
HIV AIDS Vaccine R&D

International AIDS Vaccine Initiative

Andrea von Lieven, Clinical Program Manager

16 December 2009, Luxembourg
EU HIV/AIDS Civil Society Forum

Overview

- Why do we need an HIV Vaccine?
- How do we know a vaccine is possible?
- Vaccine Field Update
- Recent Results from Thai Study, RV144

HIV continues to devastate

- 33.4 million people living with HIV worldwide; 7,400 new HIV infections daily
- 25 million AIDS-related deaths to date
- 2.7 million people a year become infected, including 430,000 children
- 40% of new infections among young people
- **For every 2 persons put on treatment, 5 new infections**

1990
7.5 million
people living
with HIV

1995
18.5 million

2000
28.5 million

2005
32 million

2008
33 million

- **Women bear the brunt of the epidemic, representing almost 60 percent of HIV-infected adults in Africa and half of adults worldwide**

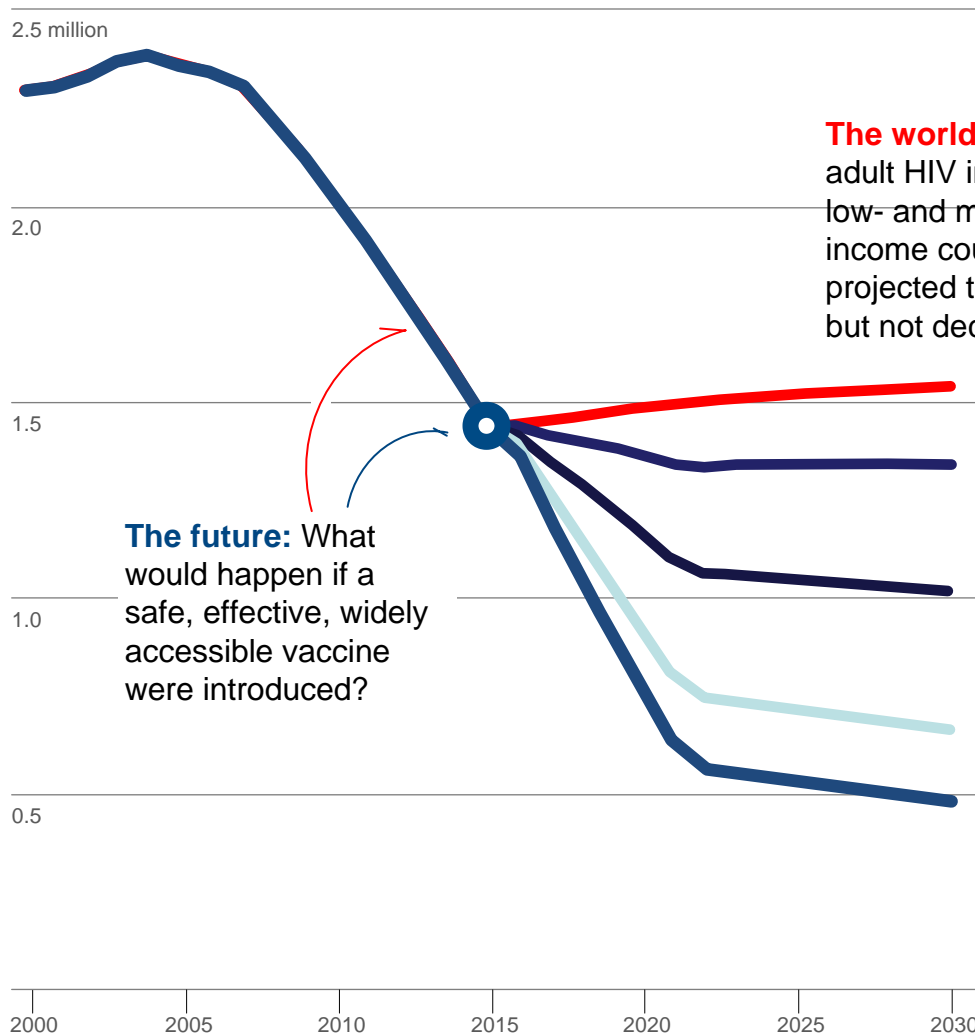


Women: AIDS vaccines part of the answer?

