global advocacy

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PHOTO ©Jaime Razuri/AFP/Getty Images

PERU / previous page

On World AIDS Day (December 1) in 2003, Peruvian AIDS organizations march for free access to antiretroviral drugs for all who need them.

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community matters: (re)-defining our advocacy

SHAUN MELLORS / south africa

THE MOST RECENT International AIDS Conference (Bangkok, 2004) showcased an enormous diversity of communities around the world and how they are responding on the ground to the epidemic. It was also striking evidence that the battles we fought to find a place for community during the first two decades of this epidemic have largely been won. Communities, including people living with AIDS (PWAs), are part of almost every platform, sentence, project proposal, abstract and conference. And although we are sometimes still referred to as a principle ("We believe in the principle of community involvement"), we as community, together with our scientific colleagues, have a responsibility to define and transform this principle into reality.

Affected communities were the first to respond to the AIDS epidemic, out of a sense of fear, survival and compassion. Our voices have changed the nature of health care and doctor-patient relationships, and we all know from personal experience the invaluable contributions of community involvement on so many fronts.

But as community advocates, activists and representatives we have perhaps taken "community involvement" for granted, and may be in danger of losing our focus and direction. We are failing to ensure (or even to clearly define) an effective and accountable response to the epidemic—from our political leaders, our scientists and ourselves. Although communities are experienced and have expertise, we also have a lot more to learn, especially when it comes to preparing the public for vaccine trials. We cannot just simply pick up the cookie cutter that defined our approaches and programs at the beginning of the epidemic and reuse them in addressing today's issues of vaccine preparedness. Instead, we need to assess what we've learned so far, and use these lessons to re-think our big-picture priorities and strategies.

We have learnt that large-scale human trials are possible, but demand much of us—especially when they take place in poor, highly affected communities. We know that better products need to be developed. We know that effective community involvement and trust are important for this research to succeed. We have known for a while that we need to act now to ensure equitable global access to AIDS vaccines and ***microbicides***, once effective products become available.

As for strategies, it's clear that success will require a far more coordinated, concerted effort over the coming years—which will depend on clearly defining roles, responsibilities, resources and mechanisms for accountability. It will also require broader public understanding and support.

The public is "AIDS fatigued," and we are not being creative enough in placing the vaccine agenda within the public sector.

But experience has shown that simply providing information will not automatically lead to broad public support. Political leaders, community and civil society are usually not instantly willing to step forward and embrace this research. The public is "AIDS fatigued," and we are not being creative enough in placing the vaccine agenda within the public sector. To do better, we will need to build new coalitions, partnerships and networks that work more effectively and efficiently on the ground than the cottage industry approach we now have.

One aim of this revamped effort and alliance-building should be to improve national coordination amongst different stakeholders and partners. This is especially important in countries doing (or planning) trials of vaccines, microbicides and treatments, which usually involve different sets of national and international sponsors. Often each initiative has its "own" communities where trials, or trial preparations, are taking place. Each of them may be doing important research, but for the most part, coordination amongst them is almost non-existent. Besides establishing separate trial sites, the different microbicide and vaccine networks develop their own literature, community mapping activities, needs analyses, socio-behavioral studies, volunteer recruitment campaigns and standards of care for trial participants—even when these groups are working in the same province or district.

Having different initiatives that reinvent the wheel rather than work together is counterproductive. It unnecessarily drains limited financial and human resources. It squanders opportunities for ***clinical trials*** to do more to expand access to treatment and prevention in the community, and to fully involve communities in these studies. It also means that they often miss chances to learn important lessons from one another—for example, lessons that microbicide advocates can teach us about gender in clinical research, that vaccine advocates can teach about community mobilization and that treatment advocates can teach about community activism.

"It's difficult to work as we are doing now, when one researcher comes along and wants to do community preparedness on vaccines, and then another one comes who works on microbicides," says Dawn Cavanagh of the Gender AIDS Forum in South Africa. "Many of us are overstretched and battling with shrinking budgets…But we're under pressure to take on these separate researcher/donor-driven needs."

from lessons learned to an advocacy agenda

By drawing on what our experience is telling us, we can see some key areas for community action.

- Ensure that trial sponsors work together at the national and community levels, especially in developing infrastructure for providing medical care, AIDS treatment and HIV prevention services—a big part of making sure that trials do in fact leave communities better off, and that this impact is sustained. [See chapter 20 for more on this issue.] And as vaccine, microbicides and treatment advocates, we must develop common agendas that all work for these goals.[1]

- Advocate for comprehensive national plans for countries engaged in AIDS vaccine development. These plans should cover strategies and timelines for pre-clinical and clinical research, regulatory review of clinical research studies and approval of vaccines and microbicides. They should also address public health use and accessibility, along with issues related to standards of care and treatment and developing the infrastructure needed to bring sustainable benefits to communities that participate in trials.

  The national plans should form part of a broader national response, and the different interventions should not be seen as separate from each other, or competing for funds or attention. On the contrary, they offer opportunities to integrate the treatment, vaccine and microbicide agendas.

- Support the acceleration of the clinical trial calendar and the strengthening of research infrastructure and capacity. This requires more investment from wealthy countries and other stakeholders, development of research staff and community representatives, and progress in understanding and grappling with preparedness work.

[1] The US National Institutes of Health (NIH) has plans to interconnect its AIDS research networks by synchronizing their funding and requiring cross-network communication and some resource sharing, including a global Community Partners structure, by 2006.

› Ensure that prevention efforts are culturally appropriate, in languages that people speak and understand, and that they are not biased against women. We also need to help focus prevention on value systems and not simply on practices, as it has done in the past and still does in many cases.

AS COMMUNITY ADVOCATES we also need to look beyond clinical trial implementation at the broader process of vaccine development and access. Vaccine preparedness encompasses public understanding of these issues, and public support and participation. Community advocates, especially from the South—where vaccine research is still relatively new—must become more effective, articulate vaccine and microbicide advocates. We also need to point out where the clinical research agenda fits in with other goals and agendas, such as reducing poverty, promoting development and strengthening women's rights. And we need to integrate the principles of benefit and justice into this research. If we do not, history will judge us harshly for failing to learn from our experience and capitalize on the lessons it offers us for fighting this epidemic.

We need to integrate the principles of benefit and justice into this research. If we do not, history will judge us harshly.

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from trial volunteer to vaccine advocate

PAUL WETAKA / uganda

Since the first ***clinical trial*** of an AIDS vaccine back in 1988, nearly 24,000 people around the world have volunteered for AIDS vaccine trials—each of them, by definition, committed to the goal of finding an effective vaccine. But what do they do once the trial ends? Here one former volunteer describes how his experience as a study participant has shaped him into an advocate who speaks frequently in the media and among Uganda's communities, emphasizing the need for the public to support—or, more accurately, to demand—the strongest possible effort to develop an AIDS vaccine.

