HIV Prevention

— Condoms and Beyond

Impact

POLICY BULLETIN TEN, JUNE 2005
New Publications

All publications and resources are available for download at www.nat.org.uk. Please check the web site for details of other forthcoming publications and events.

POSITIVE PEOPLE’S INVOLVEMENT PROJECT

NAT is currently engaged in a Positive People’s Involvement (PPI) Project, funded by the Big Lottery Fund, which aims to enable people living with HIV to influence and shape health and social care services at a local level. More information about the project can be found on the PPI section of NAT’s web site. Recent outputs include:

Involving people living with HIV
Regional seminars were held in Bristol, Leicester, London and Newcastle in 2004 to identify the experiences of people living with HIV, what their needs were, and any gaps in their skills and knowledge. Contact NAT or visit the web site for a copy of Involving people living with HIV, the report from these seminars. Reports from each regional seminar are also available on request.

Web feasibility study
NAT carried out a feasibility study to investigate how Web technology can be best used to encourage, promote and support positive people’s involvement. The study will be used to further develop the proposal for a ‘one stop’ HIV web site in the UK. Contact NAT or visit the web site for a copy of the Web feasibility study report.

Changing Tomorrow
A UK conference of people living with HIV was held in September 2004. NAT worked with partner organisations to enable people with HIV to develop their skills in managing their own condition and influence health and social care providers. Contact NAT or visit the web site for a copy of the conference report.

What impact can an HIV conference have on the lives of people living with HIV?
Research by Bab Evans, National AIDS Trust, on the effects of the 2004 Changing Tomorrow conference of people living with HIV and AIDS. Published in HIV Medicine, May 2005.

CRIMINALISATION

A revised version of NAT’s paper on the criminalisation of HIV transmission has been produced. It includes information for HIV positive people, and updates the paper to take account of recent convictions and court judgements.

NAT SUBMISSION

NAT has submitted a response to the Scottish Executive opposing their proposal for mandatory blood test orders for those allegedly involved in criminal incidents.

FACT SHEET

NAT has produced a new fact sheet on new prevention technologies.

PRISONS PROJECT

NAT is working with the Prison Reform Trust to assess and produce a report on the needs of prisoners in the UK in the context of HIV and hepatitis.
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Cover courtesy IAVI (photo: Vanessa Vik)
Deborah Jack is Chief Executive of the National AIDS Trust.

The scale of the HIV epidemic in 2005 is horrifying. Forty million people are now living with HIV, infection levels are increasing throughout the world and if current trends continue a further 45 million people are predicted to contract HIV by the end of the decade.

There is, as we know, still no cure. To make progress on the Millennium Development Goal of halting and beginning to reverse the spread of HIV and AIDS, and to tackle effectively the complex biological and social phenomenon that is HIV, there isn’t simply a ‘magic bullet’. Instead an array of responses is necessary, covering the various aspects of treatment, care, stigma and discrimination, as well as prevention. This is clearly a challenge to politicians, to the voluntary sector, and to campaigners — since it is always easier to focus on, and advocate for, one simple solution.

The recent emphasis on increasing access to treatment is welcome and necessary. Commentators are quite right to criticise a ‘treatment for the rich, prevention for the poor’ response to HIV, as it is fundamentally contrary to human rights. Yet in spite of international campaigning, we are on course to fail the target of securing antiretroviral therapy for 3 million people in developing countries by the end of 2005.

The National AIDS Trust (NAT) believes that access to treatment for all must be scaled up urgently, and we welcome the recent commitment by G8 Finance Ministers to achieving universal access to care and treatment by 2010. But we risk ultimate failure in tackling HIV if, in boosting access to treatment, we take the spotlight off prevention. HIV prevention must remain a priority. Advocating for prevention using the means we already have available, as well as advocating for research and development of new prevention options, does not mean advocating less for treatment. The challenge to world leaders as the G8 summit approaches is to deliver an ‘and . . . and’ outcome, not ‘either . . . or’, with all the implications for significant increases of funds that this entails.

In any event, treatment and prevention strategies are not really separable — in fact they reinforce each other. Treatment significantly reduces infectiousness so is preventive in impact also. The offer of treatment is a great incentive to take an HIV test, and when people are aware of their status (and, if positive, are receiving care) this has an impact, behaviourally, on reducing unsafe sexual behaviours. Furthermore, both treatment and prevention interventions share health infrastructure and service requirements, so investing in one benefits the other.

The bottom line is that without progress in prevention — reducing the number of infections — then the number of people living with HIV will outstrip, by an ever-widening

“Forty million people are now living with HIV, infection levels are increasing throughout the world and if current trends continue a further 45 million people are predicted to contract HIV by the end of the decade.”
It is vital for communities in the UK to engage with the development of new prevention technologies and the establishment of the UK Community Advisory Board on new preventive technologies, for instance, is very encouraging. We need to do more to make the case for better HIV prevention in this country, and some ideas are found in our ‘Talking Heads’ section.

Some might say though, that resources directed at developing any new prevention technology could be better spent on increasing access to and promoting the use of the range of HIV prevention methods already in existence. Condoms, for instance — male and female — are, of course, a reliable way of preventing transmission of HIV and other sexually transmitted infections. Increasing their availability, complemented by education on sexual and reproductive health, is important.

But to rely only on condoms is to leave millions of people, particularly women, at continuing risk. This was clearly illustrated in a recent article by International Planned Parenthood Federation director general Steven Sinding. He noted that “in Sub-Saharan Africa, the majority of newly HIV-positive women are contracting the virus within marriage from their husbands. This pattern is reflected around the world. In Cambodia, prevalence is falling among sex workers but rising rapidly in married women: fifty percent of all married women who contracted the virus in 2002 were infected by their husbands. Furthermore, in one recent study, more than 80% of HIV-positive women were monogamous, and in a study in Rwanda, 25% of women who were HIV-positive said they had had only one sexual partner in their lifetime.”

Consistent condom use is simply not an option for millions of people — women find themselves unable to insist on their use, and they are obviously not feasible for couples wishing to have children. As Stephen Lewis, UN Special Envoy for HIV/AIDS in Africa, chillingly puts it, “ironically, and lethally, in the age of AIDS in Africa, marriage can be dangerous to women’s health”.

We have to address the issues that keep women vulnerable, but new prevention options do not mean advocating less for treatment. It is vital for communities in the UK to engage with the development of new prevention technologies and the establishment of the UK Community Advisory Board on new preventive technologies, for instance, is very encouraging. We need to do more to make the case for better HIV prevention in this country, and some ideas are found in our ‘Talking Heads’ section.

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technologies could offer real hope of protecting people most at risk. An HIV vaccine could do this, but it is widely acknowledged that development of a microbicide is likely to happen sooner. Crucially, a partner would not need to know about or consent to a microbicide’s use, and contraceptive and non-contraceptive forms would enable even a woman wishing to become pregnant to protect herself. Microbicides could have benefits in the developed world too — tackling rising rates of sexually transmitted infections in the UK for instance, as well as HIV.

A microbicide would not be designed to replace condoms — rather it would be another weapon to add to the arsenal of prevention methods available. Experience in the contraceptive field shows that when a new product is added to the range of existing options, there is an increase in the overall use of contraceptives. There is every reason to believe the same applies to HIV and that HIV transmission rates would be reduced by the introduction of a microbicide. Until the introduction of a 100% effective vaccine, no one method of prevention will ever eradicate HIV alone. And even when a vaccine is discovered, early versions are likely to be only partially effective and it will of course take time to implement vaccination programmes worldwide, so new prevention technologies should work in parallel with existing methods of prevention.

NAT is campaigning to make microbicides and vaccines a reality — to secure the support necessary to speed their development and effective and ethical introduction throughout the world - in developed, as well as developing, countries. This year provides an important opportunity to influence world leaders on this issue, through the UK’s Presidencies of the G8 and the European Union (EU). There are some clear messages for politicians ahead of the G8 and EU Presidencies — as Frans van den Boom of the International AIDS Vaccine Initiative (IAVI) says in his article on vaccines, more and better investment, financial incentives and political will are required if vaccine development is to be taken forward. The same is needed for microbicides if we are to secure this much-needed product by the end of this decade.

Ultimately, developing these new prevention technologies is about respecting and upholding human rights, about maximising the ability of all at risk to protect their own health and that of their sexual partners. This is the necessary alternative to the simplistic mantra of ‘ABC’ (abstinence, be faithful, use condoms) coming from the United States which ignores the rights of many vulnerable people, and in particular women.

With the G8 focus on Africa’s development, we would like to see increased commitment from all G8 and EU leaders to advance the development of these new technologies, as part of the wider fight against the disease which is exacerbating poverty and reversing years of development progress.

Effectively preventing HIV has to be our ultimate goal.

Deborah Jack
Chief Executive, National AIDS Trust
The global scourge of AIDS calls for immediate actions to save lives and prevent disease, through significant expansion of HIV prevention programmes and access to AIDS treatment. Yet even if treatment reaches millions more, the steady toll of around 14,000 new HIV infections every day places the goal of universal access increasingly out of reach. Much wider implementation of existing prevention strategies could potentially control the epidemic to some degree, but these approaches have limitations, which make them inherently difficult and costly to sustain. Immediate actions must therefore be balanced by long-term efforts to develop far more effective tools than any we have today. An effective preventive vaccine remains our best — probably our only — hope of ending the pandemic.

With the UK hosting the G8 summit and assuming the EU presidency next month there is an opportunity to place AIDS prevention research and development (R&D) high on the international agenda. This fits well with the Government’s priorities for reducing poverty, especially in Africa, where the AIDS epidemic deepens household poverty and has a negative effect on national economies. The International AIDS Vaccine Initiative (IAVI) is calling on this year’s G8 to back previous commitments on AIDS vaccine R&D with real investment, renewed global leadership, and measures aimed at stimulating private sector engagement and securing eventual access to a vaccine.

There is still a long way to go. Despite significant funding increases since 2000, AIDS vaccine research still lacks necessary resources and the full engagement of private sector expertise and innovation. Key priorities include ensuring the best possible science is supported; developing enhanced capacity for clinical trials; engaging private, public and civil society partners from North and South; and increasing commitment from the world’s most powerful nations.

**WHY A VACCINE?**

History shows us that infectious disease epidemics — like smallpox, polio and now HIV and AIDS — can only be conquered through mass immunisation programmes. Existing vaccines against other diseases prevent three million deaths each year. Smallpox has been eradicated globally, polio is close to elimination and vaccines for tetanus, measles, mumps and hepatitis A and B are saving millions of lives worldwide. Plus, in many cases vaccines have proved to be the most cost-effective interventions available in the long term. In the case of HIV, the main difference between a vaccine and existing preventive methods lies in durability of protection, enabling more sustainable interventions. Existing methods need to be maintained indefinitely; for instance, condoms must be used in every high risk sex act. At a community or national level, this entails sustained activity to educate all young people and to maintain high levels of awareness and avoid complacency among those in sexually active age groups. By contrast, a vaccine could provide lasting protection via a number of courses per person with occasional re-vaccination — or ideally even a “one-time” intervention.
But how effective would an AIDS vaccine be? What impact could it have on the epidemic? How many lives would it save? No vaccine is 100% effective, and many researchers believe that when the first AIDS vaccine becomes available its efficacy rate may be lower than many other vaccines in use today. But epidemiologists estimate that even a ‘partially effective’ vaccine could have a dramatic impact on HIV incidence. For example, a study by the World Bank and the European Commission indicates that even a 50% effective vaccine, administered to 65% of all adults at risk, could reduce rates of infection by 25% to 60%.