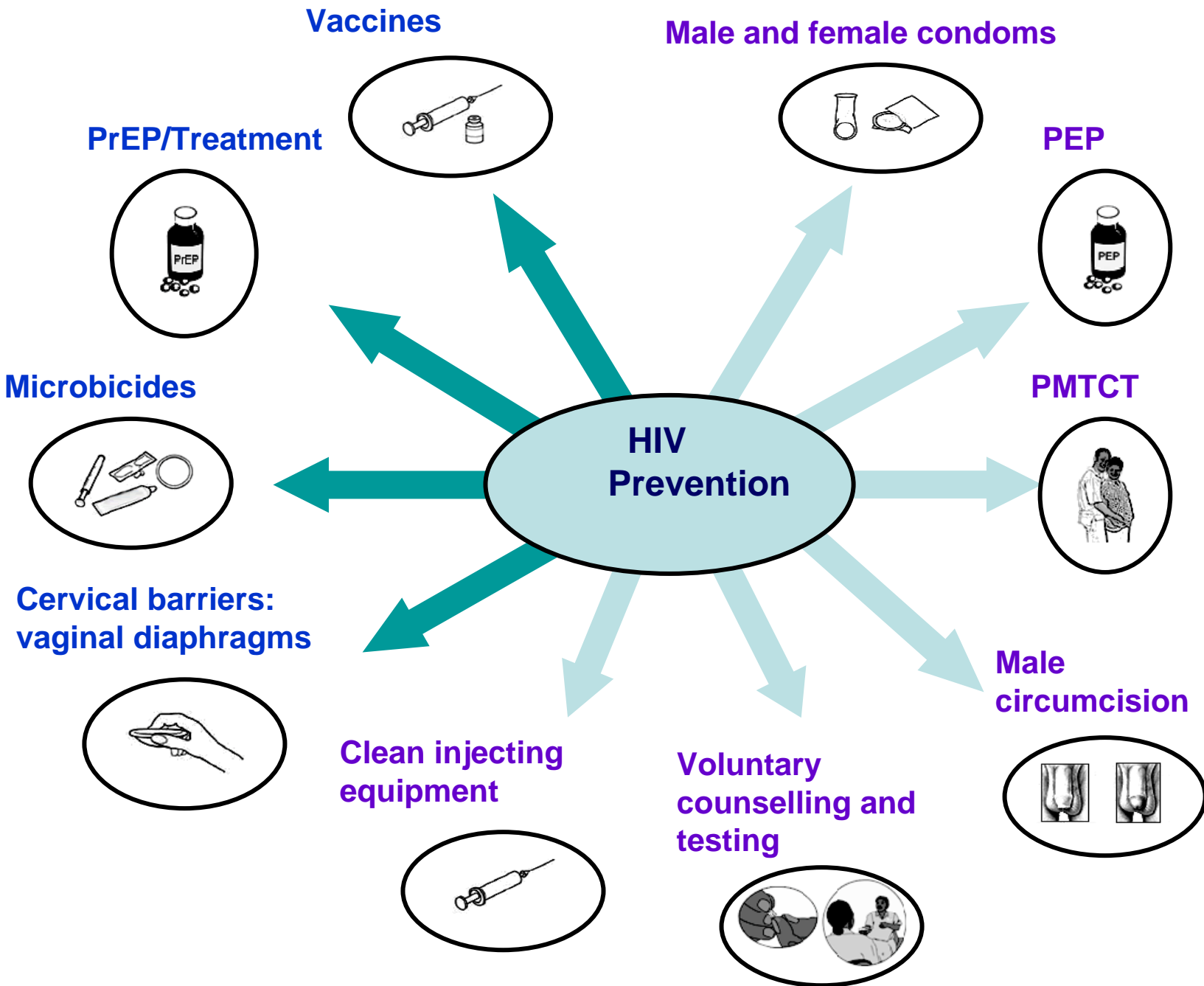
- Can be used with or without a partner's knowledge or cooperation
- Girls could potentially be vaccinated as pre-adolescents before the onset of sexual activity or other potentially high-risk behaviors
- Lessons from family planning about the need for choices to meet women's varied needs and preferences ("method mix"); increases utilization
- We do not know when new technologies will be available or how effective they will be, so we must pursue a range of options



A vaccine would give millions new hope



	Vaccine effectiveness	New infections prevented by 2030
LOW IMPACT	Cuts infections 30%, available to 20% of population	2.1 million
MEDIUM IMPACT	50% effective, 30% coverage	5.6 million
HIGH IMPACT	70% effective, 40% coverage	9.8 million
VERY HIGH IMPACT	90% effective, 40% coverage	12.0 million



