

## SPOTLIGHT

### CABs that help make trials transparent

Shree Venkatram

**F**orty-eight-year old Usha, a former sex worker, now peer leader, is playing an important role in the AIDS vaccine trials in India. She is a member of the Community Advisory Board (CAB) and her views and suggestions are sought after by members of the research team in Chennai. She is their link to the community where the trials are taking place.

She was 15 and already a mother of a child, when her husband deserted her. She was forced into the sex trade and it was her only avenue to survival. Some years ago, she began working for an NGO in improving the lot of sex workers by bringing to their knowledge ways in which they could protect themselves from sexually transmitted diseases. Usha knows only too well the hardship and the struggle these women face. She realises what an AIDS vaccine would mean to women who sell sex and to those who are at risk of HIV because their

husbands visit sex workers. It would be their passport to better health and a life free from HIV.

When YRG Care, the NGO coordinating the trials in Chennai, invited Usha to be

#### Simply put...

A CAB is generally made up of 20 to 30 people representing various sections of the community, such as religious groups, the academia, the media, lawyers, social workers, NGOs and people living with HIV/AIDS. The members serve as primary liaison between the community and trial researchers.



*CAB members link the community to the researchers*

a CAB member, she accepted. She went through an orientation programme along with other CAB members. They learnt more about HIV, the proposed vaccine trials, and the role and responsibilities of CAB. The orientation also made them sensitive to the need to maintain confidentiality of volunteers. Most of the CAB members are from non-medical fields, but each of them is a leader in his/her respective areas.

Sashi Kumar, an auto rickshaw driver, is a CAB member too. He has been involved with YRG Care for the past nine years, ever since he fell seriously sick, and the NGO ensured that he got treatment and was on the road to recovery. He became a peer leader, teaching others in the slum where he resides, and fellow auto drivers how to safeguard themselves from the virus. He takes those who fall ill to YRG Care for treatment. He plies his vehicle in the morning, and spends

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the afternoons at auto stands educating drivers about the virus and the trials taking place in the city. The chats are usually during games of carom that the auto drivers play as they wait for passengers at the stands.

The CAB plays a vital role in making clinical trials transparent. Its members uphold the rights of volunteers and safeguard the interests of the community where the trials are held. The CAB in Chennai has 17 members including a priest, a lawyer, a psychiatrist, NGO representatives and housewives. The CAB for the Pune trial site has 34 members, including commercial sex workers, people living with HIV/AIDS, men who have sex with men, doctors, nurses, slum women, social workers and academicians. They range from those in their late twenties to those above 60 years. Each CAB member is expected to ensure that the concerns of the community are brought to the notice of the researchers.

### **Decisions by consensus**

The research team periodically updates CAB members about the status of the trials. Findings of new studies on HIV and vaccines are shared with them. CAB members also meet regularly among themselves when senior research team members are present where they discuss issues related to the trials like information dissemination, rights of volunteers or concerns expressed by them. Mary Jessi, a CAB member, says that the members come from diverse backgrounds, everyone is encouraged to speak, and they have free and frank discussions. The beauty of working in a CAB, says lawyer Anita Sumanth, is that decisions are taken by consensus after the intense discussions among members who have varying levels of education.

## **CAB members are responsible for:**

- General community outreach and education
- Support for volunteer recruitment by disseminating information about the trial
- Providing feedback on trial protocols, including criteria for participation, informed consent forms and processes
- Advising investigators regarding potential participants' perspectives about the trial
- Providing a safeguard (in addition to institutional ethics review committee) for participants well being

CAB also acts as a watchdog, looking after not only the volunteers, but also the community. Members make certain that the community has adequate knowledge of the trials, and the participants know their rights and have agreed to take part of their own free will and are under no duress or compulsion to do so. They ensure that trial sponsors and researchers work towards developing infrastructure including improved services for HIV/AIDS prevention and care that will leave the community better off after the trial has been completed.

