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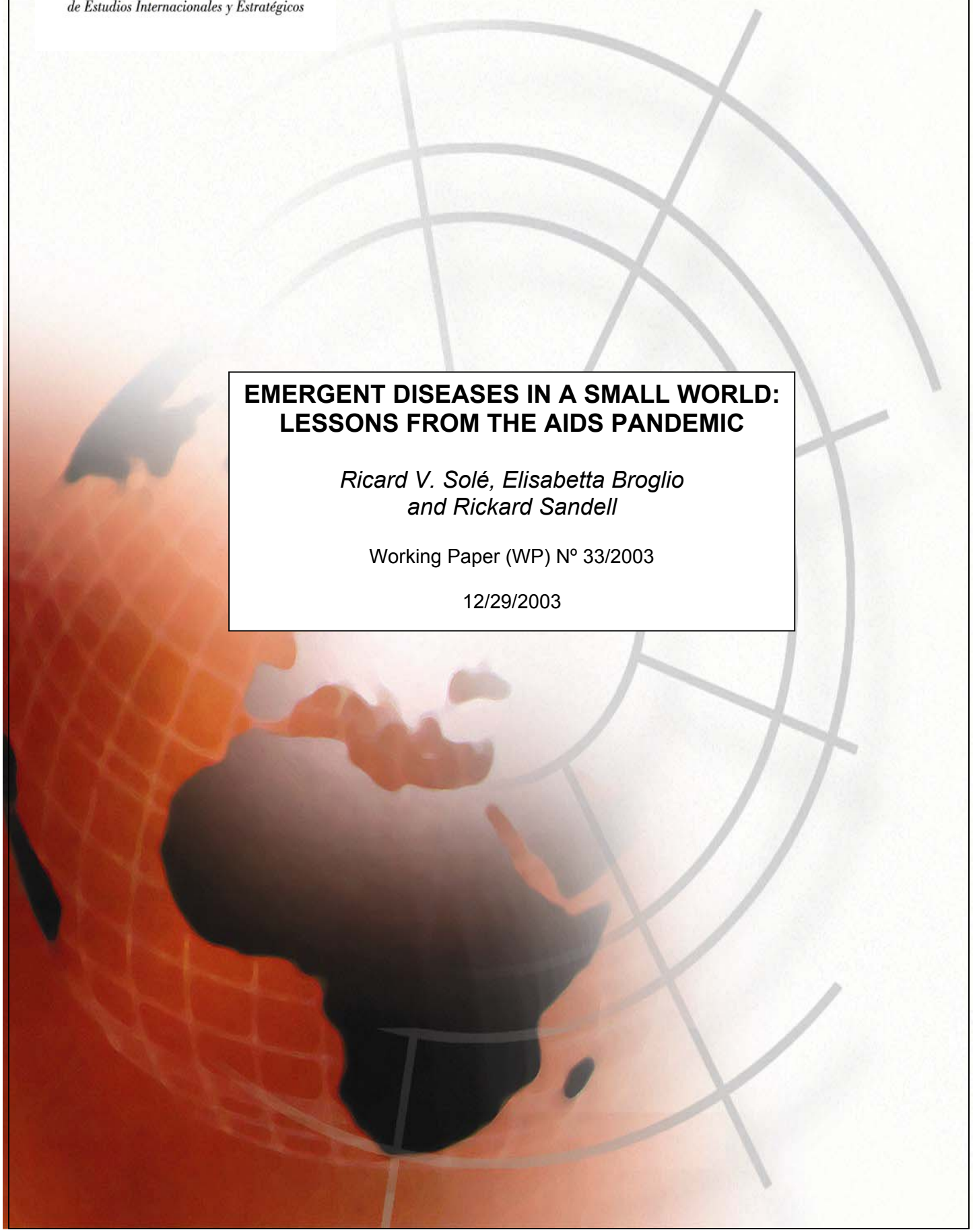

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Emergent Diseases in a Small World: Lessons from the AIDS Pandemic

Ricard V. Solé, Elisabetta Broglio* and Rickard Sandell ***

'Some say that AIDS has made us ever vigilant for new viruses. I wish that were true.'
Joshua Lederberg

Introduction

Over the past few decades, the concepts of 'emergent diseases' and 'emergent viruses' have attracted the attention of both scientists and politicians as a new threat to the economic and social stability of our world (Morse, 1993; Garrett, 1994). Not surprisingly, these two concepts are associated with other sources of environmental change, including the increasing evidence of an accelerated modification of our current climate and the degradation of the world's ecosystems.

To a large extent, the fact that new viruses are 'emerging' is intimately associated with the increasing deterioration of natural ecosystems and the human-driven modification of local animal populations, particularly of rodents. These populations experience rapid, sometimes exponential increases in their size due to the resources provided by growing human settlements, often in conjunction with local climatic imbalances. An example is provided by *hantaviruses*. High precipitations in the south-western US during the early 90s increased mice populations and led to an outbreak of this virus, transmitted by exposure to rat faeces. A previously unknown pathogen, the so-called *Sin Nombre* virus (SNV), was identified as the cause of hantavirus pulmonary syndrome (HPS). The virus was highly effective: it killed almost half of those exposed by causing severe breathing difficulties.

A similar situation is shared by the so-called *arenaviruses*. The South American viruses of this group, also carried by rodents, offer a good example of how exploitation of new geographical areas and intensive agriculture increase the likelihood of the emergence of diseases. The so-called Argentine hemorrhagic fever, first described in the rich agricultural zones of the pampas in the late 50s, has spread widely, causing the infection of thousands of people each year. Neither its origin nor the cause of its spread to the rodents that serve as its reservoir and vector are known.

By far, the most devastating effects of emergent viruses are those of the so-called *lentiviruses* (*lenti* = slow), a virus family to which the Human Immunodeficiency Virus (HIV) belongs. The basic structure of these viruses is shown in Figure 1. The prototype lentiviruses cause 'slow virus' infections of sheep. These viruses were first described in the 1950s by Bjorn Sigurdsson, who studied maedi/visna, a progressive infection of Icelandic sheep which, after an incubation period of roughly two years, caused a pneumoencephalitic disease.

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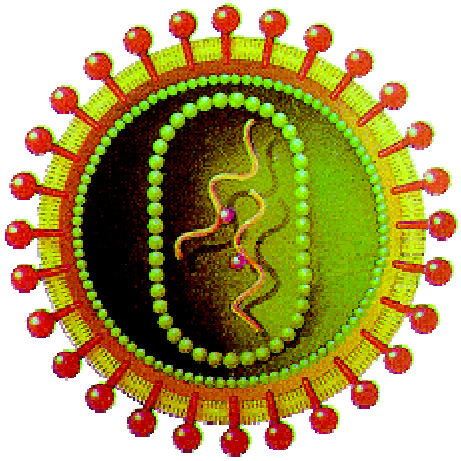
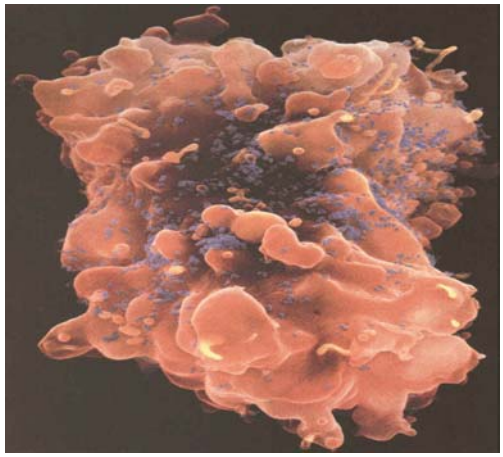
Lentiviruses are characterized by a number of common features. First of all, a remarkable complexity of their viral genomes that distinguishes them from other retroviruses (a class of viruses containing a RNA molecule as the genome which, after infection, is transcribed into the host's DNA genome). In particular, they have a lifelong persistence. This is a function of both their ability to integrate into the host genome and to evade host immunity but is also related to their very high mutation rates and their capacity to infect both dividing and non-dividing cells, such as immune cells (macrophages, Figure 1, right) and, in the case of HIV, T-cells (see Table 1).

