Certainly my colleague will address this point with brilliance.

In these trials the importance of the care of research subjects is secondary to the importance of the results and the accessibility of the treatment at large. These trials are being held "for the good of society". Celebrated authors such as Beecher, state that a trial is ethical or not since its inception; the ends do not justify the means. This is my conviction.

But let us stress that many of the benefits of these trials are not accessible to the target population yet. An example is the trial on short course AZT in South Africa for pregnant women with HIV, where wide access to it is long due and authorities do not even recognize the relation between HIV and AIDS. What about participants who join the trial taking into account that there will be a benefit for their communities? For this reason, "Ethics and basic human rights require not a thin promise, but a real plan as to how the intervention [to the population] will actually be delivered are needed" Annas, G.J. and Grodin, M. A. Human Rights and Maternal-Fetal HIV transmission Prevention Trials in Africa. Who should require this: the researchers, the local IRB, the foreign IRB? Who is responsible, accountable, liable?

Can we perform these trials because they can be used to provide a stronger argument to present to national authorities?

This would mean that any cheaper treatment than the best treatment could be tested since some time some authority may be sensitive to it. This is only marketing policy.

(*)An author asks "... [if access to AZT for pregnant women does not exist yet] So, why are these trials undertaken? My assessment is that since placebo trials could no longer be conducted in the USA or other developed countries, there was still an interest in knowing whether cheaper regimens would be effective. So the only people who will benefit will be people in developed countries, and the few mothers who receive AZT and not placebo in the trials [since pregnant women with HIV do not even have access to it] ". Laing, R. If a lower dose was effective, would it make any difference, Procaare 13, October, 1997(*)

Approval of clinical trials of suboptimal interventions on the basis of the future availability, may raise some problems for the IRBs of the developed countries involved.

According to **Guideline 15(CIOMS)**: Obligations of sponsoring and host countries "...An external sponsoring agency should submit the research protocol to ethical and scientific review according to the standards of the country of the sponsoring agency, and the **ethical standards should be no less exacting than they would be in the case of research carried out in that country...**" (emphasis added)

Since they do not provide the same standard of care, how can this approval be obtained? Some authors say that the ethical principles can be the same, but their expression varies locally. Ethics and international research. Halsey, N. et al BMJ (1997) 315: 965-966

Certainly the 1981 Guiding principles for Human Studies at the Massachusetts General Hospital are not the same principles since "concern for the individual takes precedence over the interests of science and society" and "A study is ethical or

not at its inception; it does not become ethical because it succeeds in producing valuable data." Guiding principles for Human Studies. Boston: Massachusetts General Hospital, 1981.

On the other hand, in the Rakai study, negative HIV partners in discordant couples were not informed by physicians on the status of their spouses, something that they would have to do in developed countries (the US?). What kind of ethics principles permits opposite behaviour in this context?

Other Resolutions related with the right to life and health, and the principle of equality.

We must recall that access to life (Art III) and health (Art XXV) are parts of the Declaration of Human Rights undersigned by every nation in this planet. This is the reason why many Medical Associations argued that accepting different standards of care in the Helsinki Declaration "...would mean to preserve inequality as a principle in the most important set of principles that regulate research in human beings. Equality and justice are a central part of all Human Rights Declarations and are widely acceptable as central principles." (British Medical Association. Com-Helsinki-Oct 1999)

Recently the Mexican Supreme Court ruled in a unanimous sentence that the right to health is not satisfied by providing some drug or some medical care. Rather the best therapeutic alternative must be provided, defined as the one which results in the best quantity and quality of life (Amparo 223/97). This should be compared with the recent draft for the Declaration of Helsinki (May 4th, 2000), where instead of the "best proven" treatment only a "proven" treatment could be offered.

(*) Further, neither the recent discovery of such treatments nor the existence of other illnesses that deserve the same or more attention can constitute an obstacle for this right since these matters are irrelevant on the right of an individual to receive treatment for his illness. (*)

Hence, we stress that the right to optimal care is universal, but unfortunately it is not provided everywhere. Nevertheless this is no reason for that right to cease, and it would be sophistical to deny the fulfillment of this right if we have the resources to do so, as is the case in the AIDS Vaccines area. Paraphrasing an author: Would you forbid people in developed countries from using triple therapy because most people in the world do not have access to it? Why do we simply accept these borders as natural restraints to our health rights? (Chris Green, Indonesia, A response to Richard Laing, Procaare, October 17, 1997)

Undue Induction and Coercion

Some contend that even in case we had the money to provide the optimal care to participants, we should not do so because this could be undue inducement or even coercion.