Paul Wetaka, a professional soldier in the Ugandan military (and former member of the President of Uganda's protection unit), began his involvement a decade ago when he volunteered for Africa's first AIDS vaccine trial. That trial was initially controversial, but nowadays Uganda is preparing for its third AIDS vaccine study—amid a strongly supportive public. (For the story of how this came about, see chapter 21.) Today Wetaka works with the Army's medical services unit responsible for care of soldiers with HIV/AIDS. The unit is now launching its own program to provide ***antiretroviral drug*** treatment.

I FIRST GOT INVOLVED with AIDS vaccines in 1995, when I was approached by the Joint Clinical Research Center in Kampala, where Uganda's first trial was done. By then I had already traveled all over the country with the President of Uganda as one of his bodyguards, and listened to his speeches. We went to many towns and villages, and he spoke about AIDS and how to guard against it. At the same time, I was seeing my commanders and friends die of AIDS. Back then we called it 'slim' disease. I spent a lot of time visiting friends in the hospital, going to funerals, trying to help the orphans they left behind, so they could pay their school fees and get the things they needed.

To be in the trial I had to have an HIV test. This worried me, but finally I did it and I was HIV-negative. This made me decide I wanted to do more about AIDS than just try to help my friends, so I made the final decision to go ahead with the trial. I had many questions about possible risks of participating, but the trial staff explained everything and answered all my questions.

The trial didn't start for two more years. During that time the volunteers learned a lot about science and research, things like ***informed consent***, ***placebos***, HIV transmission, and how to know if a vaccine works. And about safer sex, and modes of HIV transmission. But we had two years of just focus groups. We said, please, give us the vaccine. We are ready.

During the trial a ***Community Advisory Board (CAB)*** was started, and I became a representative for the volunteers. Most of the volunteers were military men, and there were also a few civilian women. The other CAB members included religious leaders, HIV-positive activists, community leaders. We were told that after this trial, there will be more trials, and that one day we would need to test the effectiveness of some vaccines, and it will take many people to do this. So I wanted to continue doing something about AIDS, especially for the AIDS vaccine movement.

The CAB couldn't continue after the trial ended, so we started our own group, called the Uganda Pioneers for Vaccine Research. Most of our activities were aimed at raising awareness of HIV/AIDS and vaccine trials in the community. We didn't have any assistance or support to move around as a group, so we each did what we could on an individual basis. I used my access to military leaders, who gave me the chance to speak with my fellow soldiers about HIV/AIDS and vaccine development in Uganda.

During that time—it was 1999—I also started speaking about AIDS on radio, TV, and at workshops. I still do this, usually about once a week. This means talking with a lot of people and hearing their questions, and what they think about HIV/AIDS and vaccines.

Distrust of clinical research is a big problem in our communities. When vaccine trials first came here, where traditional culture is observed, the new idea wasn't always welcomed quickly. And HIV/AIDS is often regarded as a public shame or disgrace.

People often ask whether I'm HIV-positive and whether the vaccine can cause HIV. There were a lot of rumors at the time of the first trial that the volunteers are HIV positive. AIDS patients were treated in the same place where the trial

was carried out, which made many people think we had AIDS. We faced a lot of stigma, and spent a lot of time explaining to people what was really going on.

When the second trial came up, I continued to talk about the need for an AIDS vaccine. Helping the community see the need and demand for a vaccine. And that we shouldn't wait a decade or longer to get a vaccine after it's been licensed for use in industrialized nations. I also speak about the importance of vaccines we already have. In some communities in Uganda, and in other parts of Africa, there's still a problem of accepting vaccines that have proven effective, like for polio and measles. But the public response to the second trial was very positive.

I was allowed to work with this trial to share my experiences as a former participant. I got involved with the CAB, and we helped with some of the preparation—looking at the language used in the ***protocol***, informed consent documents and educational materials. We also started a newsletter with IAVI [the International AIDS Vaccine Initiative], who sponsor the trial.① But the trial came to an end in February 2005.

There will be another study starting soon at Makerere University with the Walter Reed Army Institute from the US, and I hope to play the same role. But I will find ways to stay involved even if all trials end. Somehow the vaccine movement will go on until we find a vaccine for HIV/AIDS. If the present products don't go forward, we shall try others. I hope scientists are having sleepless nights to find the best product for us to try. So we will still need to prepare communities for more trials.

Many people don't realize that the AIDS vaccine movement needs support from the public.

A big challenge is that many people in Uganda don't realize that the AIDS vaccine movement needs support from the public—this is a new idea to them. All the vaccines and drugs we depend on come from industrialized countries in the Western world. So people don't know that the scientific research to make them goes beyond the laboratory and involves people. We need people to understand that developing an AIDS vaccine which can save lives and economies will be one of the world's greatest achievements. And that not to do so would be one of its greatest failures.

reference

① www.iavi.org/uganda
Website of the Uganda Virus Research Institute/IAVI AIDS vaccine program, with the quarterly newsletter published by the site's CAB; information on volunteering for trials and frequently asked questions.

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speed and equity:
why political leadership is important

CHRIS COLLINS

THERE IS A LOT OF ANGUISH in being a US citizen these days if you care about public health. It means watching your country use global health policy to advance the causes of gargantuan profit and religious conservatism at the expense of treatment access and scientific knowledge.

Of course, many governments fall terribly short in addressing health priorities, not just the US. That was part of the initial appeal of the AIDS vaccine movement for me. It seemed that an AIDS vaccine might be able to circumvent political limitations because, like the polio vaccine, it could be delivered universally, including to marginalized groups. A vaccine might overcome social obstacles to effective HIV prevention, like the unequal status of women, intolerance for sexual diversity, and the rights of drug users.

I was wrong. Politics is as important in AIDS vaccines as it is in other areas of health. Political leaders help determine the pace of scientific discovery and the ethics of ***clinical trials***, and they will be crucial in determining who gets a vaccine quickly when one is developed. Fortunately, there are examples of political leadership on AIDS vaccines, and they should serve as models for policy makers around the world.

It's rare that the leader of a nation shows up to launch an AIDS vaccine trial. But by November 2003, when President Paul Kagame of Rwanda came to inaugurate AIDS vaccine research in his country, he had done much more than make speeches about the epidemic. He had created a climate in which AIDS could be talked about with increasing openness, and where AIDS vaccine development was treated as a high priority.

This leadership produced tangible results. Administrative aspects of the country's first vaccine trial were handled efficiently. The Health Minister made sure research supplies were imported duty-free to the trial site. A local ethics committee was formed, asked hard questions, and then decided to approve the trial.

