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Nigeria: HIV/AIDS Rate Now Below 4.6 Percent, Says NACA
Victoria Ojeme
30 October 2010
Abuja — Director General of National Agency For the Control of AIDS, NACA, Dr John Idoko, said preliminary reports had shown that national prevalence rate of HIV/AIDS was below 4.6%. This comes as National Toll Free Counselling lines have been made available to Nigerians for more information on HIV/AIDS.

Dr Effiong Eno, who represented the Director, Idoko, made this known at an awareness programme on HIV/AIDS, Nature, Causes and Prevention held at Kotonkarfe, Kogi State, at the weekend.

According to him, Nigeria is beginning to win the battle against HIV/AIDS.
He said in 2008, Nigeria had a prevalence that was far above 6%, adding that it had now been brought down to 4.6% by the current assessment.

"If you want to look at the actual number of people before on treatment, it was 800,000. Currently, we have close to 400,000 people on treatment.

In her remark, Executive Secretary, Kogi State Agency for the Control of AIDS, KOSAKA, Hajia Rabiatu Ajanah, blamed local government officials for non-performance at the grass root.

"We have our various support groups that we are working with and we have about 113 support groups we are working with in Kogi State and some of them are up to 200_500 HIV/AIDS positive in the group and mostly are women.

"The local governments are not helping matters, they need to support the community by carrying out sensitisation as we just did now into various communities," she added.

US Panel Debates Value of HPV Vaccine for Boys
On Thursday, CDC’s Advisory Committee on Immunization Practices (ACIP) discussed several topics relating to human papillomavirus vaccination. In addition to data on uptake, the committee reviewed whether HPV vaccination of males is cost-effective and should be recommended. Merck’s Gardasil, the only HPV vaccine approved by the Food and Drug Administration for males, is marketed for male patients ages 9-26 to prevent genital warts caused by HPV types 6 and 11.
“In fact, 50 percent of patients who end up being diagnosed in an STD clinic didn’t even notice [genital warts] or were not overly concerned about them,” said ACIP member Dr. Franklyn Judson, a professor at the University of Colorado.

“I would say that the men that I see would rate genital warts on the quality scale just above death,” said Dr. James C. Turner, an ACIP liaison from the American College Health Association. The warts are a concern, he said, “not because of the medical consequences, but because of the social consequences.”

HPV is the cause of most cervical cancers, as well as anal cancers and some head and throat cancers.

At the meeting, Dr. Richard M. Haupt of Merck Research Labs presented data on Gardasil’s efficacy against lesions that can lead to anal cancers. Another study suggested that when female vaccine uptake is as low as it is now, vaccinating males is not as cost-effective as improving the female rate. When female uptake is high, vaccinating males still is not cost-effective, it said.

Anal cancer rates have risen in recent years, partly because gay men with HIV have been living longer. Less than 1 percent of boys ages 11-17 have received an HPV vaccination, while up to 15 percent of men on some college campuses have gotten the shots, Turner said.

Facebook Blamed for Vaccine Woes

Taranaki Daily News (New Plymouth), (10.28.2010) Esther Taunton

Slow uptake of a government-funded human papillomavirus (HPV) immunization program and a subsequent unsuccessful catch-up effort may be due in part to the lack of marketing on social networking sites, said Dr. Peter Catt, deputy chair of the Taranaki District Health Board.

Two years ago, the board launched a catch-up HPV vaccination program to boost the number of girls who receive the vaccine. But data show just 46 percent of Taranaki girls born between 1992 and 1996 have started the three-shot series. “Where we missed out was not using technology,” said Catt. “We weren’t on Facebook.”

According to Catt, a New Plymouth general practitioner, the message from his nurses is that girls are choosing to believe what they read online over the advice of medical practitioners. “The feedback from my nurses is that what was on Facebook was believed,” he said.

Sandra Boardman, general manager of planning, funding, and population health, said negative publicity at the time of the campaign’s launch impacted vaccination rates. Some in the community objected to vaccinating girls against an STD. Others expressed concern about adverse reactions to the vaccine.

The $164.2 million (US $126 million) national HPV immunization program began in 2008 and was hailed as New Zealand’s most significant step toward cancer prevention in half a century. But uptake was slow, leading to the catch-up program.

Boardman expressed hope that a larger percentage of girls would start and complete the vaccination program next year.

A New Class of Chinese Escorts


Women in universities and aspiring professionals looking to advance themselves amid China’s economic boom are increasingly turning to sex work, advocates and academics in Beijing say. This semester, at least two universities have banned students from working as escorts and mistresses.

“Years ago, when people heard somebody was a prostitute, [society] would criticize her very harshly, so girls who might want to copy her would change their minds,” said Xiao Yi, 27, who became a mistress to her boss while interning at an advertising agency. “These days, people’s attitudes have totally changed. They laugh at poor people, but they don’t laugh at prostitutes.”

Yi’s boss gives her money, helped with business ventures, and gave her “financial aid” for her relatives, she said. “He can look after people,” she said. “There are quite a few of us girls. We are thinking of ways to make our lives better.”

“More and more, students are making this choice, taking a shortcut to a better life,” said Lan Lan, a former sex worker who now runs an organization to raise HIV awareness and distribute condoms. “They find a rich lover, post services on the Internet, or just walk into a high-end club and sell themselves.”

Students reluctant to see themselves as sex workers can be lax about protected sex, Lan said. “If they’re trying to become a mistress, they won’t take a condom when they go to meet this man,” she said. “They want to show their purity and loyalty.”
“Most of the girls are financially comfortable, but they see their classmates carrying Louis Vuitton or Gucci bags, and they’re jealous,” said “Student Ding,” who takes a 10 percent commission for linking moneyed men with students. These men would find cruising karaoke bars and hotels for prostitutes degrading and time-consuming, he said. “They don’t have time and they don’t know how to find them. They can’t drive their posh cars around campus asking girls if they want to be their mistresses,” he said. “I act as a bridge.”

**Black Patients Fare Well on Vertex Hepatitis C Drug**

*Reuters*, (10.30.2010) Bill Berkrot

In a Phase III study, Vertex Pharmaceutical Inc.’s experimental hepatitis C drug telaprevir boosted sustained viral response rates among black patients, suggest data presented to the 61st annual meeting of the American Association for the Study of Liver Diseases in Boston.

Among black patients taking telaprevir with standard treatment, 62 percent achieved a sustained viral response (SVR), compared with just 25 percent for those taking pegylated interferon and ribavirin alone. As previously reported, the SVR rate was 75 percent for all patients receiving telaprevir in combination with pegylated interferon and ribavirin, compared with 44 percent for those on standard treatment alone. The new data are important because of higher hepatitis C prevalence and lower SVR rates among African Americans.

“If you look at that treatment difference and then you look at the difference in the overall population, in fact the benefit relatively speaking is even greater,” said Robert Kauffmann, Vertex’s chief medical officer. “African Americans bear a large proportion of the burden of hepatitis C in the United States, compared with Caucasians and the overall population.”

In a subgroup analysis, 62 percent of patients with advanced liver fibrosis or cirrhosis taking telaprevir achieved SVR, compared with 33 percent on standard therapy.

Another study showed 58 percent of telaprevir patients met criteria for a 24-week treatment. Criteria were undetectable viral levels in the blood at weeks four and 12. Another study showed no benefit from extending therapy to 48 weeks once these criteria were met.

Telaprevir and a similar treatment candidate being developed by Merck & Co. are generating excitement due to their comparatively better SVR rates in a shorter time than standard therapy alone. It is believed that thousands of people with hepatitis C are awaiting approval of these drugs before they initiate treatment.

Vertex plans to complete its application for telaprevir for Food and Drug Administration review this year. Many expect FDA approval to be granted in 2011.

**Kenya First Of Four Countries To Launch UNICEF, Partners Initiative Aimed At PMTCT Of HIV**

On Friday, UNICEF and the Kenyan government announced a partnership aimed at preventing mother-to-child transmission (PMTCT) of HIV by providing HIV-positive mothers with packs of medicines they can easily administer to themselves or their babies at home, IRIN/PlusNews reports. According to the news service, the “mother-baby pack” contains antiretroviral drugs (ARVs) and antibiotics that women can easily administer themselves at home to reduce the risk of infecting their babies and is colour-coded to make it easy to use even for illiterate mothers; each colour shows which drugs are to be taken during pregnancy, during labour and after delivery” (10/29).

“The ‘Mother-Baby-Pack’ is part of the [Kenyan] government’s Maisha MTCT-free Zone Initiative,” according to a UNICEF press release. "This innovative programme is designed to help virtually eliminate mother-to-child-transmission of HIV and pediatric AIDS by 2013 in Nyanza and Rift Valley provinces, where about half of all Kenyan children with HIV live, and by 2015 in the entire country. Without treatment, around half of all children born with HIV will die before their second birthday," the press release states (10/29).

"This initiative has the potential to save many lives and I believe it is [an important] component towards the realization of our goal," UNICEF Executive Director Anthony Lake said at the launch Friday, according to IRIN/PlusNews (10/29).

The launch of the mother-baby packs in Kenya "marks the beginning of a phased implementation in four countries, including also Cameroon, Lesotho and Zambia," according to the UNICEF press release (10/29). *Capital FM* writes that the program in Kenya "is scheduled to run through mid-2011,” during
which it "will be monitored by UNICEF and its partners" to monitor distribution of the drugs as well as mothers' acceptance and use of the medicine.

Capital FM reports that low rates of prenatal care in Kenya, "with less than a half of all pregnant women actually completing four antenatal care visits before giving birth and more than a half of pregnant women giving birth at home," complicate efforts to reduce MTCT. Lake explained, "Other factors hindering scale-up of prevention of mother to child transmission services is that a third of all pregnant women living with HIV and AIDS still receive less efficacious drug regimens; and that babies born to mothers with HIV/AIDS are often not tested early-on" (Wambui, 10/31).

"The pack was developed by UNICEF in collaboration with the World Health Organization, USAID, Elizabeth Glaser Pediatric AIDS Foundation and other partners," VOA News writes. "The idea was inspired by healthcare workers in Lesotho, who gave HIV-positive pregnant women plain paper bags filled with pre-measured drugs along with instructions on how to administer them during and after pregnancy. The experiment proved highly effective at stopping HIV transmission from mother to child," according to the news service (Ryu, 10/29).

In addition to the mother-baby packs, the "Maisha Initiative further aims at increasing the number of deliveries with assistance from skilled birth attendants through intensified follow up of pregnant women by community health workers, and by supporting the roll out of a Health Services Support Fund. The Fund provides incentives to health facilities that improve their performance and reach more pregnant women, especially in remote communities," according to the UNICEF press release (10/29).

"According to the 2010 report on universal access to HIV prevention, care, and treatment released last month by WHO, UNAIDS, and UNICEF, the global health community is reaching more than half of pregnant women (53%) in need of services to prevent transmission of HIV from mother to baby," according to a press release from the Elizabeth Glaser Pediatric AIDS Foundation. "However, nearly 1,200 babies are still newly infected with HIV every day, emphasizing the need to reach more mothers and children" (10/29).

Even though Kenya has made progress in adding PMTCT programs in the country, some "22,000 children are infected annually through mother-to-child transmission," the Daily Nation writes in an article that examines the factors that present challenges to driving down the number of children infected with HIV/AIDS (Otieno, 10/30).

"The initiative is being supported financially by a number of partners including the U.S. Government, UNICEF National Committees, the Clinton Health Access Initiative (CHAI) and the Mothers-to-Mothers (M2M) programme," according to the UNICEF press release (10/29).

**Human Immune System Assassin’s Tricks Visualized for the First Time**

ScienceDaily (Oct. 31, 2010) — Scientists from the UK and Australia have seen the human immune system's assassin—a protein called perforin—in action for the first time. The UK team is based at Birkbeck College where they used powerful electron microscopes to study the mechanism that perforin uses to punch holes in rogue cells.

The research is published on October 31 in Nature. Professor Helen Saibil, who leads the UK team at Birkbeck College, said: "Perforin is a powerful bullet in the arsenal of our immune system—without it we could not deal with the thousands of rogue cells that turn up in our bodies through our lives."

"Perforin is our body's weapon of cleansing and death," said project leader Professor James Whisstock from Monash University, Melbourne, Australia.

Perforin works by punching holes in cells that have become cancerous or have been invaded by viruses. The holes let toxic enzymes into the cells, which then destroy them.
If perforin isn’t working properly the body can’t fight infected cells. And there is evidence from mouse studies that defective perforin leads to an upsurge in malignancy, particularly leukaemia, so says Professor Joe Trapani, head of the Cancer Immunology Program at the Peter MacCallum Cancer Centre in Melbourne, Australia.

The first observations that the human immune system could punch holes in target cells was made by the Nobel Laureate Jules Bordet over 110 years ago, but we have had to wait for the latest advances in structural molecular biology to find out how exactly this happens.

Professor Saibil continued: "From our previous work we already knew that bacterial toxins, such as the one involved in pneumonia, dramatically change shape to punch holes in membranes. We were fascinated by perforin and wanted to know its structure and how that might change in order for it to act as a hole-punching machine."

The structure was revealed by combining information about a single perforin molecule—visualised using the Australian Synchrotron—with Professor Saibil’s electron microscope images (taken in London) of a ring of perforin molecules clustered together to form a hole in a cell membrane.

Professor Whisstock added: "Now we know how it works, we can start to fine tune it to fight cancer, malaria and diabetes."

Another interesting finding is that the important parts of the perforin molecule are quite similar to those toxins deployed by bacteria such as anthrax, listeria and streptococcus, showing that this method of making holes in cell membranes is quite ancient in evolution. "The molecular structure has survived for close to two billion years, we think," said Professor Trapani.

Perforin is also the culprit when the wrong cells are marked for elimination, either in autoimmune disease conditions, such as early onset diabetes, or in tissue rejection following bone marrow transplantation. So the researchers are now investigating ways to boost perforin for more effective cancer protection and therapy for acute diseases such as cerebral malaria. And with the help of a £600K grant from the Wellcome Trust they are working on potential inhibitors to suppress perforin and counter tissue rejection.

Professor Douglas Kell, BBSRC Chief Executive said: "New technologies in microscopy and synchrotron experiments have opened up tremendous opportunities for molecular biologists. This is a great example where the knowledge we gain about the normal structure and function of a molecule has the potential to underpin important developments in our health and well being."

Scientists 'Watch' Formation of Cells' Protein Factories, Ribosomes, for First Time

Scientists 'Watch' Formation of Cells' Protein Factories, Ribosomes, for First Time

ScienceDaily (Nov. 1, 2010) — A team from The Scripps Research Institute has revealed the first-ever pictures of the formation of cells’ "protein factories." In addition to being a major technical feat on its own, the work could open new pathways for development of antibiotics and treatments for diseases tied to errors in ribosome formation. In addition, the techniques developed in the study can now be applied to other complex challenges in the understanding of cellular processes.

Identifying and observing the molecules that form ribosomes—the cellular factories that build the proteins essential for life—has for decades been a key goal for biologists but one that had seemed nearly unattainable. But the new Scripps Research study, which appears in the October 29, 2010 issue of the journal Science, yielded pictures of the chemical intermediate steps in ribosome creation.

"For me it was a dream experiment," said project leader James Williamson, Ph.D., professor, member of the Skaggs Institute for Chemical Biology, and dean of graduate and postgraduate studies at Scripps Research, who credits collaborators at the Scripps Research National Resource for Automated Molecular Microscopy (NRAMM) facility for making it possible. "We have great colleagues at Scripps to collaborate with who are willing to try some crazy experiments, and when they work it’s just beautiful."

Past studies of the intermediate molecules that combine to form ribosomes and other cellular components have been severely limited by imaging technologies. Electron microscopy has for many years made it possible to create pictures of such tiny molecules, but this typically requires purification of the molecules. To purify, you must first identify, meaning researchers had to infer what the intermediates were ahead of time rather than being able to watch the real process.

"My lab has been working on ribosome assembly intensively for about 15 years," said Williamson. "The basic steps were mapped out 30 years ago. What nobody really understood was how it happens inside cells."
Creating a New View

The NRAMM group, led by Scripps Research Associate Professors Clinton Potter and Bridget Carragher and working with Scripps Research Kellogg School of Science and Technology graduate students Anke Mulder and Craig Yoshioka, developed a new technique, described in the Science paper and dubbed discovery single-particle profiling, which dodges the purification problem by allowing successful imaging of unpurified samples. An automated data capture and processing system of the team’s design enables them to decipher an otherwise impossibly complex hodgepodge of data that results.

For this project, second author Andrea Beck, a research assistant in the Williamson laboratory, purified ribosome components from cells of the common research bacterium Escherichia Coli. She then chemically broke these apart to create a solution of the components that form ribosomes. The components were mixed together and then were rapidly stained and imaged using electron microscopy. "We went in with ‘dirty’ samples that contained horribly complex mixtures of all different particles," said Williamson.

Mulder, who is first author on the paper, collected and analyzed the particles that were formed during the ribosome assembly reaction. Using the team’s advanced algorithms, they were able to process more than a million data points from the electron microscope to ultimately produce molecular pictures.

The Pieces Fit

The team produced images that the scientists were able to match like puzzle pieces to parts of ribosomes, offering strong confirmation that they had indeed imaged and identified actual chemical intermediates in the path to ribosome production. "We always saw the same thing no matter how we processed the data, and this led us to believe this was real," said Williamson.

Further confirmation came as the researchers imaged components from different timeframes. After breaking down ribosome components, the scientists prepared samples at various stages allowing enough time for the molecular mix to begin combining as they do during ribosome creation in cells.

Imaging this time series, the team was able to show higher concentrations of larger, more complex molecules and fewer smaller molecules as time elapsed. These results fit with the limited information that was already available about the timing of formation steps, providing further confirmation of the team’s success.

Interestingly, this work also confirmed that there are more than one possible paths in ribosome formation, a phenomenon known as parallel assembly that been suggested by prior research but never definitively confirmed.

Long-Term Potential

Williamson says that with the information now at hand, they will be able to move forward with studies of which additional molecules might be present in cells and essential for ribosome formation. Such data could offer exciting medical potential.

All bacteria contain and are dependent on ribosomes. Identification of molecules required for ribosome assembly could offer new targets for antibiotic drugs aimed at killing bacteria. "If we can figure out how to inhibit assembly, that would be a very important therapeutic avenue," said Williamson.

There are also indications that some diseases such as Diamond Blackfan Anemia might be caused, at least in some cases, by errors in ribosome production. Better understanding of that production could also reveal ways such errors might be repaired to cure or prevent disease.

At the more basic level, this successful project has also proven techniques that Scripps Research scientists and other researchers can apply to allow similar imaging and understanding of other complex but critical cellular processes.

Journal Reference:

Common Stomach Bacteria May Fight Off Inflammatory Bowel Disease Caused by Salmonella

ScienceDaily (Nov. 1, 2010) — *Helicobacter pylori*, a common stomach bacterium, reduced the severity of inflammation of the colon caused by *Salmonella* in mice, according to research from U-M Medical School scientists.

More than half the people in the world are infected with *H. pylori*, although it is very unusual to find it in the United States. But this research shows there may be an inflammation control benefit to hosting the *H. pylori* infection, says Peter Higgins, M.D., Ph.D., M.Sc., lead author of the study published last week in the journal Inflammatory Bowel Diseases.
"If we have evolved to live with certain bugs, maybe there is a reason," said Higgins, assistant professor of gastroenterology in U-M's Department of Internal Medicine. "This research demonstrates that having *H. pylori* in your stomach could have beneficial immune effects in other parts of the body."

In the study, mice were infected with *H. pylori*, allowed to develop immune tolerance for a month, and then infected with *Salmonella*, which induces the inflammatory bowel disease colitis. The data provided the first evidence that *H. pylori* infection in the stomach alters the immunological environment of the lower gastrointestinal tract and reduced the severity of *Salmonella*-induced colitis.

"This was surprising because *H. pylori* infects the stomach, not the colon. It appears to have a more global effect on the gut immune system," says John Kao, M.D., senior author of this study and assistant professor in U-M's Department of Internal Medicine.

"But it may explain why people in regions with lots of *H. pylori* infection—such as Asia and Africa—get fewer inflammatory bowel diseases, like ulcerative colitis and Crohn's disease."

It also may explain why *H. pylori* infection is so common, Higgins says. *Salmonella* was historically a rampant fatal infection that caused the plague of Athens, which led to rise of Sparta. It also likely led to the early death of Alexander the Great. So it would make sense that many humans carry the *H. pylori* bacteria, if it truly reduces the severity of inflammation caused by *Salmonella*, Higgins says.

The *H. pylori* infection is now more commonly found in developing countries or those with poor sanitation, where *Salmonella* and inflammatory bowel diseases are more common. Most people contract *H. pylori* in their first seven years of life, most commonly through exposure to feces. Higgins does not recommend that inflammatory bowel patients should be infected with *H. pylori*, however. In the U.S., *H. pylori* infection is treated with antibiotics because it can lead to stomach ulcers or cancer, even though most people don't notice they have it.

"There may be a reason we co-exist with *H. pylori*. Maybe we should not be so quick to get rid of it in patients who do not have stomach ulcers," Higgins says, adding that this may be especially true in places where *Salmonella* remains a common threat.

"It would be reasonable for researchers to look at whether *H. pylori* infection is associated with reduced severity of other gut infections like cholera or Clostridium difficile. Many more studies are needed, however, to see if *H. pylori* could actually prevent inflammatory bowel disease."

**Antibiotics Have Long-Term Impacts on Gut Flora**

ScienceDaily (Nov. 1, 2010) — Short courses of antibiotics can leave normal gut bacteria harbouring antibiotic resistance genes for up to two years after treatment, say scientists writing in the latest issue of *Microbiology*, published Nov. 3.

The researchers believe that this reservoir increases the chances of resistance genes being surrendered to pathogenic bacteria, aiding their survival and suggesting that the long-term effects of antibiotic therapy are more significant than previously thought.

Antibiotics that are prescribed to treat pathogenic bacteria also have an impact on the normal microbial flora of the human gut. Antibiotics can alter the composition of microbial populations (potentially leading to other illnesses) and allow micro-organisms that are naturally resistant to the antibiotic to flourish.

The impact of antibiotics on the normal gut flora has previously been thought to be short-term, with any disturbances being restored several weeks after treatment. However, the review into the long-term impacts of antibiotic therapy reveals that this is not always the case. Studies have shown that high levels of resistance genes can be detected in gut microbes after just 7 days of antibiotic treatment and that these genes remain present for up to two years even if the individual has taken no further antibiotics.

**Journal Reference:**

Peter D.R. Higgins, Laura A. Johnson, Jay Luther, Min Zhang, John Y. Kao. Prior *Helicobacter pylori* infection ameliorates *Salmonella typhimurium*-induced colitis: Mucosal crosstalk between stomach and distal intestine. *Inflammatory Bowel Diseases*, 2010; DOI: [10.1002/ibd.21489](https://doi.org/10.1002/ibd.21489)
The consequences of this could be potentially life-threatening explained Dr Cecilia Jernberg from the Swedish Institute for Infectious Disease Control who conducted the review. "The long-term presence of resistance genes in human gut bacteria dramatically increases the probability of them being transferred to and exploited by harmful bacteria that pass through the gut. This could reduce the success of future antibiotic treatments and potentially lead to new strains of antibiotic-resistant bacteria."

The review highlights the necessity of using antibiotics prudently. "Antibiotic resistance is not a new problem and there is a growing battle with multi-drug resistant strains of pathogenic bacteria. The development of new antibiotics is slow and so we must use the effective drugs we have left with care," said Dr Jernberg. "This new information about the long-term impacts of antibiotics is of great importance to allow rational antibiotic administration guidelines to be put in place," she said.

**Journal Reference:**

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**Size of Protein Aggregates, Not Abundance, Drives Spread of Prion-Based Disease**

ScienceDaily (Oct. 28, 2010) — Mad Cow disease and its human variant CreutzfeldJakob disease, which are incurable and fatal, have been on a welcome hiatus from the news for years, but because mammals remain as vulnerable as ever to infectious diseases caused by enigmatic proteins called prions, scientists have taken no respite of their own. In the Oct. 29 edition of the journal Science, researchers at Brown University report a key new insight into how prion proteins—the infectious agents—become transmissible: In yeast at least, it is the size of prion complexes, not their number, that determines their efficiency in spreading.

"The dogma in the field was that the misfolding of the protein is sufficient to cause disease, and the clinical course of the infection depended on the amplification of the misfolded protein," said Tricia Serio, associate professor of molecular biology, cell biology and biochemistry. "But over the years in mammals it has become clear that the abundance of misfolded protein is not a good predictor of disease progression. The question is, What else has to happen for you to get the clinical pathology?"

Cells make prion proteins naturally, although biologists do not understand what their normal role is in mammals. When those proteins misfold in cells, they assemble into structures called aggregates, but other proteins, known as chaperones, attempt to break down the aggregates. The rates at which this assembly and disassembly occurs are determined by the shape or conformation that the prion protein has adopted.