Enjoying the right to life (without harm to others) cannot be coercive, because the right to life precedes all other rights.

Following this kind of reasoning, couldn't we argue that conducting an unethical trial (with different standards than those in developed countries) in a country extremely afflicted by AIDS, (*)offering some future benefit of access to the product if shown efficacious (*) is also **undue inducement or coercion on the country** to participate in these trials ?

A Suggestion

The subject we are discussing can be examined as an equation:

standard of treatment in developing countries must be = to standard of treatment in developed countries

I believe that in a clinical trial II.3 of the Helsinki Declaration has to be respected. (*)"Thus, scientific research does not admit any inequality among participants in clinical trials. And it also states implicitly equipoise, that is "a state of genuine uncertainty on the part of the clinical investigator regarding the comparative therapeutic merits of each arm in a trial" "Freeman, B. Equipoise and the ethics of clinical research, NEJM 317(3);141-145 In this case the trial could be conducted in any country. (*)

But in order to continue the discussion let me propose the following idea: During an academic meeting, in a discussion about testing a subtype B vaccine in South Africa, some people from developed countries saw no obstacle to test a vaccine constructed on a subtype which is not the prevalent in South Africa. A colleague from South Africa did not agree and she just returned the question: would you agree to test a subtype C vaccine in the US or Europe, where this subtype is not prevalent?

That is, to test a subtype B vaccine in South Africa would be **as ethical as** testing a subtype C vaccine in the US or Europe.

Returning to the equation, let me stress that it does not establish any standard of treatment at all, only **an equality of standards**. A way to evaluate exploitation in a clinical trial is verifying whether equality holds or not: if it does not hold then we may be in the presence of exploitation.

Inspired by her assertion, my suggestion is that whenever the best proven treatment is not provided in a trial in a vulnerable community then **the trial must be matched**, that is, **there will be an identical trial in population, standard of treatment, endpoints, etc, being conducted simultaneously in a developed community.**

Conclusion:

I think that the problem is mostly of access to treatment and prevention. Not access to trials, and even less to unethical trials. The International Covenant on Economic, Social and Cultural Rights (Art. 2.1, Res. 2.200-A XXI UN General Assembly, December 16th, 1966) established the need to **progressively** achieve "...the full realization of the rights...". Here we are not progressing. It is not through reductions of rights of the most deprived and the consolidation of inequalities that we shall obtain better health for all and more dignity for the human being.

(*)"We believe that much of the debate in the past few months is the result of an unrecognizable confusion about the role of clinical research in a public health crisis. Although clinical research may be justified by such a crisis and is indeed expected to contribute to its solution, it is not in itself the solution. Research in developing countries proved years ago that vitamin A supplementation could decrease infant mortality by 30% and that a vaccine could prevent the perinatal transmission of hepatitis B, and yet, these lifesaving, cost-effective, public health interventions are still not available in the countries that need them most. No one can guarantee that the discovery of an effective, easier-to-use, more affordable method to prevent perinatal HIV will lead to its widespread application. This sad reality mandated that human subjects, particularly the politically and economically vulnerable, as well as those who cannot provide consent - children in this case - should be protected during research. Indeed, as recently as last year, the good-practice guidelines recommended by the International Conference, on Harmonisation restated that the researcher's primary ethical responsibility is for the welfare of subjects participating in the research, not for the welfare of future patients who may benefit from it." Lallemant, M et al. Letter to the Editor NEJM (1 998) 338(12):836-844(*)

I believe that in a clinical trial III.3 of the Helsinki Declaration has to be respected. (*) "'Thus sicentific research does not admit any inequality among participants in clinical trials.' And it also states implicity equipoise, that is 'a state of genuine uncertainty on the part of the clinical investigator regarding the comparative therapeutic merits of each arm in a trial.'" Freeman, B. etc.