Six years earlier, then-US President Bill Clinton came to Morgan State University in Baltimore and issued a challenge to the nation. "If this is the Age of Biology," Clinton declared, "let an AIDS vaccine be its first great triumph." That day he announced plans to build a new Vaccine Research Center (which opened in 2000 and is now an important contributor to AIDS vaccine development), and soon he would propose incentives to spur development and delivery of AIDS vaccines globally.

Governments play an essential role in mobilizing resources, determining how effectively they're used and in creating an enabling environment.

Every country brings different resources to the AIDS vaccine effort. Governments play an essential role in mobilizing these resources, determining how effectively they are used to address the country's needs, and creating an "enabling environment" that allows AIDS vaccine development work to flourish.

Achieving this involves a wide range of activities. On the most basic level, government leaders can marshal support for AIDS vaccine research and define how it fits into broader national goals—as, for example, Thai leaders did when they included vaccines as part of the country's early, aggressive response to the epidemic, a prescient decision that has made Thailand a key player in the field today. Governments can also influence this research through their policies and laws. For example, many countries, including Brazil, Canada, Ethiopia, Tanzania, and Uganda, have signaled their political

Former US President Bill Clinton speaking at a conference for HIV/AIDS researchers (Boston, February 2003). Since leaving office in early 2000, he has made HIV/AIDS one of his main priorities. In 1997, while still President, he called for the world to develop an AIDS vaccine within the decade.

commitment by incorporating vaccines into their national plans for combating the AIDS epidemic, which in turn helps in establishing infrastructure and momentum for vaccine work. In October 2003, parliamentarians from around Asia issued a joint declaration pledging stepped-up efforts on behalf of vaccine research, placed within a context of legislative activities on HIV prevention and treatment, human rights, and anti-stigma efforts. And most recently, the G8 countries have endorsed—and will hopefully help finance—a "Global HIV Vaccine Enterprise," a coordinated plan to tackle scientific and infrastructural obstacles to a vaccine, under the auspices of the Bill & Melinda Gates Foundation.

But how can a government actually speed up the pace of scientific discovery? How does it make sure that health-related research truly meets the needs of its population?

Financial support for targeted research is one answer. For example, although the South African government has been widely criticized for its overall response to HIV/AIDS, it has demonstrated strong leadership in the area of vaccines, founding and supporting the South African AIDS Vaccine Initiative (SAAVI) to fund what is now a robust pre-clinical and clinical research program on vaccines suited to the country's epidemic.

Another approach is to support multilateral organizations involved in AIDS vaccine development. Eight governments provide direct funding to the International AIDS Vaccine Initiative (IAVI), a public-private partnership that supports work on vaccines for use in the developing world. As another example, numerous African countries (plus the World Health Organization) fund the African AIDS Vaccine Programme, which advocates and builds local capacity for accelerated research on AIDS vaccines. Countries can also band together: In July 2004, Brazil, Thailand, China, the Russian Federation, Nigeria and Ukraine signed a Joint Declaration to work more closely with one another to produce AIDS treatments and develop AIDS vaccines and ***microbicides***.

By far the largest financial commitment to AIDS vaccine research has come from the United States, which will spend well over $400 million on this research in fiscal year 2004 through its National Institutes of Health (NIH). And in the 1990s, with lagging interest in AIDS vaccines from pharmaceutical companies (where most of the world's expertise in vaccine development is found), NIH moved beyond its traditional basic-science approach to provide more funding for product development.

But governments are still struggling to find additional ways of filling the gap left by industry's relatively minimal engagement in the search for an AIDS vaccine. Some funding

agencies (including NIH and IAVI) are attempting to harness private sector know-how by providing direct support to companies doing AIDS vaccine research. More indirect measures have been used as well: for example, in 2002 the United Kingdom introduced a tax credit for companies working on drugs or vaccines targeting AIDS and other infectious diseases primarily affecting people in developing countries.

In the late 1990s, proposals in the US Congress would have created similar incentives (for work on microbicides and vaccines against malaria, tuberculosis and HIV). These proposals were never enacted. But when governments are sufficiently motivated they *can* act decisively. The threat of bioterrorism inspired the US Congress, in 2004, to pass a package of incentives aimed at encouraging industry to develop bioterror "countermeasures," such as anthrax and smallpox vaccines. Those incentives, which include not only direct funding for research but also liability protections, accelerated regulatory review and guaranteed purchase of new products once they are licensed, could all be extended to vaccines against AIDS and other major infectious diseases.

US government incentives to develop vaccines against bioterror diseases could be extended to vaccines against AIDS and other major infectious killers.

promoting clinical trials

When an AIDS vaccine candidate moves out of the lab and into humans, it enters the collective (and political) sphere. Clinical trials of these products are expensive, they can present ethical conundrums, and they often receive intense media scrutiny. Their success depends on public trust. For these reasons, government support is also crucial to their success—especially in countries new to such research, or where past clinical trials helped identify effective products which then took many years (or even decades) to become widely available locally.

Again, Thailand provides an example of how government can lead the way. The Kingdom has made AIDS vaccine research a high priority, partnering with industry, academics and government researchers from several countries to conduct

more than a dozen *Phase I* and *II* trials and launch two *efficacy* trials (one completed, one continuing through 2009). Thailand has also used this research to enhance the country's overall response to HIV and the broader health problems facing its population. Its ongoing AIDS vaccine efficacy trial is helping the country expand prevention and treatment services, build health care and research infrastructure, and achieve a new level of community involvement in research. Increasingly, other developing countries are joining in the effort: In the last five years, nearly two dozen countries in Africa, Asia and Latin America have launched, or are preparing for, AIDS vaccine trials (see appendix 2).

©SAAVI

SOUTH AFRICA

Nelson Mandela, South Africa's former president, visited the vaccine trial site in Soweto shortly before it began the country's first AIDS vaccine trial. Mandela has devoted much of his time since leaving office to the battle against AIDS. From left to right: researchers Glenda Gray, Carolyn Williamson, Atom Dilraj; Nelson Mandela, Community Advisory Board (CAB) member Winnie Serobe, former SAAVI head Tim Tucker and researcher Andrew Robinson.

These trials require extensive preparation of laboratories, clinics and participating communities (see chapters in Clinical Trials, section 3), and one of the most important roles for rich countries is to support the buildup of this capacity in the developing world. The HIV Vaccine Trials Network (through the US National Institutes of Health), the US Military Program, the International AIDS Vaccine Initiative and the European and Developing Countries Clinical Trials Partnership are all important examples of agencies involved in this effort.

