The AIDS epidemic: social, scientific and economical impacts and perspectives

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“There have been as many plagues as wars in history; yet always plagues and wars take people equally by surprise.”

(Albert Camus, The Plague)

Introduction

In the last few years, several new diseases have been discovered, some of them very serious and difficult to control. Since the discovery of the Human Immunodeficiency Virus (HIV), in the beginning of the 1980’s, more than twenty pathogens have been described and found to be involved in several diseases. These new diseases add to existing ones – whose incidence has been increasing – and, among the new microbial agents, there are several viruses against which the currently available therapeutic arsenal is insufficient.

The current situation has peculiar features, among which are:

a) Increased size of the world population (more than six billion people);

b) Large population movements, both spontaneous (leisure or business travels) and induced (wars, droughts and other environmental disasters);

c) Higher number of people suffering from diseases due to higher exposure of specific groups to risk situations - such as prisoners, residents in senior citizen homes and orphanages, schools students, migrants, homeless populations and citizens living in precarious conditions;

d) Intense and rapid environmental changes, related to economical and industrial development;

e) Lower social support, higher unemployment, disorganized urbanization;

f) Intense use of anti-microbial drugs, favoring, on the one hand, the emergence of resistant strains and, paradoxically, contributing on the other hand to the development of resistance caused by lack of compliance with treatments.
It is a well-known fact that infectious and parasitic disease agents are part of our habitat (our ecology), surely making it unlikely (and many times undesirable) that they ever be completely eliminated. The complex ecological relationships (host-environment-parasites) are yet to be entirely understood, and the importance of maintaining this balance for the balance of life itself should be underscored. On the other hand, the technical knowledge accumulated in the last few decades has already indisputably demonstrated the close relationship between improvement of basic sanitary conditions and lower incidence of infectious and parasitic diseases. Those conditions include, but are not limited to availability of safe water supplies, adequate sanitary sewage systems, healthy diets, education and employment.

The hegemony of the market culture

The dismantling of the former Soviet Union and the current hegemony of the central capitalist single current of thought in peripheral countries has brought serious problems to their populations. The drive for efficiency at any cost, concentration of wealth, weakening of social public policies have contributed to discard the notion of nation in favor of a large global market, where actions and policies are decided by the central countries.

The Aids epidemic

As Camus has suggested, Aids took the world by surprise, as did other plagues. This happened even as industrialized societies boasted at the end of the 20th century that they were able to control all infectious diseases by means of immunization or treatment.

The emergence, in the end of the 1980’s, of this serious and mortal epidemic, involving several aspects of human relations (sex, death, prejudice), may serve as an example for the fight against other diseases. The immodest expectation to be able to control infectious diseases by the end of the 20th was crushed, in the specific example of the Aids epidemic, by the difficulty to put into effect proven preventive strategies (change of behavior, use of condoms, safe blood banks, use of disposable syringes), to develop truly effective and affordable drugs and to develop efficient vaccines and make them available.

Contradictorily and positively, there were beneficial by-products brought by the response to the global dissemination of this serious epidemic. such as the involvement of civil society clamoring for access to information, for more funds for research and new drugs, as well as the opportunity to expand the discussion on complex themes (such as sexuality, death, use of illicit drugs, confidentiality). Additionally, the participation of persons living with HIV/Aids in medical conferences and governmental disease control committees has contributed to change the paradigm of vertical programs, in which decisions were usually taken top-to-bottom, with no broader discussions or correct assessment of possible risks and benefits.
Brazil has been facing the epidemic in an unusually courageous way – comparatively to other programs of disease control -, by distributing (and locally producing) condoms and anti-retroviral drugs at no additional cost to patients, as well as implementing a public network of laboratories for diagnosis, patient follow-up and research support. These measures, even if not sufficient to interrupt the dissemination of the epidemic, have increased survival rates and improved the quality of life of people living with Aids, as well as improved the techno-scientific conditions of healthcare professionals.

**Scientific, economical, social and ethical impact**

**Science and ethics**

As far as science is concerned, the amount of knowledge related to HIV/AIDS has been truly remarkable since the first clinical cases were reported in 1981 (Okie, 2006), and, even before the discovery of its etiological agent, it was found to be infectious and sexually transmissible. The discovery of HIV took little more than two years, and its causal relationship to Aids was established in 1984. In 1985, there were tests available for serologic diagnostics. Not long after that, these tests began to be used in triages of blood to be transfused and, in 1987, the beneficial, albeit ephemeral, effect of zidovudine against HIV was demonstrated. About ten years later (1996), the efficacy of the association of anti-retroviral agents was proven, inaugurating a new era for the control of the epidemic and providing relief to millions of people infected with HIV. However, this scientific victory, as it had also been the case in similar situations, has not reverted into global benefits, being instead restricted mainly to the central, industrialized countries, and highlighting the pressing need to discuss the ethics of access to scientific progress by all the people who need it.