I would like to end by quoting from two African authors who while referring specifically to the African situation, also depict the Latin American reality.

"Until the educated use their links with Western institutions and research centres for the benefit of the mass of Africans, rather than for ephemeral dollars, unethical research will go on in Africa. Africa's problem is not that of resources. But of priorities misplaced." The response of People with conscience , Oyewale Tomori, Procaare 13, October, 1997.

"Unethical research will not benefit developing countries in the long run, since it undermines human rights, which are the very foundation on which sustainable development needs to be built. In addition, it violates the principle of justice that a continent impoverished through colonialism, and forced to continue to be unable to provide gold-standard treatment because of debt traps, will continue to provide the human laboratory where placebo-controlled trials can be conducted because locally affordable care is often no more than placebo treatment." Ijsselmuiden, Carel B. Letter to the Editor NEJM (1992) 338 (12): 836-844

Thank you

Stefano Vella the New President and Joep Lange the New President-Elect of the International Aids Society

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Stefano Vella is the new President of the International Aids Society (IAS) and Joep Lange is the new President-elect elected: the appointments took place on 11th July during the XIII International Aids Conference on Aids together with the election of the new Governing Council membership. Mark A. Wainberg, former IAS President, is now Past President. Lars O. Kallings has been re-elected IAS Secretary-General.

Members from each of five geographic regions are asked to nominate five members every second or fourth year to serve terms of four years on the IAS Governing Council. Elections are held by ballot among members within each region to determine who these representatives will be. The President of the IAS is then elected from among the members of the Governing Council. These five regions are North America, Europe, Africa, Latin America/Caribbean, and Asia and the Pacific.

The new membership of the IAS Governing council includes, for the first time, members from India and China that further expands the panel of members from countries mostly affected by HIV/Aids. This testifies the IAS global worldwide approach to HIV/Aids: with its more than 10,000 members the IAS is among the few societies that can develop national driven agendas almost in all the countries.

IAS Governing Council Election 2000

President

Stefano Vella, MD
National HIV Aids Clinical Research Program, Istituto Superiore di Sanita', Rome, Italy.

President-elect

Joep Lange, MD
NATEC Amsterdam, The Netherlands.

Region 1 (USA/Canada)

Helene D Gayle, MD, MPH
Director for the National Center for HIV, STD, and TB Prevention (NCHSTP), Centers for Disease Control and Prevention (CDC).

Scott Hammer, MD
Professor of Medicine, Columbia University College of Physicians and Surgeons and Chief of the Division of Infectious Diseases, Columbia Presbyterian Medical Center, New York, USA.

Region 2 (Europe)

Gunnel Biberfeld, MD, PhD
Professor of Clinical Immunology, Karolinska Institute, Stockholm and Head of the Department of Immunology, Swedish Institute for Infectious Disease Control.

Jap Goudsmit, MD, PhD
Chairman of the Institute of Infectious Diseases, University of Amsterdam, The Netherlands.

Ian V D Weller, BSc, MD, FRCP
Head of the Department of Sexually Transmitted Diseases, Royal Free and University College Medical School, University College London (UCL), UK.

Region 3 (Africa)

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Region 4 (Latin America/Caribbean)

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Professor of Infectious Diseases at BAUMS, Buenos Aires, Argentina.

Gloria Echeverria De Perez, MD, MSc
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Region 5 (East Asia/Oceania)

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Roy K W Chan, MBBS, MRCP, FRCP, FAMS
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John Kaldor, MD
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Chaiyos Kunanusont, MD
Director of the Aids Division, Department of CDC, Ministry of Public Health, Thailand.

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The Role of STD Detection and Treatment in HIV Prevention – CDC – Centers for Disease Control and Prevention

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Testing and treatment of sexually transmitted diseases (STDs) can be an effective tool in preventing the spread of HIV, the virus that causes Aids. Consequently, HIV programs and STD testing and treatment programs should develop strong linkages. This is especially important for programs targeting sexually active young women, who represent one of the fastest growing populations with Aids.

What is the link between HIV and other STDs?

In the United States, the spread of HIV infection among women through sexual transmission has followed in the footsteps of other STD epidemics. For example, the geographic distribution of heterosexual HIV transmission in the South closely parallels that of syphilis. Most of the health districts with the highest rates of syphilis and gonorrhea are concentrated in the South, where HIV prevalence among child-hearing women also is high.