The CABs in Chennai and Pune have examined educational packages relating to the trials and the informed consent forms. They ensure that the information material is culturally appropriate, in languages that people speak and understand, and is gender sensitive. They have been actively involved in the translation of these packages into Tamil and Marathi. Dr Seema Sahay from the National AIDS Research Institute, coordinating the vaccine trial in Pune, cites the example of the informed consent form that initially stated that 100 ml of blood would be drawn from a volunteer during a visit. CAB members felt that a technical measurement like this would not be appropriate as a grassroots community would find it difficult to understand a measurement like 'millilitre'... The CAB suggested that the volume should be indicated in terms of

a tablespoon or a cup. The consent form was suitably modified.

CAB members also play an active role in stalling rumours. In Pune, a peer reported a rumour that NARI was "selling blood". A CAB member probed the issue and found that many people were suspicious why sophisticated tests were being conducted free of cost. The only motive, they thought that NARI may have, was to 'sell blood'. The CAB member, peer and the research team called for a meeting of the community where they explained why the research staff was collecting blood samples and treatment and tests were being offered free to the research participants. The rumour subsequently died down.

### **Building trust**

For research scientists, CABs open a vital window. The members are its eyes and ears in the community. They also inform the research team about the risk behaviour prevalence in the community, ways to recruit volunteers and give community perspectives on education and communication strategies related to the informed consent process. For the community, CABs are their link to the research team. The members are in a position to give them information, or see that it becomes available to them on any aspect of the trial. They play a very important role in building trust in the community, and on it depends the success of any trial. ■

**IN CONVERSATION****“Site buddies help spread the health network further”**

An Interview with Sunil Menon



*Sunil Menon founded Sahodaran, a community based organisation for men who have sex with men in 1998. He has a background in anthropology and ethnography and has presented papers on MSM and transgender issues at national and international conferences. He also co-founded the Community Actions Network, under the aegis of WHO, and was the first to initiate targeted interventions amongst MSM in Chennai as early as 1993. He serves as a resource person and consultant on MSM and transgender issues to many organizations including Naz Foundation International (NFI) U.K. He spoke to Sankalp about the challenges faced by MSM in trying to lead a life without stigma and discrimination.*

**What would you say are the three most important challenges being faced by the MSM community today?**

Firstly, the legal system and other enforcement agencies often exploit the MSM community. This is not always directly due to section 377 of the

Indian Penal Code. A fear of maltreatment prevails among the community that hampers both intervention processes as well as accessing the community to catalyse behaviour change. The second challenge involves the stigma and discrimination that exists regarding sexual minorities among the general public. This has severe implications on intervention programmes as many ‘hidden’ MSM are not reached. Thirdly, media plays a big role in over-sensationalising such issues and need to be trained to cover such stories sensitively.

**Does the MSM community access the public or private health care system? Are there any gaps in the public health care system and how can these services be strengthened?**

The community does access the public health care system in the absence of any other ‘free or cheaper’ service. Many MSM approach the only government hospital in the vicinity for a monthly check up. The counsellors and doctors at the departments of venerology and Sexually Transmitted Infections are usually very approachable and sensitive to the needs of the MSM. But sensitisation of the new staff and interns is a continuous process and key to ensuring that the community accesses these services without any reservations or fears. The outreach staff of Sahodaran often accompanies the new members for care and treatment.

**How does your NGO reach out to those MSM who do not openly**

**disclose their identities or are not part of any organized group?**

Sahodaran tries to reach out to the ‘hidden’ MSM through the existing ‘friendship networks’ that they use by word-of-mouth, phone, email, etc...The staff is trained to initiate contact with new MSM. On gaining their trust and confidence, they disseminate information on safe sex and the importance of regular health checks. The staff has also cultivated ‘site buddies’, local MSM of the areas, who help spread the health network further. These buddies are also involved in disseminating condoms and accompanying new MSM to health facilities.