In terms of ethics, Aids has unveiled a myriad of legal and, particularly, ethical challenges – several of which date from before this epidemic – both in industrialized countries (Beecher, 1996; Rothman & Michels, 1994) and in developing nations (Bayer & Gostin, 1989; Connor, 1989). These challenges belong to well-known categories:

- Allocation of scarce resources;
- Prevention;
- Secret and confidentiality;
- Discrimination;
- Public health protection vs. individual protection (public health vs. individual needs);
- Research involving human beings;
- Application of the principles of distributive justice.

On the topic of research, for many years internationally collaborative research projects have occurred almost always with financing agencies,
researchers, institutions and, many times, the projects themselves coming from developed countries and the participation, usually small, from researchers and institutions from developing countries.

The Aids pandemic increased the need for effective international collaboration, and the role of the World Health Organization (WHO), initially by means of the Global Program on Aids and its successor, UNAIDS, has been undoubtedly important in this process. More recently, other philanthropic, independent or non-governmental organizations, such as the Global Fund for Malaria, Tuberculosis and Aids (whose aim is to increase the availability of anti-retroviral drugs through new funds)(www.unitaid.eu) and foundations (Bill and Melinda Gates, Bill Clinton, among others) have been created. If the latter, on the one hand, expands the amount of available resources, on the other hand, it risks lowering State resources and decreasing the pressure for the State to fulfill its mandated role in public health care. Another risk is that the agenda gets to be defined solely by the financing entities (with all the associated political and financial consequences).

Collaboration in AIDS research has made it necessary to re-examine legal and, especially, ethical aspects of research in general. The practical difficulties faced by collaborative efforts are not exclusive to AIDS research, but the particular characteristics of this epidemic have made many points more visible and sensitive. The issues specific to the epidemic and the problems that are expected to be solved will be useful in the fight against other endemic or epidemic diseases. Many publications, seminars and debates have been held to discuss these topics and it is worth emphasizing some points:

It is crucial to develop universally acceptable ethical principles, which should consider culturally relevant approaches for the implementation of research projects. The Declaration of Helsinki (2000) can and should serve as one of their main ethical references.

All researchers, both from developed and developing countries, should collaborate during all stages of the study, from the development of the protocol to the publication and application of the results.

Decisions about access to the products which result from the studies should be made based upon the principles of justice, meaning that those who have to cope with the heaviest burden should receive the appropriate benefits. Volunteers should have access to drugs, vaccines, interventions, prevention strategies and any other benefits resulting from the study.

Financing of studies should include funds for strengthening local capacities, not only those related to the specific aims of the project, but also local infra-structure, institutions and host country capacity to conduct research projects.

It is extremely important to deepen the discussion on the informed consent process. Such consent should be obtained in ways that respect the
dignity and cultural values of the volunteers. The confidentiality of the data should be protected during the whole project. The inclusion of vulnerable individuals shall warrant special justification and appropriate protection and should occur only when the aim of the project is to benefit those persons. Individuals may be considered vulnerable when: (a) they are incompetent to give valid consent; (b) they are potentially vulnerable to induction, coercion or exploitation. These groups include, but are not limited to: children, people with mental illnesses or disorders, and prisoners.

Despite the existence of several international and national ethical rules, the urgent need to find mechanisms to control the exponential dissemination of the AIDS epidemic, the raise in deaths by tuberculosis and the increase in the incidence of other diseases, old and new (such as malaria, dengue fever and cholera), have been used as an argument (Greco, 2000) to lower the ethical standards required to carry out studies involving human beings, especially in developing countries. With the justification that poor countries do not have access to the ideal treatments anyway, there seems to have emerged a concerted action to modify several items of the Declaration of Helsinki – a declaration which has been considered by the Canadian Medical Association as the “stone tablet of medical research ethics” – especially those related to access to healthcare and to the use of placebo as an experiment control.

**Double-standard in clinical research**

The migration of randomized trials to developing countries brought with it the risk of lowering ethical requirements. There is no intention here of demonizing the pharmaceutical industry - which has an important role in the development of many products - by attributing all non-ethical trials to them, since such trials have also been carried out by national and international agencies, with the collaboration of local and/or international researchers.