An AIDS vaccine **is possible**

A recent study showed for the first time in people that an experimental vaccine could provide a modest level of protection against HIV infection

But we also know:

Immune control is possible

- Majority of HIV-infected individuals initially suppress viral load
- Populations resistant to HIV infection
 - Long-term non-progressors: control infection for many years
 - Highly exposed, uninfected: commercial sex workers, men who have sex with men



Clinical research in Africa

Phase I/II vaccine trials

- Generally populations with low risk behaviour
- 6 phase I/II trials conducted at a total 7 centres to date
- Approximately 400 volunteers enrolled so far

Epidemiology studies

- Preparatory research for STOC trials.
- Study HIV prevalence, incidence, retention.
- Research natural history of disease, early infection, neutralizing antibodies, immunology of exposed individuals.
- 5 ongoing studies at 9 centres involving around 3000 volunteers
- **100.000 people received VCT**

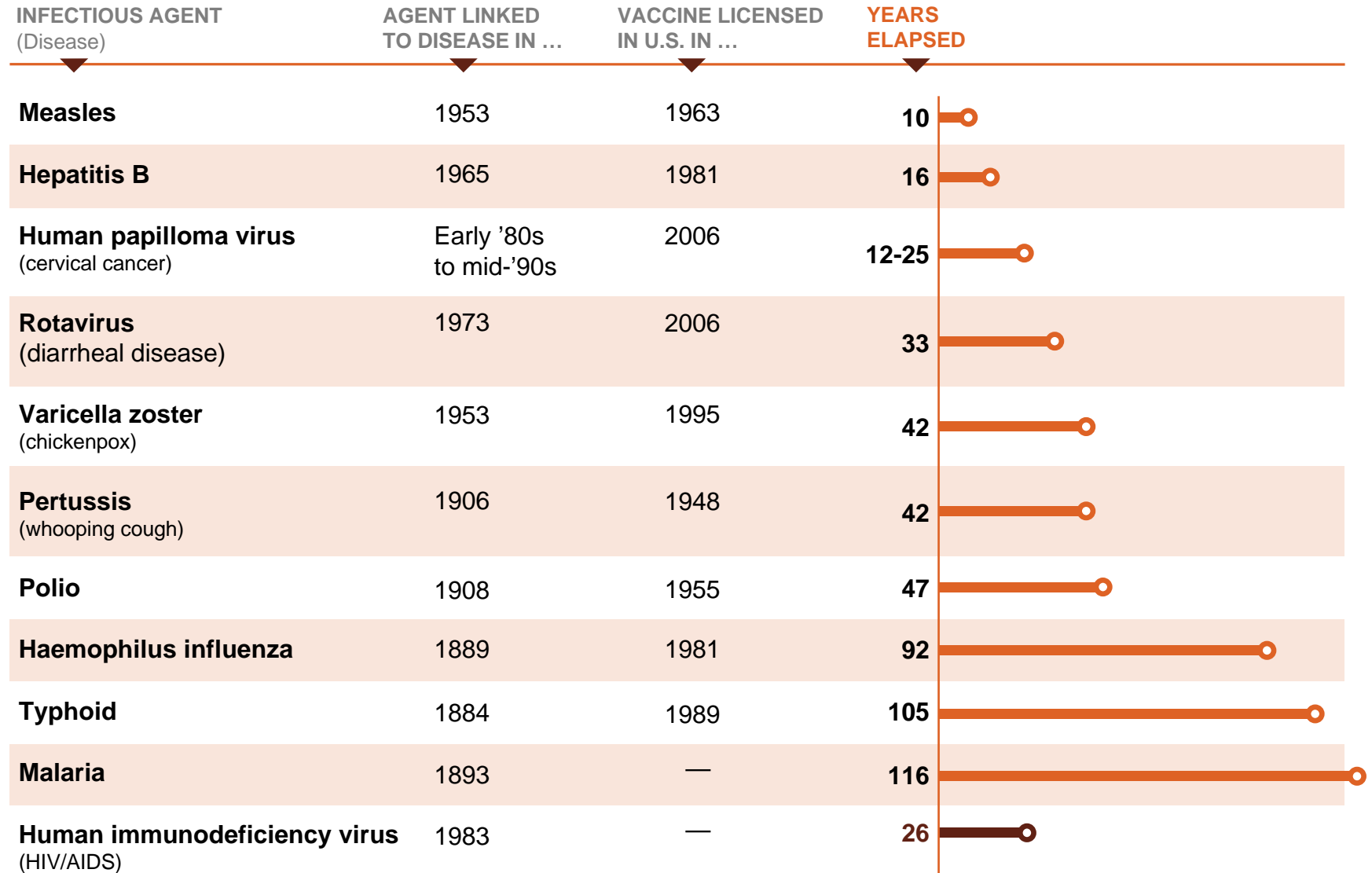
Social Science

- MSM, Fishing Community

Budget

- 430 FTE staff funded

Persevere: Vaccines can take decades to develop



The AIDS Vaccine Pipeline; where are we today?

Efficacy Trials Completed

- Sanofi + VaxGen: ALVAC + gp120: *Initial results show 31.2% efficacy*
- VaxGen gp 120 alone: *No efficacy*
- Merck: Ad 5-gag-pol-nef: *No efficacy*

Efficacy Trials underway

- NIH-VRC: DNA + Ad-5: *started 2009, results ? 2012*

Other Candidates Currently in Clinical Trials

- Phase II: Range of Cellular immunity candidates
- Phase I: Range of Cellular immunity candidates

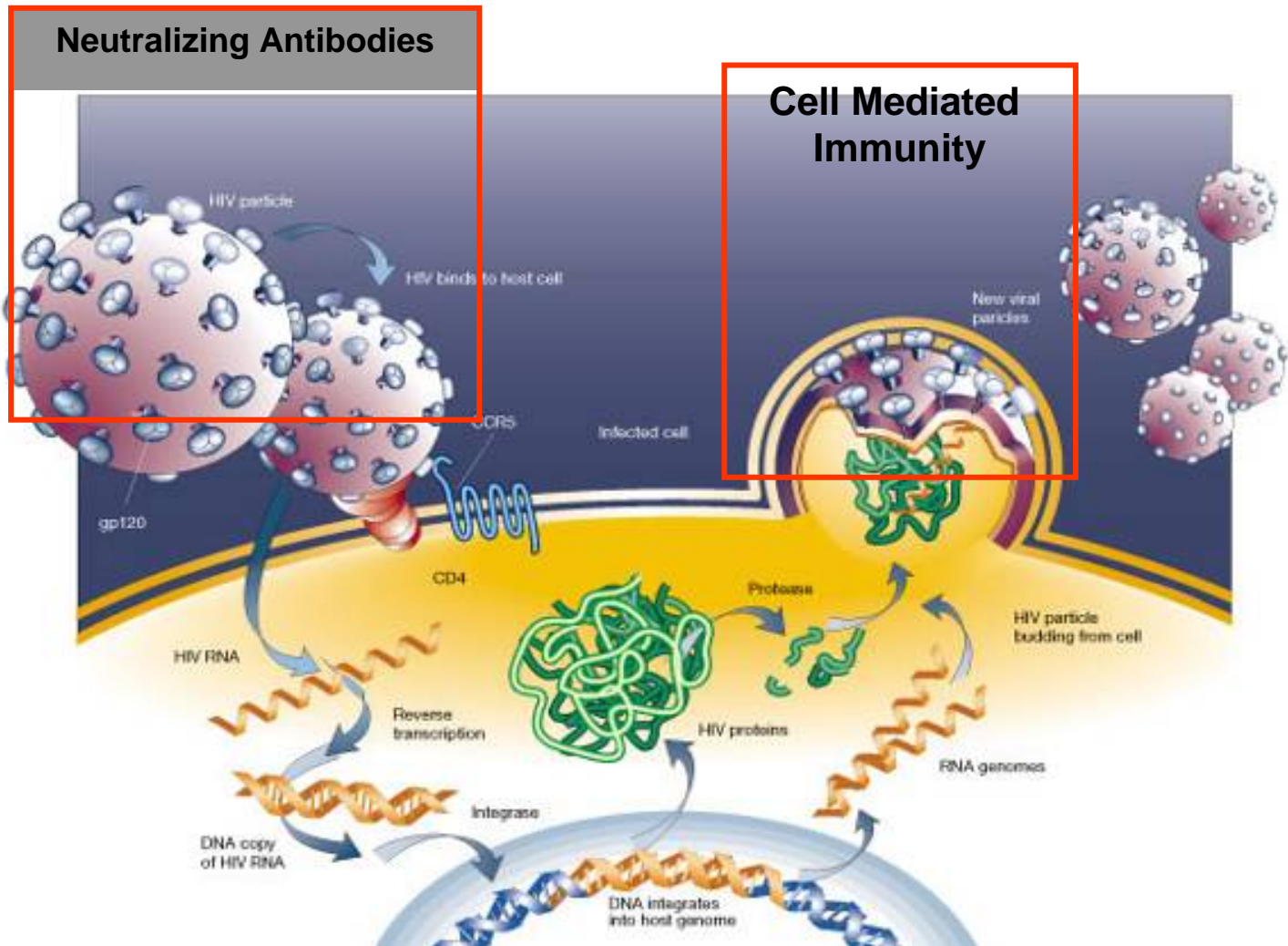
Our Assessment:

