Supplement

The Global Fund
To Fight AIDS, Tuberculosis and Malaria

Ten-year fight for world health

Each year millions of people die from avoidable or curable illnesses. Since 2002, an unprecedented financial effort has helped transform world health. Malaria is on the wane, a third of those in need receive treatment for Aids, and the fight against tuberculosis is under way. The 10 year-old Global Fund, which collects money from donor countries for programmes in 150 countries, is the main mechanism for this progress. But the present financial crisis may impact on its work

KEITH HARING FOUNDATION, NEW YORK

KEITH HARING –
'International Volunteer Day' (1988)

South Africa gets to grips with AIDS

BY OUR SPECIAL CORRESPONDENT ANDRÉ CLÉMENT

It was a Wednesday in late October. Fifteen or so children were lining up outside the HIV clinic in Site B, Khayelitsha, Cape Town's largest township. Accompanied by their parents or, for orphans, an adult relative, they patiently waited their turn. The nurse weighed them, checked for coughing and handed out a month's supply of anti-retroviral medicines (ARVs).

Some of the children were 8 to 10, others a bit older. Adolescence was just round the corner, rebellious and prone to risky behaviour, a period of difficult existential questions and emotional rollercoasters. It was time to explain the reasons behind their daily diet of tablets and pills to subdue the virus and prevent it from developing into AIDS. A group of older children gathered in a prefab, while a counsellor, Nombasa Dumila, took the adults aside to discuss "how to help the children understand and come to terms with their status, and teach them to take responsibility for their own health".

"We work in three sessions," explained Dumila. "These children are beginning to ask questions, especially 'Can I stop now?'. The first session deals with germs, tuberculosis and basic hygiene, while parents learn the elemental science behind HIV. The next week we give them a more detailed description of viruses and bacteria." There were illustrations to explain the importance of CD4 cells, which reflect the strength of the immune system, and of antiretrovirals. Next, Dumila said, "We counsel adults about how to tell their children about their status. Parents who are themselves infected struggle with this part, but tend to take the process more seriously and personally than those who aren't, who try to get it out of the way as quickly as possible." The last session is used to answer the children's questions.

These children do not know they were the first babies to receive ARV treatment in South Africa. Their tenth birthdays coincided with the anniversary of a battle which began here in Khayelitsha, heartland of the Treatment Action Campaign (TAC) led by Doctors without Borders (Médecins sans Frontières, MSF) clinic. In 1998 the TAC consisted of a handful of people living with AIDS, gay activists and women who had lost children to HIV. The world took notice in July 2000 during the XIII International AIDS Conference in Durban when the TAC held public demonstrations, and assisted the South African government in its legal battle against 39 pharmaceutical companies trying to block access to affordable generic drugs. The TAC's campaign gave a face to victims of the international patent cartel.

The protests paid off, and the pharmaceutical lobby eventually dropped its case. Hope spread that the sick would receive treatment. But the activists who had defended the government were soon disappointed. Manto Tshabalala-Msimang, then health minister and a loyal supporter of President Mbeki, delayed the distribution of ARVs to the public health sector, citing toxic side-effects and recommending an alternative cure of garlic, beetroot, lemon and African potato. In 2002 the Constitutional Court upheld a High Court decision of the previous year (1), ordering the state to provide Nevirapine (a drug which greatly reduces the risk of mother-to-child transmission) to HIV-positive mothers across all state-funded clinics.

Further court proceedings led to a ruling in 2004 to implement a national treatment strategy and ARV rollout. However Mbeki and Tshabalala-Msimang (who died in 2009) continued to spread confusion by openly questioning the link between HIV and AIDS and promoting various quack remedies (such as those peddled by the German-American vitamin salesman, Mathias Rath). Two independent studies estimated that the government's foot-dragging over the provision of ARVs may have resulted in over 300,000 preventable deaths (2). Mbeki's refusal to acknowledge the severity of the AIDS epidemic contributed to the ANC's ousting him as president following its 2007 party conference in Polokwane.

Kgalema Motlanthe, who became interim president, appointed a new health minister, Barbara Hogan (the first white woman to be convicted of treason by the apartheid regime in 1982). Hogan took over a ministry that had lost its bearings and, with the help of Fatima Hassan, a lawyer and member of the AIDS Law Project and TAC, set about reversing previous policies. "Our party had inherited a somewhat Stalinist political mindset," said a longtime ANC member. "Today, those cadres who

Continued on page ii

André Clément is a journalist

A war chest

BY KOFI ANNAN

One of my great concerns as a Secretary-General of the United Nations was the crushing burden of infectious diseases on developing countries.

Ten years ago very few people in the developing world were receiving AIDS treatment. They knew that, while AIDS had ceased to be a death sentence in rich countries, they themselves had little reason to hope, because the drugs were just too expensive for the developing world. I recall a visit to a hospital in Maputo, where a dying woman looked me straight in the eye and asked if I could help her. She knew that medication could save her but, as she was poor, for her the disease was a death sentence. I will never forget that look, which was much more powerful than her words.

In 2000 the global outlook was bleak: HIV had infected a tragic proportion of the population in southern Africa in just over a decade and we feared the spread would continue at that pace – not only in Africa, but also in Asia and the former Soviet states.

In the absence of a cure and with life-sustaining medicines costing $10,000 per patient per year, many of us feared that AIDS would greatly affect economic and social development and cause political instability as country after country succumbed to the pandemic.

At the pivotal international AIDS conference in Durban in July 2000, Nelson Mandela made an unforgettable appeal in his closing address: "In the face of the grave threat posed by HIV/AIDS, we have to rise above our differences and combine our efforts to save our people. History will judge us harshly if we fail to do so now, and right now."