"Different conformations of the same prion protein can dramatically alter the spread of pathology and the incubation time of prion diseases," Serio said. "We wanted to learn how."

By combining experiments in yeast cells with mathematical models, the Brown team found that what affects a prions' ability to transmit from cell to cell is the size of the structures into which they assemble, Serio said. If the aggregates become too large, they lose their transmissibility among cells. Prion aggregates that remain small are transmitted with greater efficiency.

"In this paper we changed the transmissibility just by shifting the size," Serio said. "We could change it in either direction."

The proof was plain to see. Postdoctoral researcher Aaron Derdowski monitored differently sized prion aggregates as they moved among cells under the microscope and could see that smaller ones fared better than larger ones. He also kept track of the spread of different prion structures through a genetic analysis of affected cell populations.
In concert with the experimental work, Suzanne Sindi, a postdoctoral researcher with a joint appointment in molecular biology, cell biology and biochemistry and the Center for Computational Molecular Biology, modeled how cells make and spread prion aggregates, providing a novel simulation of the process that she ran on a computing cluster in the Center for Computation and Visualization at Brown. The model that best replicated experimental observations was the one in which aggregate size, rather than abundance, was the key factor.

**Implications for disease**

Serio says the insights the team has gained in yeast may better explain what others have observed in mammals as well.

"Previously it was not clear why you would have those outcomes," she said.

Ultimately the findings could inform future strategies for developing a treatment for prion infection. If researchers unaware of the importance of aggregate size developed a therapy to hinder prion aggregate formation, they might inadvertently make things worse by producing smaller aggregates, Serio said. "A more effective strategy might be to control the size of the aggregates," she said, "rather than their presence or absence."

The findings may also relate to other neurodegenerative diseases that depend on misfolding proteins, such as Alzheimer’s disease or Parkinson’s disease, Serio said.

**Shuttle Mice to Boost Disease Research: Experiment on Last Flight of Discovery Will Probe Spaceflight-Induced Immune-System Impairment**

ScienceDaily (Oct. 30, 2010) — When the space shuttle Discovery lifts off on its final flight Nov. 2, its six astronauts will be joined by 16 rodent passengers on a historic mission of their own.

Riding in special self-contained modules that automatically supply them with food and water, the mice will be part of a long-term NASA effort aimed at understanding why spaceflight makes humans more vulnerable to infection by viruses and bacteria.

The agency has studied the phenomenon aboard its space shuttles for more than 25 years, collecting data from laboratory animals and astronauts themselves. The mouse experiment—a collaboration between teams at the University of Texas Medical Branch at Galveston and NASA’s Ames Research Center in Mountain View, Calif.—will be the final immunology investigation planned for the shuttle program.

"Since the Apollo missions, we have had evidence that astronauts have increased susceptibility to infections during flight and immediately post-flight—they seem more vulnerable to cold and flu viruses and urinary tract infections, and viruses like Epstein-Barr, which infect most people and then remain dormant, can reactivate under the stress of spaceflight," said Dr. Roberto Garofalo, a professor at UTMB Health and principal investigator for the project. "We want to discover what triggers this increased susceptibility to infection, with the goal both of protecting the astronauts themselves and people with more vulnerable immune systems here on Earth, such as the elderly and young children."

The mice aboard Discovery will be in orbit for 11 days, during which time shuttle astronauts will perform daily checks on their health and well-being. Within two hours of the shuttle's return to Earth, eight of the animals will be infected with respiratory syncytial virus—a pathogen that infects almost all human children by age two and ordinarily causes a relatively harmless cold-like upper respiratory disease. In some children, however, the infection spreads to the lungs, where the inflammation it generates causes coughing, wheezing and extreme difficulty in breathing.

Another group of mice kept in nearly identical conditions on the ground will also be exposed to the virus. Garofalo’s team will conduct genetic and protein studies of the lung and nasal tissues of both sets of mice, evaluating lung inflammation, viral replication and other key factors related to RSV infection in mice.

"We have substantial experience using mice to study immune response to RSV infection, and that will enable us to look at all the aspects of the immune responses of these mice as well as the pathological manifestations of the disease, looking at ways in which the space environment affects this respiratory infection," Garofalo said.

Understanding how spaceflight impairs the immune system and finding ways to make sure that infection doesn’t threaten the health of space travelers are expected to become increasingly important, as NASA plans human expeditions beyond the relative safety of Earth orbit—to Mars, for example, or the asteroids. The developing commercial spaceflight industry, which hopes to launch large numbers of private citizens into orbit in the near future, also has a stake in ensuring that its passengers stay safe and healthy.
Despite the shuttle program's end, Garofalo said, immune system experiments in space may well continue on the International Space Station.

"The space environment incorporates many factors that we know affect the immune system—microgravity, radiation, even different nutritional standards—all acting in a relatively short period of time," Garofalo said. "The space station provides a unique environment for generating answers to fundamental questions about the human immune system. Those answers will benefit people here on Earth, and there's been a lot of interest in pursuing them."

**CDC Reports First Blood Transfusion HIV Transmission since 2002**

**SUMMARY:** Public health investigators described an unusual case of HIV transmission through a transfusion of infected blood in the October 22, 2010 issue of the CDC's *Morbidity and Mortality Weekly Report*. The donor gave blood soon after becoming infected, during the "eclipse period" before HIV RNA is detectable on a screening test. Transmission via transfusion remains very rare; this case, which occurred in 2008, was the first reported since 2002.

By Liz Highleyman

In the early years of the AIDS epidemic, many cases of *HIV infection* were attributable to blood transfusion, especially among people such as hemophiliacs who received blood products frequently and from many donors. Blood collection facilities at first tried to protect the blood supply by asking prospective donors about risk factors including men having sex with men, injection drug use, and exchanging sex for money.

The first blood screening test, introduced in 1985, tested for antibodies against the virus and had a "window period" of at least a few weeks after exposure before the body produced enough antibodies to be detected. Newer methods test for HIV genetic material (RNA or DNA) or antigens directly, and can reveal infection sooner. As of 1999, blood banks have used nucleic acid amplification tests, which detect HIV gene sequences. But such tests still have an "eclipse period" of about 9 days after exposure during which they may not detect the virus.

The recently described case involved a blood donor in Missouri. When this man first donated in June 2008, he reported no HIV risk factors. Enzyme immunoassay screening did not reveal HIV antibodies and nucleic acid amplification of pooled blood from 16 donations did not detect HIV genetic material.

This individual donated again at the same center in November 2008, and this time his blood tested positive for HIV. The Centers for Disease Control and Prevention (CDC) indicated that the man likely became infected within several days before the first donation.

Unfortunately, during the period between the 2 donations, blood plasma from the infected donor was given to a patient undergoing kidney transplantation in Colorado. Missouri health officials notified Colorado authorities in December, and the recipient was tested for HIV. The patient did not have detectable HIV antibodies, but had an HIV RNA viral load of 7240 copies/mL and a CD4 T-cell count of only 48 cells/mm3; no symptoms of HIV infection were noted. Genetic sequencing showed that the recipient's virus was 99% identical to that of the donor.

At this time the patient started *antiretroviral therapy (ART)* and was also taking mycophenolate mofetil (CellCept)—used to help prevent organ rejection after a transplant—which also inhibits T-cell proliferation and HIV replication in activated T-cells and macrophages.

Extensive tracing found that blood products from the initial donation had only been given to the Colorado patient and 1 other person in Arkansas who died of heart disease 2 days after receiving the infected blood.

The donor initially refused to be interviewed by the Missouri Department of Health and Senior Services, but eventually consented in April 2009. He then admitted having extra-marital sex with both men and women—often anonymous and while intoxicated—including an instance just before the June 2008 donation.

In an accompany editorial, CDC officials noted that the agency received reports of 3 similar cases during 2000 and 2002, in which blood that tested negative for HIV by both ELISA antibody assays and nucleic acid amplification resulted in HIV transmission to a blood product recipient.

The CDC authors noted that the risk of HIV transmission via blood transfusion is "extremely low"—estimated at 1 case per 1.5 million procedures—but "likely is under-recognized." This might happen, for example, if a recipient dies due to another cause before testing positive; in the present case, the donor's infection was only detected because he gave blood a second time. The authors estimated that there
might be approximately 11 donations of HIV infected blood and 20 instances of HIV-containing blood products released each year.

"Even though such transmissions are rare, health-care providers should consider the possibility of transfusion-transmitted HIV in HIV-infected transfusion recipients with no other risk factors," the CDC authors advised. "It is the responsibility of persons who donate blood to answer screening questionnaires accurately to ensure the safest blood supply possible." 10/29/10

Reference

Inflammation Biomarkers Linked to Increased Risk of Death in People with HIV

SUMMARY: HIV positive people with elevated levels of C-reactive protein (CRP) and fibrinogen, 2 biomarkers associated with inflammation and blood clotting, had a significantly higher risk of death over 5 years, according to a report in the November 1, 2010 Journal of Acquired Immune Deficiency Syndromes. These findings suggest that inflammation remains an important risk factor for mortality even among individuals with relatively high CD4 cell counts, the researchers concluded.

By Liz Highleyman
A growing body of evidence indicates that chronic immune activation and persistent inflammation contribute to increased rates of non-AIDS conditions such as cardiovascular disease in people with HIV, well before they experienced severely impaired immune function.

Phyllis Tien, Carl Grunfeld, and fellow investigators with the Fat Redistribution and Metabolic Change in HIV Infection (FRAM) study looked at the relationship between mortality and blood levels of the inflammation biomarker C-reactive protein and the coagulation (clotting) biomarker fibrinogen among HIV positive individuals over the course of 5 years.

CRP and fibrinogen are released as part of the inflammatory and clotting cascades that occur with development of atherosclerosis, a build-up of cholesterol, immune cells, scar tissue, and other material in the arteries. Atherosclerosis plaques and blood clots can block arteries, leading to a heart attack or stroke can result.

The present analysis included 922 HIV positive FRAM participants. The majority (about 70%) were men, the median age was just over 40 years, and about 40% were smokers. About 90% were on antiretroviral therapy (ART) and about 80% had undetectable viral load. The average CD4 count was approximately 350 cells/mm3—the level at which HIV positive people should definitely start treatment, according to current U.S. ART guidelines.

Participants with baseline fibrinogen levels in the highest tertile, or third, were on average older, more likely to be black, and had higher total cholesterol, lower HDL ("good cholesterol"), higher HIV viral load, and lower CD4 cell counts.

Results
- Over a 5-year period, baseline levels of both CRP and fibrinogen were significantly associated with increased risk of death due to any cause, after adjusting for traditional cardiovascular risk factors.
- Participants with high CRP levels (> 3 mg/L) had a 2.7-fold higher likelihood of death than those with low levels (< 1 mg/L).
- Patients with fibrinogen levels in the highest tertile (> 406 mg/dL) had a 2.6-fold higher likelihood of death compared with those in the lowest tertile (< 319 mg/dL).
- When stratified according to CD4 cell count, fibrinogen remained independently associated with elevated mortality for all categories:
  - CD4 < 200 cells/mm³: odd ratio (OR) 1.93 per 100 mg/dL increase in fibrinogen;
  - 200-350 cells/mm³: OR 1.43;
  - 350-500 cells/mm³: OR 1.43;
  - CD4 > 500 cells mm³: OR 1.30.

Based on these results, the investigators concluded, "Fibrinogen and CRP are strong and independent predictors of mortality in HIV-infected adults."
“Our findings suggest that even in those with relatively preserved CD4 counts > 500 [cells/mm3], inflammation remains an important risk factor for mortality,” they continued. “Further investigation should determine whether interventions to reduce inflammation might decrease mortality risk in HIV-infected individuals.”

“The lack of a substantial interaction of fibrinogen and CRP with CD4 also strengthened our hypothesis that the association of inflammation with mortality is independent of the absolute CD4 count,” they elaborated in their discussion. “These findings could suggest that the CD4 cells remain immunologically activated despite CD4 cell restoration. The subsequent persistent inflammatory state could contribute to non-HIV-related comorbidities such as liver and cardiovascular disease, which have been reported as the leading causes of non-HIV-related death in the HAART era.”

Reference

Tests Show Haitian Cholera Strains Match Ones From South Asia, CDC Says
Tests have shown that the strain in Haiti’s cholera outbreak is similar to cholera strains found in South Asia, the CDC said on Monday, Agence France-Presse reports (11/1).

“The new findings from CDC’s laboratory are based on a method of ‘DNA fingerprinting’ called pulsed field gel electrophoresis (PFGE), which analyzes DNA patterns that can then be compared with PFGE patterns of cholera strains from other regions of the world,” according to a CDC press release. The test, which was performed on 13 samples from Haitian cholera patients, found that they "are the same strain and similar to a cholera strain found in South Asia," the CDC states, noting that the findings are "not unexpected." According to the press release, additional "information about this strain, including the possibility that it might be found in other regions of the world, is anticipated from additional studies" (11/1). But further testing might not explain how the outbreak in Haiti started, the CDC said, AFP notes.

"Although these results indicate that the strain is non-Haitian, cholera strains may move between different areas due to global travel and trade," Haitian Minister of Health Alex Larsen said of the findings, AFP writes. "Therefore, we will never know the exact origin of the strain that is causing the epidemic in Haiti. This strain was transmitted by contaminated food or water or an infected person," Larsen said (11/1).

"The finding intensifies scrutiny on a U.N. base above a tributary to the Artibonite River that is home to a contingent of recently arrived peacekeepers from Nepal, a South Asian country where cholera is endemic and which saw outbreaks this summer," the Associated Press/Seattle Times reports. The CDC's Christopher Braden pointed out that South Asia is the region around the Indian subcontinent, which includes India, Pakistan and Nepal. The finding rules out some theories, "including a hypothesis that the strain might be related to a 1990s South American outbreak, Braden said. He said the strain was 'fairly common.'"

"Following the CDC report, U.N. mission spokesman Vincenzo Pugliese said U.N. personnel took environmental samples around the [Nepalese] base Oct. 24, including from septic tanks, and tests by a private laboratory found no cholera. He added that the mission ‘welcomes the scientific contribution of the national public health laboratory in Haiti and the CDC to the understanding of the current cholera outbreak in Haiti,’” according to the news service. The article also describes recent visits to the Nepalese U.N. base, which the AP/Seattle Times said "reeked of human waste" in an area nearby (Katz, 11/1).

In related coverage, The Atlantic examines the outbreak in Haiti and looks at how the situation is being addresses on the ground. "As the crisis continues, the government and international institutions are distributing Clorox as widely as possible. And their efforts have diminished the number of new cases and deaths. But in Haiti, cholera is here to stay. Even if the epidemic can be contained in the near term, infected bodies buried without being sanitized will contaminate ground water," the magazine writes.

Jean William Pape, director of the Haitian health organization GHESKIO, said he "hoped the epidemic would 'create an incentive' for the government to provide 'what we have needed for a long time: adequate sanitary conditions for the population'" (Gaestel, 11/1).

In Afghanistan, Leprosy Still Strikes Despite Billions Of Aid Money Pumped Into Country
“Despite tens of billions of dollars in aid money flowing into [Afghanistan] since 2001, living conditions for millions of Afghans have changed little from those of centuries ago,” when diseases like leprosy were more common, Agence France-Presse reports in an article that describes the efforts of a doctor in the
region against leprosy and an Afghan family with two members impacted by the disease. The article also examines how misuse of development funds have kept the country from moving forward and looks at recent efforts by government officials to maintain better oversight of development projects. "Earlier this year, Afghanistan’s Western backers agreed to give the government greater control of aid money – up to 50 percent from 20 percent – and to improve their own oversight of development funds," AFP writes. "What provincial officials say they need is the basics – roads, power, hospitals and schools – to drag their regions into the current century," according to the news service (11/1).

New study re-examines bacterial vaccine studies conducted during 1918 influenza pandemic
WHAT: Secondary infections with bacteria such as Streptococcus pneumoniae, which causes pneumonia, were a major cause of death during the 1918 flu pandemic and may be important in modern pandemics as well, according to a new article in the Journal of Infectious Diseases co-authored by David M. Morens, M.D., senior advisor to the director of the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health.

The researchers examined 13 studies published between 1918 and 1920. During this time, many scientists erroneously believed that influenza was caused by bacteria, not a virus. As a result, researchers began performing and publishing results from clinical trials testing bacterial vaccines designed to prevent the flu. In their new study, Dr. Morens and his colleagues used modern statistical and evaluation methods to re-analyze the vaccine effectiveness data from these old studies in an attempt to correct for any statistical biases in the original analysis.

In addition to confirming the importance of bacterial infections associated with the 1918 influenza pandemic, the new analysis suggests that the use of bacterial vaccines containing S. pneumoniae could reduce pneumonia rates and deaths in modern influenza pandemics as well. During the 2009-2010 H1N1 influenza pandemic, the authors write, autopsy results implicated bacterial infections in 29 to 55 percent of deaths. In light of this study, the authors recommend more research into the use of bacterial vaccines to prevent illness and death associated with influenza.


Antibody locks up West Nile's infection mechanism
November 2, 2010
WEST LAFAYETTE, Ind.—Researchers have learned the structure that results when an antibody binds to the West Nile virus, neutralizing the virus by locking up its infection mechanism. The information could help scientists develop a vaccine against the mosquito-borne disease.

"The findings show precisely how a key part of the antibody, called the antigen binding fragment, or Fab, attaches to two adjacent protein molecules that make up the virus's outer shell. This "crosslinking" attachment between molecules is repeated over the entire shell, interlocking the 30 molecular "rafts" that make up the shell and preventing structural changes needed for the virus to infect host cells," said Michael Rossmann, the Hanley Distinguished Professor of Biological Sciences in Purdue's College of Science.

"The antibody crosslinking causes the virus to become rigid, and this rigidity prevents conformational changes to the virus needed to fuse with host cells," Rossmann said.

Findings are detailed in a research paper that appeared in October in Proceedings of the National Academy of Sciences. The team included postdoctoral researcher Bärbel Kaufmann, other researchers at Purdue, the Washington University School of Medicine in St. Louis and the biotechnology company Crucell Holland B.V. in The Netherlands.

"Learning how antibodies neutralize viruses is important for developing effective vaccines," Rossmann said.

"There are many antibodies that can neutralize West Nile virus," he said. "These findings concern a specific antibody, called CR4354. It uses an unusual approach to neutralize the virus. Normally an antibody binds to a single molecule, but now we see this crosslinking, which is quite clever because it ties everything rigidly together."

The researchers used a process called cryoelectron microscopy to take detailed pictures of the Fab-virus complex. They also used X-ray crystallography to learn the antibody's precise crystalline structure.

West Nile belongs to a family of viruses known as flaviviruses, which includes a number of dangerous insect-borne disease-causing viruses. West Nile virus causes a potentially fatal illness and has infected
thousands of people in the United States over the past five years, killing more than 400 people in that time frame, according to the Centers for Disease Control and Prevention. The virus is endemic in parts of Africa, Asia and Europe and in the past decade has spread throughout North America and into Central and South America.

NSAIDs Cause Stem Cells to Self-Destruct, Preventing Colon Cancer, Study Finds

ScienceDaily (Nov. 1, 2010) — Nonsteroidal anti-inflammatory drugs (NSAIDs) prevent colon cancer by triggering diseased stem cells to self-destruct, according to researchers at the University of Pittsburgh Cancer Institute (UPCI) and the University of Pittsburgh School of Medicine. Their findings, reported in the early online version of Proceedings of the National Academy of Sciences, could lead to new strategies to protect people at high risk for the disease.

Doctors have long known that NSAIDs, such as aspirin, can lower the risk of colon cancer, but it’s not been clear how they do it, said senior investigator Lin Zhang, Ph.D., associate professor, Department of Pharmacology and Chemical Biology, Pitt School of Medicine, and UPCI.

“Our study shows NSAIDs target stem cells that have accumulated mutations that could lead to cancer development, and initiate a biochemical pathway that makes those cells undergo programmed cell death, a process called apoptosis,” Dr. Zhang said.

The researchers studied mice that have a genetic defect similar to one that is present in patients with familial adenomatous polyposis, a condition that accounts for about 1 percent of all cases of colorectal cancer, and is typically present in non-hereditary colon cancer, too.

Mice that ate the NSAID sulindac in their feed had within a week markedly elevated rates of apoptosis in their intestinal polyps, and specifically in stem cells that had accumulated some dangerous, precancerous changes causing abnormal cell signaling, the researchers found. If the mice also lacked a gene called SMAC, which makes a protein that is released during apoptosis, sulindac was less effective at killing the diseased stem cells.

“That leads us to think that SMAC is an important regulator of this process,” Dr. Zhang said.

He and his team then took a closer look at polyps removed from patients and found higher levels of apoptosis in cells with stem cell features among those who were taking NSAIDs. The findings indicate that apoptosis measures could be a useful way of assessing the effectiveness of cancer-prevention drugs, as well as lead to the development of new agents to further sensitize abnormal stem cells to NSAIDs.

Journal Reference:

HIV Test Rules for Foreigners to Be Eased

Korea Times (Seoul), (10.25.2010) Bae Ji-sook

Ministry of Health and Welfare officials say they plan to submit a bill to the National Assembly that would scrap mandatory HIV testing for foreigners applying for certain visas. Those seeking non-professional work in South Korea on an E-9 visa would no longer have to submit HIV test results or be tested to renew their residency status.

Currently, those seeking an E-6 entertainment visa to work more than 91 days either must submit HIV test results or be tested within 72 hours of arrival. About 4,000 such visas are granted each year. They are commonly sought by singers and dancers for work in bars and hotels, as well as by athletes.

Last year, UN Secretary-General Ban Ki-moon urged South Korea’s former Health Secretary Jeon Jae-hee to end mandatory HIV testing of foreign workers. Just last month, the Ministry of Justice repealed automatic deportations for foreigners testing HIV-positive while on entertainment and non-professional work visas. The repeal has been submitted to the National Assembly for confirmation.

Under the health ministry proposal, HIV testing would still be required for language instructors seeking an E-2 teaching visa.

“Education is considered a very intimate relationship,” said an official with the Ministry of Education, Science and Technology. “According to an unofficial survey by the Prime Minister’s office, the majority of parents wanted solid evidence of their children’s teachers’ HIV status ... it is just intended to reassure parents.”

Last year, an English professor with Kyung Hee University filed a complaint with the National Human Rights Commission over the HIV testing requirement. Several other English teachers joined Benjamin
Wagner’s protest. Wagner claimed the visa requirement reflects unfounded perceptions about Westerners as being promiscuous and drug users.

In July, a group of lawyers filed a petition against the requirements with the Constitutional Court.

**Comparative Effectiveness of HIV Testing and Treatment in Highly Endemic Regions**

*Archives of Internal Medicine* Vol. 170; No. 15: P. 1347-1354. (08.09.2010)  Eran Bendavid, MD, MS; Margaret L. Brandeau, PhD; Robin Wood, MD; Douglas K. Owens, MD, MS

“Universal testing and treatment holds promise for reducing the burden of [HIV] in sub-Saharan Africa, but linkage from testing to treatment sites and retention in care are inadequate,” according to the study’s introduction.

The researchers developed an HIV epidemic and disease progression simulation in South Africa to compare the outcomes of the present HIV treatment campaign (status quo) with four HIV testing and treatment strategies that increase access to antiretroviral therapy: (1) universal testing and treatment absent changes in linkage to care and loss to follow-up; (2) universal testing and treatment with enhanced linkage to care; (3) universal testing and treatment with reduced loss to follow-up; and (4) comprehensive HIV care with universal testing and treatment, improved linkage to care and reduced loss the follow-up. Survival benefits, new HIV infections, and HIV prevalence were the main outcome measures.

“Compared with the status quo strategy, universal testing and treatment (1) was associated with a mean (95 percent uncertainty bounds) life expectancy gain of 12.0 months (11.3-12.2 months), and 35.3 percent (32.7 percent-37.5 percent) fewer HIV infections over a 10-year time horizon,” the authors reported. Enhanced linkage to care (2), prevention of loss to follow-up (3) and comprehensive HIV care (4) provided substantial additional benefits, they noted: “Life expectancy gains compared with the status quo strategy were 16.1, 18.6 and 22.2 months, and new infections were 55.5 percent, 51.4 percent and 73.2 percent lower, respectively.” Sensitivity analysis showed comprehensive HIV care reduced new infections by 69.7 percent to 76.7 percent under a broad set of assumptions.

“Universal testing and treatment with current levels of linkage to care and loss to follow-up could substantially reduce the HIV death toll and new HIV infections,” the authors concluded. “However, increasing linkage to care and preventing loss to follow-up provides nearly twice the benefits of universal testing and treatment alone.”

**Finding Ways to Help the Youngest with HIV**

*Plain Dealer (Cleveland, OH)*, (10.05.2010) Angela Townsend

The Pediatric AIDS Clinic at University Hospitals Rainbow Babies & Children’s Hospital is conducting what is believed to be the only study on HIV-positive children and cardiovascular disease. Dr. Grace McComsey, chief of Pediatric Infectious Diseases, Rheumatology, and Global Health at Rainbow and a professor at Case Western Reserve University School of Medicine, is heading the four-year study.