Individuals who are infected with STDs are at least two to five times more likely than uninfected indivuduals to acquire HIV if exposed to the virus through sexual contact. In addition, if an HIV-infected individual also is infected with another STD, that person is substantially more likely than other HIV-infected persons to transmit HIV through sexual contact (Wasserheit, 1992).

How do STDs facilitate HIV infection?

There is substantial biological evidence demonstrating that the presence of other STDs increases the likelihood of both transmitting and acquiring HIV.

- *Increased susceptibility*. STDs probably increase susceptibility to HIV infection by two mechanisms. Genital ulcers (e.g. syphilis, herpes, or chancroid) result in breaks in the genital tract lining or skin. These breaks create a "portal of entry" for HIV. Nonulcerative STDs (e.g., chlamydia, gonorrhea, and trichomoniasis) increase the concentration of cells in genital secretions that can serve as targets for HIV (e.g., CD4+ cells).
- *Increased infectiousness*. Studies have shown that when HIV-infected individuals are also infected with other STDs, they are more likely to have HIV in their genital secretions. For example, men who are infected with both gonorrhea and HIV are more than twice as likely to shed HIV in their genital secretions than are those who are infected only with HIV. Moreover, the median concentration of HIV in semen is as much as 10 times higher in men who are infected with both gonorrhea and HIV than in men infected only with HIV.

How can STD treatment slow the spread of HIV infection?

New evidence from intervention studies indicates that detecting and treating STDs can substantially reduce HIV transmission at the individual and community levels.

- *STD treatment reduces an individual's ability to transmit HIV*. Studies have shown that treating STDs in HIV-infected individuals decreases both the amount of HIV they shed and how often they shed the virus.
- *STD treatment reduces the spread of HIV infection in communities*. Two community-level randomized trials have examined the role of STD treatment in HIV transmission. Together, their results have begun to clarify conditions under which STD treatment is likely to be most successful in reducing HIV transmission. First, *continuous* interventions to improve access to effective STD treatment services are likely to be more effective in reducing HIV transmission than *intermittent* interventions through strategies such as periodic mass treatment. Second, STD treatment is likely to be most effective in reducing HIV transmission where STD rates are high and the heterosexual HIV epidemic is young. Third, treatment of symptomatic STDs may be particularly important. The first trial, conducted in a rural area of Tanzania, demonstrated a decrease of about 40% in new heterosexually transmitted HIV infections in communities with continuous access to improved treatment of symptomatic

STDs, as compared to communities with minimal STD services, where incidence remained about the same (Grosskurth et al., 1995). However, in the second trial conducted in Uganda, a reduction in HIV transmission was not demonstrated when the STD control approach was community-wide mass treatment administered to everyone every 10 months in the absence of ongoing access to improved STD services (Wawer, 1998).

What does this mean for HIV prevention programs?

Strong STD prevention, testing and treatment can play a vital role in comprehensive programs to prevent sexual transmission of HIV. Furthermore, STD trends can offer important insights into where the HIV epidemic may grow, making STD surveillance data helpful in forecasting where HIV rates are likely to increase. Better linkages are needed between HIV and STD prevention efforts nationwide in order to control both epidemics.

In the context of persistently high prevalence of STDs in many parts of the United States and with emerging evidence that the U.S. HIV epidemic increasingly is affecting population groups with the highest rates of curable STDs. CDC's Advisory Committee on HIV and STD Prevention (ACHSP) has recommended the following:

- Early detection and treatment of curable STDs should become a major, explicit component of comprehensive HIV prevention programs at national, state, and local levels.
- In areas where STDs that facilitate HIV transmission are prevalent, screening and treatment programs should be expanded.
- HIV and STD prevention programs in the United States, along with private and public sector partners, should take joint responsibility for implementing this strategy.

The ACHSP also notes that early detection and treatment of STDs should be only one component of a comprehensive HIV prevention program, which also must include range of social, behavioral, and biomedical interventions.