The rapid spread of tuberculosis and malaria added to this burden and to a strong feeling of powerlessness: would these diseases of poverty really destroy our tremendous common efforts to achieve development and progress?

When I called for the creation of a global fund – a "war chest" to fight the diseases of poverty – in Abuja in 2001, I did not dare believe that the turnaround would be so quick and dramatic. The plan of action I built with the help of WHO Director-General Gro Harlem Brundtland, UNAIDS Executive Director Peter Piot, UNICEF Executive Director Carol Bellamy and others had five goals: prevention of the spread of the disease, especially by getting young people involved; stopping the transmission of the virus from mothers to their children; giving people access to care and treatment; quickening the pace of scientific research; and protecting the most vulnerable.

The plan was ambitious. I said clearly at the time that leaders in all countries needed the foresight and courage to firmly commit to the fight against AIDS and to make it a priority in their national budgets. The creation of the Global Fund to Fight AIDS, Tuberculosis and Malaria was a big part of the response. It drew on expertise in the United Nations system, government bodies and nongovernmental organisations – especially with associations of people living with HIV/AIDS and the other diseases – and the private sector.

At the time, many people said that the plan was unrealistic and the call for a war chest was a dream, but great achievements always start with a dream, and the progress we have made in the fight against the three diseases is proof that dreams can be realised.

It would not have happened unless prices of drugs were made affordable. The large pharmaceutical firms were therefore crucial to realising this dream. I met with them often during this time, together with Gro Harlem Brundtland and Peter Piot.

In April 2001 these companies performed a spectacular volte face when they dropped legal action that they had begun against South Africa's efforts to lower the price of AIDS-related and other drugs. Increasingly driven by competition from generic drug companies using the safeguards in World Trade Organisation treaties the price of one AIDS drug after another plummeted. Today, a year's treatment for AIDS cost less than $100 per patient.

I also encouraged many leaders to talk openly about AIDS, asking them to break a code of silence and dispel the prejudice and discrimination that surrounded the disease. Keeping quiet about AIDS costs lives. Unfortunately this message sometimes fell on deaf ears, especially when it came to the subject of condom use.

As we look back on this revolutionary decade in the fight against AIDS, we can celebrate equally remarkable gains in the fight against TB and malaria. The annual number of new TB cases has fallen every year for the last five years, and we are on track to achieve the global target of halving TB mortality by 2015. In country after malaria-endemic country, we see remarkable falls in child mortality thanks to the widespread availability of bed nets and effective treatment.

While all of us can be proud of what has been accomplished in this decade, we know there is more to be done. Today it is time to dream anew – of the end of AIDS, TB and malaria once and for all, a dream that can become real if only we keep up the fight.

Kofi Annan is former Secretary-General of the United Nations (1997-2006) and Chairman of the Kofi Annan Foundation; kofiannanfoundation.org

Towards a world without HIV

BY FRANÇOISE BARRÉ-SINOUSSI

Despite the progress made in the field of medical research since the discovery of AIDS in 1981, it is too early to speak of a cure. In 1983 we identified the agent responsible for the progressive failure of the immune system, later naming it the human immunodeficiency virus (HIV). The last 30 years of research have provided us with profound insights into how the virus replicates itself, spreads and lies dormant in latent reservoirs within the human body. This understanding led to the revolutionary breakthrough of combination antiretroviral (ARV) therapy in 1996, which has reduced patient mortality rates by more than 85%. Not only are ARVs effective in treating HIV, they also have preventive applications. As early as 1994, the ACTG076 clinical trial showed that zidovudine (AZT) effectively prevented mother-to-child transmission of HIV. Recent studies confirm that ARVs significantly reduce the risk of the virus being sexually transmitted.

These are major developments. The fact that ARVs not only save lives, but also prevent new infections and thus check the AIDS pandemic, is a powerful argument in favour of speeding up universal access to treatment. In Botswana, where 90% of patients are under treatment, new data released by UNAIDS (1) suggests that "the number of new HIV infections … is 30% to 50% lower today than it would have been in the absence of antiretroviral therapy".

STR/GETTY IMAGES

Activists from the Treatment Action Campaign (TAC) marched to the second National AIDS Conference in Durban in June 2005 to demand provision of antiretroviral drugs

Yet many countries cannot afford the high cost of treatment and depend heavily on international aid. Unfortunately, the global financial crisis threatens to disrupt the flow of funds, as donor countries renege on their commitments. Several recipient countries are already starting to run out of ARVs, impeding their ability to increase treatment coverage and even to secure treatments for those already treated. Even more worrying is the risk that this situation could lead to the development of newly resistant strains of HIV and produce a fresh pandemic.

We cannot allow the fight against an enemy as devastating as HIV to be undermined by politics. It is essential that innovative, durable sources of funding are found, such as the airline ticket levy used to finance the Unitaid fund. For several years now a number of voices have been calling for proceeds from a possible financial transaction tax to be channelled to health initiatives in developing countries. We must do all we can to bring this proposal to the attention of G20 leaders.

Concurrently, we must redouble our efforts to develop new therapies. Though significantly alleviated by ARVs, living with HIV remains a heavy burden. Combination ARVs must be taken for life, and they are not without side effects. They do not completely eradicate the virus: its persistence in latent reservoirs is associated with chronic generalised inflammation of the immune system. Thus patients do not recover a full life expectancy, compared with the general population, and are under increased risk of cardiovascular and neurological diseases, cancer and premature ageing.