THE SEARCH

Last autumn saw a number of articles cast doubt on the prospects for an AIDS vaccine. Observers lamented the long list of scientific unknowns and the frustratingly slow progress of research in the midst of this terrible, and growing, epidemic. But similar things were once said about polio, a disease now close to being eradicated. It is true that progress on AIDS vaccine research has been slow, but not historically — it took 42 years to develop the measles vaccine. One of the main reasons for creating IAVI was to accelerate AIDS vaccine R&D. But whatever the sceptics’ views, there are sound scientific reasons to be optimistic. Yes, HIV is complex and yes, it is variable. But most people are able to control the initial high viral levels circulating in the blood and hold that in check for close to a decade. We have already seen experimental vaccines against SIV (a close cousin of HIV that infects monkeys) preventing AIDS infection in inoculated animals and infusion of the right type of antibodies can also prevent infection in this model. Plus, there are a very small number of humans who appear to show natural resistance to infection, and whose immune response have provided scientists with vaccine ideas. The route to a vaccine may not be an easy one, but it is one that we think is possible, and one which offers by far the best long-term solution to combating AIDS.

Five years ago, the pipeline of AIDS vaccine research was looking pretty bleak. Vaccine candidates were few and far between and progress to find new ones was slow. Today, despite some setbacks, progress is under way. More candidates are being trialled, and there is a renewed effort on trying to solve some of the fundamental research questions that have plagued the field. More countries are involved in research and testing, and we’re seeing increasing interest from the private sector. And in the last two years we’ve seen one really major milestone — the completion of the first ever large-scale trial on an AIDS vaccine candidate. If the outcome of the trial was disappointing, the trial itself was a resounding success. Recruiting thousands of volunteers and retaining them over a three-year period, the trial has set an important precedent — and an example that is being repeated around the world.

There are now some 30 candidates in small-scale clinical trials. That’s double the number in trials in 2000. There are also more private pharmaceutical companies with vaccine candidates being trialled. At the same time, there has been a big increase in the number of countries — and particularly developing countries — engaged in the search. Four African countries have already started small-scale trials and another five are gearing up to join in. Throughout Africa, Asia and Latin America there are state-of-the-art clinics and laboratories, staffed by local physicians and technicians, where, four years ago, there were virtually none.

But despite all this progress — in developing candidates, in carrying out trials, and in building up expertise and capacity to host trials — there are still some big challenges ahead.

THE BOTTLENECKS

One problem is that almost all the vaccine candidates that are in trials at the moment are based on the same basic idea. They’re all designed to provide protection through ‘cell-mediated immune response’, which means that the vaccine can enable immune system cells to recognise other cells infected with specific pathogens — in this case HIV — and destroy them.

But there are other ways an AIDS vaccine might work. If this first approach is only modestly or not successful, we will need to be ready with some alternatives. It’s time to look again at some of these other options as potential blueprints for vaccine design.
At IAVI we’re doing all we can to explore the potential of alternative vaccine candidates. We’re expanding our Neutralising Antibody Consortium to look for vaccines that can induce broad-spectrum antibodies, which can neutralise the effects of the virus. And we’re setting up a new consortium to look at why so-called ‘live-attenuated’ candidates work. These ‘live’ vaccines are essentially weakened versions of the real virus, which act by preparing the immune system, in advance, to defend itself against infection. Vaccines like this are the most promising in monkeys. But the problem is that inoculation with these ‘live-attenuated’ vaccines could potentially not be safe in humans. Keen to replicate these effects, while minimising the risks, researchers are now trying to understand how these vaccines actually work. A third vaccine design possibility involves stimulating an immune response in the mucous membranes of the urogenital, respiratory or gastrointestinal tracts, which can act to prevent entry of the virus and infection in the first place.

Once really promising candidates are found, carrying out large-scale clinical trials is vital. Despite the successful experience with the first two large-scale trials (one in North America and Europe, and one in Thailand) and further trials that have gone ahead in Thailand, most developing countries simply do not have the capacity to conduct this kind of trial. The paradox is that these are the countries who need a vaccine most and would get the most benefit from participating early in these trials. We have made huge progress recently, particularly in East Africa and Asia, but more capacity is still needed in other countries where there are high infection rates and different sub-types of the virus are circulating. These include developing countries in Africa, Asia, Eastern Europe and Latin America.

Even once a vaccine is ready the work isn’t over. Manufacturing and distributing the vaccine will present major challenges that the world needs to start preparing for now. Building the manufacturing capacity demands a five-year lead, and preparing the vaccination infrastructure poses a mammoth task. In the past it’s taken up to 25 years for some vaccines to get to where they were needed most — time which we can’t afford to lose. We’re already working closely with the public sector on this — encouraging and working with governments to start preparing for access; to sort out transport, delivery venues, counselling, storage and personnel.

**THE ULTIMATE STICKING POINT**

What’s needed to speed up AIDS vaccine research is pretty clear. But diversifying vaccine design, developing large-scale testing and setting up global delivery mechanisms all require major funding. And at the moment investment into AIDS vaccine research is just too low. Even after a boost from US$160 million in 1996 to US$690 million in 2004, public spending on vaccine research is still less than 5% of the total public money spent on AIDS each year. And it’s less than 1% of the world’s total annual spending on public health. At the same time, there’s very little incentive for private companies to invest heavily. The anticipated market in industrialised countries is limited and the largest demand by far will be from those countries that are least able to pay.

We’re tackling this problem from two angles. We’ve been reminding the world’s decision makers about the urgent need for an AIDS vaccine, and we’ve been calling for an increase in global spending — to US$1.1 billion a year. We’ve also been promoting public policies that stimulate innovative financial mechanisms to attract the private sector to invest in R&D. These include ‘push’ incentives like subsidies, tax credits and reducing risk through supporting some of the costs. At the other end we’re working on ‘pull’ mechanisms — like advance purchase commitments (APC), where donor governments and institutions guarantee to pay a pre-agreed price for a vaccine once it has been developed.

These APC guarantees are designed to ensure people in poor countries can have access to a vaccine while protecting companies from intense pressure to drop their prices so low they have no chance of recouping their investment. Assessing a suitable price for an APC requires some understanding of what the real market could be — by finding out who would be prepared to pay what. In practice, uptake for vaccines is always lower than public health needs, and in the case of an AIDS vaccine, researchers predict an uptake of between 20% to 40% depending on its efficacy. Even so, we expect that if...
donors commit to pay only a modest price per person vaccinated, we could still be looking at a multi-billion dollar need in the developing world. This is the APC value that world governments need to offer to attract private investment.

**POLITICAL CLOUT**

The world’s most powerful governments have already agreed that an AIDS vaccine is a global priority. At several G8 summits in recent years they have acknowledged the need for a vaccine. Most recently, in June last year, they endorsed the establishment of the Global HIV Vaccine Enterprise (GVE) — an alliance of independent agencies working towards an AIDS vaccine globally, in which IAVI is a founding partner. Proposed by the Bill and Melinda Gates Foundation, GVE aims to foster cooperation and provide a forum for discussing best vaccine concept. The GVE has already agreed a “Blueprint”, similar to IAVI’s, setting out the scientific consensus on key priority areas for research.

In the run-up to this year’s G8 summit in July we’ve been working closely with our partners to make sure that AIDS vaccine stays high on the G8 agenda. Only with the backing of these governments — to provide funding, financial incentives and political will — can the vaccine programme move on at a reasonable pace. The top priorities for these governments now are to:

- Increase and better target investment in AIDS vaccine research
- Create a multi-billion dollar APC for AIDS vaccines
- Strengthen political leadership and provide greater assistance to developing nations for AIDS vaccine R&D

The Gleneagles summit is a great opportunity for the G8 to signal a new era in tackling HIV and AIDS. It’s time to commit to concrete actions towards developing and delivering an effective AIDS vaccine. Working together with partners in the developing world, the G8 need to champion vaccines and other new preventive technologies. With the right vision now and the commitment to match that vision, they have a chance to save millions of lives and billions of dollars by ending the most devastating epidemic in centuries.

Frans van den Boom
Executive Director, European Programme
International AIDS Vaccine Initiative

For further information, visit www.iavi.org

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**ABOUT THE INTERNATIONAL AIDS VACCINE INITIATIVE**

Founded in 1996, IAVI is the world’s largest organisation focused on AIDS vaccine research. As a global organisation working in 23 countries, we are committed to accelerating the development of AIDS vaccines that are suitable for use in the developing world — the world in which AIDS has been at its most devastating. IAVI brings together expertise from industry and academia, and from government and philanthropic sources to speed the development of vaccine candidates. We partner with NGOs and governments in developing countries to run clinical trials, and we integrate our research efforts with public policy and advocacy campaigns to ensure AIDS vaccine research gets the resources and support that it needs.
Almost five million people became infected with HIV in 2004 and more than three million were killed by AIDS. Over 20 million have died since the first cases were identified in 1981. The number of people living with HIV continues to grow and now approaches 40 million worldwide — people in the most productive years of their lives, or with their whole lives still ahead of them.

Shocking, numbing, sobering — the tragic testament to an epidemic that rages on.

No matter where we live, what our HIV status is, with whom (or whether) we have sex, we are all affected by HIV and AIDS — a fact that’s often ignored. Not by those who live in communities where AIDS-related funerals are a daily reminder of the scourge. But in places where relatively few people are infected, the epidemic is more easily overlooked. Yet HIV and AIDS continues to change our collective global future by the devastation it wreaks on families, villages, cities and countries.

Besides the immediate crisis it presents, HIV and AIDS also undermine global development, nullifying or even reversing decades of progress — deepening poverty, reducing life expectancy, contributing to political and economic instability, exacerbating food shortages and increasing the divide between rich and poor. In many places, AIDS continues to take its biggest toll on racial and ethnic minorities, the poor and the disenfranchised, leaving the well off relatively unscathed.

Against this background, though, one important statistic is too easily forgotten: Even in the most affected regions of the world, the vast majority of people have not acquired HIV. Providing people — especially youth — with access to the information, tools and support to remain HIV-free is an enormous challenge. Today’s AIDS prevention efforts, including HIV counselling and testing and behaviour change (from promotion of abstinence or mutual fidelity to reducing the number of sex partners, delaying sexual debut and increasing condom use), must be expanded, so they can reach more places and more people.

A massive scale-up of access to treatment for infected people is also critical. First and foremost, it will help tens of millions of people live many more productive years when they can raise their families and contribute to the economy. It’s also crucial to increasing people’s willingness to learn their HIV status, and to avoid infecting others.