Eighty patients from across Ohio (the youngest is two; the oldest is 21; mean age is 9) are being followed. At the study’s start, participants underwent blood tests to assess cholesterol levels and diabetes or prediabetes, and to look for markers of heart inflammation—a condition more common among HIV patients.

“In adults atherosclerosis is checked with a CT scan. But that test involves too much radiation for it to be routinely used on children safely,” explained McComsey. Instead, the team used noninvasive ultrasound to measure carotid IMT (intima media thickness) and to assess whether there was any plaque buildup. “Whatever happens in the neck artery is a reflection of what happens in the heart vessel,” she said.

The initial study findings show that HIV-positive children have significantly higher IMT, cholesterol levels, and prediabetes compared with HIV-negative healthy kids. “All of these cardiovascular risk factors put them at higher risk even though they don’t show signs of heart disease, such as chest pain,” said McComsey.

After one year, during which researchers observed the participants but otherwise did not intervene, the HIV-positive group showed improvement in lipid levels compared to the HIV-negative control group. Participants’ CD4 counts also improved after one year, linked with IMT improvements.

According to McComsey, the patients and their parents adopted improved diets and increased activity levels. These changes were not prompted by researchers, but instead by parents more aware of potential cardiovascular risks. “When you give a consent form to the parents, even without us trying to influence the results of the study, they changed the way [their children] were eating and exercising,” she said.
The initial findings, “Heightened Inflammation Is Linked to Carotid Intima-Media Thickness and Endothelial Activation in HIV-Infected Children,” were published in the journal Atherosclerosis (2010;211(2):492-498).

1 November 2010 Last updated at 04:56 ET

'Jesus had HIV' sermon sparks South African fury

By Mohammed Allie BBC News, Cape Town

"Today I will start with a three-part sermon on: Jesus was HIV-positive," South African Pastor Xola Skosana recently said in a Sunday church service. The words initially stunned his congregation in Cape Town’s Khayelitsha township into silence, and then set tongues wagging in churches across the country.

Some Christians have been outraged, saying he is portraying Jesus as sexually promiscuous. HIV is mainly transmitted through sex, but can also be spread through needle-sharing, contaminated blood, pregnancy and breastfeeding.

However, as Pastor Skosana told those gathered in the modest Luhlaza High School hall for his weekly services, in many parts of the Bible Jesus put himself in the position of the destitute, the sick and the marginalised.

"Wherever you open the scriptures Jesus puts himself in the shoes of people who experience brokenness. Isaiah 53, for example, clearly paints a picture of Jesus who takes upon himself the infirmities and the brokenness of humanity," he told the BBC.

He is also quick to emphasise that he is using the metaphor to highlight the danger of the HIV/Aids pandemic, which still carries a stigma in South Africa’s townships.

"Of course, there’s no scientific evidence that Jesus had the HI virus in his bloodstream," says the pastor, whose non-denominational Hope for Life Ministry is part of a growing charismatic movement in South Africa.

"The best gift we can give to people who are HIV-positive is to help de-stigmatise Aids and create an environment where they know God is not against them, he's not ashamed of them."

But Pastor Mike Bele, who officiates at the Nomzamo Baptist Church in nearby Gugulethu, said most clergy in Khayelitsha and other Cape Town townships are strongly opposed to associating Jesus with HIV.

"The subject of my Jesus being HIV-positive is a scathing matter," he says.

"I believe no anointed leader with a sound mind about the scriptures and the role of Christ in our lives would deliberately drag the name of Christ to the ground."

For Pastor Bele portraying Jesus as HIV-positive means he becomes part of the problem, not the solution.

"The pastor needs to explain how it came about for him to bring Christ to our level, when Christ is supreme and is God," he says.

"There is a concern that non-believers would mock Christ and try to generalise Christ as opposed to the powerful force we believe him to be."

But Pastor Skosana, who has been in the ministry for 24 years and lost two sisters to Aids, argues that religious leaders have to play a much bigger role in combating the spread of the pandemic in South Africa where more than 5.7 million people live with the virus—more than in any other country.

And he concluded the last of his three-part sermon by taking an HIV test in front of the congregation—after which 100 churchgoers followed his example.

"The message to the church is that it is not enough for us to give people food privately and give them groceries, we must create an environment that’s empowering because most people who are HIV-positive will not necessarily die of Aids-related sickness but more of a broken heart, out of rejection," he says.

'Fear and ignorance'

Amid the controversy, Reverend Siyabulela Gidi, the director of South African Council of Churches in the Western Cape, has come out in support of Pastor Skosana, saying his standpoint is theologically correct.

HIV in South Africa

- 5.7m carry Aids virus
- 18% of those aged 15 to 49 HIV-positive
- 460,000 receiving ARVs (estimated in 2008)
- 350,000 deaths due to Aids (estimated in 2007)
- 1.4m Aids orphans


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"What Pastor Skosana is clearly saying is that Christ at this point in time would be on the side of the people who are HIV-positive—people who are being sidelined by the very church that is attacking him," the Anglican priest says.

"Pastor Skosana has fortunately got the country talking, he’s got the world talking and that is what theology is all about."

Outside religious circles, Pastor Skosana has also received support from Aids activists.

"The pastor’s sermon takes away the stigma that HIV is a sin and that it’s God’s punishment," says Vuyiseka Dubula, general secretary of the powerful Aids lobby group Treatment Action Campaign.

"To associate Jesus with HIV is powerful, particularly for those who go to church. Now people are starting to think: ‘If Jesus could be HIV-positive who am I not to have it even if I go to church?’"

Jan Glazewski, a professor of marine and environmental law at the University of Cape Town who has been HIV-positive for 25 years, wrote in a letter to the Cape Times newspaper that he identified with the idea that God was on the side of the poor and marginalised.

"The pastor’s metaphor gives strength to us all," he said.

"In aligning Jesus to HIV, his sermon has prompted an outcry as well as expressions of anger."

"This is because of fear and ignorance."

"It is this fight against fear and ignorance that Pastor Skosana is determined to continue.

"The more we talk about it in our pulpits, the more we ask people to test voluntarily in the church the better."

"One of the most powerful things we can do as a church right now is to say Jesus was and is HIV-positive."

**A sweet discovery raises hope for treating Ebola, Lassa, Marburg and other fast-acting viruses**

New research published in the Journal of Leukocyte Biology suggests that a purified form of a product modified from simple sugar molecules can eradicate killer viruses by mobilizing white blood cells

When a team of European researchers sought to discover how a class of antiviral drugs worked, they looked in an unlikely place: the sugar dish. A new research report appearing in the *Journal of Leukocyte Biology* (http://www.jleukbio.org) suggests that a purified and modified form of a simple sugar chain may stop fast-acting and deadly viruses, such as Ebola, Lassa, or Marburg viruses, in their tracks. This compound, called chlorite-oxidized oxyamylose or COAM, could be a very attractive therapeutic option because not only did this compound enhance the early-stage immune defenses in mice, but because of sugar’s abundance, it is derived from easily obtainable sources.

"We modified and purified a safe drug from natural sources and discovered how it can protect against deadly virus infections," said Ghislain Opdenakker, M.D., a researcher involved in the study from the Laboratory of Immunobiology at the Rega Institute for Medical Research and the University of Leuven in Belgium.

To make this discovery, researchers infected mice with a virus that kills in less than a week. When one group of these infected mice was treated with an unpurified version of the compound, about half of the infected mice were protected from the effects of the virus. Researchers then purified the compound and treated another group of infected mice. In that group, more than 90 percent survived the deadly infection. These results suggest that the purified compound almost completely blocked the killer virus by speeding the response of the body’s fast-acting immune cells, called white blood cells or leukocytes, at the early stage of infection.

"This is an exciting discovery because it offers hope that we will finally be able to really do something about some of the world’s deadliest viruses – rapidly mobilizing antiviral immune cells is critical in the race between these killer viruses and the host," said John Wherry, Ph.D., Deputy Editor of the *Journal of Leukocyte Biology*. "The fact that this compound comes from something as abundant as sugar just sweetens the findings."

**Florida to Drop 350 Patients in AIDS Drug Program**

*South Florida Sun-Sentinel (Fort Lauderdale),* (11.02.2010) Bob Lamendola

About 350 uninsured HIV/AIDS patients will be dropped from Florida's AIDS Drug Assistance Program in a month in a cost-cutting move by state health officials. Another 2,000 ADAP patients are at risk of losing treatment coverage unless more funding can be tapped for the program, Florida Department of
Health (DOH) officials said Tuesday. The $100 million-a-year program is $16 million short of the funds it needs through April 1, 2011.

ADAP previously covered patients making up to four times the federal poverty level. That will drop to only three times the poverty level, or $43,710 for a family of two, making about 350 current clients ineligible, officials said.

Many will be eligible for low- or no-cost treatment through HIV drugmakers’ charity programs, said Tom Liberti, chief of the state Bureau of HIV/AIDS. The state has helped many of the more than 2,300 patients who are on Florida’s ADAP waiting list access treatment through these programs.

Loss of jobs and job-related health insurance has boosted ADAP demand, and clients are living longer because of effective treatments.

“We are all pursuing every possible legal and financial option we can to make up the deficit,” said Liberti, noting that he is asking DOH for emergency funds and for federal clearance to allow Florida to negotiate lower drug prices. If neither happens, “a minimum of 2,000 people, maybe more” could be temporarily dropped from ADAP, Liberti said.

Next year, the state expects more ADAP funding through different sources, Liberti said. States with ADAP waiting lists could receive $50 million in a budget bill that will come before Congress after the Tuesday elections, a federal health official said.

A New Resource for LGBT Seniors


A social service and advocacy organization for LGBT senior citizens recently launched the online National Resource Center for LGBT Aging. The one-year project by SAGE was underwritten by several foundations and the US Department of Health and Human Services’ Administration on Aging.

Together with 10 other groups, SAGE is soliciting community feedback as it begins building the website, which will address issues including health care access, HIV and aging, and transgender elders. The site will offer publications, program directories, personal stories, interviews with prominent experts, and other items.

SAGE is asking individuals and organizations to say what they need and want in the site—information that will be used to inform its directories and listings.

Other contributors to the center include the MAC AIDS Fund; the Gill Foundation, one of the nation’s largest foundations focused on LGBT rights; and the H. van Ameringen Foundation, a personal foundation that concentrates on HIV/AIDS and other LGBT community issues. For more information, visit www.lgbtagingcenter.org.

'B Being Faithful' in a Sexual Relationship: Perceptions of Tanzanian Adolescents in the Context of HIV and Pregnancy Prevention

AIDS Care Vol. 22; No. 9: P. 1153v1158, (09..2010) Joy Noel Baumgartner; Helen Lugina; Laura Johnson; Tumaini Nyamhanga

The “B” in the “ABC” HIV prevention strategy stands for being faithful. Little is known, however about what adolescents think about faithfulness and reducing one's number of partners, including their understanding of its implementation within relationships. Because youths face the dual threats of HIV and unintended pregnancy, “it is important to understand how adolescents may integrate their thinking on pregnancy prevention if they are using faithfulness or partner reduction as their HIV prevention strategy,” wrote the authors of the current study.

The researchers conducted 20 focus group discussions with 158 adolescents ages 14 to 20. The groups were stratified by age, sex, current school attendance, rural or urban residence, and marital status. The results indicated that “the vast majority” of groups felt the “B” messages are important and relevant for both unmarried and married youths to hear, but that the messages need to be stated explicitly “(e.g., ‘being faithful means having only one tested sexual partner at a time’).”

The youths acknowledged the risks of multiple partners; a few recognized that concurrent partnerships are riskier than serial partnerships. “Faithful relationships are perceived as ideal in terms of romantic expectations and HIV prevention, but were considered unrealistic if the relationship had a power imbalance,” the authors wrote.

“Condoms were given as the primary method for pregnancy prevention among youth, yet faithfulness was usually seen as precluding condoms use, and many youth considered condom use as evidence of a lack of faithfulness,” the team concluded. “Overall, adolescents recognized that practicing fidelity is
complex. Young people need life skills education for how to establish and maintain faithful relationships with one tested partner and how to integrate condom use for pregnancy prevention within that relationship. Programs also need to more explicitly address the issues of trust and repeat HIV testing within ‘faithful’ relationships, which is an uncomfortable but necessary reality for many adolescents.”

**A Parallel Process Growth Mixture Model of Conduct Problems and Substance Use with Risky Sexual Behavior**

*Drug and Alcohol Dependence Vol. 111; No. 3; P. 207-214, (10..2010)* Johnny Wu; Katie Witkiewitz; Robert J. McMahon; Kenneth A. Dodge; Conduct Problems Prevention Research Group

“Conduct problems, substance use, and risky sexual behavior have been shown to coexist among adolescents, which may lead to significant health problems,” explained the study investigators, who sought to examine relations among these problems in a community sample of children at high risk for conduct disorder.

A latent growth model of childhood conduct problems revealed a decreasing trend from grades K to five. A parallel process growth mixture model identified four concurrent conduct problems and substance use trajectory classes during adolescence: high conduct problems and high substance use, increasing conduct problems and increasing substance use, minimal conduct problems and increasing substance use, and minimal conduct problems and minimal substance use.

“Across all substances (tobacco, binge drinking, and marijuana use), higher levels of childhood conduct problems during kindergarten predicted a greater probability of classification into more problematic adolescent trajectory classes relative to less problematic classes,” the investigators reported. For tobacco and binge drinking models, childhood conduct problem increases over time also predicted a greater probability of classification into more problematic classes. For all models, individuals classified into more problematic classes demonstrated higher proportions of early sexual intercourse, infrequent condom use, receiving money for sex, and ever contracting an STD. Tobacco use and binge drinking during early adolescence in particular predicted higher levels of sexual risk taking into late adolescence.

The results “highlight the importance of studying the conjoint relations among conduct problems, substance use and risky sexual behavior in a unified model,” the investigators concluded.

**South African Province to Circumcise Prisoners in Hopes of Halting HIV Spread**

*Los Angeles Times*, (10.29.2010) Robyn Dixon

KwaZulu-Natal province is offering circumcision to men in its prisons as part of South Africa’s campaign to halt HIV transmission. KwaZulu-Natal’s health department hopes to circumcise 2.5 million men overall by June 2014, and so far, more than 10,000 men have undergone the procedure, said Dr. Sinbongiseni Dhlomo, the provincial health chief. The province is a stronghold of the Zulu tribe; Zulu King Goodwill Zwelithini recently endorsed a return to the practice, which has not been common among Zulus for many years. Multiple studies have shown that male circumcision reduces the risk of female-to-male HIV transmission by up to 60 percent. National health authorities have set a goal of performing HIV testing on 15 million South Africans, about a third of the population, by June 2011.

**Overcrowded Prisons Serve as Incubators for Tuberculosis**


The packed prisons of sub-Saharan Africa are dangerous incubators for TB, according to information presented at a recent conference in Cameroon. Christopher Kuaban, a University of Yaounde researcher, identified overcrowding, promiscuity, malnutrition, poor health care, and bad ventilation all as contributing to the problem. As an example, Kuaban cited the central prison in Douala, Cameroon, which was built in 1930 to house 700 prisoners but now holds 3,200 to 3,500. While some prisons have begun TB screening of inmates at intake, Kuaban said all detainees should be tested “at least once or twice a year.” He also called for better health care and ventilation and for setting up comprehensive TB control programs.
Experts: Did UN Troops Give Haitians Cholera?

Suspicion That a U.N. Peacekeeping Base on a Tributary to the Infected Artibonite River Fueled Protests of the U.N. Last Week

AP: Researchers should determine whether United Nations peacekeepers were the source of a deadly outbreak of cholera in Haiti, two public health experts, including a U.N. official, said Wednesday.

The U.S. Centers for Disease Control and Prevention found that the strain of cholera that has killed at least 442 people the past three weeks matches strains found in South Asia. The CDC, World Health Organization and United Nations say it’s not possible to pinpoint the source and investigating further would distract from efforts to fight the disease.

But leading experts on cholera and medicine consulted by The Associated Press challenged that position, saying it is both possible and necessary to track the source to prevent future deaths.

"That sounds like politics to me, not science," Dr. Paul Farmer, a U.N. deputy special envoy to Haiti and a noted expert on poverty and medicine, said of the reluctance to delve further into what caused the outbreak. "Knowing where the point source is — or source, or sources — would seem to be a good enterprise in terms of public health."

The suspicion that a Nepalese U.N. peacekeeping base on a tributary to the infected Artibonite River could have been a source of the infection fueled a protest last week during which hundreds of Haitians denounced the peacekeepers.

John Mekalanos, a cholera expert and chairman of Harvard University's microbiology department, said it is important to know exactly where and how the disease emerged because it is a novel, virulent strain previously unknown in the Western Hemisphere — and public health officials need to know how it spreads.

Interviewed by phone from Cambridge, Massachusetts, Mekalanos said evidence suggests Nepalese soldiers carried the disease when they arrived in early October following outbreaks in their homeland.

"The organism that is causing the disease is very uncharacteristic of (Haiti and the Caribbean), and is quite characteristic of the region from where the soldiers in the base came," said Mekalanos, a colleague of Farmer. "I don't see there is any way to avoid the conclusion that an unfortunate and presumably accidental introduction of the organism occurred."

Cholera, which had never before been documented in Haiti, has killed at least 442 people and hospitalized more than 6,742 with fever, diarrhea and vomiting since late October. It is now present in at least half of Haiti's political regions, called departments.

Death occurs when patients go into shock from extreme dehydration. The epidemic has diverted resources needed for the expected strike of a hurricane this week, and could spread further if there is flooding.

Suspicion that the Nepalese base could have been a source of the infection intensified Monday after the CDC revealed the strain in Haiti matches those found in South Asia, including Nepal.

But nothing has been proven conclusively, and in the meantime the case remains politically charged and diplomatically sensitive. The United Nations has a 12,000-strong force in Haiti that has provided badly needed security in the country since 2004. But their presence is not universally welcomed, and some Haitian politicians have seized upon the cholera accusations, calling for a full-scale investigation and fomenting demonstrations.

Laurie Garrett, senior fellow for global health at the Council on Foreign Relations, said it is clear that the disease was imported to Haiti but that it is still not clear by whom or how. She said the epidemic will contain lessons for humanitarian relief work and disaster relief around the world.

"It has to be either peacekeepers or humanitarian relief workers, that's the bottom line," she said.

Mekalanos said researchers might be more aggressive in finding the source of the infection if the case was less sensitive.

"I think that it is an attempt to maybe do the politically right thing and leave some agencies a way out of this embarrassment. But they should understand that ... there is a bigger picture here," he said. "It's a threat to the whole region."

He also cast doubt on U.N. military tests released this week that showed no sign of cholera. The tests were taken from leaking water and an underground waste container at the base a week after the epidemic was first noted and processed at a lab in the neighboring Dominican Republic, U.N. spokesman Vincenzo Pugliese said.
Mekalanos said that it is extremely difficult to accurately isolate cholera in environmental samples and that false negatives are common.

The Nepalese troops were not tested for cholera before their deployment if they did not present symptoms. But health officials say 75 percent of people infected with cholera bacteria do not show symptoms and can still pass on the disease for weeks.

A spokesman for the World Health Organization said finding the cause of the outbreak is "not important right now."

"Right now, there is no active investigation. I can’t say one way or another (if there will be). It is not something we are thinking about at the moment. What we are thinking about is the public health response in Haiti,” said spokesman Gregory Hartl.

The Harvard experts said more conclusive evidence would be available following closer examinations of the genetic material in the strain.

CDC spokeswoman Kathryn Harben said in an e-mail that the center will make the full genomic DNA sequence available when it is confirmed.

"At some point in the future, when many different analyses of the strain are complete, it may be possible to identify the origin of the strain causing the outbreak in Haiti,” she said.

Farmer, who co-founded the medical organization Partners in Health that is a leading responder in the epidemic, said there is no reason to wait.

"The idea that we’d never know is not very likely," he said. "There’s got to be a way to know the truth without pointing fingers."

**Anti-nausea drug has anti-HIV effect too**

Keith Alcorn
Published: 04 November 2010

A drug used to quell nausea caused by chemotherapy has a strong anti-HIV effect in the test-tube, and this effect is intensified if the HIV protease inhibitors saquinavir or ritonavir are also present.

The drug, aprepitant (Emend, manufactured by Merck & Co), also returns the favour by intensifying the antiretroviral effect of ritonavir and saquinavir, and blood levels of aprepitant are boosted by ritonavir.

The findings, reported in an advance online publication of the journal *AIDS*, have resulted in a clinical trial that is now testing the safety and pharmacokinetics of aprentin in HIV-positive people.

Aprepitant is one of a class of neurokinin-1 receptor antagonists that block the neuropeptide substance P, which is involved in interactions between the nervous system and the immune system.

The interaction between substance P and the neurokinin-1 receptor is critical for viral infection of a cell, and HIV is no exception.

Previous experiments have shown that a substance P antagonist – a chemical that can block its normal receptor on human cells – reduces HIV infection of macrophages by reducing the display of CCR5 receptors on these cells. Most types of HIV require the CCR5 receptor in order to gain access to CD4 cells and other immune system cells.

Aprepitant is licensed for the prevention and treatment of nausea due to cancer chemotherapy. It was selected for this experiment after the discovery that it could prevent HIV infection of macrophages.

Further tests showed that it had the strongest anti-HIV effect of any neurokinin-1 receptor antagonist.

In this study the drug was incubated alone and in combination with a number of antiretroviral drugs from different classes: ritonavir and saquinavir (protease inhibitors); nevirapine (non-nucleoside reverse transcriptase inhibitor) T-20 (entry inhibitor) and AZT, ddI and 3TC (nucleoside analogues).

The researchers looked at the synergistic effect of the drugs in peripheral blood mononuclear cells infected with a wide range of HIV isolates representing all global sub-types and major recombinant forms, and viruses adapted to use the CCR5 and CXCR4 receptors.

The researchers found that the antiviral effect of aprepitant used together with the two protease inhibitors was greater than would be expected from adding up the antiviral effect of each drug alone, in other words, synergistic. Use of aprepitant with a protease inhibitor resulted in double the expected antiviral effect. A smaller synergistic effect was observed with 3TC and AZT. No synergy was observed with other drugs.

The researchers found no difference in activity according to viral subtype or receptor usage.

**Reference**

Manak MM et al. *Anti-HIV-1 activity of the neurokinin-1 receptor antagonist aprepitant and synergistic interactions with other antiretrovirals*. AIDS, advance online publication, October 21 2010.
Firefighter’s HIV-related death occurred in the line of duty
By Neal Mcnamara
Federal Way Mirror
It has been four years since South King Fire and Rescue veteran Doug Waller died as a result of contracting HIV on the job, but his death is just now being recognized as having occurred in the line of duty.

In September, a contingent of South King personnel traveled to Colorado Springs, Colo., with Waller’s wife, Sharon, her two sons and other family to witness Waller’s name engraved on the International Association of Firefighters’ Fallen Firefighter Memorial.

Waller’s former colleagues at Station 65 in Auburn gave Waller’s family a medallion from the memorial at a ceremony on Sunday morning, the fourth anniversary of Waller’s death. A plaque will hang in the station in his honor.

The recognition of Waller as a casualty took so long due to the nature of his death; it had to be proven to the state of Washington that he contracted HIV on the job, as opposed to a more obvious firefighting-related injury.

It is believed that Waller contracted HIV after being stuck by a needle on a medical call. A test immediately after the injury came up negative. He did not find out he had the virus until 2006, two months before he died.

Waller retired from the department in 2000, said IAFF Local 2024 President Ryan Herrera, and since Waller’s HIV diagnosis came years later, it was outside a 60-month window that would have allowed his death to be recognized as in the line of duty. The state Department of Labor and Industries, which handles workers’ compensation claims, needed proof that Waller contracted HIV while he was on duty as a firefighter.

Herrera said that the claim was finally approved in February 2008. Waller’s family allowed the release of his records in May to the International Association of Firefighters, which allowed his name to be inscribed on the fallen firefighter memorial. Waller’s name was engraved under the year 2006.

There are efforts to have Waller’s name placed on memorials in Olympia and on the national monument in Washington. Herrera said he is working on submitting Waller’s name to the national monument. Washington State Council of Fire Fighters President Kelly Fox could not immediately be reached for comment on whether Waller is in line to be included on the state memorial.

Waller joined South King as a volunteer in 1976, and was hired full time in 1981. Herrera could not confirm that Waller was the first firefighter from Washington to die from contracting HIV on the job. Labor and Industries spokeswoman Elaine Fischer said that Waller’s death was treated like any worker who died on the job as the result of a blood-borne pathogen.

“We certainly wouldn’t look at it any differently than any other occupational illness or disease,” Fischer said. She said that the certification of Waller’s death as in the line of duty took longer because of the time it took to identify when he was exposed to HIV.