Eradicating HIV will long remain a dream. Even so, some models lead us to believe part of the dream could eventually come true if we succeed in developing new shortterm therapeutic strategies, which may result in life-long remission without the need for drug therapy.

The recent case of Timothy Ray Brown, known as the "Berlin patient", suggests such strategies may one day become feasible. Brown had been living with HIV for over ten years when, in his early forties, he underwent a bone marrow transplant to treat leukaemia. His doctor searched for a compatible donor with a particular genetic characteristic: a mutation of the CCR5 co-receptor, a molecule which acts as a "docking station" on the surface of

Françoise Barré-Sinoussi is a researcher at the Institut National de la Santé et de la Recherché Médicale (Inserm) and the Institut Pasteur. She was awarded the Nobel Prize in Medicine in 2008

South Africa gets to grips with AIDS

Continued from page i

supported Mbeki and Tshabalala-Msimang are ashamed to admit they lacked courage." In May 2009 South Africa's newly elected president, Jacob Zuma, ended the government's policy of denial by entrusting the health portfolio to Aaron Motsoaledi, a respected medical doctor.

"Things have vastly changed these past years," said Lynne Wilkinson, an MSF doctor in Khayelitsha. "Here, 20,000 residents are currently under treatment. We have almost stopped seeing terminally ill patients brought to the clinic in a wheelbarrow."

During the Mbeki era the number of deaths had reached 600 a day – mostly young people – and life expectancy had dropped, from 62 in 1990 to 51 in 2005. That may be over, but huge problems remain. Tuberculosis (TB) is spreading, and developing resistant strains. To make matters worse, 70% of TB sufferers also have HIV, meaning two epidemics must be treated concurrently. The challenge is immense: with 3 million patients in need of ARVs, the country's medical, human, financial, planning and logistical resources will be stretched to their limits.

Section 27 in Johannesburg is an NGO specialising in public health. It works to promote section 27 of South Africa's constitution, which states that every citizen has the right to access adequate health services. Mark Heywood, its director (and one of the founders of the TAC), admitted that "activists are tired" after eight years of battling the state. But government, activists and doctors are now more or less on the same wavelength, as Heywood's election to the post of deputy chairman of the National AIDS Council (Sanac) attests, though who knows for how long? "Motsoaledi has driven the implementation of the health programmes over the past two years," said Heywood. "Ironically, civil society has struggled to keep up. The progress so far is undeniable: 1.5 million patients are currently on treatment and adult circumcision has been actively promoted (3). The improvement and expansion of treatments preventing mother to child transmission have reduced the risk of postnatal infections to 3.5% (4). These results are not superficial, but continued success is not guaranteed. There is still a very long way to go."

South Africa has unequivocally rejected AIDS denialism; even so, according to Heywood, "dark clouds lie on the horizon". The Zuma government's ambitious national health insurance scheme, designed to reduce the extreme disparities in the quality of health care, will take several years to implement. A modern, costly private sector serves 30% of the population, while the debilitated public sector must cater to the needs of everyone else, especially the poorest. Heywood criticised the plan as being "very weak at the moment. It's already under fire from the private sector, which falsely claims that it will frighten doctors into leaving overseas. But our health care system will function only if we manage to reduce the enormous gap between the private and public sectors. We need a strong system to share the HIV burden evenly across the entire [health] sector. And I'd like to see an investigation into why private sector prices are exploding, while their costs haven't increased that much."

> 'The financial crisis is making matters worse. Aid donors are cutting back on funding. Civic organisations are the first in line to get the chop, despite having been the main catalysts for change up until now'

"The TAC's 2001 victory over Big Pharma has been undermined by the time and effort the activists have since spent in fighting their own government," he continued. "The drug companies have regrouped and bought out their generic competitors. WTO patent agreements have been enforced in India and Thailand, curtailing their manufacture and export of cheap generics. Already, the global health community, which had initially identified clear goals such as challenging patent rights and establishing a Global Fund, is finding itself weakened and divided." He was concerned that "the financial crisis is making matters worse. Aid donors are cutting back on funding. Civic organisations are the first in line to get the chop, despite having been the main catalysts for change up until now."

Back in Khayelitsha, at the TAC headquarters, Andile Madondile, in charge of the Treatment Literacy programme, expressed concern over the funding shortage that has led to the forced closure of two offices: "We have 17 branches in Khayelitsha servicing 500,000 residents. Our counsellors visit the clinics to talk about opportunistic diseases and the importance of regularly taking their medicines. Unfortunately, we may have to start thinking about government subsidies to continue our work."

Hogan felt the prospect of a reduction in international aid was "crazy". She said: "ARV treatment is a longterm commitment. These drugs literally give people their lives back; they must be taken over a period of 20, 30, even 50 years. We had to move heaven and earth to obtain urgent medicines from the UK and US during the 2009 shortfall which occurred in some provinces. If funding dries up, the virus risks becoming resistant, with global implications. Not the least of which could be a new epidemic, for new research shows that people under ARV treatment are far less likely to pass on the infection."