Small Test of Concept Phase II trials will determine whether any of these approaches provide advances over candidates above

Vaccine Delivery: Bioject™/Electroporation



Immune Mechanisms for an AIDS Vaccine



The Thai trial demonstrates an AIDS vaccine is possible

Thai research draws closer to a vaccine for Asian strain of virus

Scientists in Thailand claim to be close to discovering a vaccine for HIV, raising hope the search may be over. Reports in the *New York Times* and BBC yesterday said despite the findings being hailed as a significant breakthrough, a global vaccine still appears far away.

THE STUDY WAS CARRIED out by the US army and the Thai government over seven years on volunteer — all HIV-negative men and women aged between 18 and 30 — in Thailand.

After administering the vaccine, known as RV 144 to some 16,402 volunteer doctors say the result of tests are "statistically significant and the vaccine is 31 per cent effective".

Half the volunteers were given six doses of two vaccines in 2006 and half were given placebos. They were then regularly tested for HIV for three years. Of those who got placebos, 74 got infected, while 51 of those who got the vaccines did.

"I don't want to use a word like 'breakthrough', but I don't think there's any doubt that this is a very important result," said Dr Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases.

"For more than 20 years,

vaccine trials have essentially been failures. Now like we were groping for an unlit path and a door opened. We can start as very important question Dr Fauci said scientists would seldom consider

Celebrate Aids vaccine but remain vigilant

The unveiling of an Aids vaccine is a uplifting news in the face of the various pandemics that have assailed humanity in quick succession.

Although the discovery may have come too late for the 33 million suffering Aids worldwide, it is a major leap for humanity. However, it is too early to celebrate the efficacy of this vaccine, even after seven years of human trials.

Also, it is also not yet clear whether it can prevent infection by the other two strains of human immunodeficiency virus (HIV) in America and Africa.

Last month, a new strain of the Aids-causing virus was discovered in a Cameroonian woman. It differs from the three known strains of HIV and appears related to a form of similar virus discovered in wild gorillas.

That notwithstanding, it is important that the non-infected,

especially sexually active youth, do not engage in tragic immorality as a clear-cut vaccine and cure only remain in the realm of possibility.

The proliferation of condoms and now the so-called morning after pill have led to explosion in unprotected sex. Aids is terminal and the consequences irreversible, whether to the infected or the affected.

SANCTUARY OF LIFE

The ABC of responsible sexuality must still be the byword. That a vaccine against HIV and cure for Aids will eventually be found is not in doubt. Indeed every little step by researchers means progress toward this goal.

But medical research is involving expensive and sometimes outwits the scientists themselves before a cure is announced. This is because the sanctity of human life has neither time nor price. ■

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Hope rekindled as scientists announce possible Aids vaccine



HOPE AT LAST

• Vaccine, known as RV 144, was conducted in Thailand but failed.
 • It had been formulated back in the 1980s by the WHO, which is now in North America and Europe.
 • Since 2003, at least 10 vaccines were being tested in 10 million countries in Africa, Asia and Latin America.

people in Thailand. Six women from 18 and 30 were (and as the trial began) groups.

Researchers found that the risk of contracting HIV had. Half of the volunteers on the vaccine, while the ones given a placebo are counselled on HIV/AIDS prevention.

The results found that 11 less for those who had this cure.

It is also the first time trials that a vaccine has a virus, which infects 7,500

Breakthrough in Aids fight

Science wins a round in fight against HIV/AIDS



DISCOVERING THE Zaidi Mural, a model and student at the University of Johannesburg, in Johannesburg. Photo: MICHELE BRITTON

For the first time, an Aids vaccine tested in human clinical trials has reduced the number of HIV infections, researchers announced yesterday.