The Department of Labor and Industries does not have public records showing specific cases of firefighters contracting HIV on the job. However, it does keep statistics on firefighters who die as a result of more general “viral diseases.” In 2008 and 2009, records show that a firefighter claimed a viral disease injury — only one claim in each year.

For all occupations claiming an injury resulting from “viral diseases,” the department showed 10 and 18 in 2008 and 2009, respectively. In 2007, there were 103 claims, and 211 in 2006. The category did not exist in 2005.

Data from the U.S. Department of Labor’s 2009 report on occupational fatalities in Washington state show no deaths from “harmful substances or environments.” There were three deaths nationally in 2009 in that category.

South King Fire and Rescue spokeswoman Kendra Kay said that two other South King firefighters have died in the line of duty. Volunteer firefighter Eugene Parsons died in 1969 when the fire truck he was riding in collided with a utility pole. Volunteer firefighter Fred Auer Sr. died in 1966 after suffering a heart attack fighting a blaze in Lake Grove.
Liver Cancer Survival Similar in HIV-Positive and HIV-Negative People

Three-year survival rates after a diagnosis of hepatocellular carcinoma (liver cancer) are similar between people living with HIV and HIV-negative people, according to a study presented at the American Association for the Study of Liver Diseases being held October 29 to November 2 in Boston.

Liver disease and liver cancer have become some of the leading causes of illness and death in people with HIV in recent years—particularly among people coinfected with hepatitis C virus (HCV) or hepatitis B virus (HBV). What’s more, some studies have suggested that people with HIV are more likely to progress to liver cancer and have more aggressive disease than HIV-negative people. These studies, however, have often been quite small, and their study designs have differed.

To better understand survival following a liver cancer diagnosis in people with HIV, Anne Gervais, MD, from the Hopital Bichat in Paris, and her colleagues examined the medical records of 687 people diagnosed with liver cancer, 23 of whom were HIV positive.

Most all of the HIV-positive participants were coinfected with HCV or HBV, nearly all were taking HIV antiretroviral (ARV) therapy, and the majority had a CD4 count over 200 at the time of their cancer diagnosis. In most regards, the HIV-positive and HIV-negative study volunteers were similar, but the HIV-positive participants were much younger at the time of their cancer diagnoses—49 years old on average—than the HIV-negative participants, where the average age was 58.

Gervais’s team found that rigorous screening, the stage of the cancer and estimates of the cancer’s speed of progression (a process called preoperative surveillance) significantly affected survival rates among the HIV-positive participants. People who had good preoperative surveillance had much smaller tumors at the time of diagnoses and were far more likely to be alive three years after receiving treatment than those who had poor surveillance. The three-year survival rates were 63 percent in those with good surveillance compared with just 17 percent in those with poor surveillance.

One encouraging finding was that on average, people living with HIV had similar three-year survival rates as HIV-negative participants. Overall three-year survival was 42 percent among the HIV-negative volunteers and 39 percent among the HIV-positive volunteers.

“Screening of the HIV-positive population should be reinforced as the prognosis after curative treatment is at least equal to that of HIV-negative [patients],” concluded the authors.

HIV-positive suspect agrees to plea deal in biting case

Christine Ferretti / The Detroit News

Mount Clemens— A plea agreement was reached today for an HIV-positive Clinton Township man who gained national media attention when he was charged with bioterrorism and assault after allegedly biting a neighbor. The controversial felony charge against Daniel Allen was dismissed in June by Macomb County Circuit Court Judge Peter Maceroni. The judge agreed to toss the charge after Allen’s attorney, James L. Galen Jr., argued the law — enacted in Michigan in 1998 in the wake of the Oklahoma City bombing and an anthrax scare — was being misapplied.

But the 45-year-old was still facing a potential sentence of up to 20 years in prison on two felony assault charges stemming from the Oct. 18 incident.

Jury selection was slated to begin this morning, but instead, Galen said attorneys for both sides agreed to the plea deal.

Allen pleaded no contest to assault with intent to do great bodily harm less than murder. If he complies with the terms and conditions of probation for the next 11 months, the charge will be reduced to a misdemeanor charge of aggravated assault and Allen will not have a felony conviction, Galen said.

Galen said the decision was a difficult one for Allen, who has maintained his innocence. But after a year-long battle, this was the "best resolution to this case."

"Mr. Allen wanted to move on with his life and put this ordeal behind him. It has affected his health, mental well-being and consumed him for the past year," Galen said. "Daniel should have never been charged, but ultimately, given the circumstances, this was a good resolution to the case."

Macomb County Prosecutor Eric Smith could not be immediately reached for comment.

Allen is accused of biting his neighbor, Winfred Fernandis Jr., on the lip during an altercation over a football in the driveway of Allen’s home. Prosecutors say Allen was the lone attacker. But Galen claimed that Allen was the victim, and was attacked by Fernandis and members of Fernandis' family because he's gay.
Allen originally was charged with the two assault offenses. But prosecutors added a count under the bioterrorism law — possession or use of a harmful device, in this case, HIV — after Allen revealed in a TV interview that he was HIV-positive.

The charge riled Civil Rights and AIDS activists across the nation that claim the law was not intended to cover an HIV-positive person biting someone. The American Civil Liberties Union of Michigan has said the charge demonized people with HIV and promoted fear and ignorance about how the disease is spread. "This case was blown way out of proportion," Galen said. Sentencing is set for Dec. 8.

One in four young Austrians see toilet AIDS infection risk
One out of four young Austrians believe they could get AIDS and HIV by going to the toilet, according to research.

Condom producer Durex polled more than 15,700 Europeans aged between 15 and 20 including around 1,000 Austrians for its "The Face of Global Sex 2010" study.

The survey has shown that 25 per cent of interviewed Austrians admitted thinking there was using a public toilet may risk becoming infected with the virus, while 16 per cent said the same about kissing.

Around half of questioned Austrians said they saw a general or no risk of becoming infected themselves, Durex announced today (Thurs).

A study by GfK Austria showed earlier this year that 26 per cent of Austrians think AIDS is a disease which only affects homosexuals and drug addicts. Researchers, who spoke to around 1,000 Austrians aged 15 and older, said they also found that 41 per cent thought "those who lead a normal life" could not get AIDS and HIV.

Around 520 people living in Austria got infected with AIDS in 2009.
About Crofelemer
Crofelemer is a locally-acting, minimally-absorbed product that is believed to possess dual novel mechanisms of action that might be effective in treating both acute infectious diarrhea and chronic diarrhea. Investigational studies support the use of crofelemer as an anti-secretory anti-diarrheal agent that may provide relief to patients through the inhibition of chloride secretion by both gut CFTR (Cystic Fibrosis Transmembrane Conductance Regulator Protein) as well as gut CaCC (calcium-activated chloride channel). Inhibiting CFTR and CaCC prevents the secretion of chloride and other ions, as well as water which passively follows chloride, out of the body into the gastric lumen. This secretion leads to diarrhea, with the associated symptoms of dehydration, electrolyte imbalance, abdominal cramping, urgency and increased frequency. Additionally, crofelemer, unlike other anti-diarrheal agents, does not affect gut motility. Crofelemer is well tolerated, and, in trials to date, demonstrates a safety profile comparable to placebo. Crofelemer, if approved, would be a first-in-class CFTR inhibitor as well as a first-in-class CaCC inhibitor that would work as an anti-secretory anti-diarrheal drug.

About HIV-Associated Diarrhea
Approximately 15-30% of the 1 million people in the United States living with HIV are affected by chronic diarrhea. HIV-associated diarrhea is a serious unmet medical condition that contributes to increased mortality and morbidity by reducing treatment compliance and efficacy as well as the quality of life in patients. The U. S. HIV-associated diarrhea market potentially represents a $300 million opportunity annually.

About Fast Track
The Food and Drug Administration (FDA) has developed the Fast Track Designation as an approach to making such drugs available as rapidly as possible. In particular, Fast Track is a process designed to facilitate the development, and expedite the review of drugs to treat serious diseases and fill an unmet medical need.

Leaders Discuss Best Practices, Challenges For Detecting Counterfeit Medications
During the opening of the 10th annual meeting of the International Society of Pharmacovigilance (ISoP) in Accra, Ghana, the country’s "Vice President John Dramani Mahama on Wednesday called on member countries of [the society] to institute effective measures that would help detect fake and counterfeit drugs," Ghana News Agency reports.

The ISoP, which includes members from across the world, "is an international non-profit scientific organisation, which aims at fostering pharmacovigilance both scientifically and educationally, and to enhance all aspects of the safe and proper use of medicines in all countries," according to the news service. During his speech, Mahama said foreign aid provided "to developing countries to fight diseases would not benefit them if vigilance is not intensified to eliminate the malpractices in drug administration." He also "called on member countries to tighten their security networks to ensure that proper drug administration is practised to repose more confidence in the existing pharmaceutical companies," Ghana News Agency writes.

The "government of Ghana is creating the necessary environment to become a global major actor in the vigilance against counterfeiting and misuse of drugs and I will like to call on all of you here to do same in your countries," Mahama said to attendees. The article also includes comments by ISoP President Alexander Doodoo, and Serge Xueref, an official with the Global Fund to Fight AIDS, Tuberculosis and Malaria (11/3).

The ISoP meeting followed the 33rd Annual Meeting of Representatives of the National Centres participating in the WHO Programme for International Drug Monitoring, that was also held in Accra, according to an agenda (pdf) released by the WHO (undated).

"This is the first time that major global drug safety events are being held in sub-Saharan Africa and the choice of Ghana reflects the increasing stature attained by the country in Global Drug Safety," Ghana News Agency reports in a separate article. According to the news service, "[m]ore than 500 participants representing pharmacovigilance professionals from across the globe" were to attend the ISoP meeting to "examine pharmacovigilance practices across the globe with a view to sharing best practices, highlighting common challenges and developing broad principles for dealing with them."

The article includes quotes made ahead of the meeting by Doodoo and ISoP’s Brian Edwards and Delese Mimi Darko(10/25).
Sanofi Pasteur's Dengue Vaccine Enters Phase III Trial In Australia
Sanofi Pasteur, the vaccines division of the pharmaceutical group Sanofi-Aventis, on Thursday announced the company had begun testing its dengue fever vaccine in a Phase III clinical trial in Australia, Dow Jones/Wall Street Journal reports. "Sanofi-Aventis already performed earlier clinical tests on children and adults with the vaccine in the U.S., Asia and Latin America," Dow Jones/Wall Street Journal adds (Landauro, 11/4).

"This study is part of a global phase 3 clinical study program aimed at advancing the development of a novel vaccine for the prevention of dengue disease in children and adults," according to a Sanofi Pasteur press release. "Currently, there is no specific treatment available for dengue fever, which is a threat to nearly three billion people and a public health priority in many countries of Latin America and Asia where epidemics occur," the release states.

It continues: "The study in Australia is the first to use dengue vaccine doses produced with industrial scale processes. The study is aimed at demonstrating that production of the vaccine at industrial scale will meet consistency criteria required for market authorization by regulatory authorities" (11/4).

"We are now entering the final laps of a long run that Sanofi Pasteur started almost 20 years ago," said Wayne Pisano, president and chief executive of the company. He added that if the vaccine is successful, the company plans to introduce it in countries where dengue is a significant public health priority, PharmaTimes writes (McKee, 11/4).

IRIN, Scientific American Examines Scientific Efforts Against Dengue, Malaria
IRIN examines scientists' desire to release genetically-modified (GM) mosquitoes into the wild in an effort to help prevent the spread of dengue. Although "[t]hese mosquitoes are engineered with an extra gene or inserted bacterium or have had a gene altered so that either their offspring are sterile and unable to spread dengue, or simply die," the news service writes that some people are concerned over possible unforeseen ramifications the release of such genetically-modified insects could present. "For half a century, scientists have released billions of engineered insects – for example, fruit flies to save plants, but to date there has not been a field release of insects engineered to save humans," IRIN writes. The article describes the decision by the NGO Pesticide Action Network-Asia and the Pacific to "oppose a since-granted request to release modified mosquitoes [in Malaysia] on the grounds that 'it may have environmental or health consequences as well as carry risks arising from horizontal gene transfer,'" as was described by Executive Director Sarojeni Rengam, according to the news service. The piece also includes comments by Imperial College London Professor John Mumford, who is also a lead researcher on the "WHO-funded regulatory group Mosqguide, founded to develop best practices for deploying genetically modified mosquitoes to fight mosquito-borne diseases, primarily dengue and malaria," IRIN writes (11/3).

In related news, Scientific American explores recent efforts to develop a vaccine that protects against malaria: "Scientists have many promising malaria vaccine candidates in the works, and for the first time one [RTS,S] has reached advanced human trials. If it or another candidate is even partly effective in people, it could save the lives of millions of children and pregnant women. It would be the only vaccine yet developed against a human parasite, an achievement of Nobel caliber. And it could, in its first-generation form, be distributed in Africa as soon as 2015."

Regarding the ongoing trial of RTS,S, Scientific American writes that its "impact could be enormous, saving hundreds of thousands of lives every year – provided that the vaccine is widely distributed." The article references several "hurdles" that will remain to be overcome even if the vaccine proves effective in the larger trial.

The article also examines the challenges that have complicated malaria vaccine development in the past, how development efforts have evolved over time and several current strategies scientists are using to approach vaccine development today, as described by several scientists involved in such work (Carmichael, November 2010).
No easy solution to genetic 'battle of the sexes'

A new study published today shows a genetic 'battle of the sexes' could be much harder to resolve and even more important to evolution than previously thought.

This battle, observed across many species and known as intralocus sexual conflict, happens when the genes for a trait which is good for the breeding success of one sex are bad for the other – sparking an 'evolutionary tug-o-war' between the sexes.

It has previously been thought these issues were only resolved when the trait in question evolves to become sex-specific in its development – meaning the trait only develops in the gender it benefits and stops affecting the other. An example of this is male peacocks' tails, used for mating displays, which are not present in females.

However, a new study by the universities of Exeter (UK), Okayama and Kyushu (both Japan) published today [4 November] in Current Biology shows this doesn’t always bring an end to conflict – as even when the trait becomes sex-specific, knock-on effects can still disadvantage the other sex.

Professor Dave Hosken, from the Centre for Ecology & Conservation (Cornwall) at the University of Exeter, said: "This kind of genetic tussle is everywhere in biology. For example, in humans, male hips are optimised for physical activity, whereas female hips also need to allow child bearing. That’s the sort of evolutionary conflict we’re talking about, and these conflicts were previously thought to be resolved by sex-specific trait development.

"What we’re seeing in this study is that this isn’t always the end of the sexual conflict. This means it’s no longer clear how or when, if ever, these conflicts get fully resolved and this means it could be more important to the evolutionary process than has generally been thought."

In this study, the researchers looked at broad-horned flour beetles, where males have massively enlarged mandibles used to fight other males for mating supremacy. The enlarged mandibles aren’t present in the females at all – meaning this is a sex-specific trait.

By selectively breeding the beetles for larger or smaller mandible size, the researchers were able to show that the bigger the mandibles were – the more successful the males were in breeding. There was a corresponding counter-effect on females, however, as females from larger mandibled populations were less successful.

Professor Takahisa Miyatake, from the Graduate School of Environmental Science at Okayama University, said: "We looked at all the possible reasons for this and found that while the females did not develop the larger mandibles, they did inherit many of the other characteristics that made the enlarged mandibles possible in males. This included a reduced abdomen size, which could affect the number of eggs a female can carry – giving a possible explanation for the disadvantage."
"So here we see a sex-specific trait which is still having a negative effect on the sex which doesn’t show it. This means that even though it looks like this genetic conflict is over, it’s still ongoing and there’s no easy way to end it."

Kensuke Okada, also from Okayama University, said: "The view that sex-limited trait development resolves this kind of genetic battle of the sexes is based on the assumption that traits are genetically independent of each other, which is frequently not true.

"What we're seeing here is that genetic architecture can provide a general barrier to this kind of conflict resolution."

**Clue to how some 'control' their HIV without medication**

By Caroline Parkinson Health reporter, BBC News

HIV infects key cells in the body’s defence which co-ordinate the response to infection

Tiny changes to an "alarm" protein which responds to infections may explain why some with HIV can control their condition without drugs.

Around one in 300 people with HIV are "controllers", and scientists want to replicate how their bodies behave.

Writing in Science, US researchers say differences in five amino acids in a protein called HLA-B are key.

But a UK expert said there was still a "long way" to go before a vaccine or a new drug for HIV could be developed.

HIV "controllers" were first identified almost 20 years ago. They are able to suppress viral replication with their immune system, keeping viral load at extremely low levels, without using anti-retroviral drugs.

It was already known that certain genes involved with the HLA system were important for HIV control. But scientists had not identified which genes were involved or how they acted.

**Drag and drop**

The researchers carried out a genome-wide association study of the genetic make-up of almost 1,000 controllers and 2,600 people with progressive HIV.

Around 300 points were found to be associated with immune control of HIV, all in regions of chromosome six that code for HLA proteins.

Scientists were then able to pinpoint specific amino acids and identified the five in the HLA-B protein as playing the key role.

HLA-B is part of the process by which the immune system recognises and destroys virus-infected cells.

Part of the protein called a binding pocket "drags and drops" peptides from inside the virus onto the cell membrane.

These then mark out the cell for destruction by CD8 "killer" T cells in the immune system.

All five of the amino acids identified by researchers are in the binding pocket.

Scientists from Massachusetts General Hospital, Massachusetts Institute of Technology and Harvard University carried out the work.

Bruce Walker of the Ragon Institute at Massachusetts General Hospital, one of the lead authors of the paper, said: "We found that, of the 3bn nucleotides in the human genome, just a handful make the difference between those who can stay healthy in spite of HIV infection and those who, without treatment, will develop AIDS.

"Knowing how an effective immune response against HIV is generated is an important step toward replicating that response with a vaccine.

"We have a long way to go before translating this into a treatment for infected patients and a vaccine to prevent infection, but we are an important step closer."

Gus Cairns, editor of HIV Treatment Update of the UK's National Aids Manual, said: "As the researchers say, this research opens the door to the development of a vaccine that could encourage the body to mimic the most effective kind of immune response, or to drugs that could interfere with HIV's ability to infect cells and derange the immune system.

"Nonetheless there is still a lot we don’t know about why some genetic variants provide a much less welcoming environment for HIV than others and, although we are becoming clearer about what kinds of
specific immune response are effective against HIV, we are a long way from being able to make them happen, or even knowing what we must do to make them happen.”

**Small Protein Changes May Make Big Difference in Natural HIV Control**

ScienceDaily (Nov. 4, 2010) — Tiny variants in a protein that alerts the immune system to the presence of infection may underlie the rare ability of some individuals to control HIV infection without the need for medications. In a report that will appear in *Science* and is receiving early online release, an international research team led by investigators from the Ragon Institute of Massachusetts General Hospital (MGH), MIT and Harvard and from the Broad Institute of MIT and Harvard describe finding that differences in five amino acids in a protein called HLA-B are associated with whether or not HIV-infected individuals can control viral levels with their immune system only.

"We found that, of the three billion nucleotides in the human genome, just a handful make the difference between those who can stay healthy in spite of HIV infection and those who, without treatment, will develop AIDS," says Bruce Walker, MD, director of the Ragon Institute and co-senior author of the *Science* article. "Understanding where this difference occurs allows us to sharpen the focus of our efforts to ultimately harness the immune system to defend against HIV."

"Earlier studies had showed that certain genes involved with the HLA system were important for HIV control," adds Paul de Bakker, PhD, of the Broad Institute and Brigham and Women's Hospital, co-senior author. "But they couldn't tell us exactly which genes were involved and how they produced this difference. Our findings take us not only to a specific protein, but to a part of that protein that is essential to its function."

It has been known for almost two decades that a small minority—about one in 300—of individuals infected with HIV are naturally able to suppress viral replication with their immune system, keeping viral load at extremely low levels. To identify genetic differences that may underlie this rare ability, Florencia Pereyra, MD, at the Ragon Institute established the International HIV Controllers Study ([http://www.hivcontrollers.org/](http://www.hivcontrollers.org/)) in 2006, with a goal of enrolling 1,000 HIV controllers from medical clinics and research institutes around the world. That goal was expanded to 2,000 controllers in 2008, and thus far over 1,500 controllers have been enrolled.

The current investigation began with a genome-wide association study (GWAS) of almost 1,000 controllers and 2,600 individuals with progressive HIV infection, through a collaboration with the AIDS Clinical Trials Group. The GWAS, which tests variations at a million points in the human genome, identified some 300 sites that were statistically associated with immune control of HIV, all in regions of chromosome 6 that code for HLA proteins. Further analysis narrowed the number of gene sites to four but could not indicate whether those differences actually affected viral control or were just located near the causal variants. Fully sequencing that genome region in all participants was not feasible, but a process developed by Sherman Jia—a medical student in the Harvard-MIT Health Sciences and Technology program, working with de Bakker at the Broad—pinpointed specific amino acids; and directly testing those sites associated five amino acids in the HLA-B protein with differences in viral control.

HLA-B is essential to the process by which the immune system recognizes and destroys virus-infected cells. Usually HLA-B grabs onto viral protein segments called peptides that are inside the cell and carries them to the cell membrane where they essentially flag the infected cell for destruction by CD8 "killer" T cells. The portion of the HLA-B protein that grabs and displays viral peptides is called the binding pocket, and all of the five identified amino acid sites are in the lining of the binding pocket.

"Amino acid variation within the HLA-B binding pocket will impact its shape and structure, probably resulting in some peptides being presented effectively and others not," de Bakker says. "Our work demonstrates that these variants could make a crucial difference in the individual's ability to control HIV by changing how HLA-B presents peptides from this virus to the immune system."

Walker adds, "HIV is slowly revealing its secrets, and this is yet another. Knowing how an effective immune response against HIV is generated is an important step toward replicating that response with a vaccine. We have a long way to go before translating this into a treatment for infected patients and a vaccine to prevent infection, but we are an important step closer."

The investigators note that these findings would not have been possible without the participation of the hundreds of HIV controllers, many of whom traveled to Boston for testing, who have enrolled in the study. "The enthusiasm among the patients we have enrolled and the HIV providers who referred them has been amazing," says Pereyra. "They tell us that being part of this collaborative study means a lot to them."
HIV Positive Children May Need Extra Vaccinations

**SUMMARY:** Children with HIV who are receiving combination antiretroviral therapy (ART) may benefit from additional “booster” doses of childhood vaccines, according to a research review published in the September 2010 issue of *Lancet Infectious Diseases*. Researchers found that in general children on ART developed low levels of immunity to vaccines that were given before starting therapy, but most responded well to revaccination once on treatment. Starting ART in early infancy, before receiving childhood vaccines, might preserve immunity to vaccine-preventable diseases, they suggested.

Below is the text of a press release from Johns Hopkins Bloomberg School of Public Health describing the research and its findings.

### Revaccination Could Benefit HIV-Infected Children

Baltimore—September 1, 2010—HIV-infected children receiving highly active antiretroviral therapy (HAART) may require revaccination to maintain immunity against preventable diseases. There remains no standard or official recommendation on revaccination of children receiving HAART, an effective intervention in reducing morbidity and mortality in HIV-infected children. Researchers at the Johns Hopkins Bloomberg School of Public Health reviewed published data to assess these children’s immune responses to vaccines and found that most children treated with HAART remained susceptible to vaccine-preventable diseases, but responded well to revaccination. Their review was published in the September issue of the *Lancet Infectious Diseases*.

"Most children on HAART responded to revaccination, although immune reconstitution was not sufficient to ensure long-term immunity for some children," said William Moss, MD, MPH, senior author of the review and an associate professor with the Bloomberg School’s Department of Epidemiology. "Because of the progressive effects of HIV infection on the ability of the immune system to mount an effective response, many infected children have poorer responses to vaccines than do uninfected children. In addition, fewer children infected with HIV achieve protective immunity, and those who do might experience greater and more rapid waning of immunity. These results suggest that children on HAART would benefit from revaccination, but levels of protective immunity might need to be monitored and some children may need additional vaccine doses to maintain protective immunity."

Researchers reviewed 38 published studies to establish whether children infected with HIV on HAART have protective immunity to vaccine-preventable diseases and to assess short-term and long-term immune responses to vaccination of children given HAART. Short-term was defined as less than or equal to 3 months, and long-term was defined as greater than 3 months. They found that starting HAART in infancy, before receipt of routine childhood vaccines, might preserve immunity to vaccine-preventable diseases. Currently, the World Health Organization (WHO) recommends giving most routine childhood vaccines to children infected with HIV, but does not make recommendations on revaccination.

"Continued efforts are needed to identify and treat HIV-infected children at younger ages and at earlier stages of disease," said Catherine Sutcliffe, PhD, lead author of the review and a research associate with the Bloomberg School’s Department of Epidemiology. "Vaccination policies and strategies for children infected with HIV on HAART should be developed in regions of high HIV prevalence to ensure adequate individual and population immunity. Without such recommendations, as treatment programs scale up and more children receive HAART and live into adolescence and adulthood, a larger proportion of these children could be susceptible to childhood diseases.”