But the unbroken spread of the epidemic and its ever-more dire social, political and development consequences are a constant reminder that none of this is enough. We must add new tools to those we already have; not just one tool, but many — vaccines, microbicides, pre-exposure prophylactics.

An effective AIDS vaccine remains the world’s best chance to reverse this relentless epidemic. But the search for a vaccine must not come at the expense of our immediate response or at the expense of developing other new technologies. And it doesn’t have to. Testing vaccines requires that we do all the other key things anyway — delivering the best possible risk-reduction counselling and prevention tools; ensuring confidential, voluntary counselling and testing; providing referral to comprehensive treatment.

“Providing people—especially youth—with access to the information, tools and support to remain HIV-free is an enormous challenge.”
Prevention, testing, treatment, and trials. Twenty-four years into the epidemic, it remains clear that we must do more in our quest for a vaccine, and we must do it as part of a truly comprehensive response. It is not “either/or”; it is “all the above”.

The development of vaccines to prevent AIDS is a long-term undertaking, a fact that’s clearer now than ever. More than 20 years into the epidemic, the answer to a simple question — “When will we have a vaccine?” — remains unanswered. And the standard response — “in ten years or so” — has not changed, as the time frame keeps getting pushed back.

The AIDS vaccine field always needs more time and money, but now, more than ever, the field needs:

- More flexibility and an open mind to new approaches and ideas.
- Increased collaboration and sharing of resources and infrastructure.
- Improved management of expectations at all levels — globally, nationally and locally.
- Better understanding and articulation of how vaccine research, and a future efficacious vaccine, fit into a comprehensive response to HIV and AIDS.
- Enhanced community participation, especially in the developing world.
- More sophisticated understanding of what it means to be ready for clinical research.

While the science of an AIDS vaccine remains undeniably hard and it is easy to be cynical about the prospects for an AIDS vaccine, there are important signs of progress:

- Over the past two years, more new candidates entered into Phase I trials than in any other two-year period previously.
- Ethical and high quality vaccine efficacy trials are taking place internationally — people are volunteering and remaining in the trials.
- The different players in the vaccine field are talking with each other about meaningful collaboration, most notably through the new Global HIV and AIDS Vaccine Enterprise which published its Strategic Scientific Plan earlier this year.

- The pot of money seems to be increasing, in large part due to new funding commitments from the Bill & Melinda Gates Foundation.

We are on a long-term quest, and now we must collectively do everything possible to keep re-defining what needs to be done and make sure we’re doing the most important things. Because vaccine development takes so long, we need to set an agenda for sustained and sustainable action that stretches out beyond the decade.

Working together, we must build a broader global movement advocating on issues that directly impact progress, including more funding and accelerated vaccine research and testing. While scientific issues remain a great challenge, without an increased sense of urgency and expanded community and public involvement, a vaccine is far less likely to bring the AIDS epidemic under control in our lifetimes.

Who is “we”? Advocates, activists, providers, scientists, policy-makers, everyone infected and affected by HIV and AIDS — it really is all of us. Men, women, children; national leaders and community leaders; teachers and students; public health and AIDS advocates; scientists and researchers; AIDS-affected individuals and communities — you name it.

And what does an agenda for sustained and sustainable action look like?

One key to sustaining momentum in AIDS vaccine research and development — and in AIDS vaccine advocacy — is to ensure that we develop some interim indicators of success. Scientists, communities, advocates and policy makers need to focus on a key issue: How the vaccine development process can leave communities better off for having taken part in a trial even if the particular vaccine being tested turns out not to work or to be only partially effective?

The infrastructure for AIDS vaccine clinical trials, if incorporated into the broader HIV and AIDS agenda, and more importantly, into the overall public health system in a collaborative effort, is certain to build long-term, sustainable capacity for research and service-delivery for a truly comprehensive response.

“An effective AIDS vaccine remains the world’s best chance to reverse this relentless epidemic.”
For example, the following “checklist” includes some ways that vaccine trials can leave communities better off and should be incorporated into broader AIDS vaccine advocacy:

- **Voluntary HIV testing and counselling.** Since vaccine trials involve HIV negative volunteers, people have to be tested for HIV before they can participate in a trial. As many AIDS vaccine researchers are now doing, the screening process should be used as an opportunity to introduce rapid HIV-testing kits to the community, and to teach local people how to administer tests and how to counsel those who test positive.

- **Support groups for those who are HIV positive.** In much of the developing world, AIDS carries more social stigma than it does in the industrialized world. By helping set up support groups for people who test HIV positive in trial screenings or turn positive during a trial, HIV vaccine researchers can provide emotional support to people with HIV while helping to break the silence and prejudice surrounding the disease. While no substitute for broad educational programmes, access to antiretrovirals and treatment for opportunistic infections, group support can provide a pathway to testing and treatment not sought for fear of societal penalty.

- **Prevention of mother-to-child transmission.** Short-course nevirapine helps prevent the transmission of HIV from infected mothers to their newborns. AIDS vaccine researchers can partner with local health officials to provide this simple and inexpensive regimen and educate HIV positive pregnant mothers about its life-saving potential. Health care should extend beyond that to include provision of antiretrovirals for these mothers on an ongoing basis. Mothers must also be counselled about the complex issues surrounding the risks and benefits of breastfeeding in resource-poor settings.

- **Antibiotics and medicines to combat malaria and TB.** Quite apart from antiretroviral drugs, many communities in the developing world have little access to standard antibiotics and medicines to fight two leading killers — malaria and tuberculosis. As many research groups are now doing, AIDS vaccine trial units in developing countries should provide these medicines to trial participants. Vaccine trial units should also make treatments available for other sexually transmitted infections which, left untreated, can greatly increase the risk of people contracting HIV.

- **HIV prevention programs.** AIDS vaccine researchers are ethically required to educate clinical trial volunteers about what HIV is and how to keep themselves from becoming infected. Vaccine trials offer the opportunity to expand HIV prevention efforts into the larger community. Community Advisory Boards play an important role in this effort. If male and female condoms are not widely available in the community, vaccine researchers can use their leverage with public health officials and international aids agencies to provide them at no cost.

- **Professional training.** Vaccine trials can be an opportunity to expand the number of medical professionals — doctors, nurses, technicians, social workers and others — in short supply in many developing countries. Trials cannot proceed without trained professionals — and the people best able to understand and respond to the needs of a community will come from the community. Trials can offer not only on-the-job training, but also the chance for classroom and laboratory training at associated academic institutions in the host country or abroad.

- **Shared laboratory facilities.** Many AIDS vaccine trials research teams will be setting up laboratories to conduct tests on blood samples drawn from trial volunteers. Depending on what’s being measured, these labs may use sophisticated equipment in a wide range of experiments. In poor communities without access to advanced testing facilities, these labs might also provide services such as antibody tests, T-cell counts and viral loads to help public health officials treat HIV-infected people and track the epidemic in the local area.

“We must add new tools to those we already have; not just one tool, but many — vaccines, microbicides, pre-exposure prophylactics.”
AIDS vaccine researchers can provide certain benefits directly or they can link up with others who can provide them. Most importantly, scientists need to make certain that whatever is put in place to improve public health infrastructure can be sustained after the trials end.

At the end of the day, the key message here is that instead of doing research on communities, scientists need to do research with communities. Instead of narrowly focusing on trial outcomes only, scientists need to care about the overall health of individuals and their communities.

Again: prevention, testing, treatment, and trials on the road to new prevention technologies is a key way to push for a broad, sustainable response — sustained funding, capacity, infrastructure and realistic expectations — to help us all withstand our long haul from basic science, to product development, through multiple clinical trials and, eventually and most importantly, to a safe, efficacious, accessible and affordable vaccine in use for the people and communities that need it most. In the end, it is not vaccine trials, or vaccine vials — it is women and men and children and their communities who will finally be protected.

Mitchell Warren
Executive Director
AIDS Vaccine Advocacy Coalition

For further information, visit www.avac.org

Founded in 1995, the non-profit AIDS Vaccine Advocacy Coalition (AVAC) uses education, policy analysis and advocacy to accelerate the ethical development and global delivery of vaccines against HIV and AIDS. AVAC is committed to translating and communicating this long, complex web of activities to a wider constituency and to ensuring that the rights and interests of trial participants, eventual vaccine users and communities are fully represented and respected in the process.

To marshal and sustain public involvement in global AIDS vaccine efforts, communities need information that not only educates but also suggests how people can play an active role. And this information and mobilization must be provided within the context of a comprehensive response to the epidemic. Hence, AVAC’s new AIDS Vaccine Handbook which was published in May 2005.

This completely revamped and international edition of the original Handbook, first published in 1998, provides an overview of the key scientific, policy, social, ethical and economic challenges, and of the diverse experience gained around the world over the past two decades. The easy-to-read, lively essays are written by people involved in this work as community educators and advocates, trial staff and volunteers, scientists and researchers, policy-makers and journalists.

AVAC hopes that this new Handbook serves well as a resource and reference guide — and that it motivates people to take action!
Manufacturing microbicides

IN MARCH 2005, THE INTERNATIONAL PARTNERSHIP FOR MICROBICIDES (IPM) OPENED A NEW MANUFACTURING FACILITY IN BETHLEHEM, PENNSYLVANIA, IN THE UNITED STATES THAT WILL PRODUCE CLINICAL TRIAL MATERIALS FOR MICROBICIDE STUDIES.

The IPM Clinical Trials Material (CTM) facility is the first manufacturing facility to be built by a public/private partnership and is designed for the production of materials to be used in safety trials of microbicide candidates. It will be used by IPM and other organisations to produce materials for microbicide trials at reduced costs and greater speed.

In the past, the need to contract the production of materials to a facility that was not dedicated to microbicide manufacturing caused delays and burdened under-funded microbicide developers with high costs. IPM's state-of-the-art CTM facility was built to address these problems.

“This facility will speed the day when a microbicide will be available to help millions of women protect themselves from HIV,” said Dr Janet Darbyshire, Director of the London-based Medical Research Council's clinical trials unit. “With the creation of this facility, IPM strengthens its role as facilitator of microbicide development.”

IPM AND MICROBICIDES

IPM is a public/private partnership created to address an urgent global public health issue as quickly and efficiently as possible. The organisation’s goal is to improve the efficiency of all efforts to deliver a safe and effective microbicide for use by women in developing countries as soon as possible. In many developing countries, nearly 60% of people living with HIV and AIDS are women; in several African countries, women aged 15 to 25 are two-and-a-half times more likely to be infected than men the same age. Interrupting the HIV transmission cycle requires better HIV prevention for women and girls, because of their greater vulnerability to infection. Microbicides are one prevention option that women will be able to control.

A microbicide is a product, such as a topical gel or cream, that could be applied vaginally or contained in a slow-release vaginal ring to reduce the transmission of HIV during sexual intercourse. Microbicides come in different classes and can work in a variety of ways. Microbicides work by killing or immobilizing the virus; by forming a barrier between the virus and vaginal tissue; by boosting the vagina’s natural defences against HIV; or by preventing the virus from replicating.