Figure 1. The drawing on the left hand side shows a schematic view of the HIV. It involves an external coat of protein (red spheres) that are recognized by the membrane receptors of their target cells (macrophages and other cells involved in immune responses). Inside the coat, the virus genome is packed together with the replication enzymes. These enzymes are characterized by high levels of error copying, and thus easily generate mutant strains. The picture on the right hand side shows an infected macrophage with virus particles (in blue) budding out from its surface. Once the virus replicates by using the internal cell machinery, many copies of it, most of them mutants of the original strain, will spread out.





The HIV has the capability of infecting the host's immune system, whose function is to protect the organism against external invaders. The resulting immunosupression eventually promotes a high susceptibility to other diseases. Infection proceeds through at least three stages. The initial (acute) infection, associated with rapid viral replication and dissemination, is often accompanied by a transient latent period during which the virus is brought under immune control and no disease occurs. At some later time, a high level of viral replication (resulting from the selection of highly aggressive virus clones or a high diversity of infecting variants) results in the disease, which might show up in the form of uncommon types of cancer or through other infections (due to virally-induced immunodeficiency), as well as encephalitis, wasting, pneumonia and arthritis.

All these scenarios are influenced by different factors including the genetic background of the host, its age (young hosts are generally more susceptible to rapid-onset disease), stress or the virulence of a certain strain. Furthermore, the way the virus persists, through a latent phase, is the key for its success since without effective prevention and detection measures the expansion of the infection cannot be blocked.

Table 1. Examples of Lentiviruses (main host, type of cells infected and major disorders provoked by the viruses) are shown. Cells target of Lentiviruses are immune cells of the host, with a consequence for the ability of the immune system to defend from further infections.

Virus	Host	Primary cell type infected	Clinical disorder
Equine infectious anaemia virus (EIAV)	Horse	Macrophages	Cyclical infection in the first year: haemolytic anaemia and sometimes encephalopathy
Visna virus	Sheep	Macrophages	Encephalopathy
Caprine arthritis-encephalitis virus (CAEV)	Goat	Macrophages	Immune deficiency, encephalopathy
Bovine immune deficiency virus (BIV)	Cow	Macrophages	Lymphadenopathy, lymphocytosis, CNS disease
Feline immunodeficiency virus (FIV)	Cat	T lymphocytes	Immune deficiency
Simian immunodeficiency (SIV)	Primate	T lymphocytes	Immune deficiency, encephalopathy
Human immunodeficiency virus (HIV)	Human	T lymphocytes	Immune deficiency, encephalopathy

Source: Levy, 1993.

HIV-AIDS: Origins, Distribution and Future

'Unequal development in different countries in the promotion of health and control of disease, specially communicable disease, is a common danger.'Constitution of the World Health Organization, 1946.

Two main subtypes of HIV associated with human AIDS have been described, HIV-1 and HIV-2, isolated in 1981 and 1986, respectively. The phylogenetic studies of primate lentiviruses provide compelling evidence that HIV-1 is closely related to a virus that naturally infects chimpanzees (SIVcpz), while HIV-2 (isolated from West Africa) is closely related to a virus that naturally infects sooty mangabey monkeys (SIVsmm).

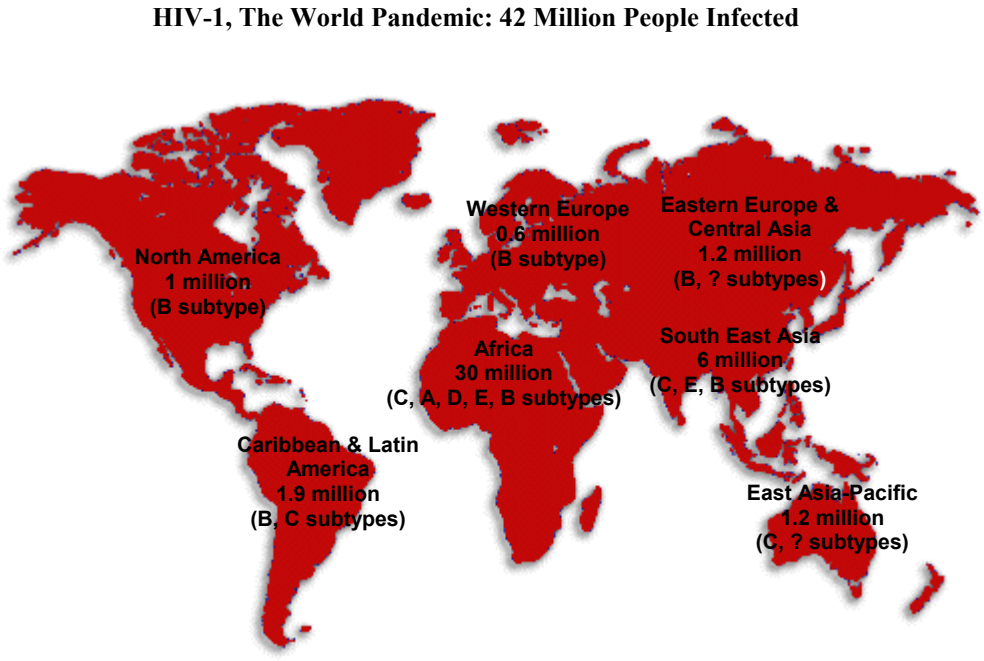
It is believed that zoonotic (or trans-species) transfer of these simian immunodeficiency viruses resulted in the emergence of HIV-1 and HIV-2. The viruses SIVcpz and SIVsmm have no effects either on chimpanzees or monkeys and have probably been with them for thousands of years. However, once the virus accidentally jumped to the human species (for example through the exchange of blood during a kill, or through the eating of undercooked monkey meat), it became a catastrophic threat. Zoonotic transfer has already been proved for other viruses, such as the Ebola virus and the Marburg filovirus. In HIV-1's case, one hypothesis is that it may have evolved through one or more initial infection events, followed by subsequent human-to-human transmission that resulted in its widespread dissemination.

At least three separate monkey-to-human transfers have probably occurred, giving rise to the three genetically distinct HIV-1 groups: groups M (for 'majority'), N ('non-M/non-O') and O (for 'outlier'). These groups are genetically distinct and have unique a geographical distribution. It is currently believed that HIV-1 group M viruses, considered to be

responsible for the global HIV epidemic, entered human populations in the early 1930s (Korber *et al*., 2000, Science 288:1789). The two other groups, O and N, are represented by fewer strains and are mainly localized in Africa and particularly Cameroon (both O and N) and Gabon and Equatorial Guinea (group O). West Africa (eg, in Cameroon, Ivory Coast and Senegal) also has the other HIV subtype (HIV-2), which has not given rise to any global epidemic, suggesting that HIV-2 might not be transmitted as efficiently as HIV-1, although it is unclear why.