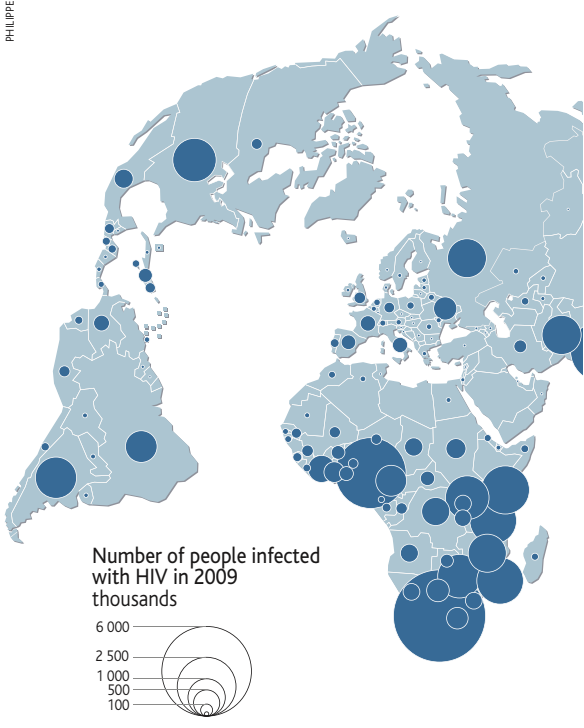
Hogan also pointed to the disastrous social repercussions: "Resolving social ills such as poverty, unemployment and violence depends on effective HIV/AIDS treatment. A new AIDS epidemic would shatter an already-fragile health system, and South Africa's unique experience in treating the virus on a massive scale, through civic participation, counselling and long-term care within communities, would be wasted."

Hassan, for her part, fretted that "fewer patients are responding to first-line treatments, and so have to be moved onto more expensive drugs, for which generics do not yet exist. I'm worried that, as in 2000, one day we will wake up and say 'Oh no! We don't have access to drugs anymore!' There is a desperate need for a clear strategy to prevent people from dying in droves again."

There is widespread consensus on the need for a decentralised health system: national clinics and hospitals are overloaded, and will not be able to cope with the addition of an estimated 6 million HIV-positive people unaware of their status, on top of the nearly 3 million patients receiving treatment. Jack Lewis is the director of Community Media Trust (CMT), producer of the weekly show *Siyayinqoba Beat It!* ("We can beat it!"), which deals extensively with issues to do with HIV/AIDS. Following a symposium on primary health care which he helped organise, Lewis said: "When one looks at the UN Millennium Development Goals, South Africa is lagging badly behind on three fronts: children's health, mothers' health and the fight against HIV/AIDS. With the [unofficial] unemployment rate at 35-40%, medical conditions are exacerbated by social deprivation. Poor people's diet is often heavy in saturated fats. As a consequence, they commonly risk developing obesity, diabetes, high blood pressure and heart problems."

South Africa faces several health challenges: HIV and TB, chronic illnesses, poor maternal and infant health, and psycho-physiological trauma sustained by victims of crime, road accidents and domestic violence. Lewis reckoned that rescuing a system on the brink of collapse will require targeting these four

PHILIPPE REKACEWICZ



Sources: Joint United Nations Programme on HIV and AIDS; World Health Organisa United Nations Population Division; The World Bank online database.

CD4+ T cells (the cells specifically targeted by HIV), through which the virus enters the cell. It has been known for some years that those (of Caucasian origin) who exhibit this rare genetic mutation, known as Delta32, are in fact protected from HIV infection.

Brown ended his ARV treatment on the day of his bone marrow transplant. Five years on, the most sophisticated tests reveal no trace of HIV in any of the compartments in which the virus establishes reservoirs throughout the body, such as the gut or central nervous system. Yet Brown's immune system continues to produce antibodies, indicating the infection may not have completely vanished. It is difficult to confirm scientifically that the Delta32 mutation alone is responsible for this "cure". Many other therapeutic elements may have contributed to the outcome of what was a very complex operation. Although such a costly and risky procedure cannot be implemented on a large scale, it opens the door to gene therapy focused on CCR5 receptors, among other targets.

Patients called HIV controllers represent the ideal model for longterm remission. They are rare individuals (only 0.3% of those infected) who have been HIV positive for at least 10 years and maintain undetectable viral load without ARV treatment, and show no sign of progressing to AIDS. Strikingly, these patients exhibit a smaller viral reservoir compared with other patients. We now know that this extremely powerful natural control of the infection is regulated by two mechanisms. The first activates cytotoxic T cells, which kill virally infected cells, while the second is linked to the immune cells' intrinsic resistance. Understanding these processes can help us develop new therapies, perhaps one day enabling all those living with HIV to suppress viral replication without ARV treatment.

A unique study in France, named Visconti, has assembled 18 patients who were tested within two to three months after HIV infection and immediately placed on ARV. Some years later, with their doctors' consent, they ended their ARV treatment and have since kept their infections in check. The study confirms the benefits of treating HIV at the very early stages of infection. There is an immensely valuable store of knowledge to be gained from analysing the immunological characteristics that made therapy redundant for these patients.

As the natural carriers of the simian immunodeficiency virus (SIV), from which HIV originated, African monkeys present a final object of study. Unlike HIV in humans, SIV-infected monkeys do not go on to develop AIDS; any immune reaction to the virus is quickly subdued. As a result, the virus multiplies freely among monkeys, without provoking the deleterious chronic inflammation observed in human infection.

The mechanisms we must induce in order to trigger a protective response against HIV/AIDS remain a mystery. A combination of vaccines and therapeutic approaches will most likely prove necessary. This is the focus of a working group formed under the auspices of the International Aids Society (IAS), composed of international scientists aiming to develop a global scientific strategy to deal with HIV persistence, in the hope that we will one day live in a world without AIDS.

Research surrounding HIV/AIDS has useful implications beyond the epidemic itself. HIV is a tool that helps us to better understand the specific mechanisms at the heart of our immune systems. There is also much to be learned from research in cancer and other chronic pathologies linked to inflammatory abnormalities. In this time of crisis, we are faced with two choices: either we work in collaboration in a spirit of solidarity, as we did at the beginning of this epidemic, or we adopt an "every man for himself" approach, to the detriment of us all.