One of the triggers of the debate on international research ethics has been the AIDS epidemic, whose causing virus, differently from other infectious diseases, does not respect national boundaries. In this epidemic, not only the need for better epidemiological knowledge but also the perceived urgency to develop and test the efficacy of anti-retroviral drugs led to an exponential increase in the number of international multi-centric clinical trials. In this context, developing countries appear as the ideal scenario: same virus, same disease, high prevalence and incidence of the infection, as well as often less demanding volunteers, authorities and researchers.

It is difficult, if not impossible, to pinpoint the origin of the heated discussions on ethical requirements for clinical studies, but it is worth mentioning at least one trigger of this ethical battle. In 1997, an incisive editorial written by Dr. Marcia Angell (1997) – then editor of the *New England Journal of Medicine* – criticized the ethics of studies financed by the United
States’ National Institutes of Health (NIH) on the prevention of maternal-fetal transmission of HIV which had been carried out in African countries, in the Dominican Republic and in Thailand. These studies were conducted at a time when the results of the ACTG 076 studies (Connor et al., 1994; CDC, 1994) had already shown that the risk of HIV transmission decreased substantially when zidovudine was orally administrated during pregnancy, intravenously during birth and orally to the newborn. In the trials criticized by Dr. Angell, zidovudine (AZT) was administered for a shorter period during pregnancy and the intravenous dose was eliminated, in comparison with a control group that received only placebo. According to her, the use of placebo in this study reminded the unethical Tuskegee syphilis study (1932-1972) (Fairchild & Bayer, 1999). This editorial and other related articles provoked intense discussions and was possibly one of the reasons for subsequent pressure from North-American regulating agencies and researchers (Levine, 1999) to modify the ethical requirements defined in the Declaration of Helsinki (1996). Their intention was to change the items related to the obligation to provide access to the best health treatments to all volunteers (item 30) in clinical trials carried out in any part of the world, as well as those related to the use of placebo when there exists an efficient treatment.

Using fallacious arguments, a proposal from the American Medical Association was sent to the World Medical Association in which those items were grossly altered, allowing for the use of placebo when there was no efficient treatment available in the country where the trial was being conducted and substituting best locally available medical care for the best medical care. This change would justify, for example, the methodological design of the trials criticized above.

This proposal was rejected, and the 52nd General Assembly of the World Medical Association (Edinburgh, 2000) maintained the restrictions on the use of placebo (item 29) and added the requirement to provide post-study access to the best medical care demonstrated in the study (item 30). However, pressures both from regulating agencies and the pharmaceutical industry were very intense, and the WMA added (2002-2004) two clarifying notes to these items. These notes made it possible to avoid the requirement to treat all volunteers with equal respect and warrants, independently from their origin or economical power, establishing the possibility of an ethical double standard in clinical research.

In the same occasion (2004), the Food and Drug Administration (FDA), responsible for approving and registering drugs in the United States, proposed that clinical research projects carried out in other countries and not conducted under an application for a Investigational New Drug (IND) need not fulfill the requirements of the Declaration of Helsinki any longer. This decision affects the rules for medication research carried out outside of the United States which has not applied for an FDA IND registration. The FDA rules used to require that studies submitted for a new experimental medication (NDA) be carried
out according to the rules that protected the volunteers the most, be them the Declaration of Helsinki or the local legislation. This new proposal requires only that the study be conducted according to the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice. These guidelines deal mainly with procedures and not with ethical issues. For example, the guidelines do not mention the issue of conflict of interests, the need to publish the results or post-study volunteer access to the treatments that have proved effective, as determined by the Declaration of Helsinki. The FDA claimed to be concerned with “ensuring the quality of data”, thus the need for the ICH Guideline. It would be more logical then to require studies to comply both with the ICH Guideline and the Declaration of Helsinki. It also stated that there was concern about the possibility of the Declaration of Helsinki being modified “independently from the authority of the FDA”. Ironically, the FDA did not consider the current version of this declaration (Edinburgh, 2000), referring to the 1989 version, which had been automatically cancelled with the approval of the 2000 version.

The FDA and other North-American agencies, as well as the Department of Health and Human Services and the US pharmaceutical industry, have opposed many improvements in several international ethical documents. Their efforts have not been entirely successful in the case of the Declaration of Helsinki, which may explain this new proposal. Since 1996, in many reports and discussion meetings on the Declaration of Helsinki and the 2002 version of the Council for International Organizations of Medical Sciences (CIOMS)’ International Ethical Guidelines for Biomedical Research Involving Human Subjects (Phanuphak, 1998), there was pressure to limit the rights of clinical trials volunteers, particularly in developing countries.