**Stigma and discrimination faced by MSM groups has repercussions in their seeking health care services too. What are some remedial measures that can be taken?**

Stigma and discrimination has to be addressed at the family level and also at the societal level. A young MSM faces a lot of trauma while coming to terms with his sexuality and his ‘apparent difference’ from other boys his age. This ‘difference’ also becomes a major cause for stigma and discrimination. MSM look for anonymity while accessing Voluntary Counselling and Testing services. But government hospitals draw big crowds. When MSM walk in, they often face lewd comments. Even young doctors and hospital staff add to the harassment by asking insensitive questions and their judgmental attitude. Hence, MSM feel uncomfortable and

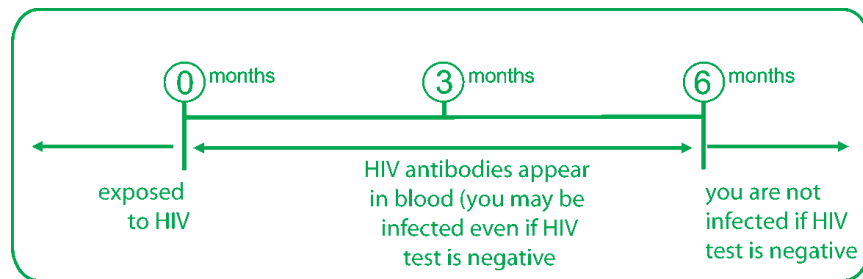
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# HIV TESTING

## The Human Immunodeficiency Virus (HIV) Test

HIV causes **Acquired Immunodeficiency Syndrome (AIDS)**, a long-term chronic disease, for which there is no cure so far. HIV infects white blood cells called **CD4+ T-cells**, which are part of the body's immune system that help fight infections. Several human immunodeficiency virus (HIV) tests can detect antibodies to HIV in the blood. This determines whether an HIV infection is present (HIV positive).

## Window Period



After the original infection, it takes between two weeks and six months for antibodies to HIV to appear in the blood. The period between becoming infected with HIV and the point at which antibodies to HIV can be detected in the blood (seroconversion) is called the 'window' period. During this period, an HIV-infected person can spread the disease, even though a test will not detect any antibodies in his or her blood.

## How do HIV tests work?

Once HIV enters the body, the immune system starts to produce antibodies - (proteins that are part of the immune system that recognise invaders like bacteria and viruses and mobilise the body's attempt to fight infection). In most cases of HIV, these antibodies cannot fight off the infection, but their presence is used to tell whether a person has HIV in his or her body. In other words, most HIV tests look for the HIV antibodies rather than HIV itself. There are tests that look for HIV's genetic material directly, but are not commonly used.

The most common HIV tests use blood to detect HIV infection. Tests using saliva or urine are also available. Some tests take a few days for results, but rapid HIV tests can give results in about 20 minutes. All positive HIV tests must be followed up by another test to confirm the positive result. Results of this confirmatory test can take a few days to a few weeks.

## Why is testing important?

A test for the human immunodeficiency virus (HIV) is done to:

- Detect an HIV infection. Testing is often done for people who are at risk of HIV infection and people who have symptoms of an HIV infection. However, a person can be HIV-infected without symptoms and transmit the virus to other people without knowing.
- Knowledge of an HIV infection will help persons take advantage of early treatment and monitoring. Appropriate care and treatment and psychological support will not only slow the growth of HIV but also ward off the illnesses and life-threatening conditions that often accompany AIDS.
- Prevent the spread of HIV through blood products, blood and organ donors.
- Screen pregnant women for HIV infection. Pregnant women who are infected with HIV and receive treatment are less likely to pass the infection on to their babies than are women who do not receive treatment.

This test is not done to determine if a person has AIDS. A diagnosis of AIDS means a person is HIV-positive and other clinical symptoms are present.

The World Health Organization issued new guidelines on expanding access to HIV testing in May 2007. It recommended that testing facilities should be made available at all the health centres, not just in certain designated ones. Until recently, the initiative for testing lay with the individual concerned (client-initiated), in which individuals actively sought an HIV test at a health or community-based facility. A compelling need for a change in approach to provider-initiated HIV testing and counselling was felt as nearly 80 per cent of people living in low and middle income countries are unaware of their status. This revised approach involves the health care provider specifically recommending an HIV test to patients attending health facilities.

Provider-initiated HIV testing and counselling has already been implemented successfully in a range of clinical settings in several low- and middle-income countries, including Botswana, Kenya, Malawi, Uganda and Zambia, as well as in pre-natal settings in parts of Canada, Thailand, the United Kingdom, and the United States.