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Rockville, MD 20849-6003
1-800-458-5231
International: 1-301-562-1098
TTY: 1-800-243-7012

CDC National Aids Hotline
1-800-342-Aids (2437)
Spanish: 1-800-344-Sida (7432)
TTY: 1-800-243-7889

CDC National STD Hotline
1-800-227-8922

NELSON MANDELA FOUNDATION

CLOSING ADDRESS BY FORMER PRESIDENT NELSON MANDELA

XIII International Aids Conference

14 July 2000, Durban

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To have been asked to deliver the closing address at this conference which in a very literal sense concerns itself with matters of life and death, weighs heavily upon me for the gravity of the responsibility placed on one.

No disrespect is intended towards the many other occasions where one has been privileged to speak, if I say that this is the one event where every word uttered, every gesture made, had to be measured against the effect it can and will have on the lives of millions of concrete, real human beings all over this continent and planet. This is not an academic conference. This is, as I understand it, a gathering of human beings concerned about turning around one of the greatest threats humankind has faced, and certainly the greatest after the end of the great wars of the previous century.

It is never my custom to use words lightly. If twenty-seven years in prison have done anything to us, it was to use the science of solitude to make us understand how precious words are and how real speech is in its impact upon the way people live or die.

If by way of introduction I stress the importance of the way we speak, it is also because so much unnecessary attention around this conference had been directed towards a dispute that is unintentionally distracting from the real life and death issues we are confronted with as a country, a region, a continent and a world.

I do not know nearly enough about science and its methodologies or about the politics of science and scientific practice to even wish to start contributing to the debate that has been raging on the perimeters of the conference.

I am, however, old enough and have gone through sufficient conflicts and disputes in my life-time to know that in all disputes a point is arrived at where no party, no matter how right or wrong it might have been at the start of that dispute, will any longer be totally in the right or totally in the wrong. Such a point, I believe, has been reached in this debate.

The President of this country is a man of great intellect who takes scientific thinking very seriously and he leads a government that I know to be committed to those principles of science and reason.

The scientific community of this country, I also know, holds dearly to the principle of freedon of scientific enquiry, unencumbered by undue political interference in and direction of science.

Now, however, the ordinary people of the continent and the world – and particulary the poor who on our continent will again carry a disproportionate burden of this scourge – would, if anybody cared to ask their opinions, wish that the dispute about the primacy of politics or science be put on the backburner and that we proceed to address the needs and concerns of those suffering and dying. And this can only be done in partnership.

I come from a long tradition of collective leardership, consultative decision-making and joint action towards the common good. We have overcome much that many thought insurmountable through an adherence to those practices. In the face of the grave threat posed by HIV/Aids, we have to rise above our differences and combine our efforts to save our people. History will judge us harshly if we fail to do so now, and right now.

Let us not equivocate: a tragedy of unprecedented proportions is unfolding in Africa. Aids today in Africa is claiming more lives than the sum total of all wars, famines and floods, and the ravages of such deadly diseases as malaria. It is devastating families and communities; overwhelming and depleting health care services; and robbing schools of both students and teachers.

Business has suffered, or will suffer, losses of personnal, productivity and profits; economic growth is being undermined and scarce development resources have to be diverted to deal with the consequences of the pandemic.

HIV/Aids is having a devastating impact on families, communities, societies and economies. Decades have been chopped from life expectancy and young child mortality is expected to more than double in the most severely affected countries of Africa. Aids is clearly a disaster, effectively wiping out the development gains of the past decades and sabotaging the future.

Earlier this week we were shocked to learn that within South Africa 1 in 2, that is half, of our young people will die of Aids. The most frightening thing is that all of these infections which statistics tell us about,

and the attendant human suffering, could have been, can be, prevented.

Something must be done as a matter of the greatest urgency. And with nearly two decades of dealing with the epidemic, we now do have some experience of what works.

The experience in a number of countries has taught that HIV infection can be prevented through investing in information and life skills development for young people. Promoting abstinence, safe sex and the use of condoms and ensuring the early treatment of sexually transmitted diseases are some of the steps needed and about which there can be no dispute. Ensuring that people, especially the young, have access to voluntary and confidential HIV counselling and testing services and introducing measures to reduce mother-to-child transmission have been proven to be essential in the fight against Aids. We have recognised the importance of addressing the stigmatisation and discrimination, and of providing safe and supportive environments for people affected by HIV/Aids.