Over 42 million adults and children are infected by HIV-1 (UNAIDS estimates published in February 2003, based on data as at the end of 2002, see Figure 2). Both in the United States and world-wide, infection is disproportionately common among minorities and among the poorest populations. The virus spreads by sexual transmission but also via infected blood and body fluids, and mothers to their newborn. In this way it has been transferred through generations and is spreading world-wide. In one year alone (2002) there were 5 million new HIV infections and 3.1 million people died. Now, the question is: if the virus was there since the early 1930s (at least), why did AIDS epidemic only take off in the 1980s? Together with the transmission processes, other events, such as changes in urbanization, rapid mass transit and new business opportunities have played a role in determine its successful dispersion.

Figure 2. The global distribution of HIV-1 infection (data from the end of 2002). Among virus subtypes, B is prevalent in the Americas and in Europe, while subtype C is the most common world-wide. The subtypes shown are variants of the main HIV-1 strain, the M group.



How Diseases Propagate in Small Worlds

'Only by facing up to the architecture of the real social world can we appreciate how truly difficult it will be to stop the AIDS epidemic. At the same time, however, a deeper understanding may suggest some powerful clues about the best way to try.'
Mark Buchanan

Understanding modern pandemics requires a certain degree of comprehension of the underlying mechanisms of disease propagation. The emergence of large-scale human

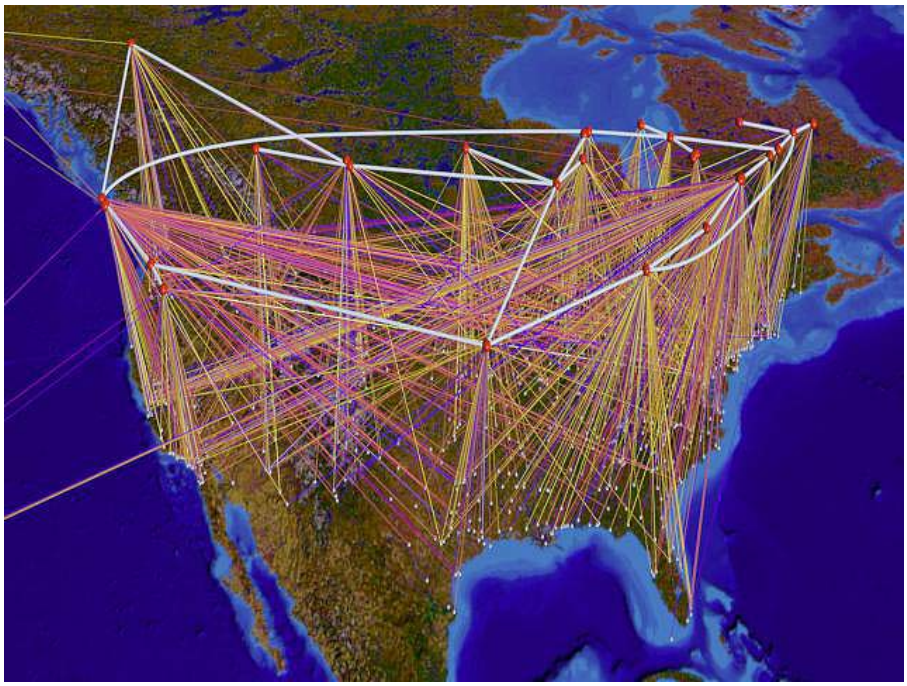
migrations, together with the architecture of social interaction strongly influences the historical course of a pandemic. The first component of this picture is crucial to understand the extremely rapid pattern of spread that pandemics can show in our time. Not surprisingly, the swift action taken to stop the recent 'severe acute respiratory syndrome' (SARS) episode was crucial to avoid its rapid spread. Since epidemics typically expand in an exponential fashion, it is crucial to introduce appropriate measures at very early stages of the process before the number of infected individuals (and the underlying virus diversity) goes beyond dangerous thresholds. In contrast with the situation that was common in the pre-industrial era, when individuals and goods moved slowly from country to country, today's global transport systems have created a *small world*.

The small-world concept has become a key issue in science, starting from the social sciences (Buchanan, 2002; Barabási and Bonabeau, 2003). Specifically, it has been shown that most interaction networks, both in natural and artificial systems, share a common trait: both information and viruses propagate very efficiently. In the Internet, for instance, it is very easy to reach a given website from any other despite the many thousands of sites forming the web.

The main property responsible for Internet's small-world nature is its highly heterogeneous structure. Most elements are connected to only one or two others, but a few of them (the 'hubs') connect many computers between them. This structure has two implications. The first is that highly connected nodes allow information to propagate at a very high speed: they act as key traffic transport pieces, since they typically collect most of the traffic. In other words, they are responsible for the web's small-world character. On the other hand, such a heterogeneous network is highly fragility: although the failure or removal of nodes at random has only a limited impact on the web's performance, a hub's failure has a huge impact on the propagation of information or viruses.

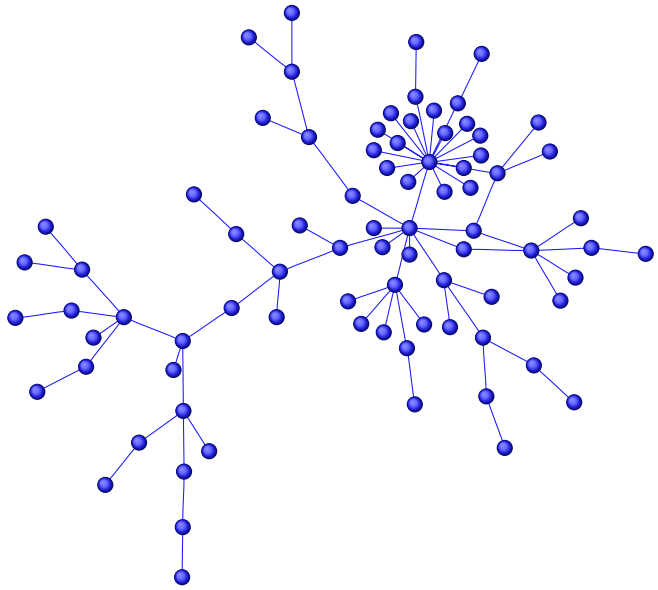
The airport network is not very different from the Internet (Figure 3). Due to the commercial expansion and common use of long-distance flights, the world has been steadily shrinking in size over the past few decades and it is now very easy for a pathogen to jump from country to country and spread further. This is actually what happens with computer viruses on the Internet: viruses spread very efficiently and are self-maintained in spite of the continuous local use of antivirus programs. Once they reach a given population size, the successful transmission of a single virus to a hub allows the epidemic to reach many other computers. Unfortunately, this situation is not restricted to the virtual world, and real viruses work in a very similar way.

Figure 3: Internet, similarly to many other technological and transport systems, is a complex network with a small-world architecture. Starting from a given node, it is very easy to reach any other node (a computer, for example) by performing a small number of jumps through the web.



At a smaller, but no less relevant scale, social interactions (including sex) also display a small-world pattern. This was shown by Fredrik Liljeros and his co-workers, who analysed the structure of networks of sexual contacts and found that they also behave as small-worlds (Liljeros *et al*., 2001). The team studied data gathered in a 1996 Swedish survey of sexual behaviour. The survey, involving a random sample of 2,810 Swedish individuals (aged from 18 to 74 years) who responded to personal interviews and questionnaires, revealed that most individuals in the network had only a few contacts with others, but that a few members of the network actually had a very large number of contacts (Figure 4, but see also Figure 5). Specifically, it was reported that the 10% most-connected men were responsible for 48% of the sexual connections, while the 10% most-connected women were responsible for 40% of the sexual connections. In contrast, for men, the 50% less-connected were responsible for 12% of sexual contacts and, for women, the 50% less-connected were responsible for 15% of contacts.