The Government of India has issued a comprehensive HIV testing policy that states:

- No individual should be made to undergo a mandatory testing for HIV.
- No mandatory HIV testing should be imposed as a precondition for employment or for providing health care facilities during employment.
- Adequate voluntary testing facilities with pre-tests and post-test counselling should be made available throughout the country in a phased manner.
- There should be at least one HIV testing centre in each district in the country for voluntary testing in the Governmental sector.

The National AIDS Control Organization has helped establish hundreds of voluntary counselling and testing (VCT) centres in India. By the end of 2005, there were 873 VCT centres in India, compared to just 62 in 1997. These centres have tested 225,600 people for HIV during 2005.

## Some Common Tests

- **Enzyme-linked Immunosorbent Assay (ELISA)** This test is usually the first one used to detect HIV infection. If antibodies to HIV are present (positive), the test is repeated to confirm the diagnosis. If ELISA is negative, other tests are not usually needed. This test has a low chance of having a false result after the first few weeks that a person is infected.
- **Rapid test for HIV** (Single Use Diagnostic System - SUDS) This screening test is more than 99 per cent accurate when used three months after possible exposure. However, positive results on a SUDS test need to be confirmed by the usual Western Blot confirmation test. The results of the SUDS test for HIV are available after 15-30 minutes, but only negative results can be reported at that time.
- **Western blot** If the sample tests positive by ELISA, the results need to be confirmed using the Western blot test. The Western blot test is more accurate, though it is also more expensive and takes longer to perform.
- **Polymerase chain reaction (PCR)/ Nucleic Acid Tests.** This test finds either the genetic material DNA or RNA of HIV. PCR testing is not done as frequently as antibody testing because it requires technical skill and expensive equipment. This test may be done in the days or weeks after exposure to the virus. Genetic material may be found even if other tests are negative for the virus. Any PCR test used to identify infection must be accompanied by a regular HIV antibody test taken three months after exposure to confirm the PCR test result. PCR viral load tests are most useful in people who already know their HIV status and to help make antiviral drug treatment decisions or in children born to HIV-infected mothers.
- **Oral fluid (saliva) and urine tests** Oral fluids (including saliva) and urine contain antibodies to HIV—they do not contain HIV itself. HIV is not transmitted through oral fluids or urine. Tests using oral fluids or urine samples have the same accuracy as the regular HIV antibody tests and the same window period limitations. The higher cost of the oral fluids tests limits its routine use in most clinics.

Testing may be done routinely or at the request of people who feel vulnerable after exposure or at specific times e.g., pregnancy.

**IN FOCUS**

# The challenge of neutralising antibodies and HIV

Sonali Kochhar and Jean-Louis Excler\*

**H**uman Immunodeficiency virus - 1 (HIV-1) causes AIDS by binding to, entering and subsequently killing T-helper cells. These cells of our immune system are necessary to fight off infections by common bacteria, viruses and other pathogens. As HIV-1 depletes the body of T-helper cells, otherwise harmless micro-organisms produce lethal infections, ultimately leading to AIDS.

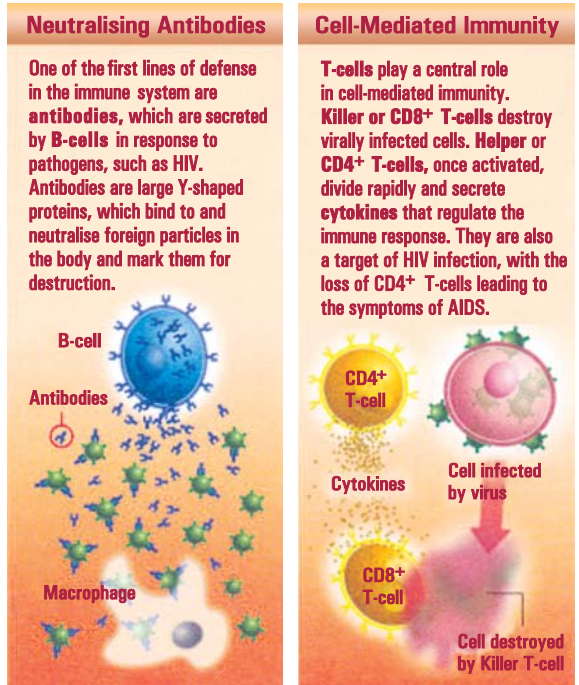
One of the most compelling medical challenges today is to develop a preventive AIDS vaccine that will provide complete protection to someone who is later exposed to HIV. Researchers believe that an ideal AIDS vaccine must work in two different ways. It must evoke an antibody response that can block HIV from entering healthy cells in the first place. The vaccine must also produce cell - me-