ADDRESSING A BOTTLENECK

Producing drugs for trials is a complex and expensive procedure because of the need to follow the universally accepted guidelines known as Good Manufacturing Practices (GMP). The guidelines aim to systematise every aspect of manufacturing so that the concentration, formulation and other physical and chemical characteristics of each drug batch are identical. This is necessary, primarily to ensure the safety of trial participants.

The new IPM CTM facility is capable of producing two to eleven kilogram batches of topical microbicide gels, lotions and creams, also known as semi-solid formulations. These batch sizes approximately equate to 500–3,000 individual uses of product. The facility is 1100 sq. ft. with several manufacturing suites and equipment for production and packaging. The facility will be able to fill tubes or applicators, the standard method of packaging for these types of products. Production of other

“In many developing countries, nearly 60% of people living with HIV and AIDS are women; in several African countries, women aged 15 to 25 are two-and-a-half times more likely to be infected than men the same age.”
product forms, such as films, sponges or rings require specialised equipment not available at the facility. The manufacturing process involves many written standard operating procedures (SOPs) that govern the entire process, from when the first raw material enters the building until the final product is ready to be shipped to a clinical site.

Once a production need is defined, a great deal of planning is required and involves three parallel processes: production, staffing and testing. The first step is to establish a set of Master Batch records that set in stone the processes for manufacturing, filling, over-wrapping, labelling and packaging. These records undergo technical and quality assurance reviews before being finalised. A second process is to define the number and type of skilled workers needed for the different tasks. This also involves technical and quality assurance reviews to ensure that workers are adequately skilled and requires training on specific procedures involved in the manufacturing campaign. The third process is to ensure that testing of the release and ongoing stability of the drug products are in place so that if any problems arise with the material, the clinical sites can be informed and corrective action can be taken.

Although many contract manufacturing organisations exist in the United States and Europe, nearly all focus on injectable and/or tablet drug products. Many topical products are produced for cosmetic uses and do not follow the above strict guidelines for their production. This facility increases the capacity to produce clinical trial material of gel and cream microbicides for safety studies.

CLOSER TO REALITY THAN MANY PEOPLE THINK
According to a report from the Rockefeller Foundation, even a partially effective microbicide could prevent 2.5 million HIV infections over three years. Addressing a significant bottleneck in the microbicide field, the CTM facility is a resource for microbicide developers and operates under IPM’s guiding principle to get a safe and effective microbicide on the market as quickly as possible, because delays translate to the loss of hundreds of thousand of lives.

Microbicides are closer to reality than many people think. Ten microbicides are under active development in preclinical tests. Fifteen are in human clinical trials, of which five are in or moving into large-scale efficacy studies. In addition, researchers have begun to identify promising new generations of microbicides that are specifically formulated to attack HIV and are likely to prove even more effective. Scientists estimate that an effective microbicide could be available within 5–10 years, and that gradual introduction of newer and better microbicides could ultimately save a generation of women.

Dr Zeda Rosenberg
Chief Executive Officer
International Partnership for Microbicides

For further information, visit
www.ipm-microbicides.org

PILOT FILLING OPERATION OF SINGLE UNIT APPLICATORS CONTAINING VAGINAL MICROBICIDE. APPLICATORS WILL BE USED IN CLINICAL TRIALS IN AFRICA.
Dr Jocelyn Moyes of the Reproductive Health and HIV Research Unit at the University of the Witwatersrand, South Africa, gives an overview of a microbicide trial. Dr Moyes has been involved in microbicides research in Tanzania and South Africa and it has become a life passion, changing a job into a vocation.

The Reproductive Health and HIV Research Unit (RHRU) situated in Johannesburg, South Africa, is participating in a number of microbicides research projects. These include: a safety and acceptability study of ACIDFORM gel used with a diaphragm, sponsored by Contraception Research and Development (CONRAD), and a safety and tolerability study of TMC120 antiretroviral containing gel, sponsored by the International Partnership for Microbicides (IPM). Both these studies are safety phase studies and involve recruiting women who are at low risk for HIV acquisition and are designed to test the safety of the gel. Generally, safety in microbicides trials is assessed by lack of vaginal irritation.

The RHRU is about to start a large phase three (efficacy trial) which is sponsored by the Department for International Development (DFID) and is conducted through the Microbicides Development Programme (MDP). The Medical Research Council (MRC) UK is intimately involved as trial monitors, providing technical support to the 6 trial sites — in Tanzania, Uganda, Zambia, and 3 in South Africa. During this trial the RHRU will recruit 2800 women over three years.

The RHRU has a very structured and successful approach to community engagement which starts prior to the intended research. RHRU recognises, and is committed to, the importance of working in partnership with communities, to build effective partnerships in research that benefits communities and researchers. The RHRU is proud of its reputation in the communities in which it has worked since 1994.

From a pure scientific point of view, identifying appropriate communities in which to conduct microbicide clinical trials hinges on factors such as HIV incidence and other risk assessments of the community or population. However, for the trial to be successful in recruiting women and retaining these women in the trial, community engagement and participation are critical.

A feasibility study conducted over two years has been completed in a number of communities in and around Johannesburg. During this study we were able to estimate important parameters such as HIV prevalence, HIV incidence, Sexually Transmitted Infection (STI) prevalence, condom use and retention issues. Generally over the communities, HIV prevalence is estimated at 25 to 30% in the cohorts of women we have recruited and retained. Women in South Africa are disproportionately infected and affected by HIV. Results from a national survey of adolescents conducted by the RHRU showed that 1 in 4 young women were infected by HIV compared with 1 in 14 young men. Women in perceived monogamous relationships and married women are particularly at risk. Women are not in a position to negotiate condom use from a partner who is her only source of financial support. Women are often further disadvantaged by having extended families to care for; nieces and nephews left in their care by siblings who have died of AIDS. An effective, affordable microbicide would provide these women with an alternative protection method that is in their control.

It is very difficult to measure the impact of HIV on large communities in sprawling urban areas such as Soweto; however, during our community preparation work what has been striking is the desperate need to find ways to address the epidemic. It is impossible to ignore HIV living in Africa. Almost every member of staff on the study team has had close and
sometimes very personal experiences of HIV. Members of family have died of the disease, often leaving children to be cared for by the extended family. This highlights the incredible burden the epidemic is placing on family units and extended society.

COMMUNITY PREPARATION: SETTING UP FOR A SUCCESSFUL TRIAL

The RHRU has successfully engaged the support of communities in and around Johannesburg in Orange Farm, Soweto, Hillbrow, Yeoville and Alexandra. This has led to the development of a repeatable framework of community entry, engagement, participation, and research dissemination.

The framework’s approach begins with cognitive mapping — a process of walking through a community identifying landmarks, activities, social situations and characteristics of the community. This information is used to define the community in terms of the physical boundaries and socio-economic factors. In parallel, a community inventory analysis is conducted whereby all identifiable community structures are documented. This includes health care providers (traditional healers, government and private), traditional and government leadership, Community Based Organisations (CBOs), Non Governmental Organisations (NGOs), informal influential groups, educational structures and religious organisations. Representatives from all identified groups are actively engaged and invited to attend a stakeholder meeting where they are briefed on the RHRU, the anticipated research, the community framework approach and the role and election of a Community Advisory Group (CAG).

A rigorous process is followed to elect a representative, motivated and engaged CAG. The CAG are initially tasked to define their own terms of reference and operating procedures, facilitated by RHRU community experts. Thereafter standard, but flexible, monthly agendas of training, understanding of research, Good Clinical Practice, ethics, HIV, study specifics, etc. are followed over the course of a year.

RECRUITMENT

Recruitment activities during the course of the trial include primary health care (PHC) clinic-based recruitment, community-based recruitment and the use of selected media.

PHC clinic-based recruitment involves research team members presenting the research and eligibility requirements to clinic staff and women waiting in family planning or well baby queues. These sessions are usually informal and outline the basic concepts of research and some basic project information. All interested women are then invited to visit the research clinic. Community-based recruitment follows a similar approach where women are approached at group meetings or in areas where women congregate, such as shopping centres. Word of mouth referral has had a strong influence on recruitment and this form of recruitment is reinforced to participants. Word of mouth recruitment is a process of active and passive spreading of study information and benefits of participation. Participants may actively encourage friends to enrol or, by sharing their positive experience of the study, passively disseminate information.

Community-based radio has provided an exciting medium for recruitment. We have funded and run a weekly reproductive health talk show. Many topics have been covered including HIV testing, condom use, contraception, sexually transmitted infection, sexuality and detailed shows on the research process, ethics and informed consent. The show provides a phone-in option and the community response has been very enthusiastic.

THE INFORMED CONSENT PROCESS

Informed consent is essential for the protection of an individual’s autonomy. Equally important is the understanding of the requirements for participation including how often study visits are, and what tests and procedures will be conducted at each visit. The RHRU makes use of a structured approach to ensure that all women participating understand what is expected of them and what risk they are taking. The informed consent process usually starts on the potential participant’s first visit to the clinic when an informal information session is held with a group of women and a staff member. Key issues are highlighted and questions answered. This information session is usually followed by some audio or audio-visual presentation either in the form of a pre-recorded tape or a video. These media are used to again highlight important information and concepts. Following this, the participant is
given an information sheet which covers in detail all the procedures, risks, benefits and reasons why the research is so important. It is only when the participant returns to her screening appointment that she will sign the informed consent. During this visit and prior to signing the informed consent, a staff member will ask a series of open-ended questions to assess the participant’s understanding of the study and requirements for participation. This may seem a very lengthy process, but informed participation respects the participant’s autonomy and aids retention of women in the study. The RHRU is committed to a process of informed consent and as part of this process consent is reconfirmed at every visit. This is usually done verbally following explanation of the procedures for that visit. The right to withdraw at any time in a study is recognised and this is included in all informed consent discussion. There is a process for participants to voice concern. This is laid out in the informed consent and the CAG is trained to handle complaints and refer them to the study team.

WHAT IS USUALLY REQUIRED FROM PARTICIPANTS IN MICROBICIDES RESEARCH?

Although this will depend on what kind of study is being conducted, either safety or efficacy, the participant will usually be expected to attend the clinic on a monthly basis for the duration of her participation in the trial. Most studies will have two or three early study visits, usually fortnightly then moving into monthly visits. Usually clinical visits or visits that involve a genital and physical examination of some kind would occur at three-monthly intervals. The monthly visit would usually involve gel dispensing and a short interview to assess adherence and identify potential problems.

All women entering microbicide trials will need to be tested for HIV and be willing to accept their HIV results. In addition, most trials will involve three-monthly HIV testing, and sometime extended genital examination, with women receiving these results. I am still amazed that women are prepared to do this over the period of a year. A risk reduction model to pre and post-test counselling has been used at the RHRU. Most of our study protocols use parallel testing — an HIV rapid test which provides the participant with a result in 15 to 20 minutes. Positive results are confirmed by a laboratory ELISA test.

STANDARDS OF CARE AND REFERRAL OF PARTICIPANTS

All women who are tested HIV positive at screening are provided with counselling until the counsellor feels the woman can be referred, at which time she is referred to an appropriate NGO or counselling service. In addition, she will receive a medical referral for assessment of her eligibility to receive antiretroviral treatment. Women who seroconvert during the trial are offered continual support until the need for referral arises. Close contact is maintained with the referral centre and the participant to ensure that adequate care is received.