The FDA concerns are related to two areas, which are conveniently absent from the CIOMS Guidelines. In relation to the use of placebo, the US agency complained that the 2000 Declaration prevented the use of placebo for simple, less serious diseases. The FDA participated in the movement to introduce in the Declaration (article 29) a clarifying note that makes it easier to use placebo. And it also supports its use in developing countries, in clinical studies on serious diseases even when there is efficient treatment, something which is not authorized by the Declaration of Helsinki.

FDA and other agencies within its parent agency, the Department of Health and Human Services (DHHS), and the U.S. pharmaceutical industry have led the charge against many of the substantive improvements in these updates, particularly in the DOH. But it is with the DOH that their efforts have met with the least success. This suggests an alternative motivation for the FDA’s proposal. In a series of published articles in medical journals as well as in a number of meetings on the DOH and a related document, the Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects, DHHS and its agencies
The global symbol of the fight against AIDS was displayed at the conference in Durban (South Africa).
have spearheaded efforts to limit the rights of clinical trial subjects and their communities, particularly in developing countries.

Furthermore, the Council and the FDA argue against the requirement that medication that proves to be efficient be given to all participants at the end of the study (Helsinki Declaration, article 30). This requirement is particularly critical in developing countries, where those who receive the study’s medication may have their treatment abruptly interrupted and those in the control group may have their access denied to treatments whose efficacy they helped prove.

Despite several criticisms made directly on the FDA’s page and in scientific literature, this substitution decision was officially taken by the agency in 2008.

**New proposals to change the Declaration of Helsinki**

In May 2007, the World Medical Association (WMA) created a new working group, with members from Brazil, Germany, Japan, South Africa and Sweden, to review the Declaration of Helsinki with the following aims: “(a) identifying gaps in content, but avoiding a complete reopening of the document for modification; (b) using the review process to promote the Helsinki Declaration”. According to the WMA’s Ethical Committee coordinator, Dr. Eva Bagenholm,

although many of the proposed changes are small, there are significant changes being proposed, particularly to enhance protection and benefits to volunteers in research projects and new items related to data registry and consent for research using human tissue.

The most controversial points of this new proposal were exactly the ones related to the use of placebo and post-study access to medications proven to be effective – WMA’s proposal (Table 1) suppresses the clarifying notes, but keeps their content within the specific items, that is, it maintains the risk of placebo use even when there is efficient treatment and reduces the obligation to provide post-study access to medication. The latter is rather weakened by the proposal that “the protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits”, which may be interpreted as it being enough to describe in the project what shall be offered (which may be nothing) for it to be ethically acceptable.

In August 2008, the Brazilian Medical Association (Associação Médica Brasileira, AMB) organized a seminar in São Paulo, together with the Federal Council of Medicine (Conselho Federal de Medicina) and the WMA, in order to expand this debate. It was followed by a meeting of the WMA Ethical Committee and national representatives of the above mentioned working group. In this seminal and exemplary event, those two controversial topics were discussed, but no consensus was reached, and the Brazilian representatives positioned themselves against the WMA’s proposal.
Table 1 – Declaration of Helsinki: Proposal by the World Medical Association (WMA) approved in the 2008 General Assembly (Seoul, South Korea) and position defended by the Brazilian Medical Association (AMB) and the Federal Council of Medicine (CFM)

<table>
<thead>
<tr>
<th>Item</th>
<th>Proposal approved in 2008</th>
<th>Proposal defended by the AMB and CFM, October 18th 2008</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Access to medical care</td>
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<tr>
<td></td>
<td></td>
<td>At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.</td>
</tr>
<tr>
<td>33</td>
<td></td>
<td>All patients entering a study must have access to the best methods proven prophylactic, diagnostic or therapeutic identified in the study.</td>
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<td></td>
<td></td>
<td>Placebo use</td>
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<td></td>
<td></td>
<td>The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention and the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm.</td>
</tr>
</tbody>
</table>
| 32   |                          | The benefits, risks, onus and effectiveness of a new method must be tested in comparison to the best proven care, except in the following circumstance:  
- The use of placebo or no treatment is acceptable in studies in which no efficient method has been proven. |

The Brazilian Medical Association, the Federal Council of Medicine, the National Commission of Research Ethics (Comissão Nacional de Ética em Pesquisa, CONEP) and the Ministry of Health (represented by the Department of Science and Technology) were in favor of maintaining the restrictions on the use of placebo and guaranteeing volunteer access to what the study proves to be effective.

In the General Assembly of the World Medical Association, held in Seoul, South Korea, in October 18th 2008, to discuss and approve the new Declaration of Helsinki, this position was defended, with the firm support from the representatives from South Africa, Portugal and Uruguay, but unfortunately it was defeated in the plenary.