diated immune responses that will kill cells already infected by HIV-1 and reduce the amount of virus spread through the body.

Today, virtually all current vaccine candidates in the pipeline are based on cell-mediated immune responses alone: they all seem unlikely to trigger the first critical arm of the human immune system, antibodies against HIV-1. Rather than preventing HIV infection, these vaccines would probably act by destroying HIV-infected cells and limiting HIV replication, thereby reducing the viral load in HIV-infected individuals. Current prevailing model suggests that the transmission of the disease to sexual partners might be reduced and in many cases prevented when the viral load decreases significantly. Thus, the current AIDS vaccines under development would probably have an impact at the individual level by preventing progression to AIDS and at the community level by decreasing HIV transmission.

Antibodies are the basis for many existing vaccines, including against hepatitis A, hepatitis B, measles and polio. Researchers hope that AIDS vaccines would be able to induce neutralising antibodies against HIV isolated from recently infected individuals and prevent the establishment of HIV infection.

This is not easily done. The body makes lots of antibodies against HIV, but they are almost always unable to neutralise



the circulating wild virus. Most antibodies bind to surface protein (called the envelope glycoprotein, Env) and, as a defence, the virus causing HIV coats its Env with a thick layer of sugars. This process fools the immune system because it identifies the sugars as being part of a healthy human cell. The virus also rapidly changes the structure of its surface proteins under antibody selection pressure to avoid detection (mutation). In addition, the Env protein is highly unstable and flexible and thus never presents the immune system with one fixed form, leading to generation of ineffective non-protective antibody responses.

However, in rare instances some people have produced antibodies that have unique structures and neutralise HIV. Combinations of these antibodies neutralise numerous HIV strains from around the world and provide strong antiviral protection in some animal

**Simply put...**

**Antigen** - Molecules that the immune system recognises as foreign such as invading bacteria or viruses; they stimulate the immune system to produce antibodies to combat invading microbes

**Antibody** - Y-shaped immune protein molecules that bind, tag, neutralise and help destroy pathogenic microorganisms e.g., bacteria and viruses making them unable to invade cells. Antibodies that can successfully stop pathogens from infecting cells are known as **neutralising antibodies**.

**Cell-mediated immune response** – The immune system response coordinated by T cell responses that target those cells that have already been infected with the pathogen.

studies. Scientists believe that by using the structural information from these antibody binding regions it might be possible to design an antigen which will stimulate the body's immune system to produce neutralizing antibodies against HIV. Such an antigen in conjugation with the cell mediated vaccines could be used in developing an ideal AIDS vaccine to provide complete protection against HIV.

Designing such an antigen (described above) is very a difficult and challenging preposition as more information is required on the -

- ❖ Nature of the HIV strain circulating in a given population
- ❖ Neutralising antibodies that neutralise the different strains of HIV to understand how to design antigens that stimulate them

#### NAC Members

- The Scripps Research Institute  
University of Pennsylvania
- Cornell University
- Dana-Farber Cancer Institute
- Harvard University
- University of Wisconsin
- Institute of Research in Biomedicine
- University of Washington

Recently, researchers in the US discovered a possible chink in HIV's protective armour. When studying the exact site where one of the already-identified broadly neutralising antibodies binds to the virus, researchers found it was the precise place where the virus would connect to the protein on cells, blocking the two from fitting together. Another promising finding is that this binding region

does not mutate as much as other regions on the virus's surface protein, since this region of the virus is needed to attach to human cells. This means that this site should be similar in most strains of HIV. This exciting news provides a new window of opportunity for AIDS vaccine researchers to design vaccine candidates that can induce antibodies to target this vulnerable point on the virus.