THE TRIAL EFFECT

As part of the screening process and the repeated testing during the trial for STIs, many women will be treated for symptomatic and asymptomatic STIs. In a large efficacy trial this may start to contribute to the public health management of STIs. The three-monthly HIV testing and risk reduction counselling is likely to change sexual behaviour and condom use. In preliminary analysis of the data from our feasibility study it seems that condom use, particularly with casual partners, appears to increase during the time of the study. These are benefits to a community that may not be measurable.

CONCLUSION

A great deal of commitment is required from women participating in microbicide research. The response from the community has been overwhelming; communities, and particularly women, are desperate to fight the epidemic that is disrupting the stability and freedom promised by the new democratic South Africa. During the feasibility study our social science team conducted interesting research into reasons for participation. Many of the young women participating in the study expressed a feeling of empowerment following testing for HIV. This was expressed in a feeling of being able to change their risk with the tools the study information and counselling had given them.

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Pre-exposure prophylaxis (PREP) is the idea that HIV negative people could take antiretroviral drugs to prevent rather than treat HIV. It is perhaps at once the most obvious and the most controversial new idea in HIV prevention.

THE NEED FOR PREP
There are good reasons to believe that testing PREP as a concept should be an urgent priority.

The main reasons are those that also apply to microbicides. Condoms are frequently not used even by high-risk populations; women are unable to enforce condom use by men or may be unaware they are at risk. The most frequent number of sex partners young women under 20 in South Africa with HIV have had is just one. A recent survey from Andhra Pradesh in India showed that half of men who have sex with men there had unprotected anal sex both with other men and with their wives.

PREP has additional advantages. It involves using a pill that exists right now rather than developing new compounds and methods of application. It would be more discreet and user-controlled than either a condom or a microbicide. It could be taken well in advance of any sex or even afterwards.

In addition, the efficacy of the first generation of microbicides is forecast even by the most optimistic researchers to be no more than 60%.

There is a crucial kind of sex those microbicides are not designed for — anal sex. Microbicides for rectal use pose considerably greater design, toxicity and testing challenges than vaginal ones. They are also an even less popular target for research funding. So far only a few small animal trials have tested the concept, and one acceptability trial, using a neutral gel, is about to start among gay men in Boston.

In addition, PREP could prevent transmission through needle sharing, which a microbicide could not.

One argument for testing PREP is that to do otherwise would be to disrespect the human rights of sexual and drug-injecting minorities who would get left behind if vaginal microbicide use becomes widespread.

THE RISKS OF PREP
But PREP is a confrontational idea too. Talking to most people who haven’t heard of the idea before elicits a response of discomfort: “You mean — give HIV drugs — to HIV negative people? What, all of them?”

This discomfort is at least partly rational, for several important reasons.

A preventative drug (or vaccine) has to be demonstrably much safer than one that treats a disease that would otherwise be fatal. The drug being trialled as a candidate for PREP, tenofovir, has only been licensed for HIV treatment for four years, and we know little about its potential long-term side effects.

The innovative drugs that treat HIV are too expensive to benefit the majority of people with HIV in the world and are proving to be a stretch even for developed-world health systems. How could we afford to give them to HIV negative people?

HIV positive people have difficulty taking their medication to the 90–95% level of...
adherence necessary to suppress HIV, and failing to do so creates drug-resistant HIV. Sporadic PREP use could mean that people who were already unwittingly infected might take it — potentially spreading tenofovir-resistant HIV round the world.

The introduction of highly active antiretroviral therapy (HAART) has meant that the terror of AIDS has ebbed in the developed world, and high-risk behaviour has become more frequent. If PREP (or microbicides) lead to similar ‘behavioural disinhibition’ among risk groups, they could have a neutral or even negative effect.

Given these reservations, it’s obvious that PREP is never likely to be on offer for sale over the counter as condoms are now, or as we eventually hope a successful microbicide will be. This raises the questions of who gets it and, more crucially, who decides who gets it. Would the universal stigma against HIV risk behaviour make people taking PREP a target for abuse, make them reluctant to ask for it, or serve as an excuse not to give it to them?

**Efficacy Trials**

However, while it is crucial to start preparing answers for these questions now if we are to turn PREP into a reality, we have to answer another question first. Does it work?

The answer is that we simply don’t know. The few trials of the idea mounted so far have given contradictory results.

Back in 1994, oral tenofovir completely stopped a group of monkeys from becoming infected via a single injection of HIV. However, in another study 10 years later it delayed but did not prevent infection when the virus was introduced rectally.

As a result several US-based institutes — Family Health International, the Centers for Disease Control, and the National Institutes of Health — have started trials of tenofovir as HIV prophylaxis in nine different countries — the USA and Peru (in gay men), Malawi (in ‘high risk’ men), Thailand (in injecting drug users), Botswana (young adults) and Cameroon, Nigeria, Ghana and Cambodia (‘high risk’ women including sex workers).

These nine trials between them would have involved 9,000 volunteers. This may sound a lot, but they are distributed among several risk groups (female sex workers, injecting drug users, and gay men) and none are as big as any of the phase III microbicide trials currently recruiting or about to start.

**Trial Problems**

So we need more trials. But in fact, two trials have now been stopped permanently, another is currently not recruiting more volunteers (though it is following up those already recruited), and another has gone ahead in the teeth of bitter activist opposition.

The first time the wider world became aware of trouble was when Cambodian sex workers, supported by the French activist group ACT-UP, demonstrated against the Cambodian trial at the Bangkok World AIDS Conference last July.

- On 12 August 2004, after an intervention from the Cambodian Prime Minister, the trial was stopped.
- On 31 January 2005, a community meeting between Thai drug users and the researchers broke up after protests that people were being coerced to participate and that tenofovir was being offered as a second-best to needle exchange.
- On 3 February this year, after a French TV documentary questioning the ethics of the trial in Cameroon and demonstrations by ACT-UP Paris outside the Cameroon embassy, this trial was suspended, with the country’s health minister saying he was going to investigate the trial. On 22 February participant follow-up resumed, but no further recruitment.
- On 16 March Family Health International itself cancelled the Nigeria trial (leaving only the Malawi and Ghana arms of the trial intact) saying that local researchers had failed to meet “necessary scientific standards”.

"Would the universal stigma against HIV risk behaviour make people taking PREP a target for abuse, make them reluctant to ask for it, or serve as an excuse not to give it to them?"
On 30 March, the Centers for Disease Control announced that the Botswana and Bangkok trial was ‘to start soon’.

In April, the trial among drug users in Bangkok began recruiting. The small US trial in gay men (only 200 volunteers apiece in Atlanta and San Francisco) has been recruiting for some time. The Peru trial is yet to start.

LESSONS LEARNED
What happened here? Among accusations and counter-accusations, a number of issues stand out.

Although trial recruiters made great efforts to consult with ‘the community’, there is a difference between consulting with well-informed activists in NGOs and ensuring ethical treatment of actual trial participants. Nigerian activist Rolake Nwagwu said: “In Nigeria, sex work is illegal. These women have no human rights and are not organised, so I don’t see how sex workers will be involved in any meaningful way.”

In Cambodia, there was a political dimension to this. US government policies had resulted in the withdrawal of USAID funding from local sex worker support groups in 2003, who were then not surprisingly disinclined to co-operate when asked to help by the same people in 2004.

Stories were widespread about local recruiters misinforming participants in order to get them on the trials. A Cameroon participant and several Cambodian participants were quoted as saying they thought that tenofovir was a ‘vaccine’ which would mean they ‘no longer had to use condoms’. Karyn Kaplan of the Thai drug Users’ Network said: “The trial looked beautiful on paper, but there has been a lot of coercion by local staff who implemented it.”

Whether these accounts are true or not they represent a failure to communicate the potential benefits and risks of the trials in a clear way. Recruiters have failed to correct an impression that PREP is all about enforcing a biomedical prevention tool for HIV negative people in order to make profits for tenofovir’s manufacturers Gilead. (In fact Gilead have said they will donate tenofovir for free to the studies.)

One complexity of a prevention trial is that in order to demonstrate the effectiveness of a new intervention (such as PREP) older interventions (such as condoms) have to ‘fail’, and yet ethically researchers have to offer safer-sex advice and condoms. This can be seen as a conflict of interest on the part of researchers, who need to make it clear that they do not want participants to take risks, they just have evidence that risks get taken. (In fact, risky behaviour tends to fall during prevention studies.)

It can also be seen as a distraction from campaigning for prevention measures that communities do want. In the case of the Bangkok trial, drug user activists saw tenofovir as a politically acceptable alternative to their own preferred prevention intervention, needle exchange. The ethical question then becomes: will more lives be saved by holding out for an intervention we know works, or will more be saved by accepting a trial of one of unknown effectiveness?

Activists in the four countries where trials have been suspended expressed frank disbelief that tenofovir would ever be made available to the local population. The Womyn’s Agenda for Change support organisation in Cambodia said: “Obviously, there is a benefit to anyone whom tenofovir prevents from HIV infection, if it proves able to do that. But it is not likely that many Cambodians would be able to use it . . . it seems clear that tenofovir is being tested mainly in poor countries because that is cheaper than doing it in rich countries.”

HIV prevention trials in general have focused attention on the issue of researchers’ responsibility to care for people who are infected with HIV or suffer drug side effects during the trial. There is a complex ethical debate around whether the standard of care offered for people infected with HIV should be the best possible, only that on offer in the host country, or something in between. There is also the issue of whether researchers have the ability or power to offer anti-retroviral treatment that might not be needed till 10 years after the trial ends.

It is in the nature of trials that more people can be harmed than helped. The classic example of this in a prevention trial was the
COL-1492 trial of the spermicide nonoxynol-9 in West Africa. This showed that using N-9, which killed HIV in the test tube, in fact doubled the rate of HIV transmission in frequent users because it disrupted the vaginal epithelium. While this trial proved that you could put on a large, double-blinded placebo-controlled trial for a microbicide, it ended up causing more women to become HIV positive than otherwise.

Given the ethical dilemmas involved in conducting PREP trials in the developing world, it is legitimate to ask why so far PREP research in the developed world has been restricted to a small US trial in gay men. PREP, if it works, is more likely to be available, at least from the start, to high-risk populations in rich countries and we are the people who should be testing the concept. Talks are under way about a possible trial among gay men in Europe and Australia, but these are at a very early stage.

THE SEATTLE CONSULTATION
A meeting between stakeholders involved in every current trial took place on 19–20 May in Seattle, convened by the International AIDS Society.

Participants included the Bill and Melinda Gates Foundation, which has sponsored the trials, the CDC, the NIH, and over 50 stakeholders representing participants in Botswana, Cameroon, Ghana, Malawi and Thailand.

The meeting’s recommendations took note of a lot of the above points. Many country-specific recommendations were made, but broad ones that applied to all the trials included:

- An immediate review to ensure that the level of counselling participants receive is significantly improved.
- Establish national guidelines to inform and improve civil society engagement — efforts so far were acknowledged to have been “at times ill-informed and inconsistent”.
- Ensure access to male and female condoms.
- Ensure that there are proper support mechanisms for individuals screened for enrolment in the trials who are found to be HIV positive.
- Clear mechanisms for feedback and conflict resolution at trial sites.