11/5/10

**Reference**


Do People with AIDS Develop Cancer Earlier or More Often?

**SUMMARY:** People with a history of AIDS diagnosis have a higher likelihood of developing—and dying from—several types of non-AIDS-defining cancer compared with the general population, and individuals who survived several years after an AIDS diagnosis had persistent excess risk for both AIDS-defining and certain non-AIDS malignancies, according to 2 recently published reports. Another study, however, found that people with AIDS did not develop most types of cancer at an earlier age on average.

**By Liz Highleyman**
It is well established that AIDS-defining malignancies—Kaposi’s sarcoma (KS), non-Hodgkin lymphoma (NHL), and invasive cervical cancer—have declined since the advent of effective combination antiretroviral therapy (ART). Studies of non-AIDS cancers in people with HIV and AIDS, however, have produced conflicting results.

**Italian Study**

As described in the November 1, 2010 issue of *Clinical Infectious Diseases*, Antonella Zucchetto and colleagues compared rates of non-AIDS malignancies among 10,392 HIV positive Italian citizens age 15 or older who were diagnosed with AIDS between 1999 and 2006, and members of the general population matched for age and sex.

The median duration of follow-up was 37 months, yielding 35,224 person-years worth of data. Risk of death during this period was estimated using standard mortality ratios (SMRs).

**Results**

- A total of 3209 people with AIDS died due to any cause during follow-up.
- Most of these individuals (about 80%) were men, half were injection drug users and the median age at the time of death was 42 years.
- 7.4% of these deaths had non-AIDS cancer as the underlying cause.
- The overall risk of non-AIDS cancer death for people with AIDS was 6.6-fold higher than that of the general population.
- The most common malignancies leading to death in the AIDS group were:
  - Lung cancer (58 cases, 24.6%);
  - Liver cancer (28 cases, 11.9% of deaths);
  - Hodgkin’s lymphoma (28 cases, 11.9% of deaths);
  - Head and neck cancers (18 cases).
- People with AIDS had elevated mortality rates for several non-AIDS cancers:
  - Anal cancer: SMR 270, or 270 times higher likelihood of death;
  - Hodgkin lymphoma: SMR 174;
  - Liver cancer: SMR 11.1;
  - Brain and central nervous system cancer: SMR 10.0.
  - Head and neck cancers: SMR 8.2;
  - Lung cancer: SMR 5.9;
  - Myeloma and leukaemia: SMR 5.9;
  - Stomach cancer: SMR 3.1.
- People with AIDS over age 45 and women had greater excess non-AIDS cancer mortality than younger individuals and men, respectively.
- Those with a history of injection drug use also had a more elevated risk of non-AIDS cancer death, especially due to liver cancer.

"In this analysis of the risk of death for non-AIDS-defining cancers among Italian people with AIDS in the [ART] era, we found a nearly 7 fold excess, compared with the general population of the same sex and age," the investigators concluded.

People with a history of AIDS had especially elevated risk of death due to cancers with infectious viral causes, including liver cancer, associated with chronic hepatitis B and C, and anal cancer, which is considered non-AIDS-defining even though it is caused by the same types of human papillomavirus (HPV) as AIDS-defining cervical cancer.

"Our findings of an excess mortality for non-AIDS-defining cancers cannot be totally explained by the well-known excess incidence of non-AIDS-defining cancers among people with AIDS," they explained in their discussion. "Some very high SMRs detected in our study should be considered as the joint result of
increased incidence of such tumors and of their worse prognosis among people with AIDS versus the general population."

They added that these findings may not extend to HIV positive people who have better-preserved immune function and never developed AIDS.

**U.S. Studies**

Researchers at the U.S. National Cancer Institute (NCI) recently published 2 related studies of cancer in people with AIDS.

In the first analysis, described in the August 9, 2010 *Archives of Internal Medicine*, Edgar Simard and colleagues assessed long-term cancer risk among people diagnosed with AIDS relative to the general population, and the impact of ART on cancer incidence.

The researchers looked at medical records from 263,254 adults and adolescents with AIDS in 15 U.S. regions, spanning the period 1980 through 2004. These records were matched with cancer registries to capture new cancers occurring 3-5 years and 6-10 years after onset of AIDS.

Standardized incidence ratios (SIRs)—which estimate likelihood of developing new cancers, while the SMRs used in the previous study estimate cancer deaths—were used to assess risks relative to the general population. Rate ratios (RRs) were used to compare cancer incidence before and after 1996 to assess the impact of ART.

As expected, people with AIDS had elevated risk for the 2 major AIDS-defining cancers, Kaposi sarcoma (SIR 5321 for years 3-5 after AIDS diagnoses and SIR 1347 for 6-10 years) and non-Hodgkin lymphoma (SIRs 32 and 15, respectively). Incidence of both malignancies declined after the advent of ART.

People with AIDS was had increased risk for all non-AIDS-defining cancers combined (SIRs 1.7 and 1.6, respectively), as well as for several specific non-AIDS cancers including Hodgkin lymphoma, mouth and throat cancers, anal and penis cancer, and lung cancer. Absolute incidence of anal cancer (RR 2.9) and Hodgkin lymphoma (RR 2.0) increased between 1990-1995 and 1996-2006.

"Among people who survived for several years or more after an AIDS diagnosis, we observed high risks of AIDS-defining cancers and increasing incidence of anal cancer and Hodgkin lymphoma," the study authors concluded.

In the second NCI study, published in the October 5, 2010 *Annals of Internal Medicine*, Meredith Shiels and colleagues compared ages at the time of diagnosis for non-AIDS cancers among people with AIDS and the general populations. They looked at data from 212,055 people with an AIDS diagnosis enrolled in the U.S. HIV/AIDS Cancer Match Study from 1996 through 2007.

The proportion of person-time contributed by older individuals (age 65 or older) was far smaller for the AIDS group (1.5%) than for the general population (12.5%), the researcher explained. Reflecting this difference, the age at diagnosis for most types of cancer was approximately 20 years younger for people with AIDS.

After adjusting for differences in the 2 populations, however, the median ages at diagnosis did not differ significantly between people with AIDS and members of the general populations for most types of cancer including colon, prostate, and breast cancer. But the age at diagnosis was significantly younger in the AIDS group for lung cancer (median 50 vs 54 years) and anal cancer (median 42 vs 45 years), and significantly older for Hodgkin lymphoma (median 42 vs 40 years).

"For most types of cancer, the age at diagnosis is similar in the AIDS and general populations, after adjustment for the ages of the populations at risk," the researchers concluded. "Modest age differences remained for a few types of cancer, which may indicate either acceleration of carcinogenesis by HIV or earlier exposure to cancer risk factors."  

**References**


**Circumcision Among Men Who Have Sex with Men in Scotland: Limited Potential for HIV Prevention**

*Sexually Transmitted Infections Vol. 86: P. 404-406*, (10.10.2010)  
Lisa M. McDaid; Helen A. Weiss; Graham J. Hart

Male circumcision has been shown to reduce the risk of HIV acquisition among heterosexual men, but the impact among men who have sex with men is not known," reported the study authors. Their aim was to
describe sexual practices by circumcision status, and to explore the feasibility of conducting research on male circumcision for HIV prevention among MSM in Scotland.

Men visiting Glasgow and Edinburgh’s commercial gay scenes were recruited to fill out anonymous, self-completed questionnaires and provide oral fluid samples. Data were analyzed using SPSS 15.0. Logistic regression was used to estimate odds ratio (OR) and 95 percent confidence interval (CI). ORs were adjusted for age and nationality, which were significantly associated with circumcision status.

A total of 1,508 men completed questionnaires (70.5 percent response rate) and 1,277 provided oral fluid samples (59.7 percent response rate). Overall, 1,405 men were eligible for inclusion in the study. Of the men, 233 (16.6 percent) reported having been circumcised. Compared to Scottish men, nationals from non-European countries (the United States, Canada, Australia and New Zealand) were more likely to be circumcised (13.1 percent vs. 50.0 percent, respectively, p<0.001).

HIV prevalence was comparable among circumcised and uncircumcised men (4.2 percent and 4.6 percent, respectively). “Although biologically, circumcision is most likely to protect against HIV for men practicing unprotected insertive anal intercourse (UIAI), only 7.8 percent (91/1,172) of uncircumcised men reported exclusive UIAI in the past 12 months,” the authors found. Few men (13.9 percent) reported being willing to participate in HIV prevention research on circumcision, and just 11.3 percent of uncircumcised men said they were willing to do so.

“The lack of association between circumcision and HIV status, low levels of exclusive UIAI, and low levels of willingness to take part in circumcision research suggest circumcision is unlikely to be a feasible HIV prevention strategy for MSM in the UK. Behavior change should continue to be the focus of HIV prevention in this population,” the authors concluded.

Scientists Identify Genes That Enable Some Immune Systems To Halt HIV; Finding Could Spur Drug, Vaccine Development

“Tiny variants in a protein that alerts the body to infection could explain how one in 300 HIV-infected people are able to resist the onset of AIDS for years without needing any treatment,” researchers said Thursday” in a study published online in the journal Science, Agence France-Presse reports (11/4). “The findings are encouraging for the development of vaccines because they tell scientists how the immune system might be manipulated to fend off HIV,” the Independent writes (Connor, 11/5).

“HIV is slowly revealing its secrets ... Knowing how an effective immune response against HIV is generated is an important step toward replicating that response with a vaccine,” said Bruce Walker of Massachusetts General Hospital, who was a senior co-author on the study, AFP adds. “We have a long way to go before translating this into a treatment for infected patients and a vaccine to prevent infection, but we are an important step closer,” he said (11/4).

For nearly two decades scientists have recognized “that a small minority ... of individuals infected with HIV are naturally able to suppress viral replication with their immune system, keeping viral load at extremely low levels,” according to a Massachusetts General Hospital press release (11/4). Such individuals, referred to by researchers as “‘HIV controllers’ do not require treatment, because their bodies suppress the replication of the virus,” Nature News writes (Milton, 11/4). Science News adds, “Scientists have long thought that finding the genetic peculiarities underlying this protection could help to create drugs or a vaccine against HIV” (Seppa, 11/4).

In search of the genetic differences that enable some immune systems to suppress the HIV virus, an international consortium of researchers “searched the genetic makeup of nearly 1,000 people with that ability and compared it with the genetic code of 2,600 others who were infected with HIV” and not HIV controllers, Reuters reports (Steenhuysen, 11/4). "The controllers had variations in five amino acids in a protein called HLA-B, which alerts the immune system to the presence of infection," HealthDay/Bloomberg BusinessWeek reports.

"We found that, of the three billion nucleotides in the human genome, just a handful make the difference between those who can stay healthy in spite of HIV infection and those who, without treatment, will develop AIDS,” Walker explained, the Massachusetts General Hospital press release adds.

"Understanding where this difference occurs allows us to sharpen the focus of our efforts to ultimately harness the immune system to defend against HIV."

Though "[e]arlier studies had showed that certain genes involved with the HLA system were important for HIV control ... they couldn’t tell us exactly which genes were involved and how they produced this difference. Our findings take us not only to a specific protein, but to a part of that protein
that is essential to its function,” Paul de Bakker of Brigham and Women’s Hospital, also a senior co-author on the study, said, according to the press release (11/4).

“"This is a really exciting step toward a kind of pie-in-the-sky goal," statistical geneticist Alison Motsinger-Reif of North Carolina State University, who was not involved in the study, said, according to Science News. "Elite controllers represent a medical mystery, she said. ‘If we can understand what’s different about their biology, it will open up new targets [for HIV] drugs or vaccines,’” she said, the news service writes (11/4).

However, Walker “emphasized discovery is not like a ‘light switch’ that turns someone into an HIV controller. It is one factor among several that increases the chances of someone being able to survive for many years with HIV and not antiretroviral treatment, he said,” the Independent writes. “We’ve identified a major determinant but there are other factors that will influence the pathway. We’ve not identified the precise mechanism to explain HIV controllers but we know that of all the genetic influences involved, this is by far the most important,” Walker said, according to the newspaper (11/5).

The Philadelphia Inquirer, also reporting on the findings of the HIV controller study, tells the story of the contributions made by patients who are HIV controllers to become testing subjects in order to advance scientists’ understanding of how to best fight the HIV virus (Flam, 11/5).

NYTimes, November 5, 2010

As H.I.V. Babies Come of Age, Problems Linger (long)

By PAM BELLUCK

WARWICK, R.I. — “They’ve been telling me since age 3 that I would die,” Tom Cosgrove said quietly. “Then age 6, age 8, age 10.”

Now 20, he is considered the longest-living person born with H.I.V. in his state, but every year has brought struggle.

As a toddler at a shelter for children infected with H.I.V. from birth, he watched others die. Then, AIDS killed his mother and newborn brother. At 8, his body rejected medication and he became temporarily unable to walk.

He raged with anger, once even striking a teacher with a chair. Classmates, paranoid about his disease, refused to shake his hand or sit at his lunch table. Friends’ parents forbade them to visit, and he could not join basketball teams or karate classes.

Even now, medications impair his short-term memory, making school, and job prospects, difficult.

“‘We call them his stupid drugs,' said Barbara Cosgrove, who adopted Tom at 3. ‘But, as I say to Tom, ‘You’re either stupid or you’re dead.’”

At a time when H.I.V. in the United States has become a manageable disease for many, Tom Cosgrove and others like him are proof of the epidemic’s troubling, lingering legacy. They are the survivors, born beginning in the 1990s to the first big wave of people with AIDS, babies practically destined to die. Improvements in drugs, along with some luck, allowed some 10,000 of them to live — and these days only about 200 children a year are born with H.I.V., thanks to vigilant drug treatment of infected pregnant women.

But life for those first H.I.V. babies now entering adolescence and adulthood has been a battle, and their experience is considered so significant — not only in this country but also for the millions of H.I.V.-positive babies worldwide — that federal health agencies have begun an extensive study to follow these young people as they grow up.

Some are weakened by years of yo-yoing symptoms that early drugs failed to treat. Some have developmental delays or other problems related to having H.I.V. at birth. And their medications often have harsher side effects than those taken by people infected more recently as teenagers or adults because complications from their illness, or previous drugs they took and became resistant to, have made their disease more stubborn to treat.

Emotionally, they grapple with hostility toward parents who infected them, grief that those parents suffered and usually died, and anxiety about trusting others with a secret that still provokes hazing and fear.

And a serious problem is emerging: some are rebelling or asserting independence by skipping or stopping medication, which can make H.I.V. spiral out of control and become impervious to previously effective therapies.

“It ain’t over yet,” Dr. Ellen Cooper, medical director of pediatric and adolescent H.I.V. at Boston Medical Center, said about keeping these young people alive and healthy. Although she has not lost a
patient in five years, she said, “I’m expecting a second wave” of these young people “dying because they’re not adherent” to medication, or because of “complications from treatment.”

Dr. Lynne M. Mofenson, chief of pediatric, adolescent and maternal AIDS at the National Institute of Child Health and Human Development, said that despite H.I.V. babies’ increased survival, their “mortality is still thirtyfold higher than similarly aged children,” and there is “a lot of research that’s needed, and interventions to improve their lives.”

Seven agencies of the National Institutes of Health are following 451 H.I.V. babies ages 7 to 16, monitoring their hearts, cholesterol, bones, brains, hearing, sexual development, school performance, language ability, behavior and mental health.

Preliminary findings show many of their current lifesaving drugs cause high cholesterol, raising fears of serious heart problems, said Dr. Russell Van Dyke, the study’s co-principal investigator. Their bone density appears poor. And many have mental health and behavioral problems, although it is unclear to what degree those problems are related to the disease or to the children’s often-difficult family circumstances.

“There is a lot of concern,” Dr. Van Dyke said, “about how the kids adapt to living and what sort of challenges they have. The lessons are going to be applicable to the rest of the world.”

‘I Was Born This Way’

Davi Morales is the kind of young person doctors worry about. He has H.I.V.-related cognitive disabilities, and spent months homeless after uncles who raised him in a Providence, R.I., housing project returned to Puerto Rico.

Davi, 20, lost Social Security disability assistance because the government now considers most H.I.V.-infected people able to work, said Scott Mitchel, a counselor with AIDS Care Ocean State, who got him into an apartment that his agency owns. But Davi has trouble staying employed, following rules, working with managers.

“I don’t think right now he can go out there and support himself,” Mr. Mitchel said. For one thing, his medication, five pills twice daily, causes severe insomnia and diarrhea.

Nowadays, people contracting H.I.V. through sex or drugs may take one easily tolerated pill, but the H.I.V.-baby generation often needs complex multipill doses with irritating side effects, making pill-skipping more likely.

In desperation, doctors sometimes allow them to stop medication altogether rather than take their “last rescue regimen poorly,” Dr. Cooper said.

Davi sometimes skips several days, and “when I feel down, like I just want to give up, I don’t want to take my medicine at all,” he said. “If I didn’t have that kid, I probably never would take them.”

That kid is the son born three years ago after Davi, who was 16, told his girlfriend at the time, who was 14, “I want to have a kid” and “she was cool with it,” he said. “I didn’t really know what I was really doing.”

She took medication during pregnancy, and their son is uninfected. Her family, fearful of Davi’s disease, blocked access to the boy for awhile, and the couple broke up. He is facing assault charges for striking her during an argument, but now sees his son regularly.

He said he wants to stay alive, but “maybe my lifespan is not as long as a normal lifespan. I was born this way and that’s what it is.”

Medication is not the problem for Elizabeth. Eighteen, white, from a wealthy Massachusetts suburb, she has been ostracized and tormented, “ ‘H.I.V. slut’ being yelled across the hallway, anything you can think of,” she said.

Elizabeth did not know she had H.I.V. until the age of 14, when her parents and physician appeared at her therapist’s appointment and told her.

“I couldn’t speak or really breathe,” said Elizabeth, whose mother was infected through a blood transfusion before she was born.

Elizabeth, who asked that her last name be withheld, said her mother “wants me to be completely closed about it,” and even Elizabeth’s little sister, who is uninfected, does not know. Keeping it inside feels “like holding your breath underwater for too long.”

But close friends she confided in betrayed her. Her best friend gossiped about it, and a boyfriend she broke up with “told everyone to get back at me,” she said. Schoolwork suffered as she constantly feared hazing and “focused on having to deal with this.”

At 16, she told a new boyfriend, who “promised that he’d never judge me upon it, that he’d never break up with me, that he’d never tell anyone,” she said. “The next day he broke up with me because of it.” They reunited, but his parents scorned her and he sometimes hid their relationship from friends, said Elizabeth, who recently stopped seeing him.
She said people in her well-educated community, who should know that H.I.V. can be well controlled with medication and protected against with condoms, have been surprisingly intolerant.

“There’s no need to think I’m dirty,” she said. “I’ve basically had my trust for people completely taken away.”

**Sharing and Trusting**

Things get harder as H.I.V. babies grow up and leave the “very nurturing network” of pediatric AIDS clinics and programs, said Rena Greifinger, who formed the One Love Project to help such young people. “At 18, all that support melts away,” plus some of them “have been completely rejected by their families, the leper child.”

At a weeklong retreat at Babson College in Wellesley, Mass., One Love provided music therapy, role-playing about disclosing H.I.V. status, and explicit discussions about sex and having children.

“When I was pregnant, I was crying all the time, worried she would be positive,” said Imani Walters, 19, who contracted H.I.V. as a teenager. Her daughter turned out healthy. “Then you get scared you might not see them grow up.”

The young people were told that having infected children was unlikely with medication through pregnancy, avoiding breastfeeding and giving the babies medication for six weeks.

“We wanted to give them so much information that we get that buy-in to stay on their meds, and they learn how to live with H.I.V.,” said Bill Kubicek, executive director of Next Step, which sponsors One Love and was co-founded by Paul Newman.

Elizabeth met other H.I.V. babies for the first time at the conference, and “here I trust everyone,” she said.

The gathering was eye-opening for Sandy Perez, 18, from Canaan, N.H., too. Her mother, infected through drug use, died when Sandy was 7. Some foster families mistreated her, she said; at one home, underfed, she slept in the laundry room, locked in, and would climb out the window and re-enter the house through the garage to grab food.

Although she now has a loving family and takes medication regularly, she has experienced serious symptoms: sunken cheeks, gaunt face, bony arms. Medication has caused diabetes, and liver and kidney problems.

Sandy rarely disclosed her H.I.V., not even to boyfriends, although she always used condoms. But she said the conference “inspired me” to feel “comfortable with myself and with having this H.I.V., so I can now share it with people that I feel I trust.”

Like her boyfriend of two years, with whom she had not had intercourse. Unable to reach him by phone from the conference, she texted him: “I have H.I.V.” He texted back: “Are you serious?” She replied: “Yes.”

Sandy felt relieved. If he did not know and “became infected, then there would be a part of me that felt responsible and guilty and just icky inside,” she said.

Soon after, the relationship ended, on good terms, she said. “He kind of didn’t really know how to handle it,” she said. But “he calmed down and we eventually talked” and “he was happy I had told him before we did anything.”

**A Family’s Acceptance**

When the Cosgroves adopted Tom, he was unruly and angry, and at 5 was further traumatized by seeing his mother “turning different colors, losing her hair,” dying of AIDS, he said. He pasted her obituary on his First Communion banner, and had “nightmares, night sweats,” he said, “very mad at her because I thought she purposefully gave me this disease.”

Since “people were petrified to take any of these children,” Ms. Cosgrove said, she adopted four other “throwaway babies,” saying she was abused as a child and “kind of a throwaway baby myself.”

All four, who arrived untested for H.I.V., turned out negative. “I really felt alone,” Tom said, and at 9, after an H.I.V.-camp friend died, he begged them to adopt someone like him.

They adopted Tyree, who had two H.I.V. strains, one from each parent, and developmental delays. For years, he took medication through a stomach tube because he would vomit it otherwise. Now 11, he often needs leg braces, and his viral load — the amount of virus in the blood — is too high.

Tyree’s adoption did not improve everything for Tom, and Tom was “very out of control” for years, he said. To tame his behavior, Ms. Cosgrove said, she had to “push him down and say, ‘You are not going to talk like that, you are not going to act like that.’ One day I dragged him across the carpet, and his teacher called and I told her this is what I did and why.”

By 12, Tom had calmed down, but he chafed at people’s reactions. Ms. Cosgrove informed his school about his H.I.V. and held a meeting for parents, but while school officials were supportive, some parents
and classmates shunned him. Tyree attends another school, whose principal advised against disclosure because parents would react badly. And a soccer coach Ms. Cosgrove told said, “Oh, we’re not taking kids like that.”

Tyree said he feels “lonely” because “none of my friends come over.” He already knows how to protect others, saying, “Don’t have sex with me.”

Tom, now mature and thoughtful, finds things more complicated. With his infection well suppressed with medication, he has started Job Corps, a federal job-training program, but his medications’ side effects affecting his memory concern him, and he said that girlfriends have not lasted long because “people have a lot of worries about going out with someone with this disease.”

Still, since his adoptive family “can accept me for who I am,” he said, “I look at it as if there’s other people out there who can probably do the same.”

**Bone loss common in patients with HIV, and often progresses**

Michael Carter  
Published: 08 November 2010

There is a high prevalence of low bone mineral density among patients with HIV, Spanish investigators report in the online edition of *AIDS*. The researchers also found evidence during follow-up of deterioration of bone health in many patients.

“Our...study revealed a marked incidence of low BMD [bone mineral density] in a large number of patients with long-term HIV infection and prolonged antiretroviral therapy”, comment the researchers.

They believe that their findings have immediate clinical significance, and write: “Clinical monitoring of BMD by DXA scan should be a priority in HIV-infected patients, specifically in those at risk of fracture.”

HIV infection has been firmly linked with an increased risk of low bone density. However, the exact causes are unclear.

Traditional risk factors for this condition include smoking, heavy alcohol consumption, malnutrition, low body weight, and lack of physical activity.

HIV itself can cause loss of bone mineral, and treatment with some anti-HIV drugs has also been associated with loss of bone mineral density.

Spanish researchers wanted to gain a better understanding of the prevalence, risks, and progression of bone loss in their HIV-positive patients.

They therefore designed a retrospective study involving 671 patients who received HIV care between 2000 and 2009 in Barcelona. All the patients had at least one DXA scan. Progression of bone loss was assessed in 391 individuals who had two or more scans.

Most (72%) of the patients were male, 6% were aged over 55, the median age was 42 years (interquartile range 37–47), 67% had a body mass index (BMI) within the normal range, 62% had an adequate calcium intake, and 35% were co-infected with hepatitis B or C.

CD4 cell count at the time of entry to the study was 496 cells/mm$^3$, 93% had experience of antiretroviral therapy, and 61% had an undetectable viral load.

Osteopenia – mild bone loss – was diagnosed in 47% of patients and osteoporosis – porous bone with an increased risk of fractures– in 23%.

Factors associated with low bone mineral density were increasing age (p < 0.001), low BMI (p < 0.001), male sex (p = 0.0078), high creatinine levels (p = 0.0047), taking HIV therapy at the time of DXA scan (p = 0.007), longer duration of antiretroviral treatment (p = 0.004), and increased amount of time taking a protease inhibitor.