TRANSLATED BY WOLF DRAEGER

(1) "Global HIV/AIDS Response: Progress Report 2011", UNAIDS, November 2011.

Europe's engagement

BY MICHÈLE BARZACH

Europe has been an ardent supporter of the Global Fund to Fight AIDS, Tuberculosis and Malaria since its inception in 2002, and its principal financial contributor, accounting for 51% of its total resources. France heads the list of European donors and is in second place overall, after the United States. Germany and the United Kingdom are respectively the second and third largest European donors.

From the beginning, Europe's commitment to the Global Fund has rested on vision and conviction. The vision that only a massive, coordinated and consolidated response can reverse the spread of the developing world's deadliest afflictions: AIDS, tuberculosis and malaria. And the conviction that an effective strategy to combat these scourges must stem from a new global health governance initiative founded on shared responsibility, respect for national programmes and strategies, transparency and unequivocal commitment on the part of all stakeholders in the fight against disease, with community and civil society in the forefront.

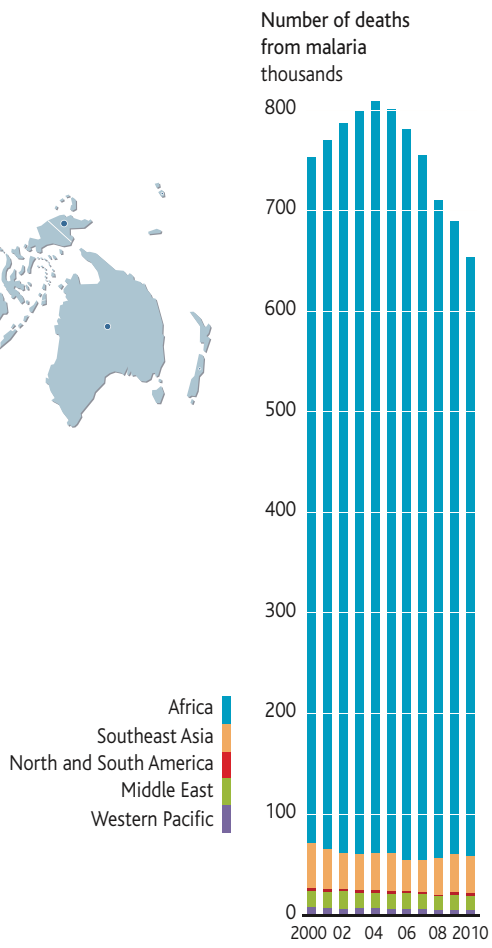
In ten years the Global Fund has, through its various funding programmes, achieved notable results unparalleled by international health organisations, as evidenced by unprecedented international financial support, by the Fund's effectiveness in channelling aid to developing countries, and by the vitality of its underlying principles.

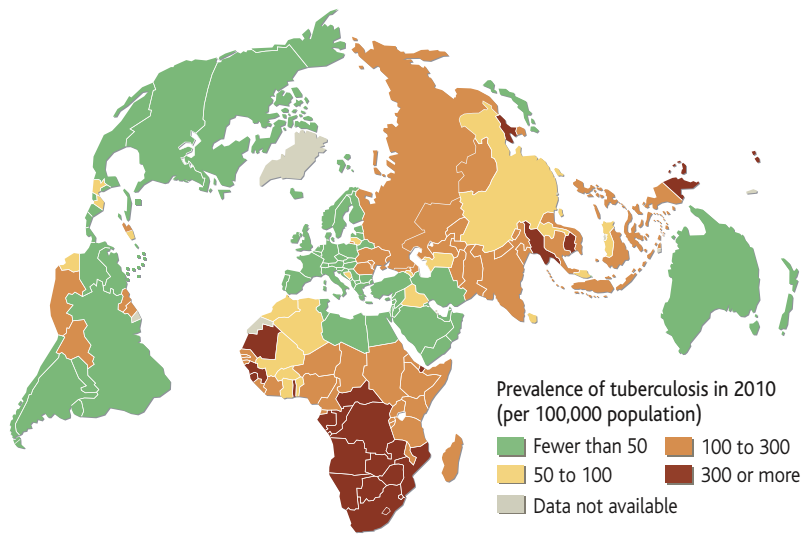
Europe's economic and financial crisis must not be allowed to undermine its convictions, or its financial commitment to the Global Fund and its founding values, which represent what Europe stands for: defending the right to health, reducing inequality of access to treatment and prevention, fighting against the discrimination of the most vulnerable – such as women and children – and marginalised members of society, and upholding human rights and democracy through greater civic involvement and public partnerships.

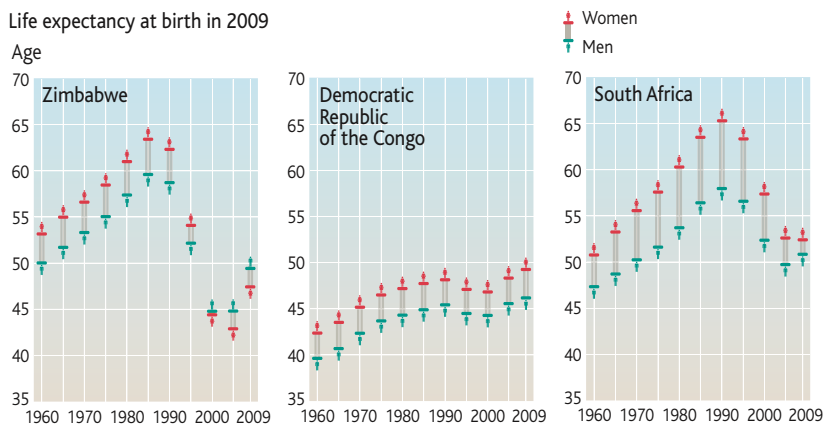
Despite the worrying economic climate, European public opinion is firmly in favour of continued aid relief: 85% support development aid, while 62% agree promises to increase aid should be kept. Europe and its member states must therefore strengthen their leadership within the Global Fund's battle against epidemics, and honour their funding obligations. To do this, European countries must resist the temptation to fall back on bilateral agreements at the expense of multilateral cooperation, and avoid the pitfalls of an overarching technocracy and the diktats of financial markets.