The experiences of Uganda, Senegal and Thailand have shown that serious investments in and mobilisation around these actions make a real difference. Stigma and discrimination can be stopped; new infections can be prevented; and the capacity of families and communities to care for people living with HIV and Aids can be enhanced.

It is not, I must add, as if the South African government has not moved significantly on many of these areas. It was the first deputy president in my government that oversaw and drove the initiatives in this regard, and as President continues to place this issue on top of the national and continental agenda. He will with me be the first to concede that much more remains to be done. I do not doubt for one moment that he will proceed to tackle this task with the resolve and dedication he is known for.

The challenge is to move from rhetoric to action, and action at an unprecedented intensity and scale. There is a need for us to focus on what we know works.

- We need to break the silence, banish stigma and discrimination, and ensure total inclusiveness within the struggle against Aids;
- We need bold initiatives to prevent new infections among young people, and large-scale actions to prevent mother-to-child transmission, and at the same time we need to continue the international effort of searching for appropriate vaccines.
- We need to aggressively treat opportunistic infections; and
- We need to work with families and communities to care for children and young people to protect them from violence and abuse, and to ensure that they grow up in a safe and supportive environment.

For this there is need for us to be focussed, to be strategic, and to mobilise all of our resources and alliances, and to sustain the effort until this war is won.

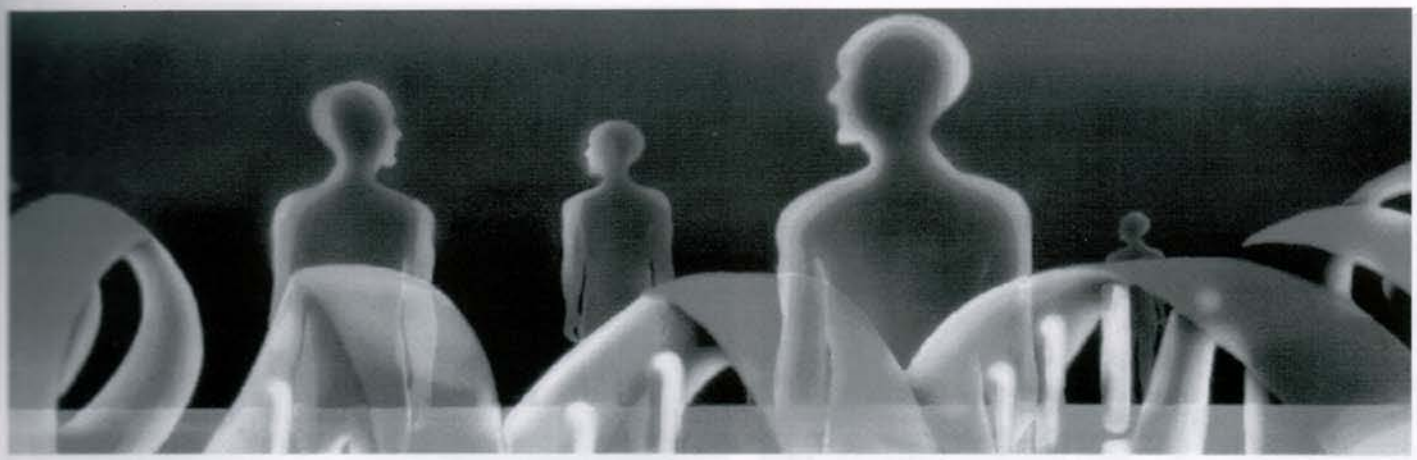
We need, and there is increasing evidence of, African resolve to fight this war. Others will not save us if we do not primarily commit ourselves. Let us, however, not underestimate the resources required to conduct this battle. Partnership with the international community is vital. A constant theme in all our messages has been that in this inter-dependent and globalised world, we have indeed again become the keepers of our brother and sister. That cannot be more graphically the case than in the common fight against HIV/Aids.

As one small contribution to the great combined effort that is required, I have instructed my Foundation to explore in consultation with others the best way in which we can be involved in the battle against this terrible scourge ravaging our continent and world.