Local and international scientists have hailed this as a breakthrough. The trial in Thailand, involving more than 16,000 volunteers, showed infection rates were nearly a third (31%) lower among vaccinees who received the vaccine than those who received the placebo.

Professor George Williams, from the medical virology department of the University of Cape Town, said: "This is fantastic news. This is the first and only we have and from here on we are in a clear position that a vaccine is possible."

Another vaccine scientist, the British Virology, or WHO International's permanent HIV research unit, said she felt euphoric.

All the hard work around the world and every bit of it were worth it. We are now in a position where we will prevent the next Aids outbreak. It is the first. Aids vaccines tested development have been shown to prevent other diseases but not Aids.

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Dr John Bredius, president and chief executive of the International Aids Vaccine Initiative, said: "It is the first time a vaccine has been shown to prevent other diseases but not Aids. It is the first time a vaccine has been shown to prevent other diseases but not Aids. It is the first time a vaccine has been shown to prevent other diseases but not Aids."

7th SEPT OF RESEARCH

Prospect for HIV vaccine gets brighter

study among Thais points to a solution to a global crisis

an HIV vaccine. The vaccine is a combination of two older vaccines that on their own had not cut infection rates. Half of the volunteers were given the vaccine, while the other half were given a placebo — and all were given counselling on HIV/AIDS prevention.

NEWS

Friday September 25, 2009 The Standard 7

RV144 trial: First HIV vaccine candidate to show efficacy



THE TRIAL

A Phase IIb test-of-concept trial, based on expected number of HIV infection endpoints (Prevention of HIV infection and ability to reduce viral load), conducted by Thailand Ministry of Public Health (ALVAC[®]-HIV (vCP1521) priming at month 0, 1, 3,6, AIDSVAX[®] B/E gp120 boosting at month 3 and 6)



THE VOLUNTEERS

26,675 Thai citizens screened; 16,402 Thai citizens (60% male, 40% female) enrolled; 16,395 received at least one dose of vaccine or placebo



THE RESULTS

Vaccine candidate provided ~30% protection against acquisition of HIV; No effect on viral load or CD4 levels in the blood of volunteers who became HIV-infected during the study

- 74 infections in placebo; 51 in vaccinees
- Trend towards limited durability; vaccine effect appears short lived
- Mode of transmission may be important factor; Vaccine possibly less efficacious in high-risk groups
- Vaccine likely not applicable to diversity of strains prominent in sub-Saharan Africa



THAI STUDY:

Different Analyses Yield Different Results

“Modified Intention To Treat” Analyses

125 infected
75 Placebo 51 vaccinees
31.2% effective
statistically significant
n=16,395

Per Protocol Analyses

86 infected
50 Placebo 36 vaccinees
26.2% effective
statistically not significant
n=12,542

The mITT analyses is the more clinically relevant analyses for a test of concept study:

- Excludes volunteers who tested HIV infected between screening and first vaccination, and reflect the study design and protocol
- Does not assume that all 4 vaccinations are important
 - Does not assume that the time of each vaccination is critical
 - Limits bias compared to PP

The per protocol analyses additionally excluded 3,853 volunteers who were analysed under mITT:

- Excluded 2,422 who did not receive all 4 vaccinations
- Excluded 1,412 who received a vaccination “out of window”
- Excluded a further 19 for other protocol violations

Discovery: Significant advancement for the field

Science briefing

Antibodies boost Aids vaccine hunt

Researchers in the US have discovered two powerful new antibodies to HIV, which may rejuvenate the flagging search for an Aids vaccine. The discovery, reported online in the journal *Science*, reveals the virus has a previously unknown Achilles heel.

Scientists at the International Aids Vaccine Initiative (IAVI) worked with the Scripps Research Institute and two biotechnology companies, Theracore Sciences and Monogram Biosciences, to find the "broadly neutralising" antibodies, which are produced by a small minority of HIV-infected people.

Both antibodies neutralise a large proportion of the many HIV strains in circulation

human immune system to produce such antibodies before exposure to HIV.

The antibodies were found by screening blood donated by 1,500 HIV-infected volunteers.

Natural cooling trend

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New Antibodies to HIV Found

By GARNETT NEASE

Gaining a Foothold Against HIV

An international team of researchers has discovered a pair of powerful new antibodies to HIV, providing fresh leads in the search for a vaccine against AIDS.