Figure 4. The local structure of sexual interactions. Here an example of a real sexual contact graph is shown. Nodes represent individuals and links indicate sexual contacts between them. Most nodes are connected to just one or two other nodes, but some show a large number of links.



As we have already stressed, this pattern of connections has consequences for the spread of sexually-transmitted diseases such as AIDS. As with computer networks, epidemics can spread in these highly heterogeneous networks even in the case of diseases with low rates of infection. The implication is that *these diseases become essentially impossible to eradicate* because they keep spreading. The reason why this happens is that individuals with many sexual contacts act as hubs for the spread of disease. If one has many partners there is a high likelihood of eventually contracting the disease. Moreover, once a person with many partners becomes infected then it is also likely that the disease will eventually be passed on to others.

This fact explains why even though people at first thought that AIDS would only attack the so-called risk groups, it then actually quickly spread to the general population. The first instance of what would later be called AIDS appeared as a relatively rare pneumonia among healthy homosexual men in San Francisco, USA. The phenomenon was initially called ‘gay cancer’, and ‘gay-related immune deficiency’ (GRID). Unexpectedly, it soon appeared that the same disease also affected drug users, both homo- and heterosexual, and that it could eventually spread to anyone. The hubs (ie, the individuals in each group that have a very large number of sexual contacts or are exposed to blood exchange) were essentially prostitutes, drug-users and blood-receptors. However, since the hubs were not isolated but had contacts with other individuals outside their groups, the disease spread rapidly. This is a general situation for diseases that mainly propagate through a network of contacts relying on some kind of social structure.

Figure 5. Regional features of the main modes of transmission for adults living with HIV/AIDS (source: UNAIDS) in 2002. Hetero = heterosexual transmission; IDU = transmission through injecting drug use; MSM = sexual transmission among men who have sex with men. Homosexual transmission seems to prevail in more highly developed countries, such as the US and Canada, Western Europe, Australia and New Zealand. In Africa, transmission is mainly through heterosexual contact, while a dangerous new trend has started in Asia, where the main sources of transmission are drug users.

AIDS: Prevalent Modes of Transmission

It becomes clear that living in such a small world, pathogens can easily jump from partner to partner. Random immunization or treatment under random conditions will often be limited to individuals with a small number of contacts and is therefore essentially ineffective. The only successful (and less expensive) strategy is to focus on prevention and treatment of individuals in the risk groups, ie, the hubs in the contact network. They allow the epidemic to propagate swiftly but are also its Achilles heel, being the key for future strategies to prevent new pandemics.

The Role of Politics

'It is hard to gain historical perspective on an event that is completely unlike any other we have seen before.'
Al Gore

As often is the case with contagious diseases it is not only the virus itself that contributes to its diffusion and lethal capacity. In the case of AIDS, the political aspects have been an important factor in aggravating the problem. The fact that the virus is sexually transmitted, and that homosexuals, sex workers and drug addicts are high risk groups have sometimes caused policy decisions to depend more on prejudice than on scientific evidence. This has led to political inaction instead of action, or triggered initiatives to counteract the spread of the virus that have been outright irresponsible.

In retrospect it is evident that a more rapid and global acceptance of the seriousness of the disease, as in the recent case of the SARS epidemic, could have led to a very different diffusion scenario than the one we are facing today. In contrast with SARS, the special characteristics of the groups initially at risk in the US (homosexual males and drug

users) was very important in terms of the social perception of the emergent disease. It took six years since the first reports of AIDS in 1981 and 41 thousand dead before the former US president Ronald Reagan used the word AIDS in public. It took the same time, until 1987, for the former president to announce the creation of an AIDS advisory panel, set up to inform the population about the emergent disease and its contagious pattern. As it turned out, and due to the socially infected debate, the advisory panel did not make efficient use of available scientific information at the time, causing additional delays in informing the public effectively. However, the US was not alone in delaying the recognition of the seriousness of the situation.

Other countries, such as China, India and particularly South Africa, chose to ignore or intentionally hide the emerging problem from their citizens and the rest of the world. These actions contributed to a steeper exponential increase in the number of infected people world-wide. For some time, several central African nations refused to report AIDS statistics to the World Health Organization (WHO). Nor did they allow external researchers to enter their countries. More than one government preferred to conceal the size of groups of people especially exposed to the HIV infection, such as the homosexual population and drug users. Many also downplayed the importance of other key groups such as sex workers, cited above as potential 'hubs' for the AIDS expansion network. Furthermore, it was especially in developing countries, which are more often deficient in hygienic measures, where the lack of politics of preventions (as for example the use of sterile needles) and blood control in exchange programmes produced the most devastating effects. An example is China, where many people from the poorer areas of the countryside contracted the HIV infection when they sold their blood to collecting centres that ignored basic blood-donation safety procedures. These centres habitually collected the blood from different people, mixing it in the same container in order to extract the plasma. Once the plasma was extracted, the remaining blood, essentially red corpuscles, was given back to the donors, very often with fatal results.

But prejudice and discrimination also drove advanced countries such as the US to make some mistaken decisions. For example, in some states, needle-exchange programmes for drug addicts were dismantled by the government, which claimed that they encouraged drug use, despite having already started to show significantly positive results in containing the spread of the HIV infection in this particular risk group. The social stigma attached to the AIDS epidemic and encouraged by some politicians produced undesired side-effects. For example, homo- or bisexual men often suffered social and work segregation. HIV-positive children were barred from schools and HIV-positive immigrants and visitors were not allowed to enter some countries. The social stigma lead infected people to hide their condition, with an increased risk of further infections as a result. This could have been avoided had more accurate information on the disease been available from the beginning of the epidemic.

In developing countries the risk of HIV infection is higher and the capacity to provide adequate treatment, care and support is much lower. Africa, with around 30 million people infected with HIV (more than 70% of the world total), is an example of this situation. There is clear evidence that the AIDS epidemic is reinforced in areas where humanitarian crises and poverty are present. Garrett (1994) has argued that the increase in violence and armed conflicts in Africa in the 1990s gave rise to conditions favourable to the spread of the HIV virus. The increased violence brought about poverty, famine and the collapse of health-care systems and other vital infrastructures. It triggered large-scale population movements, which are ideal for the spatial diffusion of the infection. Furthermore, since AIDS is primarily a sexually transmitted disease, it affects the most productive members of society (those aged between 15 and 45), which make up the working population and are critical to the economic development of any country. Violence and war destroy family

units and dismantle protective networks for women, making them far more vulnerable to infection.

In turn, this has triggered a downward spiral that has resulted in an even higher risk of contagious diffusion, contributing even further to instability and conflict on the continent. There is a feedback between disease and political instability. War clearly creates better conditions for the emergence and propagation of disease. Recent studies on the origins of HIV-2 reveal that the transfer of HIV-2 during the first half of the 20th century and the start of an epidemic in Guinea-Bissau coincided with the war of independence (1963-74). The authors (Lemey *et al*., 2003) conclude that 'war-related changes in sociocultural patterns had a major impact on the HIV-2 pandemic'. In the opposite direction, the AIDS epidemic has been considered not only a public health problem, but a security issue. As noted by Clinton in 2000, AIDS can ruin economies and threaten the very survival of societies. The CIA considers HIV/AIDS one of the main dangers for the future stability of developing countries, mainly because its economic impact will intensify the struggle for both political power control and key resources. The connection was made more explicit by Botswana's General Bakwena Oitsile at a recent meeting with other representatives of sub-Saharan military forces: 'if the security forces become weaker due to ill health, the countries' constitutions could easily be challenged. The political structures that ensure democratic governance could be threatened.'