Furthermore, Brazil also voted against the approval of the text of the new Declaration of Helsinki, being consistent with its disagreement on these two items.

Thus, the new version of the Declaration of Helsinki maintained the texts shown in Table 1.

As mentioned before, the Brazilian representatives voted against the proposals for these two items because they understood that: in relation to the
placebo, there is no plausible ethical justification for not using as a comparison a medication that has been proven to be effective, and the reasons for the use of placebo in these situations are purely economic and/or related to markets; on the post-study access: because keeping the phrase “or other care or benefits” opens the possibility of not guaranteeing post-study access to interventions identified as beneficial. These “other care or benefits” may be interpreted in several ways which are harmful to the volunteer, especially in conditions of greater vulnerability.

**Resource allocation**

Confirming a World Bank report, urban poverty has turned into one of the most explosive political and economical problems of the 21st century. The emergence of megalopolises, cities with more than ten million inhabitants, typical of underdeveloped nations, where more than 50% of the population does not have access to treated water or a sewage system, is a portrait of these problems. In the beginning of this 21st century, 20 out of the 25 largest urban centers in the world are located in the poorest regions of the planet.

According to estimates, almost one billion people still suffer from hunger today and approximately 25% of the urban population of the Third World lives in conditions of absolute poverty. The budget dedicated to health is usually insufficient: in PPP (parity purchase power) terms, the largest investment was made by the United States (12nd place in the Human Development Index), US$ 1.520 by Brazil (70th in the HDI) and about US$ 34 by Sierra Leone (last place in the HDI: 177th) (WHO, 2007).

Much has been written about the enormous additional investment in healthcare imposed by the AIDS epidemic, both in terms of direct costs (medications, ambulatory care, hospitalizations) and in terms of indirect ones (education, prevention, loss of years of work). Even considering all the possibilities to reduce these costs through the involvement of all society groups (family, friends, NGOs, day hospitals), the necessary investments will still be much greater than the resources made available. The global investment in AIDS control raised exponentially (US$ 1 billion in 2001, reaching US$ 8.2 billion in 2007), although it is estimated that US$ 20 billion will have been necessary in 2008, and the need shall increase in the coming years. This need may be illustrated by the fact that, for each new treatment that is instituted, there are 2.7 people who get infected by HIV. This rise in investments coincided with the historical commitment of the United Nations to combat the AIDS epidemic, defined in the General Assembly Special Session on HIV/AIDS (UNGASS).

One must also highlight the fact that, in most Third World countries, the AIDS impact adds to an existing long list of endemic or emergent diseases (such as tuberculosis, leprosy, schistosomiasis, leishmaniasis, malaria).

The idea that funding for health expenses should be prioritized in relation to other public expenses has been gaining momentum; for example,
funding for health should be raised by decreasing the budget for military expenses, which reached US$ 1.2 trillion, half of which spent by the United States. Unfortunately, the most common scenario is usually one in which expenses for AIDS control are taken from the total health budget, and any rises may mean less money for other diseases. Here, pressure from society to change this kind of resource allocation is certainly in order.

The structural adjustments determined by the World Bank and the International Monetary Fund (IMF) in the last decades of the 20th century, associated with the capital crisis that happened after the fall of the Berlin Wall and that in 2008 is represented by the serious North-American and global economic crisis, have worsened the social conditions of a substantial part of the world’s population, which will certainly further facilitate the worsening of the health situation globally. Thus, the most efficient application of the available resources, the decision on where and how to use them and how to counteract the interference of international agencies (World Bank, IMF) on this decision are only some of the challenges to be faced.

**Lessons**

**Confronting AIDS in Brazil**

In 1986, the Ministry of Health created the Brazilian Program on STD/AIDS (PNDST/Aids) and put it in charge of establishing a national plan to confront the epidemic. Table 2 shows some important milestones in the establishment of this program and in the access to anti-retroviral treatment. In 1996, the National Congress promulgated, with the support and pressure from organized civil society, a law that made it compulsory to provide universal access to anti-retroviral therapy to all that need it, at no additional cost (Portela et al., 2006; Teixeira et al., 2004). This decision went into the opposite direction from the common sense idea according to which developing countries should focus on prevention efforts to confront AIDS, because the complexity of the therapeutic schemes would make patient adherence to treatment difficult, increasing the risk of dissemination of resistant viruses. From 1996 to 2002, the Brazilian government’s total investment in this sort of treatment reached US$ 1,6 billion. Along with its enormous social impact, by diminishing mortality, morbidity, as well as the number of hospitalizations, medical leaves and early retirements (Teixeira et al., 2004), almost US$ 2 billion were spared. Today, the program’s good results are internationally acknowledged (Parker & Camargos Jr., 2000) and the rates of resistant virus transmission are lower than those of many developed countries. The provision of universal access to anti-retroviral drugs (ARV) and to adequate AIDS healthcare proved that it is possible for a developing country, even one with so many inequities, to treat people equally, independently of race, gender or economic power. Here we are talking not about the controlled and self-limited situation existent in a clinical trial, in which
the cost of providing such care to the volunteers is a fraction of the millions of dollars spent not only on the trial itself but also, in significant amounts, on marketing.