The two HIV antibodies, discovered in a study by Scripps and the first of their kind to have been identified in a human blood sample, are thought to be a key to developing a vaccine.



Expert science analysis and comment on our blogs.nature.com/science

Discovery raises hopes for HIV vaccine

Antibodies attack weak spot in the virus

Mark Henderson, Science Editor

Scientists are closer to creating a vaccine for HIV after discovering two powerful antibodies that attack a vulnerable spot common to many strains of the virus that causes AIDS.

The discovery highlights a potential way around HIV's defences against the immune system, which have so far thwarted efforts to make a workable vaccine. The hope is that a vaccine that stimulates the production of these antibodies could remain effective even as the virus mutates. HIV kills ten million people world



published in *Science* magazine in 2010. The antibodies are thought to be a key to developing a vaccine. The discovery highlights a potential way around HIV's defences against the immune system, which have so far thwarted efforts to make a workable vaccine.

SCIENCE

Hope in Aids vaccine search

Researchers discover anti-bodies which kill virus, renewing hope of HIV vaccine

By PAUL REDFERN, NATION Correspondent, London

Scientists have scored a major victory in the search for an HIV vaccine after discovering antibodies that attack the virus which causes AIDS.

The discovery could pave the way for a vaccine against the virus, which kills over two million people worldwide each year. About 35 million people are living with AIDS globally.

A report in yesterday's *Times* newspaper in the UK said the discovery was important because it highlights a potential way around HIV's defences against the human immune system, which have so far thwarted efforts to make a workable vaccine.

The hope now is that a vaccine that stimulates the production of these antibodies could remain effective against HIV even as the virus mutates.



The report said the antibodies would not have been identified without a new method of hunting for them, developed by a company called Monogram Biosciences. Basil Christian Petropoulos, its chief scientific officer, said: "If you think of it as a full-time effort, you can do the rest of the field."

A woman living with AIDS takes her daily dosage of life-saving drugs. New scientific findings have raised hopes for a vaccine. The report said the antibodies would not have been identified without a new method of hunting for them, developed by a company called Monogram Biosciences. Basil Christian Petropoulos, its chief scientific officer, said: "If you think of it as a full-time effort, you can do the rest of the field."

The Star

The Star newsweek 7 2010

NEWS

Finding may result in Aids vaccine breakthrough

SA experts caution there is still a long way to go before it's workable

SCIENTISTS have found two powerful new antibodies to HIV, offering fresh clues in the hunt for a vaccine. The antibodies were found in blood samples of volunteers in regions hit hardest by HIV, including SA.

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New 'cling-wrap' antibodies disarm HIV

TAMAR KAHN Science and Health Editor

CAPE TOWN — Scientists have found two powerful new antibodies that disarm HIV, offering fresh clues in the hunt for a vaccine. The antibodies were found in blood samples of volunteers in regions hit hardest by HIV, including SA.

The discovery was one small step towards developing a vaccine against HIV infection as scientists still needed to discover how the antibodies worked and turn these properties into an effective jab, said Linda-Gail Bekker, joint director of the Desmond Tutu HIV/AIDS Centre at the University of Cape Town, who collaborated with US scientists

on the research. Despite the history of disappointments, the discovery of areas of vulnerability in the virus was cause for optimism, she said.

Wayne Koff, senior vice-president of research and development at the International Aids Vaccine Initiative, said: "The findings themselves are an exciting advance towards the goal of an effective AIDS vaccine because now we've got a new, potentially better target to focus our efforts on."

"And having identified one, we've set up to find more, which should accelerate global efforts in AIDS vaccine development."

strains from getting a grip on CD4-T cells, which are a key part of the body's immune system.

