IAVI India Newsletter

SANKALP

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SPOTLIGHT

When Volunteers say YES

'Informed Consent' in AIDS Vaccine Trials

Creating awareness about AIDS vaccine trials in the community

In ethical medical research, the phrase 'informed consent' holds great significance. In fact, it is an essential part of any ethical research study involving human volunteers.

IAVI describes informed consent as "an agreement between the researcher and the volunteer, showing that the volunteer fully understands and agrees to all aspects of participating in the trial". The agreement is in the form of a document, which the volunteer signs, thereby giving his or her consent. Preceding it is the entire process of reaching out to the community, educating the people about the proposed research, getting volunteers that fit a required profile, setting up a dialogue with them to ensure that they fully understand what the drug or vaccine is expected to achieve, what is expected of them during the trial period, the risks they face, and in case of injury or infection, the type of care and treatment that would be available to them. The entire process of informed consent could take months.

Medical researchers find they are called upon to explain scientific terms in easily comprehensible ways - in the idiom and language of the community from where the volunteers will be drawn. Not surprisingly, they find they have to work with social scientists, communicators, counsellors, social and community workers to reach out effectively to people with information.

Informed consent was articulated as a principle of medical research in 1947 when the Code of Nuremberg, a set of principles for conducting experiments on humans, was formulated. The code followed the trial of Nazi doctors who had carried out inhuman experiments on prisoners in concentration camps during the Second World War, which had shocked the world. Nuremberg is the name of the German town where the trials took place of the doctors and those connected with the excesses during the War. Apart from informed consent, the Nuremberg code includes such principles as the 'absence of coercion', 'properly formulated scientific experimentation' and 'beneficence' towards experiment participants.

Simply put...

Informed consent is a process (and not just a piece of paper) that has both legal and ethical aspects. Legally, it is a formal record of a person's willingness to participate in a clinical trial. Ethically, it is a decision-making process during which a person who is thinking about volunteering collects and then weighs the available information.

AIDS Vaccine Handbook

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Though not as bad as the Nazi experiments, there have been cases in the recent past in different parts of the world of people being subjected to trials without their knowledge and permission. Often these were poor illiterate men and women who had not been provided full information.

Informed consent process

For the AIDS vaccine trials at the National AIDS Research Institute (NARI) in Pune and the Tuberculosis Research Centre (TRC) in Chennai, IAVI and its partner, the Indian Council of Medical Research, put together community education programmes, information kits, volunteer information brochures and the informed consent form. Experts were involved in screening the documents to ensure they had the vital information and were easy to comprehend. They also worked at getting them translated into Marathi and Tamil, the local languages of the sites.

The informed consent process began with outreach. At both the sites, NGOs working in the region and Community Advisory Boards (CAB) played an important role in educating the public. In Chennai, TRC along with the NGO, YRG Care, conducted meetings at institutions, while YRG Care's outreach workers met with community gatekeepers and held mass education programmes. In Pune, NARI developed a slide presentation as part of its community education, where scientific concepts like 'recombinant DNA technology', 'randomisation', 'double blinding' and study procedures were explained in a simple language. The Pune CAB members helped the outreach staff organise community interaction.

Workshops were held for journalists in both Pune and Chennai to explain the nature of the trials and enlist their help in reaching out to the wider community. NARI also put up the announcement on its website. Interestingly, at both sites, many volunteers came forward after reading about the trials in the media.

The outreach efforts saw persons from diverse backgrounds interested in enlisting as volunteers. There were business executives, social workers, teachers, paramedical staff, homemakers, students, drivers, and even labourers between the ages of 18 to 54 years, married as well as single, male and female, all literate with varying degrees of educational qualifications, and keen to volunteer.

At both sites, many volunteers came forward after reading about the trials in the media.

At Pune, 245 persons stepped forward to enrol as volunteers at small group meetings and 135 came up at one-on-one meetings. Of these, 30 were enrolled, 16 men and 14 women. Chennai had a total of 340 persons interested in enrolling as volunteers. In the end, 15 women and 17 men were enrolled. How was the selection done?

Principal Investigator of the trial at TRC, Dr V.D. Ramanathan, says all the 340 individuals were invited for a one-to-one consultation, during which they were given focussed information and the social and biological implications of participating in an experimental AIDS vaccine trial. NARI, on the other hand, organised small group meetings of interested persons as the second level of interaction. Says Principal Investigator of the trial at NARI, Dr Sanjay Mehendale, "We expected those interested to contact us for further one-to-one meetings, where detailed procedures would be explained, risk assessment done and any questions the volunteers asked would be answered. The volunteers were given additional time to make up their mind and report to NARI for screening with prior appointment."