This approach has been defended (Steinbrook, 2006) and has already been adopted by many other developing nations, with WHO support. One example is the 3 by 5 Initiative, which aimed to make anti-retroviral medication available to 3 million people by 2005, mobilized efforts from all over the world and received funding from many sources.

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**Table 2 – Relevant events for Aids treatment policy In Brazil**

<table>
<thead>
<tr>
<th>Year</th>
<th>Relevant event</th>
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<tbody>
<tr>
<td>1986</td>
<td>Establishment of the National Program on STD/Aids</td>
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<tr>
<td>1988</td>
<td>New Brazilian Constitution (Single Health System, SUS)</td>
</tr>
<tr>
<td>1991</td>
<td>AZT distribution begins</td>
</tr>
<tr>
<td>1995</td>
<td>Local production of anti-retroviral medication begins</td>
</tr>
<tr>
<td>1996</td>
<td>Legislation secures the right to anti-retroviral medication</td>
</tr>
<tr>
<td>2001</td>
<td>57º Session of the UN Commission on Human Rights: access to medication to treat pandemics is a basic human right; Brazil produces seven out of the thirteen medications</td>
</tr>
<tr>
<td>2003</td>
<td>Presidential decree makes it easier to import generic medication produced under compulsory licensing</td>
</tr>
<tr>
<td>2007</td>
<td>Compulsory licensing is issued for the anti-retroviral medication efavirenz</td>
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</tbody>
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**Perspectives**

Despite all the problems and difficulties listed above, it is actually possible to fight for the improvement of the current state of poverty and badly-distributed wealth, a backdrop for disease dissemination. Among the viable mechanisms for this is the involvement of professionals and civil society, acting together in the Health Councils and participating in budget decisions. These fora can, among other things, influence decisions to fund studies that are really relevant and ethical, in order to improve basic sanitary conditions and epidemiological surveillance, as well as the access to quality healthcare for all.

**Internationally respected ethical rules for research**

A good example was set by the intense discussions which have taken place in the past ten years in relation to proposed changes to the Declaration of Helsinki: activists, ethicists and scientists have been able to work together to resist maneuvers to lower the ethical standards for clinical trials which can increase even more the abyss that separates affluent populations from developed countries from most of the rest of the world’s population.
Civil society participation

One of the ways to counterbalance the use of power in decision-making and funding allocation related to public health policies is through the strengthening (emancipation) of people/citizens. One example to be followed is that of people living with HIV/Aids in the fight for their rights in all possible fora, including international conferences, national and international AIDS organizations and even in regulatory agencies. This made a great deal of difference in all aspects of the struggle to control this epidemic – from prevention to treatment, from debates about rights to pressure for the development of efficient drugs and vaccines. One does not hear much, however, about effective participation of people living with malaria, schistosomiasis, Chagas disease or hepatitis in conferences or discussion tables about these diseases. But there are millions of people living with one (or more than one) of these diseases in developing countries. Here, education may be a sine qua non condition to change the situation, taking into account that it was especially from people with access to education that the great pressure exerted by civil society emerged in relation to the necessary measures to face the HIV/Aids epidemic.

Challenges to the sustainability of the Brazilian program to control Aids

There are challenges to the sustainability of the Brazilian program and they include:

The weight of success: The very existence of a successful program may contribute to a lower degree of involvement – and consequently lower political pressure – from civil society, including the media. By the same token, since the Brazilian program offers the best treatment available internationally, there is also the risk that healthcare professionals do not worry enough about follow-up and change the treatment too early to more complex anti-retroviral schemes. If this happens, the use of alternatives prematurely will raise the costs of the new drugs, which are generally more expensive, usually patent protected and have been tested for a shorter period of time.

The monopolistic or oligopolistic configuration of the active ingredients market: Despite the fact that Brazil produces eight anti-retroviral medications locally, except for the efavirenz, all active principle ingredients (API) are imported, generally from Asia. This situation is particularly serious because of the possible scarcity of APIs due to the rise in consumption of anti-retroviral drugs by public and private programs all over the world.