I thank all of you most sincerely for your involvement in that struggle. Let us combine our efforts to ensure a future for our children. The challenge is no less.

I thank you.

Nelson Mandela



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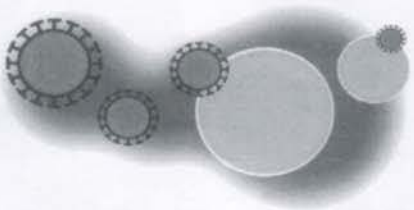

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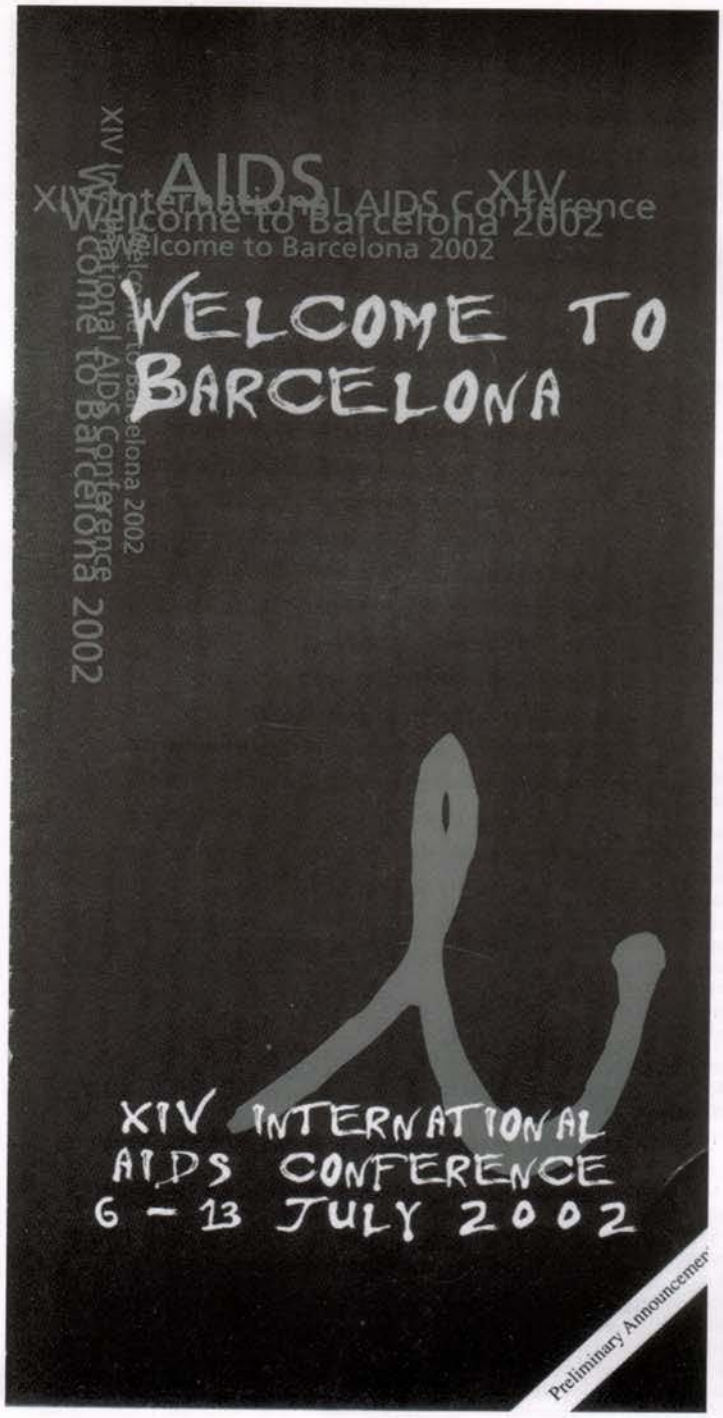

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Página de rosto: Deve conter (a) o título do artigo, conciso e explicativo, evitando termos supérfluos; (b) versão exata do título para o idioma inglês; (c) título abreviado (para constar na capa e topo das páginas), com máximo de 50 caracteres, contando os espaços; (d) primeiro e último nome dos autores e iniciais dos sobre-nomes; (e) a titulação mais importante de cada autor; (f) instituição ou serviço ao qual os autores estão vinculados; (g) nome, endereço, telefone, fax e E-mail do autor responsável pela correspondência; (h) fonte financiadora ou fornecedora de bolsas, equipamentos e materiais, quando for o caso.