Essentially, there were three levels of meetings from the broad and general to the focussed in Chennai and Pune. At every level, the volunteers were given time to decide and then initiate contact with the researchers for the next level.

Information educational materials

An information kit containing FAQs about HIV/AIDS, vaccines and vaccine trials, and details about the trial organisers, was given out to all potential volunteers. These informational materials used language and concepts appropriate to the local culture and social context. The volunteers also received an information brochure giving details of the regulatory authorities who have approved the initiation of the study, and exactly how the trial would proceed. The brochure lists the number of times a volunteer would be expected to visit the clinic, how often the blood and urine samples would be taken, and the kind of tests (pregnancy, TB and HIV) that would be conducted. The brochure also informs that the participant would be required to answer questions on his or her complete medical history and on possible risk behaviour for HIV infection.

At each meeting, the volunteers were encouraged to seek information or clari-

fication. They had questions on the long and short-term side effects, the possibility of HIV infection, the blood draws, the need for condom use, the type of care and support offered after trial participation, particularly long term support, the responsibility of the institution if something goes wrong, and about AIDS vaccine trials being held in other parts of the world.

The research team has the vital task of ensuring the participants have fully understood the risks involved and are under no kind of pressure from anyone to enrol for the trial, and that, they are doing so of their own free will, in a spirit which is altruistic.

A test of understanding

A comprehension test is given to the volunteers, which they have to clear in a maximum of two attempts. The criteria for test of understanding are strictly followed and no less than 75 per cent correct answers are considered for eligibility. The criteria also includes correct answers to some critical questions without which the comprehension and understanding is considered incomplete.

Then, and only then, are they expected to sign on the informed consent form entering the screening process. The volunteers undergo medical tests to ascertain their fitness to enlist for the trial. Those found to be suffering from TB, HIV infected or pregnant are not enrolled.

Only if the comprehension test and medical examination indicate eligibility, does the volunteer receive the study vaccination. The trial evaluates how well the vaccine is tolerated (safety) and how it induces the defensive response of the immune system (immunogenicity). The participants are clearly told that the clinical trial is not designed to study if the vaccine can protect against HIV infection (efficacy). Therefore, they are impressed upon to avoid any behaviour that may put them at risk of contracting HIV. They are not to consider themselves as protected from HIV after receiving the study vaccination. Participants are given regular risk-reduction counselling.

Personal autonomy

Given the stigma attached to HIV/AIDS, the volunteers are assured of confidentiality. However, they are free to inform whosoever they wish to about their participation in the trial. They are also informed that they can leave the trial any time during its course if they change their mind and are not obliged to give any explanation. The whole issue of informed consent is based on personal autonomy. An individual decides whether to participate or not without coercion or temptation from anyone and the research team has to ensure that it is indeed so.

Dr Mehendale says most participants consult their partners or family members. In fact, NARI encourages them to do so, given the intensity of the study visits and follow-up schedule. NARI's Ethical committee and the Central Ethics Committee of ICMR strongly recommend that families be involved in the decision making, if desired by the volunteer. "Hence, we explained to all of our study participants the significance of family support and involvement," Dr Seema Sahay, Senior Research Officer, National AIDS Research Institute adds. At TRC, 70 per cent of the male volunteers, chose to bring their spouses along with them, Dr Ramanathan says. Of course, this also meant that some eligible volunteers who were interested in joining the trial, could not do so due to pressure from the spouse or family members.

The Phase-I trials at both sites in Pune and Chennai had 100 per cent retention of volunteers showing their high motivation. With no material benefit to themselves or their families, their selfless action is in the larger interest of humanity, for a world without AIDS. We are greatly indebted to them. ■

Illustrations: Shibani
Adapted from South African HIV Vaccine Action Campaign

HIV EPIDEMIC IN INDIA

About 5.21 million adults are estimated to be living with HIV infection in the country as per the latest official estimates of the National AIDS Control Organization.