CONCLUSION
Generally, the PREP trials have happened historically at a time when a stronger activist movement is starting to develop in the host countries, which are wary of further trials that provide no benefit to local people.

One example given was the AIDSVAX gp120 HIV vaccine trial in Thailand, which was widely criticised as pointless at the time by researchers as the vaccine had already proven ineffective. The Thai Drug Users’ Network’s comment was “At the time we weren’t organised enough to resist the AIDSVAX trial. Now we are.”

Researchers involved in all trials of new prevention technologies should take account of the above concerns and establish maximum clarity of communication with trial participants and their communities, without overstating the benefits or fluffing the risks of a trial.

If they don’t, they could make prevention technology trials far more difficult to put on and delay or even prevent implementation of vitally needed new weapons against HIV.

Gus Cairns

An excellent summary of the issues involved in the PREP trials has been written by the AIDS Vaccine Advocacy Coalition. It can be found at http://avac.org/pdf/tenofovir.pdf
FC female condom is an important technology that has a vital role to play in sexual and reproductive health programmes around the world. It provides women and men with an additional choice to prevent both unintended pregnancies and the transmission of STIs, including HIV and AIDS. It is the only new prevention technology invented since the advent of the HIV pandemic and the only female initiated device currently available. To date FC female condom has been introduced in more than 100 countries throughout the world and extensive research has consistently demonstrated acceptability and demand for the device. The addition of FC female condom to a country’s contraceptive mix is not intended to replace the male condom but to increase the number of protected sex acts. This need becomes even more critical when women are not in a position to negotiate the use of a male condom due to personal and cultural constraints.

Female-initiated prevention methods offer the opportunity to address both the immediate need of prevention and, for the longer term, initiating change in the underlying issues of empowering women and promoting gender equality in sexual and reproductive health. The availability of FC female condom through national AIDS prevention programmes and reproductive health services leads to increased access to female-initiated prevention technologies and has a positive impact on overall condom use. As a product, FC expands the existing basket of contraceptive and prevention choices available for men, women and young people. Women have been hit particularly hard by the HIV and AIDS pandemic; male-to-female transmission is estimated to be twice as high as female-to-male. More alarmingly, the infection rate data shows most sexually transmitted HIV infections in females occur either inside marriage or in relationships that women believe to be monogamous (UNAIDS). In light of these statistics it is difficult to understand why the female condom is not available alongside male condoms in every government HIV and AIDS prevention policy and reproductive health programme around the world. It is not a magic bullet but a product which evidence has repeatedly demonstrated does increase the number of protected sexual acts and can and does save a significant number of lives.

**CHALLENGES OF INTRODUCING THE FEMALE CONDOM**

As with all new technologies there have been challenges and obstacles to FC introduction but what factors have prevented its widespread integration and use? Is it the product itself, its appearance? The female condom as a device has many advantages: it is made of polyurethane which is stronger than latex, odourless and causes few, if any, allergic reactions. Additionally, unlike the male condom it can be used with both oil and water based lubricants. Polyurethane conducts heat, which can make sexual intercourse feel more natural. It can be inserted up to 8 hours before intercourse, is not dependent on male erection and does not require immediate withdrawal after ejaculation. A recent research paper based on studies of pilot programmes in the field concluded that female condoms are acceptable to a wide range of women including those at most risk of contracting HIV providing they are introduced within carefully designed programmes. This is confirmed in findings of a 1997 review by WHO of 41 acceptability studies indicated that 50–70% of women and men found the female condom acceptable.

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1 The Female Health Company is the sole manufacturer of FC female condom and all studies and information contained in this article are for FC female condom only. Other female condom products are available but none of these have US FDA and European Kite mark approval for use as either contraceptive or STI prevention methods.
studies, conducted in a diverse range of cultures and settings which indicated that 50–70% of women and men found the female condom acceptable. Given the vast proliferation of acceptability studies that have been implemented and the similar results that have been found, further studies in this area are unlikely to produce any surprises so it seems acceptability is not the issue.

Is cost the issue? The relatively high cost of the female condom is widely cited as the reason which inhibits its widespread distribution. The counter-argument to this is that in terms of cost-effectiveness the female condom is not expensive if you rate it against the cost of anti-retroviral treatment and costs associated with STI treatment. The riposte is that for the price of one female condom four to six male condoms can be purchased that will also protect against HIV infection. However, the female condom is not attempting to substitute the male condom. It is aiming to increase the number of people protected overall. There can be an extra 100 male condoms available but if a man will not wear one and a woman cannot negotiate its use, it will make no difference. By providing a choice of male and female condoms, more sex acts will be protected.

Is it because we haven’t learnt effective lessons for programming? Not so. Factors common to programmes which have successfully launched and maintained FC female condom distribution have been identified and integrated into new planning and programming initiatives. These include: a multi-sectoral collaboration for introducing, promoting and sustaining FC programmes; the integration of female condoms into existing policy aims and activities such as reproductive health programmes or HIV and AIDS prevention policy or both; a comprehensive cascade training approach; a wide range of distribution outlets; an effective monitoring and evaluation system; and crucially involving men in all aspects of FC programming.

Thus we do have the knowledge and experience to demonstrate effective and efficient female condom use but how do we convey the urgent need, indeed the rights of women to have access to the only barrier method available to them for protection against STIs, HIV and AIDS? Donors and governments have been provided with the evidence of female condom efficacy, acceptability and appropriateness. A programme of assistance for the integration of the female condom into RH and HIV and AIDS prevention programmes is available. Yet, what is the missing link? What is that elusive piece of research which will convince donors and governments alike of the need to make female condoms available alongside male condoms around the world?

Esther Bayliss
Operations Manager, The Female Health Company

2 The Female Health Foundation (FHF) offers free programming assistance for all agencies involved in female condom programmes. FHF is currently developing an intervention toolkit to assist programme implementers at all stages of female condom programming.

*By providing a choice of male and female condoms, more sex acts will be protected.*

*“It is not a magic bullet but a product which evidence has repeatedly demonstrated does increase the number of protected sexual acts and can and does save a significant number of lives.”*
The male condom has been around since Egyptian times when it was used to protect against such diseases as syphilis.

Since then history has seen condoms produced in a variety of materials including oiled paper, fish bladders, animal gut, leather and even tortoiseshell, which was favoured by the Japanese.

Today, though, condoms have come a long way.

Since the onset of AIDS in the 1980s, condoms have been at the forefront of the safer sex message — and remain the only effective barrier against HIV and AIDS, other sexually transmitted infections and unplanned pregnancies.

Durex is an active advocate of the safer sex message. Each year we invest time, resources and money into helping to raise awareness of the fact that condoms are our best means of combating such ferocious and life changing sexually transmitted infections — including HIV, syphilis, chlamydia and trichomoniasis.

This involves working with politicians, healthcare providers, opinion formers and of course the public directly. In Brazil, for example, Durex is actively involved in Program H — a project which involves working with young men in the favelas (shanty towns) to promote the safer sex message with the help of rap artists and its own condom — Hora H, which translates to “in the heat of the moment”.

But making people aware of the need to use a condom to protect their health is only half the battle as far as we are concerned.

It is our belief that if we can make condoms that are easy, effective and exciting to use then we can prove to people that safer sex can be better sex.

This dedication has led Durex to the forefront of condom innovation. The company has an active programme of contact with universities and research establishments and invests in excess of £12 million in research and development (R&D) each year.

For example, in response to consumer insight which indicated condoms can be difficult to put on and uncomfortable, Durex carried out a scientific penis size survey of 3,000 men and used the research to develop the first major shape change in condoms for some considerable time. This means that the majority of the Durex range of condoms are now ‘easy on’, allowing them to be easier and quicker to put on and more comfortable to wear.

Durex also produced the first benzocaine condom, Performa, and the first commercial polyurethane condom for men, Avanti. Over the past few years we have experimented with every sort of size, shape, colour and material in our quest to make condoms the most effective, easy to use and exciting method of contraception.

“It is our belief that if we can make condoms that are easy, effective and exciting to use then we can prove to people that safer sex can be better sex.”
In addition to this, we have broadened our product range to include pleasure enhancing lubricants and personal massagers which we are selling online and in the UK through selected stores — all in a quest to make safer sex better sex.

All this research, combined with increasing condom sales and a more liberal attitude to sex lives, all convince us that not only are condoms here to stay but they will remain the most effective weapon in the fight against HIV and AIDS.

Last year’s Global Sex Survey, which was carried out by Durex in 41 countries, found that 55% of people in the UK were more worried about HIV and AIDS than any other sexually transmitted infections or unplanned pregnancies. It also showed Britain’s preferred method of contraception to be the condom.

While there is a lot of research going on into the development of microbicides and vaccines, many companies remain at their first stage of clinical studies. The way I see it is microbicides will be a supplement to a condom and not ever something that will replace it — and therefore it is important that we work closely with companies that are working towards their development.

Whilst Durex is not in a position to disclose commercially sensitive information about the future development of condoms and other sexual enhancement products, we are consistently looking at new innovations including different condom designs and new pleasure enhancing features. Recent additions have included the Pleasuremax condom which includes ribs and dots on both sides for the benefit of both sexes and Play Tingle — a condom designed to create tingling sensations for both partners.

Our commitment to product development and innovation helps us target not only established condom users, but new and lapsed ones too. We feel it’s an investment well worth making to help win the fight against HIV and AIDS.

“All this research, combined with increasing condom sales and a more liberal attitude to sex lives, all convince us that not only are condoms here to stay but they will remain the most effective weapon in the fight against HIV and AIDS.”

Suren Solanki
Head of Innovation and Development for Durex

For further information, visit www.durex.com
Sperm washing — a way of conceiving safely

DR CAROLE GILLING-SMITH AND SISTER REBECCA WOOD OF CHELSEA AND WESTMINSTER HOSPITAL'S ASSISTED CONCEPTION UNIT EXPLAIN HOW SPERM WASHING IS HELPING COUPLES AFFECTED BY HIV TO HAVE CHILDREN.

INTRODUCTION
The discovery, over ten years ago, that the progression of HIV could be effectively halted through the use of antiretroviral medicine has transformed the lives of those infected with the virus. Now increasing numbers of infected men and women are asking the medical profession to help them have children safely. In the case of positive men, concern has always been raised over the transmission of virus in semen to his uninfected partner. Sperm washing is a technique which was pioneered in the late 1980s by Dr Enrico Semprini in Milan as a method of reducing the risk of transmitting virus in semen. The technique is based on the observation that sperm itself does not have receptors for HIV and that in semen HIV is only found in the seminal fluid or non-sperm cells. During sperm washing, sperm is separated from seminal fluid and non-sperm cells by a centrifugation process through a density gradient. The clean sperm pellet is then mixed with a solution resembling seminal fluid and allowed to ‘swim-up’ to the surface. As a final test to check the method has effectively removed HIV from the sperm, a small sample of the washed sperm is tested for HIV. If no HIV is detected then it can be used to inseminate the female partner at the fertile time of the month. The method should however only be regarded as a ‘risk-reduction’ as opposed to ‘risk-free’ method since HIV could still be present in the washed sample but be below the detection limit of the HIV test used.