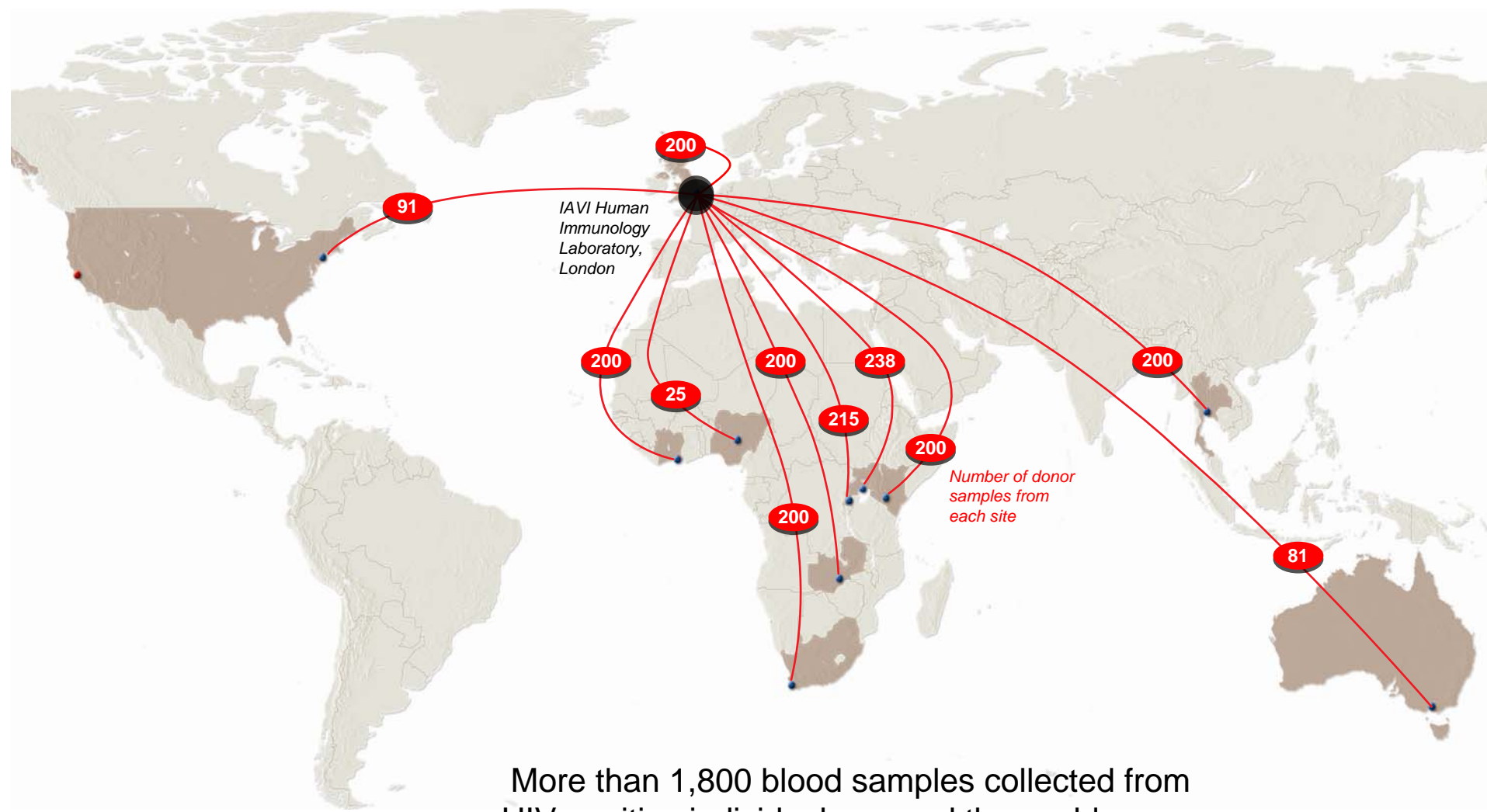
"They cling-wrap the virus, and stop it from being able to attach to the host target cell," said Bekker. The two broadly acting neutralising antibodies, PG9 and PG15, described in a paper published last week in the *US Journal of Science*, are the first to be found in more than a decade. They appear to be more powerful than those previously studied, and as they stick to parts of the HIV virus that are more accessible scientists hope they will prove easier to turn into a vaccine.

The antibodies were also the first ones to be isolated among people in the developing world, where

the majority of people infected with HIV lived. The breadth of the antibodies' effect against HIV was important as an effective AIDS vaccine had to work against the ever-increasing number of strains of the virus, said Bekker. HIV mutated fast, and different subtypes dominated in different regions. SA was primarily affected by the C-elite.

The antibodies were discovered using new technology developed by biotechnology companies Theracore Sciences and Monogram Biosciences that screened blood samples from 1,800 HIV-infected volunteers in seven sub-Saharan African countries, Thailand, Australia, the UK and the US.

Protocol G: An example of the IAVI network in action



More than 1,800 blood samples collected from HIV-positive individuals around the world



International AIDS Vaccine Initiative

IAVI gratefully acknowledges the generous support provided by the following major donors



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