At the heart of the Global Fund are the public-private partnerships between donor and recipient nations, private enterprise and foundations, civil society and technical experts, which sustain its public health programmes. They remind us that the work of the Global Fund is first and foremost the work of solidarity, of men and women seeking to alleviate the suffering of the poorest and most vulnerable people on our planet.

Michèle Barzach is a former cabinet minister and current president of Friends of the Global Fund Europe; www.afmeurope.org







epidemics: "No prevention programme will succeed without a revival of primary health care." Based on the observation that "50% of a [medical] protocol's success depends on the patient understanding his/her responsibilities", Lewis stressed the need for "Treatment Literacy to be conducted on a national scale. This would require forming teams of health workers, headed by nurses, with the capacity to keep track of 250 households in every ward. Knowing who is sick, coughing, pregnant, undergoing treatment or losing weight… Assisting patients to take their medicines regularly. At the slightest sign of TB, they must urge people to go to a special clinic and make sure they have been properly tested."

Too many people wait until the last minute before seeking hospital treatment, placing a greater burden on the system. On 14 September Motsoaledi unveiled a programme to "re-engineer primary health care" aimed at "reversing the current system of delivery, which largely focuses on curative hospital-based services, to a decentralised community-based primary health care system" (5).

The country's 4,200 health centres are being audited and revamped. Elsewhere, the health ministry may recruit up to 40,000 personnel for an extensive door-to-door campaign. That may not be enough. But on a positive note, over the past ten years South Africa's position as the world's AIDS epicentre has brought an influx of health-oriented NGOs, building up a unique wealth of expertise and experience.

Doctors without Borders is currently looking at measures to ensure treatment compliance (for patients to take their medication regularly, without interruption). "Prevention campaigns are no longer sufficient," said Wilkinson. "We need to broadcast the message on television and radio channels: 'Don't forget to take your medication', 'Call us if you need help'." She has called for a comprehensive strategy taking account of regional migratory patterns. "Most of Khayelitsha's residents are migrant workers from the Xhosa tribe in the Eastern Cape [adjoining Western Cape province], who return to their rural villages during the holidays. The number of people under treatment falls drastically during these periods. Other factors complicate matters further. Prescribed dosages differ from one country to another [South Africa hosts a migrant population of 4 million Zimbabweans, many of whom frequently travel back and forth], and drug companies manufacture their pills in different shapes and colours. To top it off, the South African government has still not adopted fixed-dose combination ARVs, which reduce pill burden and are easier to swallow." Yet fixed-dose combinations, which amalgamate multiple antiretroviral drugs in a single pill, are available in poor countries such as Malawi.

Doctors without Borders is organising local support groups to monitor patients' health and ensure they are following their drug regimen. "It's not feasible to make so many people visit the clinic each month," said Wilkinson. "Transport is expensive, and they have to take a day's leave (or two, if they're coming for TB as well) and queue the entire day just to get their medication. In Mozambique the treatment retention rate after four years is 97% in support groups, compared to 87% in clinics."

In Khayelitsha, the young "ARV babies" will soon be starting their own support groups.

ANDRÉ CLÉMENT
TRANSLATED BY WOLF DRAEGER

(1) See "Living with AIDS in Soweto," *Le Monde diplomatique*, English edition, August 2002.
(2) Nathan Geffen, *Debunking Illusions: the inside story of the Treatment Action Campaign*, Jacana Media, Johannesburg, 2010.
(3) One of the rare preventative measures which yielded quantifiable results within a local community. See Bertran Auvert and Dirk Taljaard, "Effect of the Orange Farm (South Africa) male circumcision roll-out (ANRS-12126) on the spread of HIV", International AIDS Society conference, Paris, 20 July 2011.
(4) Medical Research Council (MRC), "SA PMTCT Evaluation shows that virtual elimination of paediatric HIV is possible with intensified effort", Durban, 9 June 2011; 31.4% of the mothers surveyed in the study were HIV-positive; www.mrc.co.za
(5) Speech, 14 September 2011.

Supplement

Finding a way to remobilise

Though the Global Fund has allowed so many lives to be saved, the financial crisis is worrying: what if it means decreased funding?

BY MICHEL KAZATCHKINE

Ten years ago, the world was becoming aware of the intolerable nature of unequal access to health care and treatment between the developed and developing worlds. At the same time, the World Health Organisation (WHO) Commission on Macroeconomics and Health was showing how health, long seen as a non-productive expenditure, should instead be viewed as a priority investment for development.