Many challenges are involved, such as expanding the genuine involvement of local researchers, sharing data and lessons learned across clinical trial sites, and maintaining these sites between trials. Another challenge is to foster local expertise in evaluating the safety, scientific and ethical aspects of these studies, efforts in which countries with established regulatory agencies, plus the World Health Organization, can play a crucial role.

ensuring access

Ensuring that an effective vaccine will rapidly reach the populations in greatest need (and avoiding a repetition of the catastrophic inequalities in access to *antiretroviral drugs*) is largely an issue of political will. But that does not mean the challenges are any less complex. For example, there are no detailed answers to the deceptively simple question of how much vaccine will be needed worldwide, since this will vary greatly according to vaccine dosage, type, effectiveness, price, peoples' willingness to be vaccinated, their access to health care facilities and other factors.

Ensuring that an effective vaccine will rapidly reach the populations in greatest need is largely an issue of political will. But that does not mean the challenges are any less complex.

Nevertheless, to achieve nearly simultaneous distribution of AIDS vaccines in wealthy and poor countries, governments and international organizations will need to take a variety of actions, such as:

- Vaccine manufacturers must be poised to produce hundreds of millions of doses very quickly once a vaccine is licensed, and governments should be ready to help—for example, by providing incentives for technology transfer to vaccine manufacturers in the South, who can help meet global demand.
- The world must be ready to pay for this large-scale manufacture, such as through pre-commitments to purchase vaccine for global use. Vaccines must be available to all, regardless of ability to pay.
- Health care infrastructure must be expanded so that vaccines can be delivered quickly to adolescents and adults, not only to infants.
- Anti-stigma efforts should be launched so that an effective vaccine will be widely accepted by marginalized and highly vulnerable people around the world.

  (These and other issues related to access are discussed more fully in chapter 36.)

PUBLIC LEADERS AND VACCINE ADVOCATES can build on their AIDS vaccine work by addressing other prevention technology priorities. For example, infrastructure created for AIDS vaccine research might be used to deliver existing vaccines and treatments, such as Hepatitis B vaccine. Vaccine advocates could also help develop an agenda for global access to tenofovir, an antiretroviral product that shows promise as a prevention tool.

An AIDS vaccine will not eliminate the need for behavioral prevention, since at least the first licensed product may be only partially effective (see chapter 9), and even with the best preparation it will take time to vaccinate hundreds of millions of people around the world. So the need for behavioral prevention will persist, as will the familiar political obstacles to providing evidence-based interventions—a reminder that the quest to produce and deliver a vaccine which can end the epidemic will continue presenting new challenges to political leaders and policy advocates for a long time to come.

resources

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ensuring rapid global access to aids vaccines

DAVID GOLD

IT WOULD BE morally unthinkable to have a safe and effective AIDS vaccine without the capacity to deliver it quickly to those most at risk of HIV infection. Yet there are enormous challenges to making a new vaccine available in developing countries at the same time as in industrialized countries—in fact, it's never been done before.

Advocates and policymakers are beginning to think about how these challenges can be overcome. As they do, they must also consider the amount of time, resources and political capital to invest in the access issue, when a safe and effective AIDS vaccine may still be at least a decade away.

At first glance, it might seem unnecessary (or even wasteful) to start planning now for delivering a vaccine that doesn't yet exist. But the world's experience with licensed vaccines demonstrates the terrible consequences of failing to tackle access issues early. Poor countries still wait an average of 20 years after a vaccine is licensed in industrialized nations before it starts reaching their own populations.

This unconscionable delay has several causes, including:

- Too little money to buy the vaccines. This is true even with the creation of new organizations dedicated to closing this gap, such as the Global Alliance for Vaccines and Immunization (GAVI) and the Vaccine Fund.
- The slow pace at which companies scale up capacity to manufacture large enough amounts of new vaccines to meet global needs.
- Needlessly long regulatory approvals processes.
- Too few effective systems for distributing new vaccines in poor countries.

Poor countries wait an average of 20 years before new vaccines start reaching their populations.

Access to AIDS vaccines first captured global attention at the 2000 International AIDS Conference in Durban, which was dominated by the issue of access to ***antiretroviral*** therapy in developing countries. Citing this glaring example of public health disaster stemming from early failure to plan for treatment access, a small number of advocates began urging policymakers to start thinking about vaccine access in advance of having a product. The meeting also featured the release of "A Blueprint for Ensuring Rapid Access to AIDS Vaccines" by IAVI and the distribution of buttons and posters calling for "An AIDS Vaccine for ALL."

One year later, at the United Nations General Assembly Special Session on AIDS (UNGASS), advocates from several countries succeeded in getting a statement on AIDS vaccines included in the final "UNGASS Declaration of Commitment." In this document, nations of the world agreed to:

> Encourage investment in HIV/AIDS-related research, in particular for sustainable and affordable prevention technologies, such as vaccines and ***microbicides***, and encourage the proactive preparation of financial and logistic plans to facilitate rapid access to vaccines when they become available.

key challenges to aids vaccine access

MOST PEOPLE IN THE FIELD agree on the main challenges to ensuring rapid, broad access to AIDS vaccines. These include:

Estimating demand

Demand for an effective AIDS vaccine is likely to be very high. Yet precise estimates of how high (and therefore how much vaccine will be needed) don't exist. That's partly because demand will depend a lot on the specific properties of the vaccine, such as its level of effectiveness, its cost and ease of use. For example, there will be much more demand for an inexpensive product that protects 80% of all vaccinated people after one dose, compared with a more expensive vaccine that gives only 40% protection and requires three injections. In the latter case, different countries will probably make different decisions about vaccinating their populations, depending on the severity of their epidemic. (See chapter 6 for more discussion of these issues).

But difficult as it is to come up with comprehensive estimates of demand, this information is crucial for planning how to finance, produce and deliver a successful vaccine. A broad group of stakeholders therefore needs to work together on demand estimates for a range of different AIDS vaccines. Vaccine manufacturers, who do not usually collaborate, must make a special effort to tackle this problem together.

Manufacturing

Building a large vaccine production plant that meets the requirements of regulatory agencies typically takes 4–5 years and costs hundreds of millions of dollars. This long time scale and high cost creates a dilemma. If building begins only after ***Phase III*** trials show a vaccine to be safe and effective, the result will be a 4–5 year delay until the new facility can produce large amounts of vaccine. If it starts early enough to avoid this delay—that is, several years before a vaccine has

been shown to work—it risks the entire investment should the product prove ineffective.

But there are ways to begin scaling up manufacturing capacity before a vaccine's ***efficacy*** is proven, yet without requiring manufacturers to assume the full financial risk. These include:

- Sharing the risk between the public and private sectors.
- Building production plants with the flexibility to shift into making other vaccines by other technologies, if the candidate AIDS vaccine turns out to not to work.
- Engaging manufacturers who already produce licensed vaccines in developing countries, to see whether they have potential for large-scale production of AIDS vaccines.