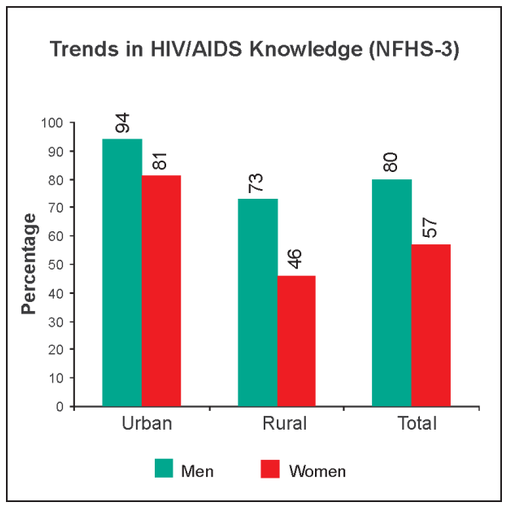
There is a growing feminisation of the epidemic with 38.4 per cent of those living with the virus being women. The virus is also increasingly moving towards the rural areas with 57 per cent of the virus load in the villages. Besides, 86 per cent of the infected persons did not know that they carried the infection.

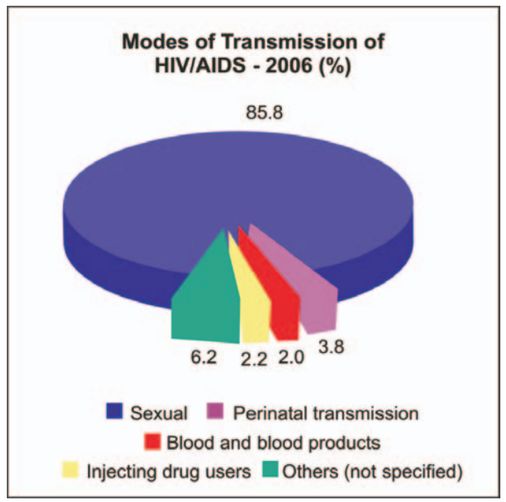
Despite this large number of HIV-infected individuals, India continues to be in the category of low prevalence countries with an overall prevalence of less than one per cent because of its large population size.

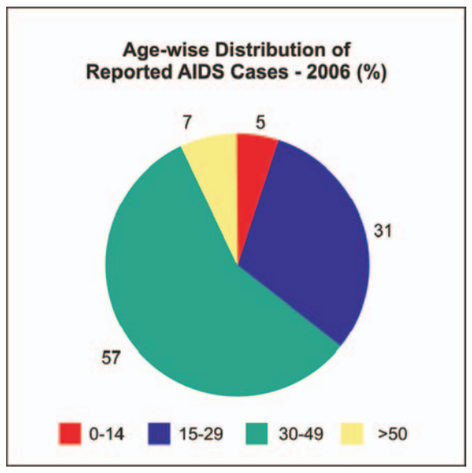
HIV was diagnosed in India for the first time in 1986 in the state of Tamil Nadu and has since then been reported by all states and Union Territories. India now holds the second largest absolute number of HIV infections in the world, following South Africa. There are several localised sub-epidemics reflecting the diversity in socio-cultural patterns and multiple vulnerabilities present in the country.

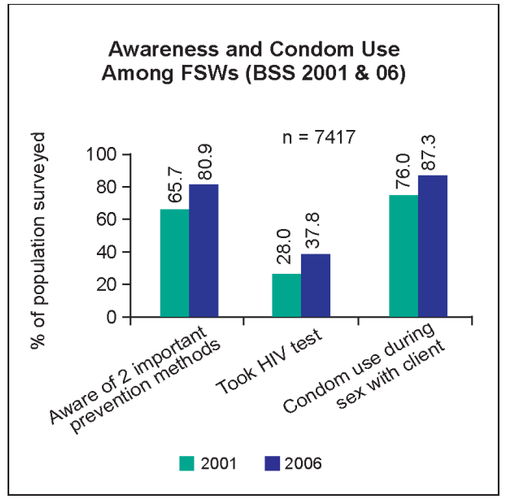
Though the overall national prevalence is low, six states have reached high prevalence (>1 per cent), namely, Manipur, Nagaland, Andhra Pradesh, Tamil Nadu, Karnataka and Maharashtra. Prevalence of HIV among antenatal clinic attendees fell below one per cent in Tamil Nadu. However, HIV prevalence among sexually transmitted disease patients has increased significantly over the previous year in Delhi, Rajasthan and Orissa. Besides, HIV prevalence was greater than one per cent among antenatal mothers in 95 districts, including nine in the low prevalence states, according to NACO.