Next the investigators looked at the progression of bone loss. Their analysis included the patients who had two or more DXA scans.

The median time between the first and last scan was 2.5 years, but in 27% of patients it was more than five years.

At the first scan, 49% of patients had osteopenia and 22% osteoporosis. At the second scan this had increased to 50% and 27%.

Overall, 29% of patients experienced progression to low bone mineral density, including 13% progressed to osteopenia, and 16% from osteopenia to osteoporosis.
When analysis was restricted to the 105 patients with five or more years of follow-up, 47% lost bone mineral density, including 18% who developed osteopenia and 29% who developed osteoporosis.

Factors associated with bone loss during follow-up included increasing age (p < 0.0001), male sex (p < 0.0001), low BMI (p < 0.0001), longer duration of treatment with a protease inhibitor (p < 0.0001) or tenofovir (p < 0.0001), and taking a protease inhibitor at the time the DXA scan was performed (p < 0.0001).

“We reveal a high prevalence of low BMD in our cohort. The longitudinal analysis – more than five years of follow-up in some cases – revealed rapid progression to demineralization”, comment the investigators.

The investigators stress the need “for close monitoring of BMD, specifically in at-risk patients who are taking antiretroviral therapy that affect bone demineralization.”

Reference

Infections the main cause of CNS neurological problems in South African patients starting HIV treatment

Michael Carter
Published: 08 November 2010

Opportunistic infections – most notably tuberculosis and cryptococcal meningitis – are the main cause of neurological problems in patients starting HIV treatment in South Africa, investigators report in the online edition of AIDS.

A quarter of patients who were diagnosed with a neurological disorder died, and a fifth were lost to follow-up. These rates were much higher than those seen in the general population of patients starting antiretroviral therapy.

“This is, to our knowledge, the first prospective study describing the spectrum of neurological disorders within the first years of ART”, write the investigators, “TB and cryptococcal meningitis together accounted for at least 60% of cases.”

Historically, neurological disease was an important cause of illness and death in patients with HIV. However, improved therapy of opportunistic infections and the advent of effective HIV treatment have led to significant falls in the number of new cases of conditions such as dementia.

But patients with HIV, especially in resource-limited settings, remain at high risk of developing neurological disorders.

Tuberculosis (TB) can cause central nervous system complications. Moreover, patients with weak immune systems have a higher risk of developing an immune reconstitution inflammatory syndrome (IRIS) after starting antiretroviral therapy. Neurological IRIS associated with TB or cryptococcus has been observed.

In addition, the anti-HIV drug efavirenz (Sustiva, also in the combination pill Atripla) has been associated with neurological symptoms such as sleep disturbances or changes in mood. Little is known about the spectrum of neurological disorders that develop in patients starting HIV therapy in South Africa.

Therefore, researchers from the GF Joote Hospital in Capte Town, South Africa, prospectively followed patients starting antiretroviral therapy over a twelve-month period in 2007-2008. They recorded the incidence of neurological disorders; the causes; treatment and outcomes.

A total of 75 patients developed neurological disease, and the overall incidence was 23 cases per 1000 person years of follow-up. The investigators believe that this is likely to be an under-estimate. Patients with mild or moderate were probably at missed, and those with the most severe disease could have died at home without receiving a diagnosis or care.

The patients had a median CD4 cell count of 64 cells/mm$^3$ at the time that neurological disease was diagnosed.

Consistent with such severe immune suppression, 36% of disease involved tuberculosis and 24% cryptococcal meningitis. Brain lesions accounted for 13% of cases, and psychosis 9%.

TB-IRIS was diagnosed in 16 (21%) of patients. Most (13) were treated with corticosteroids and after six months 15 individuals were still alive. The other patient was lost to follow-up.

Five patients (7%) developed a cryptococcal IRIS. Only one of the patients received therapy with corticosteroids.
“No patients in our cohort who presented with IRIS died during 6-months follow-up and only one patient with TB-IRIS and one with CM-IRIS were lost to follow-up”, comment the researchers.

Lesions were the cause of neurological disease in ten patients (13%). Toxoplasmosis was identified as the cause in one individual. Two patients died.

Overall, nine (12%) of patients were diagnosed with psychosis. Five of the cases were attributed to therapy with efavirenz, one case to isoniazid, and two cases to HIV itself.

After six months, 57% of patients were alive, 23% had died and 20% were lost to follow-up. These outcomes were much poorer than those seen in the general cohort of patients starting HIV therapy. Only 8% of these individuals died and between 3-5% were lost to follow-up.

“In our setting, opportunistic infections, notably TB and cryptococcus were the most important causes for neurological deterioration during the first year of ART”, conclude the investigators. They believe the rate of neurological disease seen in this study is probably an under-estimate.

They believe that their study “has particular relevance to ART programmes in high TB prevalence regions. We highlight the challenges associated with the management of these patients in resource-constrained settings.”

Reference

**HIV-positive women in Chile face forced sterilization**

By Pascale Bonnefoy

**Report says women in Chile with HIV face abuse and sterilization without consent.**

Byline: Pascale Bonnefoy

SANTIAGO, Chile — Hours after Francisca gave birth to her first child, a midwife came into the recovery room and bluntly informed her that she would never have children again. She had been sterilized, unknowingly, during her cesarean delivery. Francisca was HIV-positive and only 21.

The young woman from Curico, a rural town in southern Chile, was diagnosed with HIV during routine exams early into her pregnancy in 2002. She immediately began treatment to avoid mother-to-child HIV transmission, but throughout her pregnancy no one in the local hospital counseled her on what it meant to be HIV-positive, the potential risks of transmission to her baby or the possibility of sterilization, claims Francisca, which is not her real name.

“As I was about to give birth, the nurse scolded me, telling me I was irresponsible for having gotten pregnant with HIV, and asking why I hadn’t aborted. It was horrible,” she said.

Even though Francisca went into labor before a programmed cesarean surgery, the doctor on shift that night nevertheless operated on her under general anesthesia. She woke up with a healthy, HIV-negative baby boy, and sterile.

Two NGOs brought her case to the Inter American Human Rights Commission in Washington. It is up to the court to decide whether the Chilean government failed to protect her from being forcibly sterilized.

There are about 3,500 women in Chile with HIV or AIDS, many of whom face widespread abuse in public health centers, discrimination and sterilization without consent, according to a report “Dignity Denied: Violations of the Rights of HIV-Positive Women in Chilean Health Facilities,” [2] published last month by the New York-based Center for Reproductive Rights and the Chilean NGO Vivo Positivo.

“Sterilization without consent or under coercion occurs with enough frequency and throughout the country to be considered systematic,” said Suzannah Phillips, primary author of the report, which included interviews with 27 HIV-positive women in five regions of Chile. “It’s not an active government policy, but it is the result of government omission and not implementing its own guidelines.”

Government health officials did not respond to repeated requests for interviews.

Coercive and forced sterilizations against HIV-positive women have also been reported in Mexico [3], Venezuela [4], the Dominican Republic [5], South Africa [6] and Namibia [7].

One-fourth of the women the center interviewed who had been sterilized said they had made a fully informed and voluntary decision. The rest said they experienced directive counseling, misleading or incomplete information and sterilization without their knowledge or consent during other procedures, especially during cesarean deliveries.

In 2000, the government issued guidelines establishing counseling and written informed consent prior to sterilization, but as Francisca’s case reveals, health professionals do not always stick to regulations.
“Today women with HIV can decide if they want a normal delivery or a cesarean, depending on their condition. But many women, especially in rural areas, don’t know that. Doctors tell them their babies will be HIV-positive if they don’t undergo a cesarean, and they won’t do the cesarean if the women don’t agree to sterilization. That’s how they scare women,” said Sara Araya, head of the women’s department at Vivo Positivo.

Chile has taken major steps to address the HIV/AIDS epidemic. It adopted a national plan for the prevention, testing and treatment of HIV/AIDS that includes specialized multi-disciplinary teams in hospitals and universal access to antiretroviral treatment. Currently more than 80 percent of people with advanced HIV infection are receiving antiretrovirals.

But this has neither guaranteed quality health care nor halted discrimination against HIV-positive patients.

Such was the case of Matilde, a 36-year-old Peruvian immigrant in Santiago who tested positive for AIDS in 2003. (Matilde is not her real name. Neither Francisca nor Matilde wanted their names published because of the stigma associated with HIV.)

A year and several hospitalizations later, Matilde’s viral load was undetectable, and given the low risk of mother-to-child transmission, she and her partner decided to have a baby.

Access to treatment and attention by specialized medical staff working with HIV/AIDS patients is usually not the problem. The lack of attention and humiliating treatment comes in the maternity wards, labs or doctors’ offices, where women go for their regular checkups or to seek help for other health problems.

“A number of women are made to wait until all the non-HIV patients are treated first. Or they may be turned away entirely because health care professionals don’t want to touch them. One woman was told not to hug or kiss her baby because she would infect him,” said Phillips.

When Matilde would go to routine check-ups at the hospital, the staff there “instead of supporting me, asked me why on earth I wanted to have a baby, if I didn’t know that I was bringing a sick child to the world and that I would live a short life. What they were subtly telling me was that I should have aborted,” she said.

Three months into her pregnancy she experienced abnormal vaginal discharges and sought help in the emergency room of a public hospital. However, when the paramedic learned she was HIV-positive, she said, he stopped short and told her to go home, scolding her for being pregnant in the first place.

She returned two days later for her regular checkup. Already hemorrhaging and in severe pain, she had to wait for the staff to assist all the HIV-negative patients first. Her baby’s heart was no longer beating.

“I am more than certain that if a doctor had attended me from the beginning, I wouldn’t have lost my baby,” she said.

The first cases of HIV/AIDS in Chile appeared in 1984, and the first HIV-positive woman was reported a year later. The number of reported HIV/AIDS cases through last year was 22,115.

Most are young adult males, and 87.4 percent were infected through sexual transmission, mainly homosexual and bisexual. However, the ratio between men and women with AIDS has steadily fallen, from 9.7 in 1990 to 5.7 in 2009, and among men and women with HIV, the ratio dropped from 6.2 to 3.7 in that same period.

“Government prevention campaigns have always focused on the general population and on occasion, specifically on the homosexual community, but never on women. Public health centers distribute condoms to sexual workers, homosexuals and people with HIV, but not to women in general because they are not regarded as a group at risk,” said Sonia Covarrubias, of the NGO EPES, which provides education to working women.

At the time, Francisca thought that the sterilization of HIV-positive women was normal procedure in hospitals. “I had absolutely no information about HIV and at that moment I was very frightened and more concerned about my son’s health,” she recalled.

She later learned her rights after being contacted by Vivo Positivo and in 2003 the NGO filed a lawsuit on her behalf in a local court against the Curico hospital staff responsible for her sterilization. The case was dismissed five years later after hospital officials claimed she had given verbal consent. She says she had not, and even if she had, Chilean law requires written informed consent.

In March 2009, the Center for Reproductive Rights and Vivo Positivo submitted Francisca’s case to the Inter American Human Rights Commission.

“I wanted to have more children,” said Francisca. “It hurts when my son asks for a little brother or sister — how can I explain to him that I can’t?”
In the first part of this series, Matthew Pilecki spoke to experts about the alarming statistics that show younger men who sleep with men are seroconverting to HIV at far higher rates than other age groups. Part of the problem may be young people fetishizing unsafe sex. at the end of Part I, Paul Morris, the founder of Treasure Island Media, perhaps the largest producer and distributor of barebacking gay videos, explained that his films don’t influence sexual behavior any more than violent films or video games turn viewers into serial killers.

Arguing that it is the job of porn producers to document all types of sex practices, Morris considers bareback sex a subculture that is “not only insane, it is also essential.”

“If you’re looking for a ‘culprit’ behind trends in young men engaging in unsafe practices, whether sexual or otherwise, I’d suggest that you look critically at a gay culture that has allowed itself to be stultified by fear-by epidemiological fear and by fear of not being accepted by a dominant world that’s increasingly ‘straight,’ uneducated and reactionary,” Morris asserted. "The straight world wants gay men to be terrified, to be careful, to be obedient.”

Morris is currently producing a series of videos that only features men who are openly positive. "They’re having sex exactly in the way that they actually have sex in their daily lives,” Morris said. "As I’ve said before, being negative is our contemporary virginity; being positive is the new closet. My aim is to demolish that closet. There is no reason not to be proud and open about being [HIV positive].”

Bob Bowers’ website dons a similar pirate theme; his message however, is one of HIV prevention and awareness. Bowers, Wisconsin-based HIV/AIDS educator and activist, uses the pirate persona as a lesson to youth that perceptions often differ from reality. With his built-up physique, Bowers appears to be the epitome of health even though he was diagnosed with HIV over 25 years ago after contracting the virus through intravenous drug use.

Since then, it has been his mission to educate others, especially youth, on HIV prevention methods and to act as a voice for the HIV/AIDS community. Over the years, Bowers has noticed a shift in the attitudes of youth towards HIV/AIDS. While he feels as though his audiences are receptive, he doesn’t feel the same sense of urgency as he did in the height of the HIV epidemic.

**Not a Death Sentence: Mixed Blessing**

“I don’t think folks really view it as a death sentence anymore, and that’s good in some regards, but then that lends for an incredible amount of apathy and complacency around it,” Bowers told EDGE. "I really break down this term of chronic and manageable and I show [students] my medications, the handful of pills I take daily. I guess then they really start to grasp that this is not a cake walk and that there really are some grave challenges. I think one of the most often asked questions is how much the medications are. Without being complicated, I expressed to them it’s one thing to know your status but what good is it if you don’t have access to the medication.”

The images in the media surrounding HIV/AIDS have changed dramatically over the past twenty years—from the Grim Reaper bowling over stacks of skeletons to the healthy face of Magic Johnson. But Bowers believes that there needs to be a better balance of both images to better portray reality.

"I think we have a responsibility to not only show the beautiful faces but to have the faces that we witnessed in the 1980s out there as well,” Bowers said. "Not for the sake of fear but for the sake of reality. That’s kind of just the tip of the iceberg. You’re only seeing the beautiful people that have a movie or have an angle but that's not representative of everyone whether they are gay, straight, black or white.”

By empowering students through knowledge about HIV/AIDS, Bowers is confident that he can encourage better choices and end some of the stigma surrounding those that are HIV positive. As a heterosexual man, Bowers asserts that the disease can affect anyone and by the end of his presentations he feels as though students understand that it is not just a gay disease. But when Bowers mentions that he still has a healthy sex life with his wife, students begin to question.

"While they may be accepting and supportive you can just see it,” Bowers said. "I have a good time with it too. I'm like, 'Hey man I hit it more than you do. What are you talking about? I ain't dead yet.' It really helps to burst a lot of that stigma and it shows me that there’s still an incredible amount of stigma. That while they will support someone with AIDS, they definitely wouldn’t sleep with them. The irony is
that my first wife felt better knowing what she was coming home to than those out there not knowing. And that’s them—they don’t know. People cheat and lie all the time. Who’s going to tell you the truth about HIV?"

"In the 2000s, during the Bush administration, a greater emphasis was placed on treating HIV/AIDS around the world as opposed to at home," he said. "The Bush administration did a great thing as far as amFAR, the emergency plan for HIV/AIDS relief, which helped a lot of people in Africa and Asia. But on the other hand, HIV was neglected at home. The media often looks at AIDS in terms of Africa or Eastern Europe as opposed to Harlem, Brooklyn, or Newark. Or in Washington D.C., which has an HIV rate of 3.4 percent which puts us on par with Kenya and Uganda."

Even though the CDC continues to release reports that HIV rates are skyrocketing among MSM Millennials, little attention has been paid by gay media circuits. Rather, political issues of gay marriage and 'Don't Ask, Don't Tell' have been sweeping headlines. McCullom believes that the lack of coverage in gay media outlets reflects a larger consensus that HIV/AIDS is passé.

"I think in many ways, HIV isn’t seen as sexy anymore," McCullom told EDGE. "In terms of gay media, a lot of the opinion leaders aiding media may not necessarily be that those are affected most by HIV. They might know survivors but a lot of them aren’t necessarily younger and a lot of them aren’t necessarily Black or Latino, which have the highest HIV rates. So it might not be seen as much of a pressing issue. In terms of black and Latino gay media and bloggers I think what happens is a fatigue factor since the numbers are so high people get tired of hearing about it."

**Getting Messages Where Gay Men (Virtually) Live**

The internet has radically transformed accessibility to resources and information on HIV/AIDS. However, sites like Manhunt and Adam4Adam have created forums for MSMs seeking anonymous sex to meet instantly—there are even smart phone applications that speed the process by utilizing GPS technology. With Generation Y on the forefront of technology, it becomes questionable whether these sex sites are playing a part in the escalation of HIV rates.

"I think it’s a symptom of our instant gratification culture—the Internet, the microwave oven," McCullom said. "Twenty or thirty years ago you had to walk into a bar to meet a guy, and maybe have a drink. Now you can do that on the internet. Now you can sit at home and you can get on Manhunt and you can filter through all of the profiles—someone tall, someone short, someone black, someone white. Technology has obviously helped our community and helped the nation but it’s also been a hindrance in many ways. Just like we can order in Chinese food no we’re can go online and find a six-foot tall blonde top."

**Portrait of a Young Activist**

Matthew Stewart, 20, a junior at American University majoring in sociology and French, is actively involved with his school’s GLBTA community. He has rallied 438 people to participate in this year’s AIDS Walk and is in the process of pledging to Delta Lambda Phi, a national gay fraternity.

Growing up in Virginia Beach, Va., Stewart was subject to abstinence only sex education. As the token gay kid in his high school, he turned to reading and the internet to understand his sexuality. At just 14 years old, Stewart came out to his mother, and while supportive, she immediately raised concerns over his health.

Stewart learned that his mother had lost several friends at the height of the AIDS epidemic, and in hindsight, he is grateful for his mother’s ability to talk about HIV/AIDS.

"At the time I was like 'Shut up! I just came out to you and you’re talking about my health and my sex life?" Stewart told EDGE. "But I think that has a lot to do with the problem. Sex education is extremely important but we’re still not talking about it in America the way we should be—especially how we relate it to homosexual sex. Without getting into the nitty gritty of it, the fact of the matter is it’s much more easily transmittable through anal sex. We still can’t talk about it. It’s like a shameful thing to talk about. We can talk about HIV—we can talk about how sad it is how many people have it. But we can’t talk about how it’s transmitted? That has always dumbstruck me."

As an HIV/AIDS advocate, Stewart reaches out to his peers to educate them on safe sex practices and HIV/AIDS. More times than not, Stewart is met with complacency with some students even responding with "That's so '80s." Stewart admits that raising awareness has been exhausting, but he feels it is worth fighting for especially in Washington, D.C., with some of the highest HIV rates in the nation. He adds that if his efforts save one life then his work has paid off.

"I think a lot of it is trying to distance ourselves from the stigma of being at an at risk group," Stewart said. "Especially since a lot of the decision making in community health are still being made by people who lived through [the AIDS crisis] but we didn’t see it. It’s tough because on one side of the coin you
don’t want to be completely boxed in to this group of people that are instantly at risk but at the same if you don’t then your needs aren’t being addressed. I think a lot of that has to do with some really good things and bad things concerning gay visibility. Everyone gets upset, and I understand, on national issues about DADT and marriage but that stuff won’t matter if you’re dead."

**A Trans Man’s Safe-Sex Awakening**

Qui Alexander, 24, works at the Mazzoni Center as a community health educator. He delivers presentations at Philadelphia schools and community centers to youth and adults on the topics of healthy relationships and preventative care.

As a trans man, Alexander’s views on HIV/AIDS have changed dramatically over the years. He told EDGE that transitioning not only opened him up to more conversations with MSMs, but also changed his level of risk.

"It definitely changed more, not because of my personal experiences, but in how I was being perceived in the world,” Alexander said. "As I transitioned to male and I was more passable, I saw a lot more gay men interacting with me and being more open to talking about their sexual practices. And because I identify as queer that became a new issue for me. I always identified as queer but I only slept with women. Opening my partners to women and trans folks, that changes my risk. That made me think differently about talking about safe sex practices with the people I choose to be involved with. This is now a conversation I have to have; I have to talk about negotiating with my sexual practices."

Native of Buffalo, N.Y., Alexander was exposed to the realities of HIV/AIDS as a teen through his mother’s social work. Many of the women that his mother helped were HIV positive, forcing him to realize at a young age that nobody was invincible to the virus.

Alexander says that a false sense of hope has made Generation Y particularly vulnerable.

"It sucks that you have to show people suffering to get the idea across but that’s the only way people are relating to the message today,” he said. "I think it’s especially true of our generation but I also think it’s the technology we have-the things we see on TV. If they can find a cure to all these different diseases then we’re on our way for HIV. I think that’s the way people think. It bothers me because it’s real-there are still people every day being diagnosed with HIV. Every nine minutes someone in the U.S. is diagnosed with HIV."

**A comparison of severe outcomes during the waves of pandemic (H1N1) 2009**

The second wave of the pandemic (H1N1) was substantially greater than the first with 4.8 times more hospital admissions, 4.6 times more deaths and 4 times more ICU cases, according to a study published in *CMAJ* (Canadian Medical Association Journal) (pre-embargo link only) [http://www.cmaj.ca/embargo/cmaj100746.pdf](http://www.cmaj.ca/embargo/cmaj100746.pdf). However, because of the larger number of people hospitalized during the second wave compared to the first, the percentage of people with severe outcomes was smaller.

The researchers compared demographic and clinical characteristics as well as outcomes of patients with (H1N1) influenza admitted to hospital during the first wave with those admitted during the second wave and post-peak period of the pandemic.

In the first wave, Nunavut, Manitoba and Quebec had the highest rates for hospital admissions. In the second wave, all provinces and territories were affected with the Maritime provinces, Alberta, British Columbia, the Yukon Territory and the Northwest Territories experiencing much higher rates of hospital admission than in the first one. Quebec and Ontario were impacted in both waves, with Quebec reporting the highest number of hospitalizations and Ontario reported the most deaths overall.

At the height of the first wave (May 31 to June 20, 2009), 9.4% of hospital admissions, 10.1% of ICU admissions and 10% of deaths occurred. At the height of the second wave (October 25 to November 14, 2009), 51% of overall hospital admissions, 49.4% of ICU admissions and 53% of deaths occurred.

ICU admissions and deaths as a percentage of hospitalizations went down in the second wave.

"The second wave was substantially larger and, although the patients admitted to hospital were older and more of them had underlying conditions, a smaller proportion had a severe outcome," writes Melissa Helferty, Public Health Agency of Canada and coauthors. "The differences are thought to be due mainly to public health and clinical interventions implemented between the first and second waves."

"A national seroprevalence survey at the end of the first wave would have allowed us to better qualify the severity of the cases in Canada and permitted a more accurate comparison with other countries,” conclude the authors.

MEDIA NOTE: Please use the following public links after the embargo lift:

DNA Fingerprinting Traces Global Path of Plague

ScienceDaily (Nov. 6, 2010) — An international team of scientists has traced major plague pandemics such as the Black Death back to their roots using DNA fingerprinting analysis.

Researchers from Ireland, China, France, Germany and the United States, including Northern Arizona University's Paul Keim and David Wagner, have turned back the clock to examine the past 10,000 years of global plague disease events. Their findings regarding the plague pathogen, Yersinia pestis, will be published in an upcoming issue of the journal, Nature Genetics.

Keim, director of NAU's Center for Microbial Genetics and Genomics and division director of Translational Genomics Research Institute, said that while the plague is less of a threat to humans than at other periods in history, such as the Middle Ages, the current plague research can be applied to ongoing health threats around the world.

This type of DNA fingerprinting can be used to characterize both natural and nefarious plague outbreaks—which is crucial when a bacterium is used as a biological weapon.

"This work is more of a model for our control of epidemic diseases such as Salmonella, E. coli and influenza," Keim said. "Plague took advantage of human commercial traffic on a global scale, just as the flu and food-borne diseases do today. Future epidemiologists can learn from this millennium-scale reconstruction of a devastating disease to prevent or control future infectious disease outbreaks."

Tracking the worldwide spread of plague required identifying mutations in as many strains as possible. But transferring live bacterium across country boundaries is highly regulated and difficult due to its potential danger, presenting a challenge to scientists.

To make this research possible, the team devised an innovative research strategy of decentralized experiments where scientists in worldwide locations worked with one or several of 17 complete plague whole genome sequences. By electronically combining all of the research data, the team identified hundreds of variable sites in the DNA while assembling one of the largest dispersed global collections of plague isolates. That data was used to reconstruct the spread of plague pandemics, calculate the age of different waves of outbreak and was linked to descriptions in the historical record to better explain the current existence of plague.

The results serve as a map of how the plague made its way around the globe.

Their collaborative research determined that the plague pathogen originated in or near China where it has evolved and emerged multiple times to cause global pandemics. The international team also identified unique mutations in country-specific plague lineages.