Not even the most advanced regulatory agencies have clear guidelines on what properties an AIDS vaccine needs for licensure.

Regulatory approval

Regulatory agencies, particularly those in developing countries, are often not well set up to review new products such as AIDS vaccines quickly. But not even the most advanced agencies have outlined clear guidelines on what properties an AIDS vaccine will need to show to be granted a license. Nor is it clear whether countries will require a vaccine that has proven effective in one (or several) regions to be tested again in local populations and/or against locally circulating HIV ***strains***. Also, since each country or region has its own licensing authority with its own requirements, it will be impossible for vaccine producers to apply for a single license that's valid everywhere; instead, many different regulatory applications will be needed.

Authorities in developing countries may look to industrialized nations for guidance in licensing a particular AIDS vaccine, but ultimately they will want and need to reach their own conclusions. Those with established regulatory capacity (such as Brazil, India and South Africa) will need to play a leading role. But many others will desperately need technical assistance to strengthen their capacity for making these regulatory decisions.

Delivering AIDS vaccines

The infrastructure for delivering vaccines in poor countries is focused almost entirely on infants and children. But an AIDS vaccine, at least initially, will be targeted to adolescents and adults—groups that are not effectively reached through existing infrastructure, even in wealthy countries.

Developing sustainable systems for getting vaccines to people is expensive, even for childhood ***immunization***. The six basic vaccines given to infants in most countries cost less than US$1 per dose, but delivering them costs 10 to 20 times more—due to the price of transporting them, sometimes to remote locations, while keeping them cold (depending on the type of vaccine), developing local infrastructure and training personnel to immunize people, and a range of other steps. It is crucial that funds to help developing countries pay for AIDS vaccines cover the cost of both purchasing and delivering them.

Financing vaccine purchase

A highly effective AIDS vaccine is likely to be cost-effective at any reasonable price (although this may not be true for low-efficacy vaccines, especially in countries where HIV infection rates are relatively low). But even cost-effectiveness does not guarantee that enough money will be available to buy AIDS vaccines for poor countries. Although childhood vaccines are among the most cost-effective health interventions ever developed, more than 2 million unvaccinated children a year still die from the diseases these vaccines prevent (see table 5.1, following page).

The cost of purchasing hundreds of millions of vaccine doses over many years will be significant, even if prices are heavily tiered (meaning that they are much lower in developing countries than in industrialized ones). Some advocates have called for donor countries to set aside funds to buy large amounts of vaccine, even before one is developed. Their reasoning: this step would give the pharmaceutical industry and international funders more confidence to invest in AIDS vaccine development and manufacturing capacity, since it

would guarantee buyers for the product. Others question these proposals, citing the desperate need for funds and commitments targeting health interventions that already exist but are under-used. (For example, much more money is needed to avoid falling even farther behind with childhood immunization coverage.) But public health advocates agree that donor organizations and governments must do more to improve vaccine coverage in poor countries—both to save millions of lives and to help build confidence in the world's willingness to buy a future AIDS vaccine and deliver it where it is desperately needed.

Table 5.1 Annual deaths from vaccine-preventable diseases (2002)

Disease	Number of deaths
Diphtheria	5,000
Measles	612,000
Polio	1,000
Tetanus	215,000
Pertussis	294,000
Hepatitis B	600,000
Heamophilus influenzae b	413,000
Yellow Fever	30,000
Total	**2,169,000**

Source: World Health Organization

conclusion

THE CHALLENGE of getting an AIDS vaccine quickly to people in poor, hard-hit regions of the world will be enormous, but not impossible—if steps are taken well in advance of having a vaccine ready for delivery. This will also require resources and political will. AIDS vaccine advocates must continue to pressure policymakers, governments in the North and South, multilateral agencies and vaccine manufacturers to work together on access issues. We must also continue to aggressively push the research and development effort, because a safe and effective product is still the bottom line.

resources

www.vaccinealliance.org
Global Alliance on Vaccines and Immunizations (GAVI) and the Vaccine Fund. Information on the levels of vaccine coverage and funding for childhood vaccines globally, plus news and updates about global immunization programs and policies.

www.who.int/vaccines
World Health Organization (WHO). Immunization, Vaccines and Biologicals. Report on the status of basic vaccine coverage globally.

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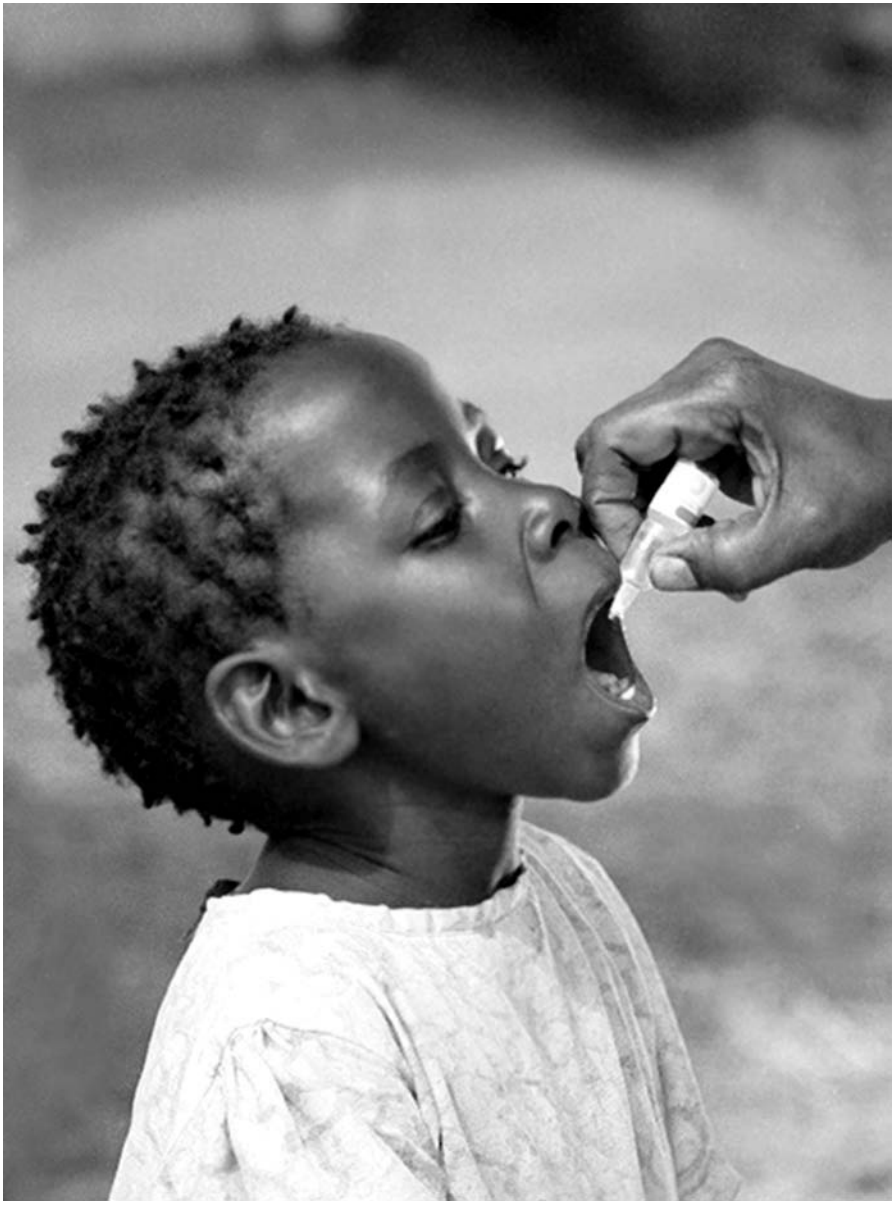
www.iavi.org/pdf/whitepaper.pdf
International AIDS Vaccine Initiative (IAVI). Two papers analyzing the policy challenges and making recommendations on how to ensure global access to an AIDS vaccine.