- ❖ Structure of the HIV surface protein against which the neutralising antibodies would need to be generated.

The Neutralizing Antibody Consortium (NAC) was established in 2002 to address these difficulties in designing molecules that would induce effective neutralising antibodies against a broad range of HIV strains so that an AIDS vaccine could be developed. Supported and managed by IAVI, this consortium is a collaborative effort of investigators from academic, non-profit organisations and US National Institutes of Health laboratories.

The Department of Biotechnology (DBT) and IAVI launched the Indian Medicinal Chemistry Programme on May 2, 2007 to complement the work of the NAC. DBT and IAVI are co-funding and co-sponsoring the programme that has top Indian and US scientists from different academic research labo-

ratories collaborating on the design of antigens to stimulate the formation of neutralising antibodies against HIV. The first component of the DBT-IAVI programme will consist of a collaboration of principal investigators from India and the US from different academic research laboratories working under a common research agreement on novel research approaches.

Through this programme, top Indian and U.S. scientists will collaborate to solve one of the most difficult challenges in AIDS vaccine development. It is hoped that this team of internationally recognised scientists working on the neutralising antibody challenge will help in the development of the next generation of AIDS vaccine. ■

\*Dr Sonali Kochhar is Medical Director, IAVI, and Dr Jean Louis Excler is Senior Medical Director, IAVI.

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hesitate in accessing the service. To counter this, a *Sahodaran* staff member accompanies a new MSM during hospital visits. Some MSM want anonymity during counselling. Therefore, *Sahodaran* offers counselling over the telephone. Sometimes, parents call us too. And we talk to them to accept the situation instead of fighting it.

#### **Mapping and in depth research about the MSM community would be key in ensuring that their information and health needs are met. What are some ways in reaching out to this hidden population?**

Mapping can take place through outreach teams, who consist of community members themselves, and exist within each MSM project. A concerted effort needs to be made to access and

assess credible data. We have mapped Chennai city and know the places favoured by MSM. *Sahodaran* outreach workers are in touch with the sex workers and provide information about accessing services and condom use. Now, the National AIDS Control Organization has a special MSM desk. This should go a long way in helping to create an environment where the MSM community can be empowered to access health services without any fear. ■

**GLOBAL NEWS**

# Contraceptive diaphragm does not prevent HIV infection

A recently completed study of a contraceptive female diaphragm indicates that the cervical barrier does not provide additional benefit over already available HIV



The diaphragm is a small, dome-shaped rubber shield that sits over the cervix and rests on the pubic bone. The diaphragm works by keeping sperm from entering the cervix and going into the uterus.

prevention strategies in reducing HIV transmission in women. Researchers at the University of California, San Francisco, conducted this first randomized controlled trial of the latex diaphragm. It involved nearly 5000 volunteers in Durban and Johannesburg, South Africa, and Harare, Zimbabwe. Results of the trial showed that HIV incidence rates among women in the control group who only received condoms and counselling were nearly identical—to around 4 per-cent—to those seen in women who also received a diaphragm and lubricating gel. During the 18-month study, 158 new HIV infections occurred in the group of women who received the diaphragm, with 151 occurring in the control group.

(Source: VAX and MIRA website)

## ASK to get ANSWERS...

If you have a question on any issue pertaining to HIV/AIDS or AIDS vaccines, write to us at:

**sankalp@iavi.org**  
**or IAVI,**  
**193 1st floor, Jor Bagh,**  
**New Delhi - 110003.**

Our experts will give the answer. The question and the answer will be published in the next issue of *Sankalp*.

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IAVI is a scientific organisation founded in 1996 whose mission is to ensure the development of safe, effective, accessible, preventive AIDS vaccines for use throughout the world. IAVI focuses on four key areas: accelerating scientific progress; education and advocacy; ensuring vaccine access and creating a more supportive environment for industrial involvement in AIDS vaccine development.

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