It was the Durban AIDS Conference in 2000, during Thabo Mbeki's presidency, and the Pretoria trial that allowed public opinion around the world to grasp the extent of this inequality and the human, social, demographic and economic costs of the AIDS epidemic. It was also a time of growing political will and commitment: by the French president Jacques Chirac and Bernard Kouchner in Abidjan in 1998; by Kofi Annan and the United Nations General Assembly in 2001; and then by the G8, which from early 2002 provided the Global Fund – still in its infancy – with the opportunity to disburse its first grants. At the time France had made significant efforts to convince people that the Global Fund should finance access to treatment and not be limited to financing prevention, as many experts were advocating. A further challenge was to broaden the activities of the Fund to include the two other major diseases in the developing world: malaria and tuberculosis.

Today, ten years on, the results are clear. A report published in November 2011 by WHO and UNAIDS showed a strong decrease in AIDS mortality and a steady decline in the number of new HIV infections worldwide, especially in Africa. Nearly seven million people – roughly 40% of those in urgent need – now have access to antiretroviral treatment. The life expectancy of a person starting treatment is now practically equivalent to that of a person not infected with HIV. Through progress in malaria control, the mortality of young children has decreased by 50% in the endemic countries of sub-Saharan Africa where nearly 80% of households now have access to insecticide-treated bed nets. With grants from the Global Fund, eight million people have been diagnosed with tuberculosis and have accessed treatment, with a success rate now above 80%.

The progress made in fighting these diseases has been unprecedented in global health. We have witnessed a clear demonstration that AIDS diagnosis and treatment can be made available and distributed to the most remote parts of even the poorest countries: a brilliant example of what can be achieved when countries, international aid and an alliance of the public and non-governmental sectors all come together with a common goal.

And yet, after ten years of progress, we are now faced with a shocking, discouraging paradox. On one hand, we are closer than ever before to ending major epidemics and attaining the Millennium goals for health, a dream since they were established in 2000. On the other, the economic crisis is imposing major budget restrictions on the development aid provided by wealthy countries, and exerting strong pressure on budgets devoted to the social sector in the developing world.

In a time of fiscal restraint it is important that we show that the Global Fund and official development aid can become even more efficient. At the same time, we cannot simply agree to do "more with less" and risk losing the gains made over the past few years due to a lack of financial resources.

With additional resources, we could actually reach the goals set by the international community: to reduce tuberculosis prevalence and mortality, come close to eliminating malaria in endemic countries, prevent millions of new HIV infections, further reduce the mortality of AIDS and ensure that virtually no child in a developing country is born with HIV, by 2015.

To do this, the G8 countries and other major Global Fund donors need only uphold their past commitments. The BRICS countries and large emerging economies also need to join this remarkable effort. And developing countries themselves, particularly in Africa, need to increase their investments in health care. At present, only six of the 53 signatories of the 2001 Abuja Declaration have reached the target of devoting 15% of their national budgets to health. In addition, we need to further increase our creativity and efforts in innovative development funding. UNITAID has shown that it is possible to mobilise sustainable funding from a tax designed to serve a global cause. The financial transaction tax is a bold idea in a period marked by uncertainty, and we need to support it.

With the birth of the Global Fund, a bridge was built between developed and developing countries. While this bridge remains fragile, we know the ingredients needed to strengthen it. These include sustained political will, continued mobilisation and activism by civil society, further progress in research and, yes, new financial resources. For now, these creative forces are subject to the headwinds of the ongoing economic crisis, with the result that donors are hesitant to sustain their commitments to foreign aid. They also face the challenge of mobilising an often indifferent public opinion at a time when aid tends to be perceived as an unaffordable luxury for donor countries, a source of expenditure without any return, rather than a necessary investment in global solidarity.

We have come a long way in ten years. Now is not the time to scale back our efforts. We have less than five years before 2015 to reach the goals set by all countries to stop the spread of AIDS, tuberculosis and malaria, increase access to health care and decrease poverty. The consequences of relenting in this fight are unimaginable. We cannot afford to fail.

ORIGINAL TEXT IN ENGLISH

Michel Kazatchkine is Executive Director of the Global Fund to Fight AIDS, Tuberculosis and Malaria; kazatchkine.blog.lemonde.fr/

Further reading

La consultation du soir, an engaging personal account of the epidemic rocking the world (in French), Gallimard, Folio documents, 2005.

Malaria, the year of hope

Each minute, a child dies of malaria. Yet medicines exist. And a vaccine may come soon

BY PAULINE LÉNA

Will mankind manage to rid itself of malaria over the next few decades? In 2011 scientific research brought high hopes of this: encouraging vaccine trials, revolutionary new therapeutic targets, identification of a protective factor against malaria, etc. Researchers working to find a cure for this global menace can finally express optimism.

The World Heath Organisation (WHO)'s 2011 report on malaria stressed that there had been a major decline in the disease worldwide. Although the overall number of cases only went down slightly (from 233 million in 2000 to 216 million in 2010), the number of deaths fell from 985,000 to 655,000. In 11 African countries, and in 32 of the 56 countries outside Africa where the disease is endemic, the number of confirmed cases, hospitalisations and deaths fell by half.

Despite these encouraging statistics, the pandemic still affects half the world's population. It is present in 106 countries and territories, particularly in sub-Saharan Africa, where the parasite plasmodium falciparum is a huge killer. "Malaria kills 1% of people who come into contact with it for the first time, but only one in a thousand of those who have been exposed to it before," explained Pierre Druilhe of the Institut Pasteur in Paris. So the disease takes a particularly heavy toll among children, who have not had time to build up immunity. The average age of death linked to malaria is four. Among adults, pregnant women, people with HIV and travellers or immigrants from non-endemic regions are the most at risk.