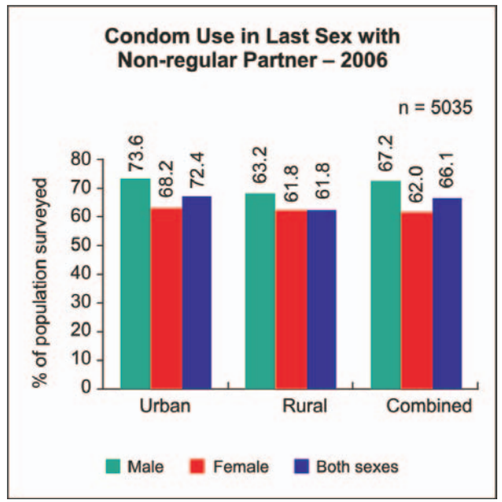
Sexual transmission is driving India's AIDS epidemic. This route accounts for approximately 86 per cent of the HIV infections in the country. The remaining 14 per cent are by other routes such as blood transfusion, mother-to-child-transmission and injecting drug use, particularly in North Eastern states and some metropolitan cities.

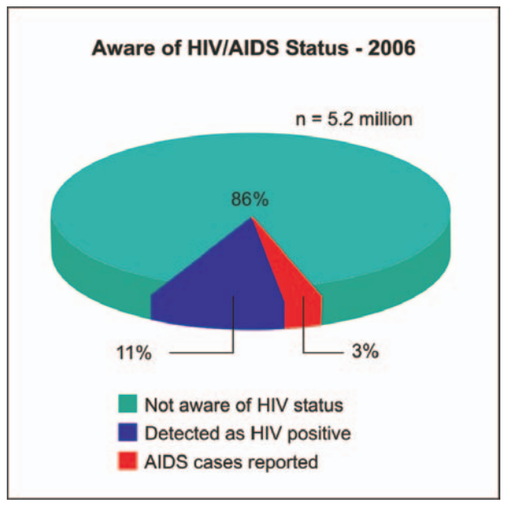


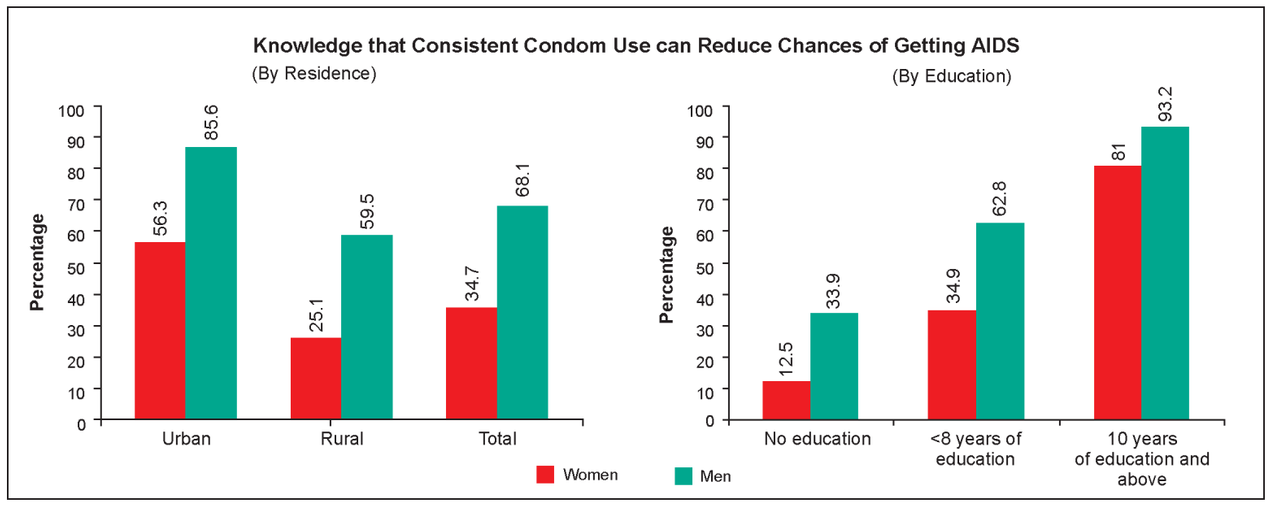


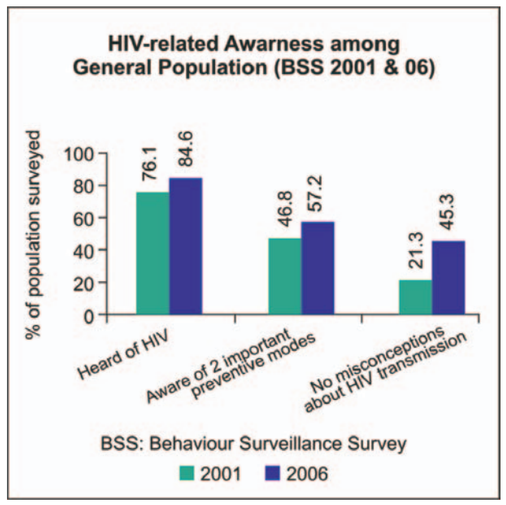












Source : National Family Health Survey — 3; NACO News Volume II(4), 2006

IN CONVERSATION

"ICMR guidelines for bio-medical research are awaiting clearance to be passed as law..."

Dr.Vasantha Muthuswamy, Senior Deputy Director General, Indian Council of Medical Research, is the Chief of Basic Medical Sciences, Traditional Medicine and Bioethics. Her contributions in the area are well recognised both nationally and internationally, so much so that she has been called the Queen of Bioethics! She has played a major role in policies related to both animal experimentation and human research and was responsible for coordinating ICMR's guidelines for bio medical research, finalised in 2000. She is also the Convenor of the Central Ethics Committee. She spoke to Sankalp *about the challenges of conducting clinical research in the country.*

What is the composition of the Central Ethics Committee? How many times does it meet? Tell us about some of the achievements of this committee.

The Central Ethics Committee (CEC) consists of 17 members from both government and private institutions. There are experts in the fields of medical science, pharmacology, law, social science, representatives of different religious groups and others. The members meet as and when a proposal of national relevance is presented. The CEC has given clearances among others for the rotavirus trial referred by the Department of Biotechnology; the mother-to-child transmission studies referred by NACO and Ministry of Health and the preventive AIDS vaccine trials being conducted jointly by ICMR, NACO and IAVI.

The guidelines for biomedical research on human subjects are required to be followed when conducting clinical trials in the country. How are these guidelines implemented? Does ICMR have a role in this?

Guidelines are always for voluntary compliance. There cannot be any forcible enforcement. Since the guidelines have been released by a national organisation like ICMR and this is a global requirement, all are expected to follow. ICMR is a research organisation and we have no legal authority to take any action against anybody.

What changes would you like to see in the current ethical and regulatory practices for clinical research in the country?