JUST 2 DROPS

Two drops of an oral vaccine (given multiple times) gives lifelong protection against polio to almost all immunized children.

37

just 2 drops: polio eradication in pictures

text by PATRICIA KAHN /
photos from the WORLD HEALTH ORGANIZATION archives

In the last century, polio epidemics killed or paralyzed millions of people around the world, mostly children. Today, nearly 20 million people live with disabilities caused by their past infection.

The development of vaccines against polio was therefore a monumental public health achievement. When the first one was licensed in 1955, its developer, Jonas Salk, became an instant international hero. A few years later, Albert Sabin developed an oral vaccine (one that can be given by mouth rather than injected). By eliminating the need for sterile injecting equipment and highly trained medical staff, an oral vaccine simplifies mass immunization programs, especially in countries without strong health care systems.

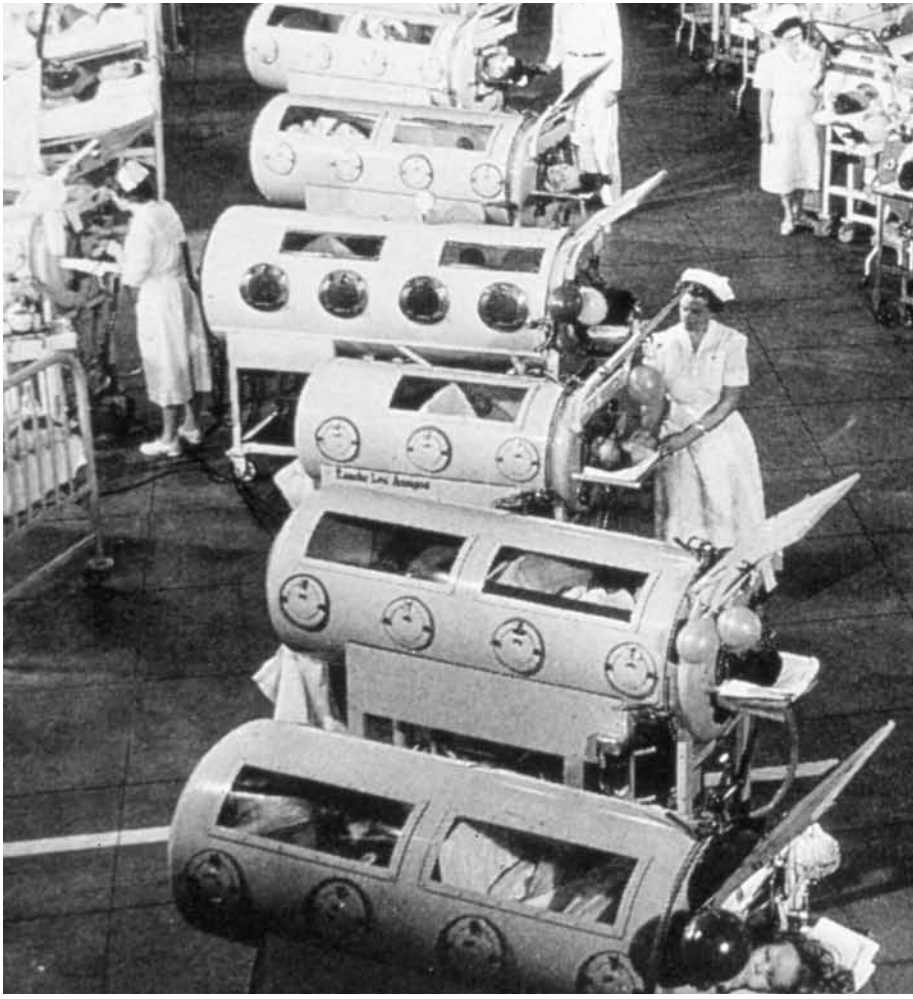
Yet it still took decades for effective mass vaccination to reach most parts of the developing world. In 1988—the year the World Health Organization (WHO), UNICEF and other international partners launched a global campaign to eradicate polio—the disease was still established in 125 countries and paralyzed 350,000 children.

Since then, the eradication campaign has immunized over two billion children and is on the verge of wiping out polio completely: in 2003, there were fewer than 800 cases recorded worldwide, and transmission had been eliminated in all but six countries. But 2004 brought a backslide, when war and other disruptions in vaccination programs caused outbreaks in areas of west and central Africa that had been polio-free. Still, WHO is hopeful that it can end polio transmission everywhere in 2005.

Polio and AIDS are obviously very different diseases, and they pose different scientific challenges for vaccines. Yet the story behind polio vaccines offers us valuable lessons today—especially about the crucial role of strong leadership and public support, and about the formidable challenges of bridging the immunization gap between wealthy and poor countries once an effective vaccine becomes available. The pages that follow portray some highlights of the polio story, from the 1920's until today.

IN THE PERIOD just before the Salk vaccine became available, about 45,000 people in the US were newly infected with polio each year.