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• Objetivo: Informar por que o estudo foi iniciado e quais foram as hipóteses iniciais, se houve alguma. O objetivo do trabalho deve resultar do final da "Introdução" e se relacionar aos "Fundamentos".

Referências bibliográficas: As referências bibliográficas devem ser numeradas e ordenadas segundo a ordem de aparecimento no texto, no qual devem ser identificadas pelos algarismos arábicos respectivos entre parênteses. Devem ser apresentadas nos moldes do *Index Medicus*, de acordo com os exemplos abaixo (quando o número de autores ultrapassar 6, somente os três primeiros devem ser citados seguidos da expressão *et al.*). No caso de ser um fascículo este deve ser indicado entre parenteses após o volume.

• Artigo em periódico

(1) BUENO, S.M.V., MAMEDE, M.V. – Comportamento das Profissionais do Sexo: relacionado a DST AIDS. *J. Bras. Doenças Sexualmente Transmissíveis, 1997:* 9(3) 4-9.

• Livro ou monografia

(2) TINKER, J. – AIDS: como prevenir, conviver e cuidar. *J. Ed. Noruega, Cruz Vermelha, 1987.*

• Capítulo em livro

(3) PAIVA, V. – Sexualidade e gênero num trabalho com adolescentes para prevenção do HIV/AIDS. *In:* Parker, R. *et al.* –A AIDS no Brasil. *Rio de janeiro; ABIA, IMS, 1994.*

• Trabalho apresentado em congresso ou similar já publicado

(4) TOMPSON, N. LILLO, P. - The Crescent Probien of DST: adolescent. *Abstracts of the XXV American Pediatrics Congress, Idaho, 1991,* 104.

Tabelas: Cada tabela deve ser apresentada em folha separada, numerada na ordem de aparecimento no texto, e com um título suscinto, porém explicativo.

• Métodos: Informar o delineamento do estudo (randomizado, duplo-cego, prospectivo, etc.), o contexto ou local (nível de atendimento, clínica privada, comunidade, instituição, etc.), os participantes (indivíduos, animais, materiais, produtos, etc) critério de seleção e exclusão, as intervenções (descrever as características essenciais, incluindo métodos e duração) e os critérios de mensuração. Para cada resultado relatado deve haver um método descrito. Os métodos não podem conter resultados.

• Resultados: Informar os principais dados, intervalos de confiança e/ou significância estatística dos resultados detalhados no trabalho. Os resultados não podem conter métodos.

• Conclusões: Apresentar apenas aquelas apoiadas pelos dados do estudo e que contemplem os objetivos, bem como sua aplicação prática, dando ênfase igual a achados positivos e negativos que tenham méritos científicos similares. Sempre que possível indicar as implicações das conclusões. Abaixo do resumo, fornecer três a seis descritores, que são palavras-chave ou expressões-chave que auxiliarão a inclusão adequada do resumo nos bancos de dados bibliográficos. Empregar descritores integrantes da lista de "Descritores em Ciências da Saúde", elaborada pela BIREME e disponível nas bibliotecas médicas.

Resumo em inglês (abstract): O "abstract" deve ser uma versão do resumo para o idioma inglês, com o mesmo número máximo de palavras e com os seguintes subtítulos: "Background", "Objective", "Methods", "Results" e "Conclusions". Os descritores devem fazer parte da lista de "Medical Subject Headings" do *Index Medicus*, conforme constam na publicação citada pela BIREME.

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Leitura Recomendada aos Autores

• International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. *JAMA, 1993, 169:* 2282-2286

• HAYNES, R.B., MULROW, C.D., HUTH, E.J., ALTMAN, D.J., GARDNER, M.J. – More informative abstracts revisited. *Ann. Inter. Med., 1990, 113:* 69,76.

BIREME – Centro Latino-Americano e do Caribe de Informação em Ciências da Saúde. DeCS – Descritores em Ciências da Saúde: lista alfabética – 2' ed. rev. amp. São Paulo: BIREME, *1992,* 111.

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