The ICMR guidelines for biomedical research on human subjects finalised in 2000 have been made into a bill, and are awaiting clearance to be passed as law. Once that is done, it will become mandatory for all clinical studies, conducted by both physicians and non-physicians, to follow the guidelines. Currently, there are laws governing research in India. Under the Drugs and Cosmetics Act, all trials in the country should follow the ICMR guidelines. The Medical Council of India Act amended in 2002 states that all research in India carried out by physicians has to subscribe to the ICMR guidelines. This is an indirect legal support to enforce our guidelines but we need more teeth!

I would like to see that all institutions make it mandatory for their researchers to undergo ethics training and only then take up clinical research and all post graduate theses should go through Institutional Ethics Committees. This will help bring about major reforms in this area.

Is there a monitoring mechanism to ensure ethical processes such as informed consent, recruitment and compensation are carried out during the clinical trials?

There is no proper mechanism in position at present. It is recommended that Institutional Ethics Committees take up the monitoring role by site visits to ensure compliance. It will take some more time to make these things really happen.

The clinical trials sponsored by IAVI and conducted jointly with ICMR and NACO have followed a very consultative and collaborative process to ensure that ethical guidelines are followed. Would you recommend similar processes to be part of other clinical research in the country?

Yes, it was an excellent process undertaken by NARI/ICMR/IAVI for the vaccine trial. It is an ideal method to be adopted as a model for all trials. However, how far this is feasible is a major question and concern. Replicating this process at all trials is desired but difficult to achieve in the current scenario. ■

IN FOCUS

Are you well?

Nalamdana – Communicating for health

A rapt audience of 300 girls from a college in Chennai are totally engrossed in the adventures of the 'hero and heroine' performing on stage. Love, comedy and family upheavals in the play all carry the undercurrent of the main health issue - HIV/AIDS. Facilitated by Nalamdana, an NGO based in Chennai, the Tamil-film style drama effectively informs and provokes discussion on HIV/AIDS among the students, breaking the silence that surrounds the infection. Issues of sex and gender, infidelity, treatment and care of the HIV infected are all handled delicately, without offending cultural sensitivities. Familiar film songs are used as background music to create the right ambience. A session of entertainment before the play ensures local participation and involvement, getting the audience to stay, sometimes two hours after the play discussing the issues.