Since the outbreak of the AIDS epidemic, scientific progress in preventing the disease has been significant. Even if a vaccine for HIV has not yet been found, there are effective ways of containing further spread of the virus. A combination of medicines, known as antiretroviral treatments or more popularly 'drug cocktails', have proved to be effective in delaying the HIV infection from developing into AIDS. The drug cocktail does not destroy the virus. It has been shown that once infected patients stop the medication the virus rebounds. This implies that a lifetime therapy is necessary since when administered properly the drug cocktail is capable of transforming the infection into a chronic rather than a fatal disease.

Moreover, if the cocktail is administered correctly it is capable of preventing HIV positive mothers from transferring the virus to the foetus, thereby eliminating the risk of generational diffusion. It is also effective in preventing or lowering the risk of contagion through exchange of body fluids among adults. Thus, if the cocktail could be administrated globally to all HIV positive people it would put an effective break on the exponential increase in the number of AIDS cases in the world as well as drastically reduce further diffusion of HIV. In addition, if such a campaign were to target infected 'hubs' the results would be even better.

The problem is that while administering the drug cocktail has proved to be extremely effective in containing the AIDS epidemic in the richer part of the world, many countries, especially in sub-Saharan Africa and Asia, have competing national priorities that inhibit the allocation of resources to expand access to HIV/AIDS care. In sum, poorer countries cannot afford wide distribution of the cocktail. Currently, more than 90% of the people with HIV in the developing world have no access to these expensive treatments.

Sometimes governments go to great length to avoid dealing directly with the costly treatment of their countries' AIDS cases. For example, South Africa's president, Thabo Mbeki, until recently insisted that poverty rather than HIV was Africa's greatest enemy. Mbeki, basing himself on a theory proposed by a well-known researcher from the University of California, Peter Duesberg, argued that retroviral drugs are ineffective. Against an otherwise unanimous scientific community, Duesberg's theory argues that HIV is a harmless retrovirus that serves as a marker for people in AIDS high-risk groups, and that there is no evidence that HIV actually causes AIDS. Under this view, AIDS is not

considered a contagious syndrome caused by a single conventional virus. Instead, the theory argues, AIDS is caused by conventional pathogenic factors such as blood transfusions or drugs, acute parasitic infections and malnutrition. The theory considers that drugs such as AZT promote AIDS, rather than fight it, thereby explaining why there is a higher number of AIDS cases per HIV-positives in America compared with Africa (the US has one AIDS case for every 20 HIV-positives; Africa has one AIDS case for every 300). Mbeki's position has led to only a tiny fraction of the millions of South Africans in need of antiretroviral treatment being able to receive it.

Part of the problem, and probably one of the reasons why Mbeki found such comfort in Duesberg's unfounded arguments, lies in the high cost of the drug cocktail. The high price is, in turn, a result of the enforcement of patent rights which allow pharmaceutical companies in possession of the patents, and with the support of the WTO, to compel countries to buy patent-protected drug-cocktails in preference to the much cheaper generic varieties. While international trade laws are quite clear on this issue, it is worth asking whether medicine manufactured with the intention to prevent deadly global infectious diseases such as HIV-AIDS should be regarded as a public good rather than a private good as assumed by the patent system.

Pharmaceutical companies driven by profit incentives can easily be accused of showing indifference to the HIV-AIDS victims' situation. However, there are some signs that they are beginning to consider the rising concerns expressed by public opinion. They have recently shifted from a purely commercial strategy to a more reasonable compromise with governments under the pressure of the AIDS catastrophe, although it could be argued that the main strategy here is less about halting the spread of the disease than countering the rising competition from the importation of illegal generics. Table 2 shows the prices charged by multinational companies in Europe compared with those charged in Africa.

Table 2: Example of the cost (in US dollars) for one-year therapy courses for a patient with different antiretroviral treatments (single, against HIV and cocktails against AIDS) in Europe and Africa, after the WTO's August 2003 proposal.

Drug/drug combinations (prices in US$)	**Europe**	**Africa**
ABACAVIR	4,635.50	985.50
ZIDOVUDINE	5475	438
LAMIVUDINE	3175	237.25
INDINAVIR	4,635.50	985.50
LAMIVUDINE + ZIDOVUDINE (COMBIVIR)	6,637.97	620.50
LAMIVUDINE + ZIDOVUDINE + INDINAVIR (TRIZIVIR)	11,487.30	1,602

Table 2 shows that the prices charged in some African countries are ten times lower than for the same product in the developed world. While this might seem to be a good deal, it is just a fraction of the difference with generic drugs produced in Brazil. A clear example is AZT (*zidovudine* in Table 2). The price per year of treatment with the generic drug offered by the Brazilian company FarManguinhos would be only US$33. In other words, buying from the Brazilian company would make the treatment available to 14 people for the same price as for one if purchased from the patent holder.

Obviously the Brazilian company does not have to consider the cost of research and development to be able to produce the drug. This cost is presumably carried by the patent holder, and it is one of the reasons why there are patent rights in the first place. However, it is easy to argue that there is a substantial difference between imposing patent rights on

a medicine that can prevent millions of people from dying, as well as preventing the spread of the disease, and on a technological innovation that simply makes life easier. Not long ago former US president Bill Clinton announced that the blueprint of the human gene would become a public good once its secret was revealed. He used the argument that it was in the interest of humanity to make such an effort. A similar arrangement for drugs like those preventing the spread of infectious diseases such as HIV-AIDS would be an important victory in the battle against the disease. No doubt preventing HIV-AIDS is also in the interest of humanity. Such measures require that richer governments invest more in research to produce the necessary drugs; if they rule out expropriation as an option, they can buy existing patents to compensate for past research initiatives. Ultimately, this could very well prove to be a small price since as long as HIV-AIDS continues its exponential growth in poorer countries, people in richer countries face an increasing risk of infection precisely due to the small-world characteristics of our seemingly big world.

When dealing with a large-scale epidemic, particularly at its early stages, certain aspects should be considered carefully. One involves the biology of the pathogen and the ecological scenario in which it emerges. Habitat destruction is driving many wild ecosystems into a new situation in which potential reservoirs of human-compatible pathogens might experience population explosions. In the future, this problem will be the main cause of a world-wide depletion of biodiversity and, as an indirect consequence, the emergence of new viruses. The AIDS virus and the recent SARS epidemic are a good illustration of this.

As discussed above, epidemics propagate at a very high speed thanks to the very large size of human populations and the small-world character of communications systems at all levels. A single infected person who reaches a highly-connected component in the air traffic system can be the trigger of further expansion. Once infected populations reach a critical mass, only strict measures of disease confinement are effective. In this context, attention should be focused on: (a) areas of the world in which human-driven ecosystem degradation are strongly affecting local fauna; and (b) appropriate measures of prevention in order to avoid the initial spread.