Tracing its evolution, the plague spread over various historical trade routes as early as the 15th century. Chinese admiral and explorer Zheng He's travels may have taken the plague to central Africa. The Silk Road, which led from China to Western Asia and on to Europe as described by Marco Polo, also may have served as an avenue for disease. The latest plague pandemic of the late 1800s still persists today in wild rodents throughout the western United States.

"The plague found its way to the United States in the late 19th and early 20th century through multiple port cities by infected ship-borne rats," said Wagner, assistant professor of biological sciences at NAU. "Based upon DNA variation detected from these comparisons, we determined that the original plague strains that infected the U.S. had their origin in Asia and likely made their way to California via Hawaii."

While plague pandemics are something of the past, the disease has never fully disappeared. The bacterium remains ecologically established in animal populations around the world, and has resurfaced in Africa and Madagascar.

"This study gives one the exciting feeling that we are able to rewind time," said Elisabeth Carniel, director of the National Reference Laboratory and World Health Organization Collaborating Center for Yersinia at the Institut Pasteur in Paris. "However, this should not lead us to consider plague a disease of
the past. We are observing its re-emergence in countries where it has been silent for decades. Therefore, far from being extinct, plague is a re-emerging disease.”

Journal Reference:
Giovanna Morelli, Yajun Song, Camila J Mazzoni, Mark Eppinger, Philippe Roumagnac, David M Wagner, Mirjam Feldkamp, Barica Kusecek, Amy J Vogler, Yanjun Li, Yujun Cui, Nicholas R Thomson, Thibaut Jombart, Raphael Leblois, Peter Lichtner, Lila Rahalison, Jeaninne M Petersen, Francois Balloux, Paul Keim, Thierry Wirth, Jacques Ravel, Ruifu Yang, Elisabeth Carniel, Mark Achtman. Yersinia pestis genome sequencing identifies patterns of global phylogenetic diversity. Nature Genetics, 2010; DOI: 10.1038/ng.705

Potential for Sexual Transmission of HIV Infection from Male Injecting-Drug Users Who Have Sex with Men in Tehran, Iran
Sexually Transmitted Diseases Vol. 37; No. 11: P. 715-718, (11.10.2010) Saman Zamani; Masako Ono-Kihara; Seiichi Ichikawa; Masahiro Kihara

Iran has responded to the threat of an HIV epidemic among injecting drug users. There is growing concern, however, over the potential for bridging HIV infection from IDUs to other populations, including men who have sex with men, noted the authors of the current study.

From 2003 to 2004, cross-sectional biobehavioral surveys were conducted among 370 IDUs recruited from drug treatment centers, a drop-in center and streets in drug-populated areas of Tehran.

Survey data indicated that about 12 percent of male, sexually experienced IDUs have had same-gender sex. HIV prevalence is high (19 percent), while condom use during last sexual encounter was low (20 percent). A multivariate analysis showed that compared to other sexually experienced IDUs, IDUs who had sex with men (MSM IDUs) are younger (adjusted odds ratio, 0.89; 95 percent confidence interval, 0.81-0.98), more likely to have used a shared needle/syringe for injecting drugs (AOR, 4.29; 95 percent CI, 1.82-10.12), and have had five or more sexual partners in their lifetime (AOR, 2.71; 95 percent CI, 1.14-.6.44).

“These results show that MSM IDUs exhibit more drug-related and sexual risk behaviors that may serve as a bridge for sexual transmission of HIV to other populations, including the broader MSM community, in Tehran,” concluded the authors. “This report intends to encourage health authorities in Iran to take serious action to prevent sexual transmission of HIV from MSM IDUs to their sexual networks.”

Porn Actor with HIV Didn’t Infect Others
Los Angeles Times, (11.06.2010) Molly Hennessey-Fiske

The Adult Industry Medical Healthcare Foundation (AIM), which diagnosed a porn actor with HIV in October, said Friday that two rounds of testing have turned up no new cases among performers. However, Los Angeles County public health officials declined to sign off on AIM’s statement.

Sherman Oaks-based AIM, which primarily serves the San Fernando Valley porn industry, routinely tests adult-film actors for STDs. After the initial positive result of the person AIM designated “Patient Zeta,” the clinic said it created a quarantine list, testing other performers who had worked with Zeta. AIM said it tested others “on two occasions, using multiple testing methods” among contacts “from both personal and professional life.”

“It has been established that Patient Zeta acquired the virus through private, personal activity and there was no transmission of the HIV virus from Patient Zeta to anyone else,” AIM announced.

However, AIM has not provided Los Angeles County Department of Public Health officials with the test results or protocols, so it is impossible to determine how Patient Zeta contracted HIV and whether everyone exposed has been tested, said Dr. Jonathan E. Fielding, the county’s public health director.

“If in fact they have used the right tests and done everything they say they have done, it’s good news for the people who were contacts, but it doesn’t reduce the risks,” said Fielding. “To have somebody work in a situation where they are forced to do things that put others at risk for life-threatening diseases is very disturbing.”

State officials say AIM has failed to promptly report cases of HIV and other STDs. State workplace safety officials are considering whether to mandate condom use and additional testing in the adult-film industry.

On Friday, one company that had suspended productions due to the infection resumed operations, and another said it would do so Monday.
Magic Johnson and HIV

On November 7, 1991, the sports world was turned upside down when Magic Johnson abruptly retired from the Lakers. Fast forward 19 years later, and Magic is still around, which might be more stunning than his initial announcement.

Nov 8, 2010—The sports world was turned upside down 19 years ago Sunday, when Magic Johnson retired suddenly because he was HIV positive. It was a giant wake up call for those of us who follow sports religiously that real life could smack us in the face at any moment, interrupting our distraction.

I can still remember the exact details of how and when I heard the awful news. I was a sophomore in high school, and after school I walked with my friends over to the mall to hangout. My mom was a hairstylist and worked at a shop in the mall, so I went to ask her for money, a daily tradition. Her first words to me were, “You’re going to be sick when you hear this,” and she then proceeded to tell me that Magic Johnson had to retire because of AIDS.

The fact that she said “AIDS” wasn’t entirely correct—Magic was HIV positive, which in many, many cases lead to AIDS, but he didn’t have AIDS yet—but that was emblematic of the time. Nobody knew anything about HIV and AIDS at the time, except that it was a death sentence. Magic Johnson, the best point guard in basketball history and my favorite athlete ever, was going to die.

This was heavy news for an idol-worshipping 15-year old to take. It was like I was in a trance. I remember telling my friends, almost in tears. We were telling as many people as we could, by word of mouth only, since this was before the internet and before any of us had cell phones. We heard that the press conference was at 3:30 p.m., so we made sure to cram into Foot Locker to watch the press conference.

From the day Magic Johnson stepped onto a basketball court, and subsequently into our living rooms, his smile and personality commanded the room. But November 7, 1991 was different. There was a somber tone to the press conference at the Great Western Forum, and rightfully so. Rather than smiling, Magic was very serious when he began the press conference, amid the audible clicks of dozens of cameras, saying “Because of the HIV virus I have attained, I will have to retire from the Lakers today.”

I was in a trance for the rest of the weekend. The announcement came on a Thursday, and as far as I was concerned school should have been canceled on Friday. Nothing else was on my mind except for Magic. I remember my friend Esfandiar ending a presentation in European history class by saying “peace to Magic Johnson.” Magic was on all of our minds.

Last week on Twitter, a trending topic was #TweetYour16YearOldSelf. I did not submit an entry, but a great one would be “Don’t worry, Magic Johnson will be okay.” I wasn’t quite 16 yet, but I’m sure in 1991 I wouldn’t have believed that Magic Johnson would be alive in 2010. Not only is Magic alive, 19 years later, but he is thriving.

Magic has been a successful business man in his post-playing days, owning several companies and even starting his own investment group. He has opened several retail stores—movie theaters, coffee shops, gyms—in urban areas, and has profited quite handsomely from his efforts. I had the pleasure recently to hear Johnson speak at a conference in Southern California, and he spoke of his business philosophy. He mentioned that a key to his success was to always over-deliver on his promises.

On November 7, 1991, Magic Johnson did not see his diagnosis as a death sentence. He said at his retirement press conference, "I’m going to beat this, and I’m going to have fun." That might just be the most over-delivered promise Magic has ever had.

HLA Genetic Variations Play Key Role in Natural Control of HIV

**SUMMARY:** People who naturally control HIV long-term without antiretroviral therapy (ART) have a unique pattern of amino acid variations in genes encoding HLA proteins, which enable immune recognition and response, according to a report in the November 4, 2010 advance online edition of *Science*. A genome-wide association analysis by more than 300 investigators with the International HIV Controllers Study found several specific amino acid changes in the HLA-B peptide binding groove associated with risk for or protection from HIV disease progression. These results, the researchers suggested, imply that the interaction between HLA and viral peptides is the key to durable control of HIV.

Below is an excerpt from a press release issued by Massachusetts General Hospital describing the research and its findings.

**Small Protein Changes May Make Big Difference in Natural HIV Control**

**Variations in protein structure impact effectiveness of immune response**
Boston, MA—November 4, 2010—Tiny variants in a protein that alerts the immune system to the presence of infection may underlie the rare ability of some individuals to control HIV infection without the need for medications. In a report that will appear in Science and is receiving early online release, an international research team led by investigators from the Ragon Institute of Massachusetts General Hospital (MGH), MIT and Harvard and from the Broad Institute of MIT and Harvard describe finding that differences in five amino acids in a protein called HLA-B are associated with whether or not HIV-infected individuals can control viral levels with their immune system only.

"We found that, of the three billion nucleotides in the human genome, just a handful make the difference between those who can stay healthy in spite of HIV infection and those who, without treatment, will develop AIDS," says Bruce Walker, MD, director of the Ragon Institute and co-senior author of the Science article. "Understanding where this difference occurs allows us to sharpen the focus of our efforts to ultimately harness the immune system to defend against HIV."

"Earlier studies had showed that certain genes involved with the HLA system were important for HIV control," adds Paul de Bakker, PhD, of the Broad Institute and Brigham and Women's Hospital, co-senior author. "But they couldn't tell us exactly which genes were involved and how they produced this difference. Our findings take us not only to a specific protein, but to a part of that protein that is essential to its function."

It has been known for almost two decades that a small minority—about one in 300—of individuals infected with HIV are naturally able to suppress viral replication with their immune system, keeping viral load at extremely low levels. To identify genetic differences that may underlie this rare ability, Florencia Pereyra, MD, at the Ragon Institute established the International HIV Controllers Study in 2006, with a goal of enrolling 1,000 HIV controllers from medical clinics and research institutes around the world. That goal was expanded to 2,000 controllers in 2008, and thus far over 1,500 controllers have been enrolled.

The current investigation began with a genome-wide association study (GWAS) of almost 1,000 controllers and 2,600 individuals with progressive HIV infection, provided through a collaboration with the AIDS Clinical Trials Group. The GWAS, which tests variations at a million points in the human genome, identified some 300 sites that were statistically associated with immune control of HIV, all in regions of chromosome 6 that code for HLA proteins. Further analysis narrowed the number of gene sites to four but could not indicate whether those differences actually affected viral control or were just located near the causal variants. Fully sequencing that genome region in all participants was not feasible, but a process developed by Sherman Jia—a medical student in the Harvard-MIT Health Sciences and Technology program, working with de Bakker at the Broad—pinpointed specific amino acids; and directly testing those sites associated five amino acids in the HLA-B protein with differences in viral control.

HLA-B is essential to the process by which the immune system recognizes and destroys virus-infected cells. Usually HLA-B grabs onto viral protein segments called peptides that are inside the cell and carries them to the cell membrane where they essentially flag the infected cell for destruction by CD8 "killer" T cells. The portion of the HLA-B protein that grabs and displays viral peptides is called the binding pocket, and all of the five identified amino acid sites are in the lining of the binding pocket.

"Amino acid variation within the HLA-B binding pocket will impact its shape and structure, probably resulting in some peptides being presented effectively and others not," de Bakker says. "Our work demonstrates that these variants could make a crucial difference in the individual's ability to control HIV by changing how HLA-B presents peptides from this virus to the immune system."

Walker adds, "HIV is slowly revealing its secrets, and this is yet another. Knowing how an effective immune response against HIV is generated is an important step toward replicating that response with a vaccine. We have a long way to go before translating this into a treatment for infected patients and a vaccine to prevent infection, but we are an important step closer."

The investigators note that these findings would not have been possible without the participation of the hundreds of HIV controllers, many of whom traveled to Boston for testing, who have enrolled in the study. "The enthusiasm among the patients we have enrolled and the HIV providers who referred them has been amazing," says Pereyra. "They tell us that being part of this collaborative study means a lot to them."

Original support for the International HIV Controllers study came through a 2006 grant from the Mark and Lisa Schwartz Foundation, and the study was expanded in 2008 through the support of the Bill and Melinda Gates Foundation. Additional supporting agencies include the Harvard Center for AIDS Research and the National Institutes of Health. 11/9/10
Study shows durable viral suppression of boosted REYATAZ in treatment-experienced HIV patients

(GLASGOW, 9 November 2010) – Results from a European Observational Study, which included 1,294 antiretroviral (ARV)-experienced patients presented today at the Tenth International Congress on Drug Therapy in HIV Infection (HIV10), demonstrated a low rate of discontinuation and sustained virologic suppression with REYATAZ® (atazanavir)/ritonavir-based regimens over a follow-up period of up to five years.¹

The aim of this study was to investigate the long-term outcomes of REYATAZ/ritonavir-containing regimens in ARV-experienced patients in a real-life clinical setting. The primary endpoint of the cohort study was the proportion of patients who remained on treatment over time by baseline HIV-1 RNA level (< 500 copies/mL and >= 500 copies/mL). Secondary endpoints were reasons for discontinuation, time to virologic failure (defined as either two consecutive HIV-1 RNA >= 50 copies/mL or one HIV-1 RNA >= 50 copies/mL followed by discontinuation) and long-term safety profile.¹

The results of the study revealed that 56% of patients with baseline viral suppression (< 500 copies/mL) (n= 722) and 53% of those with detectable viral load (>= 500 copies/mL) (n= 540) remained on treatment after 3 years with a median time to discontinuation of 4 versus 3.6 years, respectively. The overall discontinuation rate in the study was low (43%) with the reasons for discontinuation including adverse events (11%), withdrawn consent (6%) and lack of efficacy (6%). After three years on a REYATAZ/r-based regimen, 75% of patients with baseline HIV-1 RNA levels < 50 copies/mL remained suppressed and 51% of patients with baseline HIV-1 RNA levels >=50 copies/mL achieved and maintained virological suppression.¹

Long-term safety outcomes from this real-life study were consistent with data observed in clinical trials: diarrhoea (4%), renal and urinary disorders (3%), nausea (< 1%) and jaundice (< 1%) were reported. Discontinuations due to hyperbilirubinemia were infrequent (< 1%) and no new or unexpected adverse events were observed.¹

"Prior to this cohort study, less was known about long-term outcomes and the length of time on treatment in experienced patients after switching", said Professor Jan van Lunzen, M.D., Ph.D. of The University Medical Centre Hamburg-Eppendorf in Germany. "This cohort study shows in a real-life setting that a significant proportion of treatment-experienced patients stayed on an atazanavir/ritonavir-containing regimen for up to five years", he added.

Study Design

This real-life long-term cohort was a non-comparative, retrospective, observational study that collected data from three European databases (France – DatAids; Germany – KompNet; Sweden – InfCare). Clinical data from 1,294 ARV-experienced adult patients who started an atazanavir/ritonavir-based regimen between October 2004 and March 2007 were collected every six months (maximum follow-up of five years). Patients were predominately male (74%); their median age was 43 years and 75% had prior exposure to protease inhibitors (PIs).

'Equal Reduction' Hope for Cervical Cancer


New genital wart cases among men and women have substantially declined since Australia rolled out its human papillomavirus vaccination program in 2007, according to the first national study of the program. Gardasil protects against four HPV types—two that cause most cervical cancer cases and two that are responsible for most genital warts. Free vaccination is offered to women up to age 26.²

Since the program began, the number of young women seeking treatment for a new case of genital warts has declined 59 percent, reported Dr. Basil Donovan, of the University of New South Wales’ National Center in HIV Epidemiology and Clinical Research, and colleagues. With fewer women infected, young men benefited nationally too, with a drop in new genital wart cases of 28 percent. No change was seen among female non-nationals, women over age 26 at the time the program launched or men who have sex with men.

“Until the HPV vaccination program began in July 2007, the proportion of women and heterosexual men diagnosed with genital warts was stable,” said Donovan. “The decline in proportion of people with
genital warts contrasted with increasing rates of chlamydia and no reported change in frequency of genital herpes."

The drop is seen as a forerunner to a future emerging decrease in cervical cancer, which unlike warts takes years or decades to develop.

The data point to Gardasil’s efficacy against “other HPV-related disease including cervical cancer,” said Gardasil’s inventor, Professor Ian Frazier of the Center for Immunology and Cancer Research at the University of Queensland.

“It points to the likelihood of a possible equal reduction in high-grade cervical lesions and, ultimately, cancer of the cervix in this cohort of vaccinated young women,” said Dr. Edith Weisberg, director of research at the Sydney Center for Reproductive Health at Family Planning New South Wales.

The full study, “Quadrivalent Human Papillomavirus Vaccination and Trends in Genital Warts in Australia: Analysis of National Sentinel Surveillance Data,” was published online ahead of print by Lancet Infectious Diseases (doi:10.1016/S1473-3099(10)70225-5).

Oral Sex Often a Prelude to Intercourse for Teens

Students who engage in oral sex within the first two years of high school are much more likely than those who do not to report having vaginal intercourse by the end of 11th grade, a new study suggests. The study involved surveying 627 ninth-grade students in two northern California high schools every six months between 2002 and 2005.

Among students reporting oral sex by their ninth-grade year, just 9 percent had abstained from vaginal sex through 11th grade, reported Dr. Bonnie L. Halpern-Felsher of the University of California-San Francisco and Dr. Anna V. Song of UC-Merced. The overwhelming majority experienced oral sex before vaginal sex, with most of those transitioning to the latter doing so within six months.

Students “who initiated oral sex at the end of the ninth grade had a 50 percent chance of initiating vaginal sex by the end of the 11th grade,” reported the authors. “In comparison, adolescents who delayed until the end of 11th grade had a 16 percent chance of initiating vaginal sex by the end of 11th grade.”

In addition, students reporting sexual activity before ninth grade or after 10th grade had a lower chance of intercourse by the final survey than those initiating oral sex in ninth or 10th grade. Of those who abstained from oral sex through 11th grade, 80 percent had also avoided vaginal sex.

“In a past publication, we showed that adolescents perceived that oral sex was more acceptable and more prevalent compared to intercourse, and that adolescents believe that oral sex carries less risk of health consequences—sexually transmitted infections, HIV, and pregnancy—as well as social and emotional consequences than does vaginal sex,” Halpern-Felsher wrote.

“These findings highlight the need for health care providers, health educators, and parents to include discussions of oral sex within a comprehensive sexual education curriculum,” Halpern-Felsher said.


Gonorrhea and Chlamydia Testing Rates of HIV-Infected Men: Low Despite Guidelines

Noting that gonorrhea (GC) and chlamydia (CT) screening for HIV-infected men “may decrease HIV transmission and reduce the incidence of pelvic inflammatory disease in female partners,” the study authors determined GC/CT testing rates in a clinical HIV cohort before and after 2003, when CDC issued guidelines for GC/CT screening.

First GC/CT testing episodes were identified for all men enrolling in a Baltimore HIV clinic from 1999 to 2007. Clinical and demographic factors associated with being tested and with having a positive result were assessed using multivariate Cox and logistic regression.

Of 1,110 male participants, the rate of GC/CT testing upon clinic enrollment increased from 4.0 percent prior to 2003 to 16.5 afterwards, while the rate of ever being tested increased from 34.2 percent to 49.1 percent (p<0.001 for both comparisons). Among men with same-sex contact, extragenital sites were included for 10 percent of first testing episodes. Among the 342 men ever tested, 5.2 percent had positive results for their first test. Predictors of testing included enrollment after 2003, younger age, frequent
visits, and black race. Positive test result predictors included CD4 count =200 cells/mm3 and younger age.

“GC/CT testing rates among men increased substantially after the 2003 guidelines but remain low,” the authors concluded. “Disseminating existing evidence for GC/CT screening and promoting operational interventions to facilitate it are warranted.”

Most patients in darunavir monotherapy trial stay fully suppressed
Gus Cairns
Published: 11 November 2010
The latest data from a European trial using boosted darunavir (DRV/r) as the sole HIV drug has found no evidence of increased treatment failure or of viral loads increasing over time, even when viral loads below the usual limit of detectability were investigated with an ultrasensitive assay.

The latest results from the MONET trial, presented at the recent Tenth Congress on Drug Therapy in HIV Infection, contrast with an African trial using boosted lopinavir monotherapy (LPV/r) also presented which, in the absence of viral load testing, found increased rates of viral failure over time.

The MONET trial randomised 256 patients who had had a viral load under 50 copies/ml for at least six months either to take DRV/r monotherapy or to take monotherapy plus the two most suitable NRTI drugs. The 48 week results, presented this time last year at the European AIDS Conference, found that 87% of people on monotherapy and 89% on combination therapy maintained a viral load under 50 copies/ml – a non-significant difference and the most successful result from a PI monotherapy trial.

Other monotherapy trials have found that while the numbers of patients with detectable viral loads may be similar, a larger number of patients on monotherapy had ‘subliminal’ viral loads – ones below 50 but detectable by ultrasensitive tests – which another study reported this week found that monotherapy was associated with some risk of eventual failure.

The 96 week results from this study were presented at the Vienna World AIDS Conference this year. They showed that after nearly two years, the study found that 75% of people on monotherapy and 81% on combination therapy had maintained a viral load under 50 copies/ml without changing therapy; when NRTIs were added back in or patients switched to new ones, then 91% on combination therapy and 92% who had taken monotherapy had a viral load under 50 copies.

The Glasgow conference heard that, using an ultrasensitive test that could detect viral loads down to five copies/ml, the investigators found that the proportion of people with low-but-detectable viral loads varied little over the study. At baseline the proportion of patients with a viral load between five and 50 copies/ml was 13% in the monotherapy arm and 17% in the combination therapy arm. At week 96 these proportions were 17% and 15% respectively.

The proportion with viral loads under five copies/ml hardly changed at all. Eighty per cent of patients started monotherapy with viral loads under five copies; the proportion by 96 weeks was 79%. In the combination therapy arm the proportion of patients with viral loads under five copies/ml rose from 79% to 81%.

None of these differences in viral load were statistically significant, and there is thus no sign of a rise in ‘subliminal’ viral loads in patients taking monotherapy. There was very little drug resistance observed during the trial. Three patients acquired protease inhibitor resistance during the trial, one of them on combination therapy, and one acquired a new NRTI mutation.

At the Glasgow conference lead investigator Jose Arribas also presented a new cost-effectiveness analysis showing that if all patients in Spain who would have been eligible for the MONET trial – which means more than six months with undetectable viral load with no history of treatment failure, amounting to 15% of all patients in care – then a year’s drug costs for each patient would be €12,250 rather than €20,650. This would save a total of €46 million a year in drug costs, though the analysis did not take viral load testing, overheads such as healthcare worker costs, or the cost of possible future illness into account.

Another study at Glasgow looked at the efficacy of LPV/r (Kaletra) monotherapy in the clinic, as opposed to on a randomised clinical trial.

The study looked at 77 patients at three Spanish hospitals who were switched to LPV/r monotherapy. They had been virally undetectable for an average of three years, had taken an average of seven previous ARV drugs, had a high average CD4 count (519). After a mean follow-up of 22 months (11 minimum), 88% had maintained a viral load under 50 copies/ml. Of the nine patients who failed, seven admitted to poor adherence, and eight successfully re-suppressed their HIV after re-introducing NRTIs.
X-rays illuminate the mechanism used by HIV to attack human DNA

Thursday 12 November 2010

Adapted from a news release issued by Diamond Light Source.

Scientists from Imperial College London have used data collected at Diamond Light Source, the UK’s national synchrotron facility, to advance the understanding of how HIV and other retroviruses infect human or animal cells. The research, which is funded by the Medical Research Council, is published in Nature today.

Using Diamond’s finely tuned pinpoint X-ray beams, the researchers were able to determine 3D structures of the key molecular machine used by viruses, such as HIV, to insert copies of their genetic material into host DNA.

This fundamental knowledge will not only facilitate design of better drugs for fighting AIDS, but may also have an impact on pioneering treatments such as gene therapy, an experimental technique using tamed versions of viruses to treat genetic disorders. One condition this could help is “bubble boy” disease, a condition where a defective gene leaves sufferers with little or no immune system, making them extremely vulnerable to infectious diseases and in some cases having to live permanently inside a sterile environment.