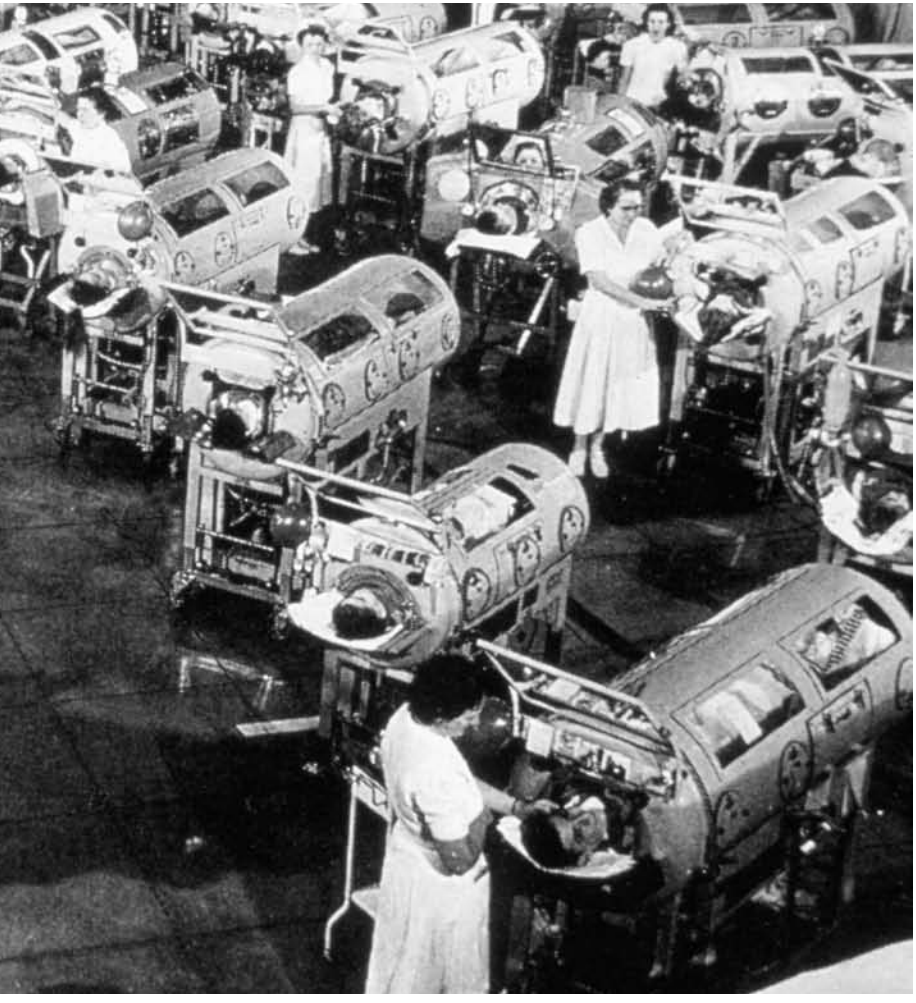
Between 5 and 10% of people contracting polio became paralyzed not only in their legs but also in their breathing muscles, putting them at risk of death through suffocation. To keep them alive, a machine called the "iron lung" was developed in the 1930's.



©March of Dimes

WHERE WE WERE – THE TROUBLING LANDSCAPE OF THE POLIO EPIDEMIC

Wards filled with iron lungs became a common feature of hospitals in North America.



IN 1921, Franklin Delano Roosevelt, Governor of New York State, was struck with polio, leading to partial paralysis. Over the following years he established a treatment center in Warm Springs, Georgia for young people rehabilitating from the effects of polio and launched a series of fundraising activities to support it.

STRONG LEADERSHIP

Roosevelt, who spearheaded the development of a polio vaccine, visits with two youngsters at the Warm Springs Foundation treatment center.

IN 1938, Roosevelt (by then President of the US) and his ex-law partner, Basil O'Connor, founded the National Foundation for Infantile Paralysis, which focused on developing a vaccine. The Foundation later became known as the March of Dimes, thanks to the practice of asking the public to support its work by sending dimes to the White House.

©March of Dimes

COMMUNITY MATTERS

The March of Dimes prioritized and funded research that led to the first effective polio vaccine, and mobilized massive public support.

The enormous public fear that came with each summer's wave of polio, combined with Roosevelt's and O'Connor's strong leadership, rallied the country behind the vaccine cause and the March of Dimes. In 1948, the March of Dimes began funding Dr. Jonas Salk's efforts to make a killed polio vaccine.

BY 1952, Salk had a candidate vaccine made from all three strains of polio ***virus***. After initial tests in people found that it was safe and induced antibodies to the virus, Salk and the March of Dimes launched an ***efficacy trial*** in nearly two million schoolchildren—the largest peace-time mobilization of volunteers in US history.

PIONEERING RESEARCH

In 1954, Salk's vaccine was tested for efficacy in schoolchildren, who were dubbed the "Polio Pioneers."

ON 22 APRIL 1955, the long-awaited results of the trial were announced: The vaccine was safe, and it protected over 60% of the immunized children against polio.

The Detroit News

HOME EDITION

POLIO CONQUERED!

VACCINE TRIUMPHS

Headlines celebrated the vaccine breakthrough, but it has taken 50 years and massive (ongoing) efforts to nearly conquer polio worldwide.

IMMUNIZATION DRIVES

Rock-and-roll icon Elvis Presley, shown here getting a polio vaccination, brought his star power to the immunization drive in the US.

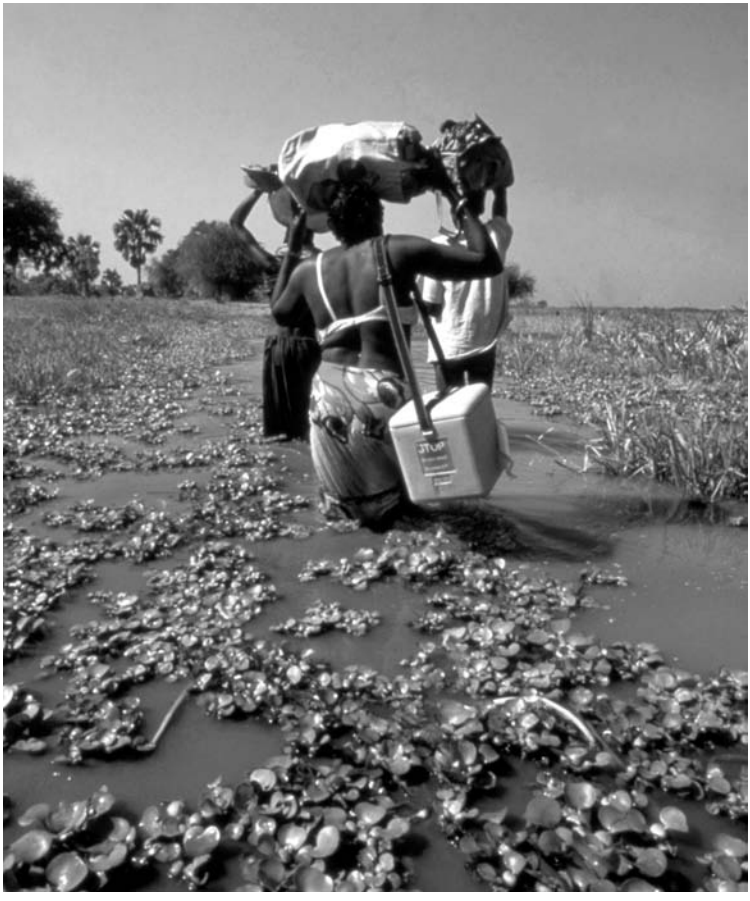
WITHIN SIX YEARS, the Salk vaccine had essentially eliminated polio in the US. In 1962, the number of new polio cases in the US was below 1000.