This is the unique approach followed by Nalamdana (meaning "Are you well?" in Tamil), a non-profit organisation. Creative, innovative and entertaining behaviour change methods are used with community participation to enable people to make better-informed decisions about their health and their families. Response-driven participatory street theatre, interactive games and puzzles, audio and video cassettes, tele films, small group workshops, television serials - Nalamdana explores the full range of communicative possibilities to reach out to people.

At a Nalamdana show: laugh and think

A scene from the play on drug abuse

A typical Nalamdana performance entails the identification of a target group followed by a focus group discussion sensitising the participants to several issues - women's rights, sex and gender and HIV/AIDS. Nalamdana counsellors use their skills and tools to make these sessions interesting and interactive. The girls are encouraged to ask questions during a discussion or put their queries in a drop box.

If a girl is sexually abused in her childhood, will she be at a risk for HIV? Once a person is infected, which part of the body does the virus attack first? If a girl has sex during menstruation, will she be infected with HIV? Are there any scientists working to discover a medicine to cure AIDS? These are some typical questions posed by the college girls after a session on HIV/AIDS. Some 20 girls volunteer for the follow up activity - an intensive theatre workshop. Asked to come up with their own issues of concern, they select 'drug abuse', much to the surprise of the counsellors.

The girls - hailing from slum tenements and lower income group communities - said this was a growing problem among them. There received no sympathy at home, their performance in college was not given any importance. Being first time college goers in their family, they had to constantly fight for their right to continue with education. Many of them resided not with their parents, but in relatives' houses, as they had come to the city to study. The boyfriend and peer pressures were driving many to join groups indulging in drugs.

The theatre group selects a story along these lines and learns to convert this story into script. Their current knowledge, gleaned from the focus group discussions as well as their misconceptions, social taboos, cultural mores and habits are all woven into the script. The trainers put them through the basics of acting, stagecraft and they finally perform for some 300 girls from their college.

There is more follow up - a post play interactive session - discussion, arguments, questions and a post-play survey. Weeks later, Nalamdana counsellors record the level of knowledge retention, action taken by the target group and the messages that have been internalised.

The principal of the college was astounded when the group dealt with the issue of drug abuse. She had no idea it was a problem among them. The college has risen to the occasion by appointing a counsellor for the girls who can now get professional help before it's too late. ■

Nithya Balaji, Executive Trustee of Nalamdana, is also part of the Sankalp *Editorial Advisory Board.*

For more information visit www.nalamdana.org

ASK to get ANSWERS...

Is there a cure for AIDS?

Suchita, Kolkata

No. There is no cure for HIV/AIDS. Since AIDS is a collection of infections, there are medicines that can prevent and control opportunistic infections (OIs) in people affected by HIV/AIDS. These OIs (such as TB) would either be harmless or at least easily managed in healthy people but they can severely affect people with damaged immune systems, as is the case with people who live with HIV/AIDS.

Today, people living with HIV are receiving treatment using several types of anti-AIDS drugs, commonly known as antiretroviral drugs (ARVs). These drugs can check the pace at which HIV multiplies in the body. But ARVs are meant to be taken life-long, on a daily basis, following a rigid schedule. If patients miss even one dose in 50, the virus can become resistant to the medicines and they lose their effect. Even in patients who remember every dose, the medicines may stop working after some time. In addition, these drugs are very expensive and some of them are known to cause severe adverse reactions. However, a strict treatment regimen and proper care and treatment have been shown to prolong survival and improve the quality of life of people living with HIV/AIDS. Babies born to HIV-infected mothers can be protected against HIV infection if the mother and baby receive ARVs during pregnancy and at delivery.

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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MANAGING EDITOR **Jyoti Bahri;** CONSULTING EDITOR **Shree Venkatram**; EDITORIAL ADVISORS **Mark Chataway, Dr Jean-Louis Excler, Sweta Das; For subscriptions** e-mail to: **sankalp@iavi.org;** or write to ***Sankalp*** **193 1st Floor, Jor Bagh, New Delhi - 110003, INDIA. Tel: 91-11-2465 2668/9, 2461 0761/2;**

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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