WHO CAN BENEFIT FROM SPERM WASHING?
Sperm washing can be an effective risk-reduction treatment for all HIV discordant couples trying to conceive where the male partner is infected and the female partner is negative. It is also advisable in couples who are both positive as each may be carrying variant strains of HIV and be on different medication. If these couples have unprotected intercourse, there is a small possibility of the female partner becoming infected with a variant ‘mutated’ strain of HIV which could also be passed on to the child and be resistant to conventional antiretroviral medication.

HOW CAN ‘WASHED SPERM’ BE USED TO TREAT COUPLES?
Many couples in whom the man is HIV positive and his female partner negative (referred to as HIV discordant couples) have never tested their fertility before. They are in effect ‘voluntarily infertile’ as they have elected to have protected intercourse at all times. Before couples embark on any form of treatment using washed sperm it is essential that their fertility is tested so that the right treatment with washed sperm is chosen. As a simple test of fertility, the woman is advised to have a pelvic ultrasound scan to check her ovaries and uterus, usually in the first week after her period, along with a blood test to check her follicle-stimulating hormone (FSH). A further blood test seven days before her expected period is done to check that she is ovulating. A simple X-ray or ultrasound test such as a hysterosalpingogram or HyCoSy is also recommended to check that her tubes are open. The man is asked to provide a sample of ejaculated sperm which is analysed carefully in the laboratory for sperm numbers and quality. If these tests show no infertility factors in either the man or woman, the couple can have relatively straightforward treatment in the form of intrauterine insemination of the man’s washed sperm at the fertile time of the woman’s cycle. This fertile time is monitored using serial ultrasound scans of the pelvis from the eighth or ninth day after the onset of the period. The scan shows the development of a follicle (sac of fluid containing the egg) and when this reaches around 18 mm in size the woman...
is given a single injection of a hormone to release the egg. During insemination, a tiny rubber tubing (called a catheter) is passed through the neck of the uterus and the washed tested sperm is gently injected. The procedure is painless and takes about five to ten minutes. When fertility issues are identified, sperm washing is combined with specific treatments, e.g. fertility drugs if the woman is not ovulating, *in vitro* fertilisation (IVF) when her tubes are blocked and intracytoplasmic sperm injection (ICSI) when the sperm quantity and quality is poor.

**HOW SUCCESSFUL IS SPERM WASHING TREATMENT?**
Since the technique was first described by Dr Semprini, over 5,000 treatment cycles using correctly washed sperm have been carried out in specialised centres in Europe and America. This has led to over 500 healthy children being born with no reports of HIV infection in either the woman or her child. There is only one case report in the world literature of a woman becoming infected through the insemination of washed sperm. In this case the sperm was not correctly processed and certainly not tested for HIV before being used. The important point here is that results to date show that sperm washing is a far safer method of conceiving than timed unprotected intercourse. Even when the man has an undetectable viral load, HIV can be present in semen and transmitted during intercourse.

The Chelsea and Westminster Hospital Assisted Conception Unit opened its Sperm Washing Programme in 1999. Since then they have treated 110 couples and performed over 300 cycles of treatment. The live birth rate per cycle attempted for intrauterine insemination, which is used when couples have either mild or no fertility issues, is 11%. This is very similar to the success rate for insemination of donor sperm. The IVF live birth rate is 32% which is similar to that achieved in IVF cycles where sperm washing is not required. To date, 27 children have been born and 14 pregnancies are still ongoing. As a rough guide to success rates, one in three couples coming to us for sperm washing treatment have had a successful outcome. The twin pregnancy rate is very low as the clinic is mindful of the risks and stresses of multiple births when one partner has a chronic disease and fertility drugs are only used if fertility is compromised.

**IS PRE-CONCEPTUAL COUNSELLING NECESSARY?**
All couples planning to start sperm washing treatment are advised to attend a counselling session together, and individually if they wish. This gives them the opportunity to discuss any issues they may have, understand the nature and risks of sperm washing, establish coping mechanisms in the event of the treatment failing or the female partner becoming infected as a result of treatment (very low probability of this happening). Counselling is also important in identifying whether the couple have really taken on board the responsibility of parenting when one partner is HIV positive and the consequences of their actions should the infected partner become ill or die. The Chelsea and Westminster has a dedicated counsellor, experienced in HIV and fertility, who runs a clinic on a weekly basis. Couples are also given the opportunity to attend counselling sessions during and after treatment if they wish to.

**ARE ANY OTHER TESTS NEEDED BEFORE STARTING TREATMENT?**
Both partners should have a full sexual health screen, including genital swabs for sexually transmitted infections, and a screen for hepatitis B and C. The female partner should have an up-to-date HIV test. We do treat men who are co-infected with hepatitis C as the sperm washing process also removes hepatitis C. However, if a man is on treatment for hepatitis C, the course of medication must be completed before he can produce sperm which is safe to use for conception.

**CAN PATIENTS BE REFUSED SPERM WASHING TREATMENT?**
The programme at the Chelsea and Westminster Hospital was established in 1999. Criteria for entry onto the programme were defined by a panel of experts and reviewed by the hospital’s ethics committee. Treatment is only offered to couples in a stable, monogamous relationship of at least one year’s duration. Couples must practise protected intercourse for at least six months before receiving treatment and neither should be abusing drugs or be involved in any other practice which might be harmful to the future child. Previous IV drug abuse is not a reason for being refused treatment, provided the problem has been addressed. The health of the infected partner is also taken into consideration. He should have stable disease with a low viral load and CD4 count greater than 200 copies per ml. In a few cases patients have been advised to start antiretroviral therapy before embarking on treatment to reduce their viral load and improve their CD4 count. There are very few instances when couples are turned away due
to concerns about the welfare of any child born through treatment. Any such cases will have been reviewed at a multidisciplinary team meeting and usually referred to the hospital’s ethics committee.

WHAT WILL TREATMENT COST?
The cost of sperm washing treatment at the Chelsea and Westminster Hospital depends largely on whether additional fertility treatment is required. All couples are encouraged to have a sample of sperm washed and frozen to be used as back-up if the sample used on the day of treatment fails to test HIV negative after washing (this happens in about 5% of cases). The cost for washing a sample of sperm and freezing it is £850. The cost of a single cycle of intrauterine insemination and sperm washing is £1,250. The cost of sperm washing IVF cycle is £3,080 and for a sperm washing ICSI cycle is £3,590.

WILL THE NHS PAY FOR SPERM WASHING?
The Chelsea and Westminster have had increasing success in securing funding for patients over the last 18 months. Both the NICE infertility guidelines published in 2004, and the British HIV Association Guidelines for the prevention of mother to child transmission of HIV to be published this month, have recommended sperm washing in HIV discordant couples trying to conceive as a method of reducing heterosexual viral transmission risk. Usually the HIV physician will write to the patient’s Primary Care Trust (PCT) to request funding and, if necessary, our centre will write to confirm that the couple fulfil the necessary criteria for funding. Most PCTs willing to fund will offer up to three cycles of sperm washing with intrauterine insemination or two cycles of either IVF or ICSI with sperm washing. They usually also fund the consultation, the necessary investigations and the cost of freezing a washed sample prior to starting treatment.

HOW CAN COUPLES GET ONTO A SPERM WASHING PROGRAMME?
Very few fertility centres in the UK have the necessary laboratory facilities to carry out sperm washing. The Chelsea and Westminster Assisted Conception Unit has a specialised laboratory for the treatment of patients with blood borne viral illnesses and is the only unit in the UK with a dedicated sperm washing programme for HIV discordant couples. Patients are referred here from all over the UK and abroad by their HIV physicians, GPs or the female partner’s Gynaecologist.

Once a referral is received, Sister Rebecca Wood, the centre’s sperm washing co-ordinator will send the couple an information pack on the programme and a checklist of investigations that are required before starting treatment (these are the fertility screen and sexual health screen). All these investigations, apart from the semen analysis, can be done locally; the fertility screen is organised by the woman’s GP or Gynaecologist and the sexual health screen is done by the HIV physician. The next step is a single visit to the centre for an appointment with the counsellor, an appointment with the doctor to review the investigations and make a plan for treatment and a consultation with Rebecca to finalise the treatment plan and complete a consent form to start treatment. Often the male partner will provide a semen analysis on the same day to minimise the number of unnecessary trips to the centre.

Treatment requires careful ultrasound monitoring of the woman’s ovaries and this can usually be organised in the local fertility clinic and the results faxed over to the Chelsea and Westminster. In this way many patients make only two or three trips to London for their treatment.

Carole Gilling-Smith
Consultant Gynaecologist and Director of the Assisted Conception Unit, Chelsea and Westminster Hospital

Sister Rebecca Wood
Junior Sister and Infectious Diseases Co-ordinator, Assisted Conception Unit, Chelsea and Westminster Hospital

For further information please contact Sister Rebecca Wood on 020 8746 8585 or e-mail rebecca.wood@chelwest.nhs.uk

LEFT: EMBRYOLOGIST AT THE ASSISTED CONCEPTION UNIT EXAMINES SPERM SAMPLES.
SPERM WASHING — A PERSONAL PERSPECTIVE
Caroline Mason

In June 2003 we decided that we wanted to have a child and chose sperm washing as the way we were going to attempt this. We have met many sero-discordant couples who have had children via natural conception and have also read the recent evidence concerning undetectable viral loads and conception and safety. However, my husband Mick was adamant that he did not want to take what he perceived as unnecessary risks. It took us a while to get our heads around the idea but by December of that year Mick had been tested, everything was fine with his fertility and we had been referred to the Chelsea and Westminster Hospital for a consultation.

BEGINNING THE PROCESS
It felt like forever before the appointment finally came through for March 2004. The first consultation gave us an overview of the procedure and we came away with a long list of fertility and STI tests that we were required to have. Thankfully, our local Women’s Hospital agreed to carry out the tests for me and also to provide follicle tracking scans as and when our treatment cycles commenced.

I had blood tests, a transvaginal scan and a hysterosalpingogram X-ray to check that my fallopian tubes were “filling and spilling” as they should be. None of the tests were particularly unpleasant and the hospital staff were really considerate and caring. However, this was one of the worst times for me — I was 37, and really convinced that I would have fertility problems. I suppose I was also just waiting for something to prevent us from trying for a baby. We also had to have the full STI screening which included HIV, hepatitis, chlamydia, syphilis, etc.

STARTING TREATMENT
In July we went back to the Chelsea and Westminster Hospital and, thankfully, the consultant advised us that everything was fine and we could start the treatment. So in August 2004 we had our first treatment. Mick had to give a sample at 8 o’clock in the morning, so we left the house at 5 am, the traffic was terrible on the M4 and we were getting really worried that we would miss the appointment time. We arrived with about 5 minutes to spare. Then we had an agonising wait until 4 pm, when we could go back to the hospital and if the sample was okay then we could have the treatment.