During the 1960's, Sabin's oral vaccine—which is less expensive, easier to use and more effective in preventing transmission (not just infection)—gradually replaced the Salk vaccine. In 1988 it became the vaccine of choice for the global eradication campaign.

THE GLOBAL POLIO ERADICATION CAMPAIGN, the largest public health project ever undertaken, remains in high gear as it works to eliminate polio from its last strongholds. One important strategy is to reach more children in remote areas. That's a tall order, especially since the vaccine must be kept cold at all times or it loses effectiveness. Some examples of the challenging logistics:

GLOBAL CHALLENGES / CENTRAL AFRICA

Vaccination teams cross rivers, mountain passes and deserts in an effort not to miss any villages.



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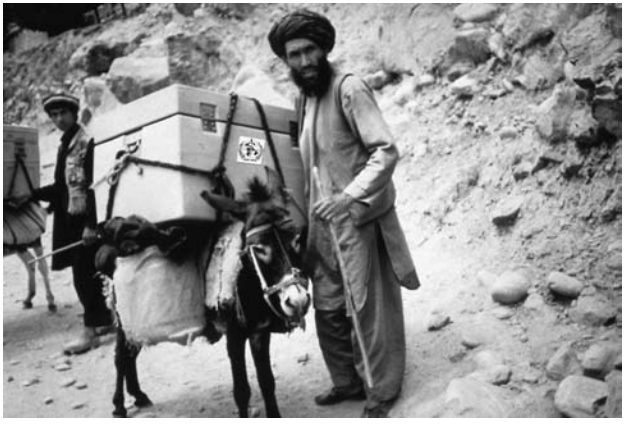
NEPAL

A porter treks polio vaccine into the Himalayas.



©WHO

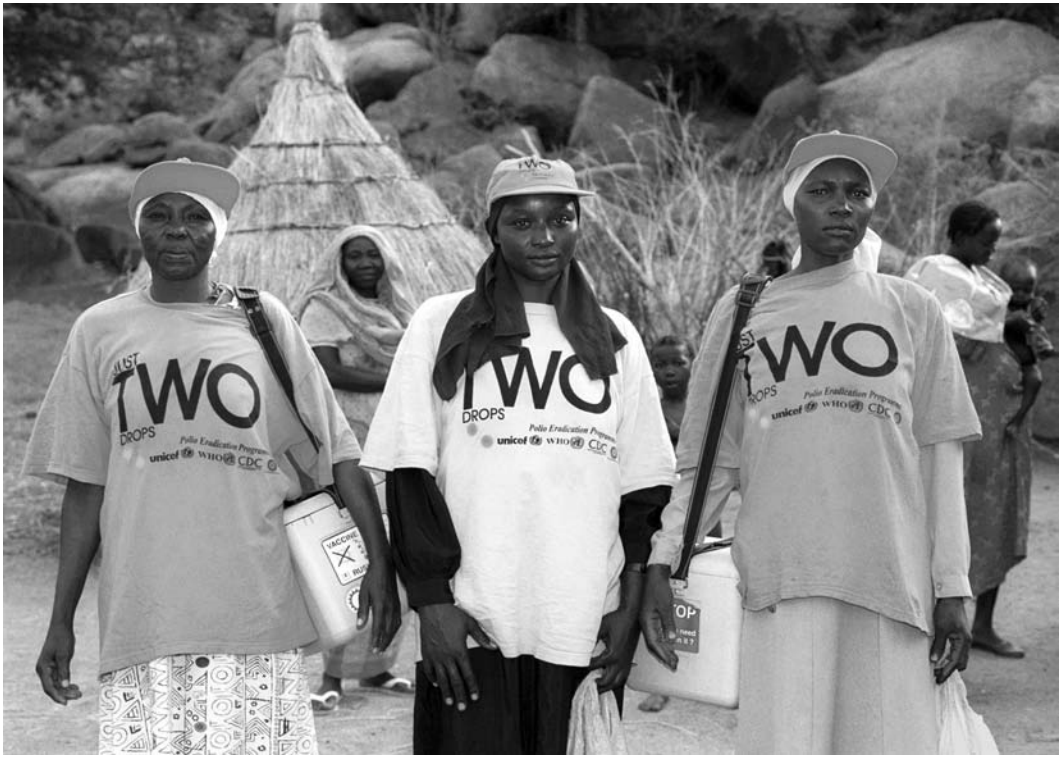
PAKISTAN

Donkeys can carry the vaccine through rugged mountain terrain in areas which are otherwise impassable.

ANOTHER IMPORTANT PART of the eradication strategy is to supplement routine vaccination with National Immunization Days (NIDs). On these days, teams of vaccinators fan out in synchronized mass campaigns to immunize every child under 5 years old, regardless of their prior vaccination status.

GLOBAL STRATEGIES / SUDAN

These women are local vaccinators selected by WHO from villages around western Nuba. Colorful T-shirts printed with the words "Just Two Drops!" clearly identify the vaccination staff and the reason for their presence.



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IN 2003, 415 million children were immunized during NIDs in 55 countries. Because the oral polio vaccine does not require a needle and syringe, volunteers with minimal training can serve as vaccinators.

©WHO/Jean-Marc Giboux

PAKISTAN

Vaccinators in Nasir Bagh Afghan refugee camp.

INDIA

A recent NID in India deployed 2 million volunteers to immunize over 150 million children in just a few days.

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THE YEARS 2005 AND 2006 are crucial as the world teeters on the edge of eliminating polio completely.

Two key challenges:

- Combating the polio resurgence in west and central Africa amid the region's armed conflicts.
- Filling the funding gap of $75 million for 2005 and $200 million for 2006.

Once again, success will demand strong political will and leadership, and public pressure.

resources

www.polioeradication.org
The official website of the Global Polio Eradication Initiative.

www.unicef.org/immunization/index_polio.html
Website of the United Nations Children's Fund (UNICEF), which plays a major role in the polio eradication effort.