At a smaller scale, sexually-transmitted diseases (but potentially other pathogens not linked to sexual intercourse) also propagate through complex social networks. These networks have a well defined architecture in which individuals with many contacts play a key role. Prevention and effective immunization will be successful provided that this information is properly used. At a national scale, politics and correct decisions on health issues are extremely important. The AIDS pandemic (and the SARS episode also) illustrate the success of the joint efforts of the international scientific community, but also the incompetence of certain political decisions, which eventually affect the life of millions of human beings. Some decisions, based on prejudice, slowed down the effective treatment and prevention of the disease and thus indirectly caused the death of many people. Examples such as South Africa reveal this incompetence at criminal levels. Prime ministers who deny the evidence reported by thousands of scientists and who accept the opinion of a minority are likely to promote a nation-wide disaster which will affect generations. This is certainly the case with Mbeki's policies, which are partly responsible for the current situation.

A similar argument can be applied to policies governing the behaviour of pharmaceutical companies. The profit-driven trade in drug cocktails that prevent the spread of HIV-AIDS and imposed patent rights have stopped or slowed down the use of much cheaper generics in countries which are in a clear state of emergency. Action such as this not only hinders the successful prevention of the pandemic but actually makes the situation worse. Each additional AIDS victim will have an impact on the global spread of the disease for

years and effectively sacrifices the lives of many thousands, if not millions of individuals. There is no reasonable excuse for governments to allow this or to prevent making the available drug cocktails a collective good.

Recent scientific developments, our knowledge about the diffusion of the HIV virus and the effectiveness of the available drug cocktails imply that the key problem to halt the AIDS epidemic is not only medical science. Until a vaccine becomes available, the real obstacle to effective prevention is politics and political will. Under politics we also include trade politics. Apart from the reluctance of governments of countries badly hit by the AIDS epidemic to admit and deal with their AIDS problem, western governments, sometimes with the help of the WTO, impose patents rights that are counterproductive in the combat against HIV-AIDS. Lack of political will in both developed and less-developed countries could easily backfire by increasing the global spread of the disease, including to countries in the developed world. Were this to occur, it is easy to see that the AIDS pandemic could become a problem that would not only bring death and despair, but also social unrest and the potential to upset democratic stability on a global scale.

Strategic Implications of the AIDS Pandemic

'We must help our partners in [developing] countries to boost awareness-raising, especially among young people, and to improve the affordability of diagnosis and care, not just for HIV/AIDS but also for other major diseases causing concern in less developed countries today.'
European Commissioner Poul Nielson

So far, the scope and seriousness of the HIV/AIDS epidemic makes it one of the greatest human tragedies in history, and its implications at the individual level are, if not impossible to comprehend, very difficult to imagine. The epidemic is by no means contained, rather the opposite; each year that passes the number of people who are HIV-positive increases across the world, as do the number of deaths from the disease.

As the epidemic progresses the damages that are directly related to it multiply and, as with all wide-ranging individual tragedies, the aggregate damage is likely to have implications far beyond the individual level. This section will discuss the strategic implications of HIV-AIDS in three interrelated areas: (a) the globalisation of the disease and the risk of an increase in the number of HIV-positive individuals in traditionally low-risk countries in the short and medium term; (b) the risk of a global economic slow-down in the long term; and (c) the increased risk of armed conflict and terrorism in the short, medium, and long terms.

The large number of infected people in Africa and Asia, and to some extent Latin America, is having, or is starting to have, negative effects on the economic growth potential of these regions. The cause of the weaker capacity for growth is the increasing deficit in human capital resulting from excess mortality due to HIV-AIDS. As this paper has clearly indicated, the disease primarily affects the working-age population. As a result, the protection afforded by the family is breaking down, bringing family resources to a minimum. Children and the elderly, who depend on the working-age population, are exposed to an increasing risk of poverty as the infection deprives families of their breadwinners. To gain an idea of the magnitude of the problem, UN forecasts put the number of parentless children in Africa at 25 million by the year 2010 (UNAIDS et al 2002).

The aggregate of all these individual problems results in a substantial loss of human capital and labour supply as well as in rapidly increasing average labour costs due to the

higher turnover rates caused by premature deaths. The consequences are weaker growth rates in local economies and eventually decreasing GDP levels for entire countries. This translates into declining resources for investment, consumption and development in the affected countries, which are likely to give rise to tensions in a variety of fields.

The high ratio of infected people also diverts substantial economic resources into emergency consumption of very expensive pharmaceuticals for combating the disease, as described in the second part of this paper. When the total medical costs of a country escalate, the potential for economic development in other areas, which could have thrived in the absence of the disease, vanishes or becomes significantly hampered. Given that a large majority of the most affected countries are developing nations, the rapidly advancing HIV-AIDS epidemic has a significant potential to thwart economic development even further in already backward economic regions.

More worrying perhaps is that the economic problems developing in the trail of the advancing epidemic initiate a series of chain reactions leading to a greater diffusion of the infection than would otherwise be expected. The reason for this is that economic deterioration triggers social mechanisms that are highly favourable to the disease's geographical spread and thus its globalisation.

There are two prime social mechanisms that are likely to spur the disease's global spread and expose regions which have hitherto been spared its ravages. Immigration research has effectively identified so-called 'economic push factors' as a principal reason for migration. Countries with a poor economic performance are potential sources of emigration even in the absence of the disease. With the presence of HIV-AIDS, economic hardship escalates, turning a situation of poverty into one of economic despair. If this continues unhindered, emigration incentives are likely to multiply, leading to a potential exodus of an even larger scale. In the first instance, emigration is directed at neighbouring countries and regions, but eventually a more global emigration flow becomes possible as the infection advances.

Apart from economic incentives to emigrate, social factors also guide people's migration choices. When family networks and social networks disintegrate, the social inertia that keeps most people from emigrating disappears. In the same way as HIV-AIDS' high death toll gives rise to economic despair, it also effectively dismantles existing social networks. If this phenomenon is wide-ranging, as it is in the hardest-hit areas such as South-East Africa, the likelihood of population movements becomes even stronger.

The strategic implications of an increased potential for population movements from regions where the HIV-AIDS epidemic has a firm grip towards regions where the epidemic has so far been contained is important to understand. This paper has indicated that one of the key factors why diseases becomes pandemics is the high incidence of population movements from areas where the infection is common to areas with low rates of infection. This is particularly true when the disease spreads through human contact, such as in the case of HIV-AIDS.

Since the infection effectively targets the working-age population and thereby destroys the economic capacity and social networks of both individuals and families, people have a higher propensity to leave their usual place of residence in search for a better life elsewhere. When this occurs, the virus travels with the people to areas where the disease is less common, thereby increasing the risk of exposure in non-infected populations. Due to its capacity to trigger social mechanisms operating on people's migration propensities, the HIV-AIDS epidemic is very effectively contributing to its own diffusion.

A larger migration from countries with a high incidence of HIV-AIDS to countries with a low incidence is further complicated by the precarious situation faced by many emigrants on arrival. In trying to cope with their new situation, a small but by no means insignificant share of the migrants take up work in the sex industry. In addition, many who want to leave their countries fall prey to traffickers and end up almost automatically in this industry.

Needless to say, increased population movements from countries affected by HIV-AIDS coupled with high ratios of new immigrants in the destination countries' sex industries is the worst possible scenario if the aim is to contain a disease which is primarily passed on through sexual contact. The discussion on sexual networks in the first part of this paper effectively shows that the key to why sexually transmitted diseases, including HIV-AIDS, become epidemics is whether a small number of people with an unusually large number of sexual contacts have the disease or not. By definition, sex workers are extremely sexually active, and when they are primarily recruited from countries where HIV-AIDS is common or very common the chances are that they unknowingly contribute to spreading the infection to parts of the world that have so far been spared.