The great challenge of poverty and inequality (Greco, 1992; Phanuphak, 1998): The relationship between poverty and dissemination of epidemics has been proven beyond doubt, and these epidemics have a very high potential of increasing poverty. The effect of increased poverty is more than financial, because the disease and consequent mortality lead to
the erosion of social capital and family unity. Poverty increases the vulnerability to infection by HIV, because it makes access to healthcare and to the complexity of therapeutic methods more difficult, besides preventing the maintenance of necessary prevention.

A last and very important obstacle for long term sustainability is a short-sighted perception, to which the pharmaceutical industry propaganda contributes, that intellectual property rights issues are not relevant. This may be an unexpected side-effect of the various programmes to scale up treatment (FGATM, PEPFAR, Gates etc.), where the opportunity to get treatment may blur the long-term debate on the need for local production and technical independence and may jeopardize long term sustainability. Also, some free trade agreements are having an impact in drug prices and that affects sustainability on a long-term basis. Use of the TRIPS flexibilities, including compulsory licensing to buy generics and to produce locally is still incipient, although there are now many ARV generic versions pre-qualified by WHO.

These challenges must be faced in order to lower the risk of not being able to guarantee long-term sustainability of the Brazilian program, because:

- There is an expectation that an increasingly high number of people will need treatment: According to estimates, there are approximately 600,000 people living with HIV in Brazil (Szwarczwald & Carvalho, 2000), 180,000 of which have already been diagnosed and are being treated, and 20,000 new treatments are started annually;
- The current investments in anti-retroviral medications is about US$ 400 million/year, an amount which will certainly increase with the expected need for imported and increasingly expensive third line treatments;
- The poverty backdrop: Even with free access to healthcare, lab tests and adequate distribution of medication in this continent-sized country, the expansion of the epidemic to poor people in small towns means that they do not always have money to buy public transportation tickets to reach healthcare centers.

**Perspectives to warrant sustainability**

The exemplary role played by Brazil and the unquestionable success of its AIDS program are reasons enough to seek viable mechanisms to warrant its long term sustainability. This mechanisms are complex and multifactorial.

**Governance**

a) Mechanisms initiated by Brazil and depended only on the country.

Many aspects related to sustainability depend only on Brazilian policies: There is an urgent need to promote the “rational use” of anti-retroviral drugs, including policies to wait until more robust scientific evidence has
been collected before including new drugs into the Brazilian treatment consensus. Although since 1996 Brazil has adopted detailed guidelines for AIDS treatment, which are revised every year, there is a need for more data on the effectiveness of the various schemes for their rational use. The strong pressures from the pharmaceutical industry to introduce new drugs must be counterbalanced by local operational research, using the enviable amount of information collected from the 180,000 people now in treatment.

To increase local production, including better formulations of existing medication: Investing in public labs (and also in national private ones) to increase local production at compatible prices – not only for drugs but also to stimulate the production of APIs. There is also the need for better pediatric formulations and also for production of fixed associations, such as the one with azt-3tc-nevirapine, which has been available for a long time in other countries.

More investments in research, including for developing more molecules and APIs. For example: the establishment of a Brazilian factory in the State of Acre with an initial production of 100 million condoms per year; the development of tests for determining viral load and for TCD4 lymphocytes determination.

b) International collaboration

Lowering the price of anti-retroviral drugs:
Even though this is a short term policy, it is a significant component of the maintenance of universal access to treatment. In this quest, the amount of resources invested annually in the production and purchase of anti-retroviral drugs is, undoubtedly, an important tool in the negotiation table. Brazilian participation in regional initiatives led by the Pan-American Health Organization (PAHO) and international ones, such as Unitaid (http://www.unitaid.eu), has contributed to expand global access to these drugs.

c) Political decision and international participation

Despite all the experience accumulated by the PNDST/Aids, which has been dealing for three decades with all this epidemic’s complex aspects, and despite all the financial and political involvement, the growing complexity and the higher costs of new drugs protected by patents are a threat to the available resources for health. Thus, the political decision to implement local production at reasonable prices becomes an unquestionable necessity. And the legal instruments to issue compulsory licensing are backed by the Trips agreement flexibility when it comes to protecting public health (Fairchild & Bayer, 1999). In May 2007, the Brazilian government decided for the first time to issue compulsory licensing for the import and future local production of the generic version of the anti-retroviral drug efavirenz. This bold decision is obviously not the solution for
the Program’s sustainability, but it showed that, in situations where universal access to public healthcare is at stake, these exceptional measures are clearly in order. With compulsory licensing, each efavirenz pill, which costed US$ 1.55 in the patented version, could be acquired for US$ 0.45, saving an estimated US$ 30 million annually. The fact is that the seriousness, visibility and accumulated experience of the Brazilian program make it easier for the country to be more vocal and act according to what is best for public health, together with other international partners, in the quest for opening the black boxes related to the cost of developing and producing these medications, with the aim of establishing mechanisms for technology transfer and local production.