The life cycle of the plasmodium parasite has not changed since the time of Tutankhamun. When a carrier mosquito bites someone, it injects an immature form of the parasite, which immediately moves to the person's liver. The parasite then goes through an initial growth phase before it is released into the blood, colonising the red blood cells. The parasite's sex cells are then able to develop, and these can be ingested by a mosquito the next time it bites. The parasite finishes its life cycle in the mosquito's stomach, giving birth to new parasites capable of infecting the next person to be bitten.

There are two ways of fighting malaria: targeting the carrier mosquitoes or the parasites themselves. The first attempt to eradicate malaria on a global scale in 1955 failed because the mosquitoes and parasites developed resistance to the insecticide DDT, and to chloroquine, the most effective synthetic anti-malarial drug.

Around 10 drugs can, singly or in combination, provide a complete cure to malaria in the vast majority of cases. But the standard drug, chloroquine, a very powerful and cheap anti-malarial medicine developed in the 1950s, is no longer as effective as it was, since plasmodium falciparum (the main strain of malaria) is now largely resistant to it. Chloroquine was replaced around 10 years ago by artemisinin, a natural anti-malarial drug used in traditional Chinese medicine. It was isolated by the pharmaceutical researcher Tu Youyou, from the Academy of traditional Chinese medicine, who won the prestigious Albert Lasker Award for Clinical Medical Research in 2011 for her work.

Artemisinin is very effective and easy to use, and is now the last defence against the disease. But specialists are already concerned about the first signs of resistance, which were confirmed in 2009 on the border between Cambodia and Thailand. To delay this eventuality as long as possible, the drug is only given in combination with another anti-malarial treatment. "If resistance to artemisinin reaches the African continent in the next 10 years, we will have no other medicine to offer," said Professor François Nosten, who set up the Shoklo Malaria Research Unit (SMRU) in Thailand.

The mechanisms involved in resistance are poorly understood. They depend on the medicine, the parasite, but also the capacity of different species of mosquito to transmit resistant strains. The WHO launched a programme in 2011 against the spread of drug resistance. The development of rapid diagnostic tests will allow clinicians to check whether a fever is really due to malaria, to avoid prescribing anti-malarial drugs unnecessarily.

For a long time research into new treatments was slow because of a lack of commercial prospects, but it was given a boost in 2002 when the Global Fund to fight Aids, Tuberculosis and Malaria (GFATM) launched an ambitious drug procurement programme. These favourable results led to a new system of financing, aimed at increasing access to treatment. Based on the recommendations of the economist Kenneth Arrow, the GFATM set up the Affordable Medicines Facility - malaria (AMFm) in 2007, reviving drug manufacturers' interest in medicines that would be sold cheaply but in very large quantities.

Last November several publications opened up promising new areas of treatment. Several Californian teams announced in *Science* magazine that they had discovered a new class of drugs that act on both the blood and liver stage parasites. In *Nature* an international team reported the discovery of a single receptor necessary for the parasite to invade red blood cells, and a German-African team explained why the red blood cells of patients with sickle cell disease were able to resist the parasite.

Most of the medicines recently released onto the market remain derivatives of existing drugs, or new combinations which are more convenient for patients to take. The not-for-profit foundation Medicines for Malaria Venture (MMV), set up in 1999, helped develop Pyramax, an artemisinin-based combined therapy (ACT) taken once a day, which is expected to be available in 2012. MMV also helped identify around 20 groups of entirely new drugs which could be used in the treatment of malaria. "Most are still at the very early stages, such as the very promising synthetic drug Oz, which is going through phase 2 trials," said Professor Brian Greenwood of the London School of Hygiene and Tropical Medicine.

Medicines are not the only weapon against malaria: the fight against mosquitoes has also proven effective. When mosquitoes are kept out by treated nets, or repelled by persistent insecticide sprayed on the walls of houses, they cannot inject parasites or ingest them. But insecticides end up losing their effectiveness too. "Resistance is a source of worry, but we must make sure that existing tools are being used appropriately," said Dr Peter Agre, director of the John Hopkins Malaria Research Institute and 2003 Nobel prize winner for chemistry. "Mosquito nets can provide 50% protection, but only if they are used by everyone."

There is still hope of finding a vaccine, one that would eradicate the parasite by blocking its transmission from one of its two hosts (human beings). Applied to infants, it would prevent the majority of fatal cases. But the ideal vaccine – cheap, and able to immunise completely, in a single shot, against every form of malaria – remains out of reach.

Clinical trials of RTS,S, a vaccine candidate developed by GlaxoSmithKline, involving 16,000 children in several African countries, should finish in 2014. "Initial results are interesting, but the level of protection is still insufficient, especially since protection seems to diminish over time," said Brian Greenwood, who took part in the research. "Some of these children will get a booster, to increase the immune reaction. It's the first vaccine, and no one thinks it will be the only one; at the very least these trials will give us information on how this model works." The outcome of trials of a second vaccine candidate is more eagerly awaited, even though it has had less media publicity: MSP3 has shown particularly promising initial results, affording protection of between 64% and 77%. Pierre Druilhe, in charge of the Institut Pasteur team which initiated the research on MSP3, had to set up a private initiative in December 2010 to pursue its trials. He was able to begin a validation trial on 800 children in eight villages in Mali. The first results are expected in February 2012.

Most people working in this field insist that a vaccine is not currently the solution to the malaria pandemic. Used properly, available methods of prevention, diagnosis and treatment should remain the principle strategies. But the battle is as political as scientific, and the issue of the distribution of funding, reduced since the economic crisis, has taken on crucial importance. While we await a technological solution, the efforts of governments and donors to improve access to treatment and the means of prevention remain the most effective weapon against this pandemic.

TRANSLATED BY STEPHANIE IRVINE

Pauline Léna is a journalist