Spain is particularly at risk of becoming exposed to this type of phenomenon. Its proximity to Africa makes it a preferred migration target for emigrants and an obvious choice for traffickers. Furthermore, the country's cultural and linguistic links make it a preferred destination for Latin Americans also. While Africa is known to be at the core of the epidemic, parts of Latin America have seen an increment in the prevalence of HIV-AIDS close to that of African countries. As for migrants entering the sex industry, the Spanish Guardia Civil has estimated that out of 300,000 prostitutes active in Spain, 70% are foreigners. Of these, 50% are Colombians, 10% are from Eastern Europe (mostly the Ukraine and Poland) and 6% are from Nigeria. All of these countries have a significantly higher incidence of HIV-AIDS than Spain and other European countries. In sum, the likelihood of HIV-AIDS gaining a stronger grip on world health through increasing migration and rising numbers of foreign sex workers from countries with high rates of individuals infected with HIV-AIDS has to be regarded as high.

The root cause for this negative assessment is that the infection continues to advance in less-developed countries, thus hampering any attempts at economic improvement. Historically, economic despair is an effective trigger for large-scale population movements, which in turn are a prerequisite for transforming diseases from a local phenomenon to a global one. Thus, the economic deterioration resulting from the ravages of HIV-AIDS in developing countries could easily come to alter the pattern of the epidemic in the developed countries in very negative ways. The most likely scenario is that developed countries will become more exposed to the disease due to some of the social mechanisms that are activated as a result of it.

Paradoxically, if migration from high-risk countries increases the result is that they suffer additional losses of human capital. The problem of course is that the people who migrate are those who are fit to work, thus depriving the country of a precious commodity when it is already facing large losses in human capital. This vicious spiral hampers the prospects for economic development even further, increasing economic despair and making emigration more attractive as a result.

The negative economic development following the expansion of the epidemic is likely to slow down economic activity, reduce trade flows and diminish exports and imports between areas where the disease is common and the developed world. This means that trade in the rapidly developing emerging markets which are currently seeing an expansion of the virus, such as China, India, South Africa and Latin America, is potentially at risk (UNAIDS and WHO 2003). While economic issues might seem a minor problem, when

millions are dying because of the disease, it is easy to see that a situation of deteriorating trade and economic activity could make the global economy more fragile in the long term and increase the potential for long spells of economic recession in the future.

The seriousness of the situation is reinforced by the unfavourable demographic developments in the western world. The lack of population growth in Europe, Japan and, to a lesser extent, the US is likely to force western countries to rely increasingly on developing markets if they aspire to continued economic growth. The progress of the HIV-AIDS epidemic in the developing countries is working against such a shift in economic focus from a western perspective. Consequently, our growth expectations should be more cautious as long as the HIV-AIDS epidemic continues to expand.

However, economic and social interaction is not only an issue between rich and poor countries. If we look at the region where the HIV-Virus has the highest prevalence –South and South-East Africa– we find that the density of HIV-infected populations is sometimes highly heterogeneous within the region, ranging from 5 %-6 % in Angola to over 20 % in South Africa and 30 % in places such as Lesotho (figures based on estimates for 2001 in the CIA's world fact book).

From a regional strategic outlook, the HIV-AIDS problem is hardly a national affair. Many of the countries in this particular region are interdependent in economic terms; in fact this interdependency is one of the reasons why the infection has spread so rapidly. When two or more countries are economically interdependent, it means that no matter how effective a particular country is in containing its own HIV-AIDS problem, it is still at the mercy of a neighbour's efforts.

Tanzania, for instance, is currently experiencing a decline in its number of HIV-infected individuals but is unable to enjoy the full economic benefits of the decline as some of its most important trading partners, and neighbours, have significantly higher HIV cases in their populations. Similarly, when the number of HIV-infected individuals reaches alarmingly high levels in countries that are economical focal points or natural centres for regional trade, this is likely to influence the economic performance of the entire region in a highly negative way. South Africa is by far the single most important country in Africa in terms of trade, and it is a dominant export-import partner for most African states, particularly in southern and south-eastern Africa. With a rate of over 20 % of HIV cases in its population, South Africa is unable to reach its optimal economic performance, thus effectively holding back the economic development of the entire region.

It is not only regional economies that are at risk because of heterogeneous HIV diffusion patterns in this part of the world. In the longer term, and if the infection is not effectively contained, the geo-strategic outlook for the region could be subject to substantial changes, with countries lagging behind South Africa today taking over as the dominant actor in the region. As in all situations of flux this does not necessarily imply an increased risk of regional instability, but the possibility cannot be ruled out. Another potential threat from the type of economic turmoil described here is that shifts in economic strength can give to situations whereby countries that manage to deal successfully with their AIDS problem come into possession of power that could be used against their neighbours. The element of insecurity resulting from a heterogeneous diffusion of the virus in a particular region of the world should not be underestimated. Avoiding conflict and economic turmoil and preserving the peace in regions where the density of HIV infection is high involves coordinated action in all affected countries simultaneously in order to avoid competitive advantages in the battle against the disease.

Other negative economic spin-offs of HIV-AIDS can easily be identified. The extremely poor economic outlook faced by many of the countries suffering from the HIV-AIDS

epidemic could convert them into 'countries for sale'. That is, the lack of economic resources could make them and their inhabitants susceptible to proposals and/or investments from anyone with economic resources regardless of their intention to remedy the situation of economic despair. Also, the lack of economic means could easily backfire on democratic institutions, leading to a break-down of the rule of law. After all, both soldiers and policemen have to earn their daily keep somehow, and when their governments are no longer able to make ends meet the risk for corruption and civil disobedience escalates.

It is no coincidence that the poorest countries are those with the largest democratic deficit and the highest rates of corruption. Needless to say, this makes many of the countries which are struggling against a growing HIV-AIDS problem and the resulting economic decline into havens for international terrorist organizations and organized crime. Organizations of this type are known to prosper in countries facing economic chaos and disintegration, and we can expect them to benefit from the negative economic effects the epidemic is causing. Currently, the risk of this occurring is greatest in South-East Africa, but the rapid spread of the disease in former CIS nations could lead to it occurring much closer to the European Union's borders. In this regard, the HIV-AIDS epidemic is a close ally of the enemy in the international war on terrorism.

The presence of organized crime and terrorist organizations could also result in administrative take-overs or partial take-overs of important democratic institutions, giving rise to 'terrorist states'. Obviously this would increase the potential for the type of security risks in other parts of the world that are being targeted by the war against terrorism. The problem is that hard power is ineffective in combating the problem since the primary enemy is a virus that benefits from an even higher stealth capacity than a terrorist. As long as the epidemic is allowed to continue contributing to economic deterioration, organized crime and terrorism are likely to prevail. Thus, a different strategy is called for in this particular struggle against terrorism and organized crime.