These examples reinforce the argument that today there is no longer room for asking IF granting clinical trial volunteers access to the best healthcare is an ethical requirement or not, as this IF must be replaced by HOW to work together to universally provide both the needed products that prove to be efficient and decent healthcare for all.

Conclusions

There are many uncertainties about what the future reserves for the AIDS epidemic, as well as for the infectious and parasitical diseases known today and those which we will certainly come to face, and the perspective of attaining health for all in the year 2000 has been irremediably postponed. The needed changes are many, and most of them are well-known:

Access to education, employment, housing; access to healthcare; all included in the Universal Declaration of Human Rights (articles 18, 25.1, United Nations, 1948).

The need for global involvement has been proclaimed as necessary for everyone to have access to health, but unfortunately this motto and the cited articles of the Universal Declaration of Human Rights are still rhetorical figures. The number of people who are starving is still intolerably high and has been getting even higher, and this growth coincides with the expansion of globalization.

In order to control endemics and epidemics, all efforts must be combined to: prevent their dissemination, with the continuous education of all on preventive methods; disseminate our urgings for solidarity and non-discrimination; encourage ethically appropriate research for new drugs, diagnostic tests and vaccines.

Unfortunately, inequality in health will not be solved by research or researchers, but, if people are treated equally in clinical studies, there will be equality in those studies, and they can be the first step for broader aims. Thus, a good start is the certainty that ethical requirements defined by unquestionable international guidelines, are applied equally all over the world. The certainty that equality shall be respected in clinical research may be an important step toward reverting the current injustice in health resources allocation, and may also
contribute to strengthen (emancipate) people (volunteers, researchers and civil society), enabling them to learn their rights as citizens and to fight for them. If it is not possible to reach this equality in such a controlled environment as is the one of clinical research, how will we make it happen in the real world?

In reality, without education, resources and healthcare, there is no perspective of controlling diseases. And access to these will only happen after considerable changes in the international order toward greater justice and equality, better income distribution and social protection. Clearly, this new international order can only be achieved with changes in each nation; it is truly difficult to cry for international justice when disparity in Brazil is so blatant. It is necessary - and it is worth repeating it – to exchange the paradigm of monetary and market values for one that values the human being. In this way, Brazil shall certainly be able to assert itself as a nation, opposing itself to the neoliberal values of the current economic order.

Will, however, the concerted action of all sorts of activists and health professionals exert enough pressure to improve the allocation of education and health resources, to improve wealth distribution? Probably not, but it means that our voices of indignation against the status quo will be heard. Our role as active citizens is to multiply and amplify the cry for justice and equality for all, independently from race, religion, origin or language.

Finally, Thucydides (465-395 b.C.) said that justice would only be achieved when those who are not victims of injustice become as indignant as those who are. I dare say that justice will only prevail when those who are affected by injustice become aware of their rights and fight for them.

Notas

1  See Declaration of Helsinki (2000) and Dismantling the Helsinki Declaration (2003).
3  See Dismantling the Helsinki Declaration (2003).
4  See Angell (2000); Lallemant et al. (1995); Portela & Lotrowska (2006); Rothman & Michels (1994); Schüklekn (1998).
5  Federal Register /Vol. 73, No. 82/Monday, April 28, 2008/Rules and regulations (edocket.access.gpo.gov/2008/pdf/E8-9200.pdf/).
7  Temple R, Ellenberg SS. Placebo-controlled trials and active-control trials in the evaluation of new treatments. Part 1: ethical and scientific issues. Annals of Internal


16. See Berkman et al. (2006).


18. See Grangeiro et al. (2006); Greco (2007).


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**Abstract** - The emergence of the Aids epidemic and the increase in the incidence of HIV infection are still a health challenge for the 21st century. The way the epidemic is being confronted and how it will be in the years to come will be of fundamental importance on the discussion of public health, ethics and human rights. The diverse aspects of the epidemic are here discussed, including the possible interventions necessary to its control. Changes in the decision-making process for the allocation of resources, both for public health care and research, as well the expansion of the ethical debate and the need to improve the standard of living of all individuals, are imperative conditions in order to face this very serious public health problem.

**Keywords**: Epidemic of the Aids, Ethics, Social impact, Scientific impact, Economic impact, Perspectives.
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