When we got back at 4 pm everything was fine and so we were ready for our first treatment. I couldn’t believe it — all these months I had been waiting for something to go wrong and finally we were going to start the treatment. I had to have a full bladder as it helps to straighten the uterus and makes it easier for the catheter to pass through. The procedure was uncomfortable but not painful, the speculum being the worst part of it. The staff were great and explained everything to us and had a really caring attitude. It was such a relief to have actually got to this point and know exactly what happens, how it feels etc.

HOPING
It is now May 2005, we have had 6 attempts, 4 intrauterine insemination (IUI) with natural cycles and 2 with IUI and Clomid which is a hormone drug designed to produce “super ovulation”. In June we will hopefully go for our seventh attempt. There are things that can get in the way: for example in May we missed a go because I ovulated on a Saturday and could not go to the hospital until the Monday, and there is always the chance that there will be a problem with the sample. We have also found that at times we have needed a break, so we have taken a month off as a way of recharging ourselves.

The experience has been a continual swing of emotions from hope to hopelessness and exhilaration to despair but I try not to focus on it too much. I keep busy at work and home. The worst time is the two week wait after the procedure to find out if I am pregnant, there is always that hope that it has worked, I start to imagine how fantastic it will be when I find out I am pregnant, and it is hard not to imagine what the baby will be like and what we will be like as parents. Obviously, it is a huge disappointment when I am not pregnant, but it is also a sense of relief that the unbearable 2 week wait is over and we know what we are dealing with.

I always get really fed up that I have to go back to my local hospital for the 3 follicle tracking scans, and then do the ovulation tests and then rush off down to London for the treatment. We have had some great days out in London but it is really hard to enjoy things when you are wondering all the time if Mick’s sample will be OK and HIV free.

I have recently started having acupuncture as I read an article that claimed it could improve chances of conception when having fertility treatment. If nothing else it has made me feel a lot less stressed and happier which can’t be bad and is all good for trying to conceive.

Despite all of the upset and disappointment and the cost of the scans and the sperm washing IUI, it has been a good experience. I am not pregnant yet, but have a firm belief that I will get pregnant. We may have to consider IVF as a next step if I don’t get pregnant in June but for us it is just having the choice that is important. The choice to try and have a child if we want to. It feels that the impact of HIV on our lives has been minimised in some way because we have been given back a choice that when we met 16 years ago we didn’t think was possible.
Dr Barry Peters
Barry is Senior Lecturer and Head of the Academic Unit of HIV/STDs at Guys St Thomas’ site of Kings College London, and a member of NAT’s Board of Trustees.

An HIV vaccine is not a myth: under controlled conditions animals have been protected from HIV infection by prototype vaccines. The difficulty is in reproducing these conditions safely in the more complex world outside the laboratory. Through an IAVI sponsored early phase HIV vaccine trial my London unit is currently doing with Nairobi, Kenya, I have a window on this complex world. There are promising aspects — healthy volunteers are very willing to participate in studies, and laboratories from all round the world are collaborating in developing the technology to assess the immune response. Barriers to an HIV vaccine remain, however. We still do not know what immune response is required for an effective vaccine, so have to rely on expensive trials in man to tell us if we have a protective vaccine. There are complex ethical issues; e.g. the possibility of inducing a positive HIV antibody test in someone who is not infected must not be allowed to disadvantage these individuals. And we must begin to prepare now for the challenges a successful HIV vaccine will bring — not least the need to ensure widespread production and access.

So let us dispel a myth — an HIV vaccine is possible. And there are few more pressing needs for global health, and social and economic stability. But to achieve an HIV vaccine sooner rather than later, will require much more realistic funding — well above the grossly inadequate levels allocated currently.

As a Trustee to NAT, I support them in presenting well-researched arguments for appropriate funding for AIDS vaccine research. Grants from non-governmental organisations such as the Gates Foundation, are vital catalysts to AIDS vaccine development. But they can never be a substitute for the resources that need to be allocated by the developed nations.

Caroline Haworth
Caroline is Director of International Programmes at Interact Worldwide. Interact Worldwide’s mission is to build support for and implement programmes which enable marginalised people to fulfil their rights to sexual and reproductive health.

The development of new prevention technologies (NPTs): vaccines, microbicides, pre and post-exposure prophylaxis, will mean increased freedom, choice and personal control for all of us over our sexual and reproductive health and well-being. That’s important for everybody.

However, I also work in developing countries with some of the most vulnerable people in the world; many of whom are stigmatised by their families, communities, judiciaries, religious leaders and governments. People who are very poor; women and girls for whom sex and protection are neither consensual nor negotiable, even within marriage; males and females who have experienced rape and gender-based violence, many of whom are also very young; jail inmates; males who have sex with males; sex workers and intravenous drug users, for example.

For these people NPTs offer the potential to exercise their right to health, often for the first time. NPTs will, in this sense, literally change the world. But development of these technologies does not ensure equitable access to them. Our job is to work together to overcome impediments to access — such as lack of investment and global political will, protectionism by the Pharma industries, conservative religious doctrine, and the machinations of neo conservatism as currently employed by the Bush administration.
Fiona Pettitt
Fiona is Advocacy and Representation Advisor at ICW, the International Community of Women Living with HIV/AIDS

ICW is the only global network of Women Living with HIV/AIDS. We are a network of activists, all of us HIV positive, seeking to raise public awareness of the issues surrounding women and HIV around the world, and to change policies and practices which fuel and fan the pandemic. ICW has a membership of around 5,000 HIV positive women from over 130 countries, and through our members, links with many more HIV positive women.

How will new prevention technologies affect the lives of ICW members and other HIV positive women? That will depend very much on whether or not they are developed to benefit HIV positive women and if they are available and affordable for all HIV positive women all over the world.

Their future potential is exciting: microbicides will provide a tool which will enable us to protect our sexual health and that of our partners; therapeutic vaccines will improve our health. We want NPTs that will impact positively on our lives and we want to be involved in their research and development so that we can ensure they are appropriate to our needs.

Julian Meldrum
Julian is a freelance writer, editor and project consultant. He has 20 years' experience in the voluntary sector responding to HIV-related issues

New prevention technologies have to be about expanding the options that people have, for protecting themselves and others from HIV. The effort has to be about exploring all avenues for harm reduction. I don't believe there's ever going to be a single, universal solution to the problem, though a first rate vaccine would be the greatest prize if it can be achieved. The epidemic is objectively going from bad to worse in terms of the number of people living with the virus, both in the UK and globally. Yet the perception of a threat, even among people who are objectively at high risk, continues to decline as people live longer with the virus and progress from one treatment to another. The effort to develop these new options is one of the few ways in which attention can be kept focused on the need to act against HIV. Everything needs exploring, vaccines and microbicides of course, but also including a pipeline of drugs for prevention — of which tenofovir should only be seen as the prototype, including new vaccines against other sexually transmitted infections, and possibly the direct induction of anti-HIV antibodies. We need new and better approaches to TB and malaria and other conditions too. This will take a lot of work to explain to individuals and communities and will involve very difficult judgements to weigh up risks and benefits. It won't be easy, but I don't see any other way to bring these epidemics under control.

Rhon Reynolds
Rhon is Senior Policy Officer and Deputy Chief Executive of the African HIV Policy Network (AHPN)

Getting African communities involved in policy and lobbying for new prevention options is key to the successful delivery of an effective microbicides in the UK. African communities need to be at the forefront of demanding new prevention options because it is only when we engage African men and women that we will start to understand if these products are going to be used, how they will be used, whether they will be acceptable, and just what a difference they might make in people's lives.

African communities deserve new options, and part of our problem is convincing ourselves that we deserve to have new options, new choices. Condom use is difficult at times, particularly for women — since they have to get their partner's consent to put one on! Having something that women can use and control is a huge step in the right direction towards us reducing some of the health inequalities that see more African women diagnosed with HIV than men in the UK.

The main barrier to African community involvement is the lack of information. The capacity of understanding in local communities is often underestimated. In addition to the near to distant prospect of an available microbicide, engaging communities in advocacy activities may seem insurmountable. As such the AHPN is facilitating an African Microbicides Working Group, to inform the work of the UK Campaign on Microbicides and to raise awareness within African communities about the legal, ethical and human rights issues related to the development and delivery of microbicides.
All publications and resources are available for download on the NAT website. Please check the web site for details of other forthcoming publications and events.

**POSITIVE PEOPLE’S INVOLVEMENT PROJECT**
NAT is currently engaged in a Positive People’s Involvement (PPI) Project, funded by the Big Lottery Fund, which aims to enable people living with HIV to influence and shape health and social care services at a local level. More information about the project can be found on the PPI section of NAT’s web site. Recent outputs include:

- **Involving people living with HIV**
  Regional seminars were held in Bristol, Leicester, London and Newcastle in 2004 to identify the experiences of people living with HIV, what their needs were, and any gaps in their skills and knowledge. Contact NAT or visit the web site for a copy of *Involving people living with HIV*, the report from these seminars. Reports from each regional seminar are also available on request.

- **Web feasibility study**
  NAT carried out a feasibility study to investigate how Web technology can be best used to encourage, promote and support positive people’s involvement. The study will be used to further develop the proposal for a ‘one stop’ HIV web site in the UK. Contact NAT or visit the web site for a copy of the *Web feasibility study report*.

- **Changing Tomorrow**
  A UK conference of people living with HIV was held in September 2004. NAT worked with partner organisations to enable people with HIV to develop their skills in managing their own condition and influence health and social care providers. Contact NAT or visit the web site for a copy of the conference report.

- **What impact can an HIV conference have on the lives of people living with HIV?**
  Research by Babbs Evans, National AIDS Trust, on the effects of the 2004 Changing Tomorrow conference of people living with HIV and AIDS. Published in *HIV Medicine*, May 2005.

**CRIMINALISATION**
A revised version of NAT’s paper on the criminalisation of HIV transmission has been produced. It includes information for HIV positive people, and updates the paper to take account of recent convictions and court judgements.

**NAT SUBMISSION**
NAT has submitted a response to the Scottish Executive opposing their proposal for mandatory blood test orders for those allegedly involved in criminal incidents.

**FACT SHEET**
NAT has produced a new fact sheet on new prevention technologies.

**PRISONS PROJECT**
NAT is working with the Prison Reform Trust to assess and produce a report on the needs of prisoners in the UK in the context of HIV and hepatitis.
THE NATIONAL AIDS TRUST (NAT) IS THE UK’S LEADING INDEPENDENT POLICY AND CAMPAIGNING CHARITY ON HIV AND AIDS. WE DEVELOP POLICIES AND CAMPAIGN TO HALT THE SPREAD OF HIV AND AIDS, AND IMPROVE THE QUALITY OF LIFE OF PEOPLE AFFECTED BY HIV, BOTH IN THE UK AND INTERNATIONALLY. WE AIM TO PREVENT THE SPREAD OF HIV AND AIDS, ENSURE PEOPLE LIVING WITH HIV HAVE ACCESS TO TREATMENT AND CARE, AND ERADICATE HIV-RELATED STIGMA AND DISCRIMINATION.

IMPACT

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