As the lack of economic development wears down democratic institutions and the rule of law, we cannot rule out that the potential for armed conflict between countries might rise. However, of all the evils resulting from the HIV-AIDS epidemic, large scale armed conflicts is probably the least likely. External conflicts require both economic resources and human resources. As this paper has indicated, the HIV-AIDS epidemic is taking a large toll from both, making military build-ups far more difficult and thus the prospect of war less likely. This is particularly true in cases where neighbouring countries are both suffering the effects of the epidemic, that is, when the density of HIV-infected individuals is homogenous. A chaotic domestic situation, with an increased risk of terrorist and organized crime activities should thus be regarded as a potentially worse security threat in the short and medium term than large-scale armed conflict in regions where HIV-AIDS is most common. However, in the long term, and as countries approach their HIV-AIDS problem in different ways, we cannot exclude that some countries will be more successful than others. This may give rise to conflicts in which a stronger nation takes advantage of its relatively superior power to overcome a less successful neighbour.

As indicated above, as a result of its extreme geographic proximity to the regions where HIV-AIDS is advancing at a faster pace, Europe is more exposed to the problems caused by the epidemic than other developed areas. The same geographical proximity also makes Europe more exposed to the infection itself, and it could face a growing incidence of contagion as the socio-economic problems caused by the infection increase. This potentially vulnerable position should be a cause for concern in so far as Europe has, or rather should have, a strong strategic interest in containing the disease. The question is: what are the available solutions?

In principle, there are two main problems that have to be considered. On the one hand, there are the economic problems caused by the infection and, on the other, the increased risk of the further spread of the disease. Both problems are interrelated. Given the implications of migration and the wider geographical diffusion implied by population movements, it would be tempting to shut down borders with countries where the infection is growing and in that way prevent the disease from entering through migration channels and networks. However, it is unlikely for this measure to be effective, nor is it desirable since the cost involved in such a venture might well outweigh the advantages given the growing demand for migrants in Europe as it starts dealing with increasing population deficits.

As for the economic problems, it may be tempting to rely on increased economic support so that affected countries can deal more effectively with their HIV-AIDS problems. The drawback, however, is that the list of success stories where financial aid has been provided is very short. To this should be added the observation made in the second part of this paper that most of the worst-hit countries have shown considerable skill in mismanaging their HIV-AIDS problems, and instead of improving are actually making the situation worse.

Ad hoc solutions such as these can at best mitigate the effects of the disease, but not eliminate them. The increasing incentives for migration and the deterioration of the economy, with its sinister spin-off effects, are merely the consequences of something much worse –the presence and diffusion of the HIV-AIDS virus. Thus, the only way to improve the strategic outlook is by effectively containing the virus and not just tackling the problems caused by it.

This paper provides some keys to which elements should be targeted to combat the virus effectively. The first key is the contagion. The notion that a small number of very sexually active people are responsible for a large number of contagious transmissions suggests that much more work is required in targeting this relatively small group of the world population when designing preventive measures to halt the spread of the disease. In doing this it is important to discard the assumption that HIV-AIDS is primarily spread among homosexuals and drug addicts. Recent developments clearly show that it is just as common among heterosexuals. Associating the virus with potential social stigmas only serves to make the struggle to remedy the situation much more difficult. Unsafe sex in general is what causes the epidemic to spread, and unsafe sex with very sexually active persons greatly increases the chances of contracting the disease. It is also important to recognize that it is not only prostitutes who are very sexually active, many of there clients falls under this category, as well as those who lead a sexually active life in terms of many partners in general. If preventive measures effectively target the most sexually active in the population the diffusion of the virus would be seriously reduced.

The second key is how to stop HIV-infected persons from developing AIDS and how to reduce the risk of HIV-infected individuals transferring the disease to others. While there is no cure available, this paper indicates that the HIV infection can be reduced to a chronic disease if those infected are submitted to available medication –the so called drug cocktail. If the drug cocktail is administered to all those who carry the infection the risk of further diffusion would be reduced to a minimum. In addition, since the cocktail is capable of indefinitely postponing the development of AIDS in infected persons, the excess mortality would also be reduced to a minimum, thereby increasing the potential for economic recovery.

Another advantage of an effective administration of the available medication is that it has the potential to contribute towards making HIV-AIDS a generational problem. If the drug cocktail is administered properly it reduces the risk of transmission from an infected

individual to a healthy individual to a minimum even if unsafe sex is practiced. That is, with time, as the current 'AIDS generation' is replaced by younger generations, the presence of HIV-AIDS in the population is greatly reduced as long as those infected have access to the drug treatment.

The problem, of course, is that no single country can carry out the mass distribution of the drug cocktail. It is simply too expensive. However, a more coherent strategy of cooperation and political commitment, for instance within the framework of the European Union and the new European centre for infectious diseases, involving the widespread distribution and financing of HIV-AIDS related research to develop medical tools to combat the disease in the future would increase the capacity to stop the disease from spreading faster and to new areas. A joint effort at the level of the European Union to make medication much cheaper and easier to access would make a big difference. At the same time, a joint effort in financing common European research on AIDS treatment and potential vaccines would have a greater chance of progress than isolated single-country efforts.

While coordination on the side of the donors is a prerequisite for being successful in this task, it is also necessary to achieve coordination on the part of the receivers. The international community's interests will only be served effectively as long as its efforts do not give rise to increased differences between the regions affected by the epidemic. As discussed above, increased discrepancies could give rise to heightened tension, which if allowed to happen could destroy any initial success of a coherent initiative to prevent the diffusion of the virus.

At the same time, and since we cannot count on a quick victory over the disease as long as we lack either an effective cure or a vaccine, European countries also have to be prepared to deal with some of the unintended side-effects of the epidemic. As with the case of finding the necessary resources for medication, the resources to deal with political instability in exposed regions need to be coordinated in order to be effective. The break-up of civil society and domestic chaos not only increase the potential for the further spread of the disease but also provide the right ingredients for terrorism and organized crime. Problems of this type call for international intervention, not excluding military intervention as a last resort.

Although some progress towards unified European missions has been made in response to other crises, Europe is still far from being in a position to answer rapidly to situations of this type. For any larger-scale aid programme to be effective, a minimum degree of rule of law is necessary. Thus, apart from the coordination of economic and medical aid, Europe also has to consider dealing with conflicts and situations of civil disobedience that might arise as a result of the disease.

In drawing up common policies to contain the AIDS epidemic it should not be forgotten that the epidemic is just one deadly disease among others, although certainly the most serious one around today. This paper has also shown that the potential for outbreaks of emerging diseases, deadly as well as others, is on the increase. In fact, AIDS is likely to be the result of the accelerating breakdown of the world's bio-diversity. Thus, efforts to contain the AIDS virus, or to halt its mutation into more serious structures, and to prevent the emergence of new deadly diseases make it necessary to adopt a wider ranging approach in order to reverse the deterioration of the planet's bio-diversity.

Being at the crossroads of the world's most exposed regions to new diseases puts the European continent in a vulnerable position for the future. It is more than likely that the real threat to European lives will be from current and emerging diseases rather than from armed conflict or terrorism. So far this 'enemy' has received far less attention than most

other threats and the time has perhaps come to take a more serious approach to European intergovernmental policies in this regard. This analysis has also shown that the struggle against epidemics such as HIV-AIDS is to a great extent a collective problem. Without an intended strategy of cooperation between rich and rich and poor countries on a variety of issues, the chances of success in containing the epidemic, and the problems it gives rise to, are likely to be limited.

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Related Web Sites

(1) MSF campaign for access to essential medicines:
http://www.accessmed-msf.org/index.asp
(2) Health Global Access Project:
http://www.healthgap.org/
(3) HIV/AIDS & Human Rights:
http://www.hrw.org/campaigns/aids/index.php

Thabo Mbeki's views are presented at:
http://www.virusmyth.net/aids/