HIV and other retroviruses carry their genetic material as RNA. After entering a human or animal cell, they convert their genomic RNA into DNA, which is then inserted into one of the cell’s chromosomes. To accomplish this, retroviruses use integrase, an enzyme that brings the ends of the viral DNA and cellular DNA together. It then irreversibly joins the DNAs, making the infected cell carry the viral genome permanently.

Earlier this year, the researchers announced an initial breakthrough, when they determined the structure of integrase from the prototype foamy virus (PFV) assembled on viral DNA ends. Crucially, because PFV is very similar to HIV in the way it integrates its DNA, the structures allowed them to explain how an important class of HIV drugs disable integrase.

Now the group has determined 3D structures of PFV integrase bound to both viral and cellular DNA. These new structures elucidate how integrase attacks cellular DNA and the mechanics of irreversible insertion of viral DNA. "It has truly been a breathtaking ride," said lead researcher Dr Peter Cherepanov, from the Department of Medicine at Imperial College London. "Only 18 months ago we had a rather
sketchy understanding of retroviral integration. Now we have obtained snapshots depicting the whole process in atomic detail. The new 3D structures capture the retroviral integration machine in action.”

These findings may enable improvements in gene therapy to correct gene malfunctions. A disabled version of a retrovirus can be used to insert a functional copy of a gene into a human chromosome. Although such approaches have proven quite successful, they are still experimental, requiring more work to make them safer.

Dr Cherepanov explains how his group’s latest findings could help. "One of the main problems with the current method is that retroviral integration is too random. While being very efficient, by its nature, integration is not very selective with respect to its target, the chromosomal DNA. Ideally, we want to insert therapeutic genes in pre-defined, safe locations of the human genome.

"Using the new structural information we have uncovered, researchers can now start trying to tweak the retroviral integration machinery to make it more suitable for practical applications. For example, we might be able to design integrase that would be highly selective for target DNA sequence."

The structural data collection was carried out on the I02 macromolecular crystallography experimental station at the Diamond synchrotron in Oxfordshire. Principal Beamline Scientist, Professor Thomas Sorensen, said: “This kind of fundamental research is vital if we are to advance our understanding of the viruses and diseases that affect millions of people around the world. Knowing the 3D structure of the mechanisms involved is like being able to see inside the engine of your car. If you can actually see what is happening, you get an idea of how you can fix it. At Diamond we produce the extremely intense X-ray beams required for looking at the molecular interactions involved in a variety of biological processes.”

Advances in structural biology have accelerated greatly as a result of access to the synchrotron facilities that have been developed around the world in the past 25 years. Biologists have been swift to recognise the huge potential that lies behind understanding the multitude of processes that take place within living organisms at a molecular level. Researchers in the UK are at the forefront of this work and Diamond Light Source plays its part in providing cutting edge facilities for protein structure determination. Diamond currently has five experimental stations dedicated to structural biology as well as an on-site membrane protein laboratory. Previous breakthroughs using structural data from Diamond include gaining a better understanding of hypertension in the pre-natal condition pre-eclampsia, learning how a key tuberculosis drug is activated, understanding how bird flu can affect humans, and solving the 3D atomic models of a single transporter protein responsible for the movement of essential chemicals into cells of the body.

Journal reference:

Injection Drug Use Fuels Black HIV Rates: Why Don’t We Talk About It?
The "poster child" for HIV/AIDS has changed throughout the years. First the media focused on White gay men who became infected through sex; then came the five H’s: Haitians, homosexuals, heroin addicts, hookers and hemophiliacs. Recently, emphasis has been placed on Black women infected heterosexually, ostensibly by "down-low" brothers. But though the risk posed to by heroin addiction has been clear from early on, the media rarely cover the role that injection drug use (IDU) has played in driving up Black HIV rates.

Injection drug use is the second leading cause of HIV infection for African American women and the third leading cause for African American men, according to the Centers for Disease Control and Prevention (CDC). The CDC also estimates that IDU directly—through actual contact with contaminated needles—and indirectly, through sex with HIV-positive partners infected from IDU, accounts for more than one-third of AIDS cases in the United States.

But talking about injection drug use is not as sexy as discussing DL Black men. And those addicted to heroin, cocaine or other injection drugs are not in a position to advocate for themselves. So Black America remains ignorant about, and powerless against, this missing link to high HIV rates in our communities.

The Cause We Don’t Talk About
"So much emphasis has incorrectly blamed the down low that there's been a lack of focus on one of the real issues of why HIV is disproportionately affecting African Americans," says Mary Beth Levin, director of programs and services at PreventionWorks! the District of Columbia's largest program focused on protecting IDUs (injection drug users). Levin notes that it’s far easier (and cheaper) to speculate about a
"mythological person" than to fund education, testing and treatment for STDs such as HIV, comprehensive mental health and drug treatment, and overdose prevention and needle exchange.

One of the most controversial but effective HIV-prevention methods—needle, or syringe, exchange (pdf)—consists of a structured process in which trained workers collect used needles from drug users, dispose of them safely(pdf) and then provide sterile needles to replace them (pdf). A large body of research exists about these programs, including a 1997 National Institutes of Health survey that found that needle-exchange programs (NEPs) reduce HIV transmission by 30 percent. In 2005, NEPs removed more than 22 million dirty syringes from communities.

Still, detractors falsely depict NEPs as programs that irresponsibly hand out needles next to playgrounds and/or promote or condone drug use. These and other "moral arguments" have prevented needle exchange from being seriously considered as a public-health strategy.

"We didn't make it universally known that syringe exchange would help to keep HIV infections to a minimum," says Beny Primm, M.D., (pdf) chair of the Addiction Resource and Treatment Corporation and the Urban Resource Institute, both non-profits that have treated drug addiction in New York City since the late 1960s, when many Black men returned from the Vietnam War addicted to heroin. Shunned by their families, communities and houses of worship, many were incarcerated, did not receive education about HIV and eventually became HIV-positive.

Injection drug use coexists with other high-risk behaviors—exchanging sex for drugs, prostitution and having sexual relationships with IDUs, for example. So in places like Washington, D.C., and Harlem, N.Y., where heroin use thrives but public health interventions have failed, AIDS rates have reached pandemic levels.

**Blood on the Hands of Congress**

"The United States is the only country in the developed world that has not reduced new HIV infections," asserts Levin. Yet in many parts of the world, NEPs help prevent blood-borne disease (pdf), including HIV. For example, in southern Australia, where 55 NEPs serve about 1.2 million IDUs, no new HIV infections occurred for three consecutive years.

Washington, D.C., where Levin’s program is based, has the highest rate of new AIDS cases in the United States. An estimated one in 20 residents, most of them Black, live with HIV, versus one in 50 Blacks and one in 200 Whites nationally.

Congress has controlled D.C.’s entire budget for 22 years, refusing to fund syringe exchange, even as other cities—some in the home states of representatives who opposed NEP in D.C.—exchanged needles. Adding insult to injury, Congress banned the D.C. government from using its own dollars for needle exchange until 2007—interference that many activists say places blood on federal legislators’ hands.

**Toward a More Compassionate Approach**

Under the Obama administration, Congress has approved money for Washington, D.C., to support needle exchange. Levin says she is "absolutely" sure that D.C.’s infection rate will go down. Dr. Primm agrees: "I think we may see some difference in the numbers."

And in the face of a growing body of scientific evidence and the support of major public figures—from former surgeon generals C. Everett Koop and David Satcher to California governor Arnold Schwarzenegger—a slow shift has been taking place nationwide.

The question remains, though: How long will it take for our nation to develop comprehensive policies to prevent injection drug use from fueling HIV’s spread? And equally important, what actions will Black people take to bring it about, and what price will Black communities pay?

**29% of pregnant women in South Africa are HIV positive**

Nov 11, 2010 1:41 PM | By Sapa

Health Minister Aaron Motsoaledi says HIV prevalence countrywide among pregnant women in 2009 was estimated at 29.4 percent

This needed to brought down to 17.3 percent by 2015, he told delegates at the National Consultative Health Forum in Johannesburg.

The national estimate and provincial figures in 2009 indicated a stable prevalence over the past four years.

"The HIV epidemic poses one of the greatest health and developmental challenges. In this country particularly the epidemic is threatening the reversal of post-apartheid developmental gains."

Since 1990 the department had been conducting a National Antenatal Sentinel HIV and Syphilis Prevalence survey. The survey was the 20th in a series of annual ones conducted in nine provinces and 52
health districts. It surveyed 33,841 pregnant women from 1457 public ante-natal clinics during October last year.

According to results the prevalence in the 15- to 24-year-old group of pregnant women was 21.7 percent. This section made up almost 50 percent of the survey population, Motsoaledi said.

Prevalence among 30- to 34-year-olds was 41.5 percent. This was the only group where HIV/Aid cases were increasing.

KwaZulu-Natal had the highest prevalence, followed by Mpumalanga and the Free State. All three had a prevalence higher than 30 percent.

The North West, Limpopo, Gauteng and the Eastern Cape had a prevalence of between 20 and 30 percent. The Northern and Western Cape were the only provinces with a prevalence below 20 percent, the minister said.

December 1 is World Aids Day. The theme for this year would be "We Are Responsible", the SA National Aids Council said.

Campaigns around the country needed to be stepped up, chairman Mark Heywood told journalists on Thursday. He said Sanac was calling for a national day of action and asked all South Africans to do something on World Aids Day.

Let the sun shine in
New prevention technologies move beyond a pipe dream
by Jim Pickett

There is now a very clear line delineating a before and an after in terms of HIV prevention history. There is a before CAPRISA, and an after CAPRISA—and the world as we know it will never be the same.

Thank Goddess.

At the International AIDS Conference in Vienna this past July, the husband and wife team of Drs. Salim S. Abdool Karim and Quarraisha Abdool Karim, from the Centre for the AIDS Programme of Research in South Africa (CAPRISA), announced that a vaginal gel had been shown to significantly reduce a woman’s risk of being infected with HIV.

The microbicide gel the Karims studied contained 1% tenofovir—an antiretroviral drug commonly used to treat HIV—and was found to be 39% effective in reducing a woman’s risk of becoming infected with HIV during vaginal intercourse and as an added bonus, it was discovered to be a whopping 51% effective in preventing genital herpes among the women in the trial. Significantly, the women who used the gel in more than 80% of their sex acts during the trial had a 54% reduction in HIV infections.

Widespread use of the gel, at this level of protection, could prevent millions of new HIV infections among women over the next two decades. This is especially important for South Africa, where the global pandemic is the most severe. In rural Vulindlela, the prevalence of HIV among young women exceeds 50% by the age of 24. Think about that. Half of all these young women are infected with HIV at such an early age—it’s absolutely horrifying, and, it goes without saying, it’s completely unacceptable.

At the conclusion of the Karims’ presentation, an overflow of more than 5,000 researchers and advocates jumped to their feet and gave them a prolonged standing ovation. Hugs, tears, and high fives—I have never seen anything like it. After 20 or so years of microbicide research and dogged international advocacy, several trials had failed and, admittedly, it was looking grim for the field. We’d seen some funders, public health authorities, researchers, and advocates turn away from the work. The naysayers were not exactly gleeful—how can one be happy, after all, about these dead ends in prevention research? But I’d say there was a lot of smug to go around.

After CAPRISA, it’s not exactly rainbows and lollipops, as there is much to be done to confirm and extend these findings and then actually make this drug available, accessible.

Finally we have a win. I must say I was feeling a little smug myself when several folks approached me at the conference to say variations of “I never quite understood why you were so passionate about microbicides... I thought you were a little nuts... You must feel vindicated...”

Lots of us feel vindicated, thank you very much.

After CAPRISA, it’s not exactly rainbows and lollipops, as there is much to be done to confirm and extend these findings and then actually make this drug available, accessible.

One study that is currently underway in a number of African countries will be able to confirm whether tenofovir gel works or not. While the 5,000 women in the VOICE trial are using a different dosing regimen than the CAPRISA participants, the data will be very important. Other studies are being planned to follow up on CAPRISA. Obtaining the necessary resources for such trials is the current—big—challenge.
But what do these new findings mean for rectal microbicides?

“The positive results from the CAPRISA study represent a very significant milestone in HIV prevention research and they increase optimism that we can develop safe and effective antiretroviral rectal microbicides,” said University of Pittsburgh’s Dr. Ian McGowan, International Rectal Microbicide Advocates (IRMA) Scientific Vice-Chair and co-principal investigator of the Microbicide Trials Network. “Phase 1 rectal safety studies with tenofovir are ongoing and these efforts need to be intensified to help us move forward to rectal microbicide effectiveness studies as quickly as possible,” he said.

Anal intercourse is a common human sexual behavior, practiced by approximately 5-10% of the world’s general population, including heterosexual women and men, gay men, and other MSM. Because an act of unprotected anal intercourse is 10 to 20 times more likely to result in HIV transmission compared to unprotected vaginal intercourse, it is likely that unprotected anal intercourse is a significant driver in the HIV epidemic overall.

We know that unprotected anal intercourse is the chief cause of HIV infection for gay men/MSM across the world. But gay men are under-represented in most national AIDS strategies, in epidemiology, surveillance, and in research—if they show up at all. They have been woefully underserved by prevention, care, treatment, and support services. Similarly, we have inadequate data regarding anal intercourse—homosexual and heterosexual—due to politics, stigma, criminalization, and outright denial. It’s hard to study a behavior that’s against the law in some places.

Globally, gay men/MSM are 19 times more likely to be HIV-positive compared to the general population. These disproportionate rates extend to Africa, where the epidemic is often characterized as “heterosexual.” For instance, according to data from Dr. Chris Beyrer presented at the Global Forum on MSM and HIV’s “Be Heard!” pre-conference on July 17, in Kenya, 15.2% of gay/MSM are HIV-positive compared to 6.1% of the general population; in Uganda, HIV prevalence rates among gay men/MSM are just above 40% compared to 5% for other Ugandan men of reproductive age.

Data released by the U.S. Centers for Disease Control and Prevention (CDC) in early 2010 revealed that gay men/MSM in the United States are 44 times more likely to be HIV-positive than other men, and 40 times more likely to be HIV-positive than women.

The bottom line is that for the men and women who engage in anal intercourse, condoms work quite well to prevent HIV, but many people do not use them, or are simply unable to use them due to a number of issues, including power dynamics in sexual relationships, stigma, and a serious lack of availability. According to the Global HIV Prevention Working Group, only 9% of individuals at risk for HIV infection had access to male condoms in 2008. Condom-compatible lubricants are also in dangerously short supply, especially in Africa. We need to do much better with what we have available now, and we should be pushing female condoms more than we are, especially since a new model has come out that has proven to be much more acceptable to women and men, and can be used for anal intercourse as well.

While the rectal microbicide field has gained significant momentum, more focus and resources are necessary. In 2010, 7.2 million U.S. dollars are being spent globally on rectal microbicide research. IRMA has calculated that annual investments must increase by 40% from 2011-2014, to $10 million per year and must increase further to $44 million in the years 2015-2020 to ensure a minimum of candidate products are moving through the research pipeline into late stage testing for effectiveness.

Advocates are optimistic that the CAPRISA proof of concept will also be translated into more financial and creative energy being put into rectal microbicide development. With five new infections for every two individuals beginning treatment, it’s absolutely imperative we find new ways to prevent HIV for individuals at risk, gay and straight, women and men. As these new methods become available, it is also of paramount importance that people who are already using condoms correctly and consistently continue doing so.

We won’t treat our way out of this global epidemic. As of this writing, over 3,400 individuals in the U.S. bide their time on AIDS Drug Assistance Program waiting lists in nine states. The new National AIDS Strategy focuses on three pillars to attack the domestic epidemic, one of which is access to care and treatment. Can we ensure this happens? Those waiting lists are made up of people who can’t wait.

The new National AIDS Strategy focuses on three pillars to attack the epidemic, one of which is access to care and treatment. Can we ensure this happens? CAPRISA enrolled 889 women into a double-blind, placebo-controlled, randomized clinical trial. They were instructed to use the gel up to 12 hours before sex and soon after having sex for a maximum of two doses in 24 hours. Participants used the gel for a minimum of one year and a maximum of two and a half years. HIV serostatus, sexual behavior, and gel and condom use were assessed at monthly
follow-up visits for 30 months. They were asked to return all used and unused gel applicators. A total of 181,000 applicators were dispensed during the study.

In a word, these women were asked to do a lot. And 843 of them did all of that to the very end, with the study achieving a truly extraordinary 95% retention rate. The standing ovation, the hugs, and the tears were as much for the scientists as for these incredibly dedicated women and their exceptional, unwavering commitment to making a difference in the epidemic.

For further information on IRMA visit www.rectalmicrobicides.org and read IRMA's new report, From Promise to Product: Advancing Rectal Microbicide Research and Advocacy.

**Scientists demystify an enzyme responsible for drug and food metabolism**

For the first time, scientists have been able to "freeze in time" a mysterious process by which a critical enzyme metabolizes drugs and chemicals in food. By recreating this process in the lab, a team of researchers has solved a 40-year-old puzzle about changes in a family of enzymes produced by the liver that break down common drugs such as Tylenol, caffeine, and opiates, as well as nutrients in many foods. The breakthrough discovery may help future researchers develop a wide range of more efficient and less-expensive drugs, household products, and other chemicals. The scientists' findings will be published in the journal *Science* on 12 November 2010.

Michael Green, an associate professor of chemistry at Penn State University and lead author of the study, explained that scientists have speculated for decades that, during the process of metabolizing chemicals in the human liver, enzymes in the family named P450 pass through a critical chemical phase-change called "Compound I," whereby an oxygen molecule is temporarily added. However, until now, no one had actually seen the process happen or even had proven that it existed. "This phase change happens quickly, and P450 just as quickly changes back to its original state," Green explained. "So the challenge was trapping the enzyme at the exact moment that it went through the Compound I stage." First, Green and his colleagues grew one of the P450 enzymes in E.coli—bacteria found in the human gut. They then developed a method to cool the enzyme at just the right rate—one one-thousandth of a second—to "freeze in time" the formation process of Compound I.

Green also explained that, while all humans have a gene responsible for making the P450 enzymes, different populations of humans vary in which version of the gene they carry, and thus, which version of P450 they produce. Such P450 variations lead to differences in the way people respond to particular drugs. "With a drug such as caffeine, for example, one population of people might be fast metabolizers, while another might metabolize the drug more slowly," Green explained. "Because the risk of caffeine-induced heart attack may be higher in slow metabolizers, the ability to actually take a snapshot of the phase changes of the P450 enzymes could help us to understand better how certain chemicals can affect people in vastly different ways."

Green's P40 research may also aid future scientific discoveries in the field of pharmacology. "Adverse drug-drug interactions are a well-known problem," Green explained. "The answer to why some people have bad interactions could be understood at the level of the P450 enzymes and their state changes. Now that we can see those state changes on a molecular level, a deeper investigation is finally possible."

**New Class of 'Dancing' Dendritic Cells Derived from Blood Monocytes**
ScienceDaily (Nov. 10, 2010) — Dendritic cells, known to be the prime movers of the body's immune response, are still notoriously difficult to study in humans. Samples, which come primarily from bone marrow or lymphoid tissue, are simply too difficult to obtain. But new research at Rockefeller University has shown scientists a way to study "authentic" dendritic cells from mouse monocytes, which are abundant in the blood, a much more accessible source in humans.

The discovery, published last week in Cell, promises to accelerate research into therapeutic uses of dendritic cells in people, particularly in vaccine development and cancer treatment; it comes from the lab of Ralph M. Steinman, who first published his discovery of dendritic cells in 1973.

"So much of the work has been done in mice because of the logistics of getting the dendritic cells to work with," says lead researcher Cheolho Cheong, a postdoc in the Laboratory of Cellular Physiology and Immunology at Rockefeller University. "We are filling in the gap between mice and humans with this new way to produce dendritic cells originated from the blood monocytes of living animals."

Cheong's breakthrough is in defining and isolating a new class of dendritic cells, called monocyte-derived dendritic cells, from the other types of specialized dendritic cells that reside in the lymph nodes, known as classical dendritic cells. After several years of searching, he found antibodies that would attach to a protein called DC-SIGN particular to the surface of monocyte-derived dendritic cells, a "handle" he could biochemically grab hold of to separate out the cells. Using this tool, Cheong was able to show that monocytes, facing an infection of gram-negative bacteria such as Escherichia coli or their cell wall component called lipopolysaccharid in the blood, migrate to lymph nodes, where they quickly develop into fully fledged monocyte-derived dendritic cells, capable of stimulating T cells and fighting the infection.

When he segregated the cells and looked at them in the microscope, he saw that they had developed the unusual shape and manner of dendritic cells, with extended arms actively probing the environment for infectious particles, taking them up and presenting them to T cells. "It looks like these regular T cells are dancing with the stars," he says. The monocyte-derived dendritic cells he had discovered outnumbered the classical dendritic cells in the infected mice and appeared to be as efficacious as their relatives in presenting invading particles to T cells, although more experiments will be required to determine their exact function in the immune response.

The work contributes to an increasingly detailed picture of how dendritic cells are derived, including work published last year in Science by Steinman's colleague and former protégé Michel C. Nussenzweig. Nussenzweig and colleagues clarified the lineages of different types of dendritic cells and in particular the point at which classical dendritic cells separate from the closely related monocytes, even though they share a common ancestor in the bone marrow.

The research also shows that monocyte-derived dendritic cells are in fact "authentic" dendritic cells, with the same functional properties as their classical cousins. Although Cheong performed the work in mice, the discovery that real dendritic cells can be coaxed from blood monocytes promises to accelerate the study of dendritic cells in humans, because it is much simpler clinically to culture monocytes from a blood sample than classical dendritic cells from lymph tissues.

"If we better understand the human counterpart of monocyte-derived dendritic cells in mice, we can design better dendritic cell-based therapeutics for human use," Cheong says.

**Journal Reference:**

**NIH scientists explore 1510 influenza pandemic and lessons learned**
History's first recognized influenza pandemic originated in Asia and rapidly spread to other continents 500 years ago, in the summer of 1510. A new commentary by researchers at the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, explores the 1510 pandemic and what we have learned since then about preventing, controlling and treating influenza.

Prior to that time, regional and local epidemics of respiratory infectious diseases and pneumonia had occurred, but no outbreaks had yet been recorded on a worldwide scale. The 1510 pandemic first arose in Asia, but it spread quickly to Africa and Europe via trade routes. Although the disease—which was then

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**Dancing stars. Dendritic cells, master immune system cells that use their long “tentacles” to probe the environment and interact with T cells, have for the first time been coaxed from monocytes in the blood of mice. Researchers say the breakthrough could accelerate research of dendritic cell therapies in humans. (Credit: Image courtesy of Rockefeller University)**
referred to by various descriptive terms such as "gasping oppression"—was highly infectious, the death rate was low, and the pandemic ended quickly.

The authors concede that the emergence of new pandemic influenza viruses remains as unpredictable as it was 500 years ago. But they outline a host of scientific and public health advances that have taken place since then—from the study of microbiology to the development of vaccines and treatment—that now allow us to better plan and prepare for both seasonal and pandemic influenza. For example, scientists at NIAID and elsewhere are currently researching the possibility of a universal influenza vaccine, which would aim to protect individuals from all strains of flu.

For more information about NIAID research on influenza, visit the NIAID Flu Web portal at http://www.niaid.nih.gov/topics/Flu/Pages/default.aspx.


30 years on in the epicenter of the African AIDS epidemic
The impact of 30 years of HIV on an area once described as the epicentre of the African AIDS epidemic will be discussed at a lecture hosted by the University of East Anglia (UEA) in London this month.

Progressive declines in agricultural production, with dire consequences for rural livelihoods, were originally predicted as a result of the long-term effects of HIV and AIDS in central and south western Uganda. However, recent research has shown that those forecasts have not come true.

The lecture "30 years into the HIV epidemic in South West Uganda and the rural economy hasn't collapsed. What happened?" takes place on November 25 at UEA London, ahead of World AIDS Day on December 1. Prof Janet Seeley, of the university's School of International Development, will report on research carried out over the last three decades that has looked in more depth at the impact of HIV-related infection and AIDS-related deaths on individuals, communities and livelihoods, in order to contribute to the design of policies and programmes that address the ongoing issues.

Prof Seeley, who has studied the effects of HIV/AIDS on rural communities in East Africa, in particular Uganda, for more than 20 years, will explore the reasons why rural livelihoods have proved to be much more resilient than had been expected in this region, and suggest lessons for forecasting.

In the mid 1980s south-western Uganda and north-western Tanzania were often referred to as the epicentre of the African AIDS epidemic. When first identified HIV/AIDS was of concern as a possible adverse factor in social and economic development because of its specific impact in the 15-50 age group.

The research carried out by Prof Seeley and colleagues Prof Tony Barnett, of the London School of Economics and Political Science, and Prof Stefan Dercon of the University of Oxford, has found that HIV/AIDS has sometimes thrown households into disarray and poverty, but more often it has reduced development and kept households poor.

"People have undoubtedly suffered terrible personal loss and distress, but those who have survived have drawn on support from family and friends and from local organisations to rebuild livelihoods. People have shown resilience and managed," said Prof Seeley. "For some the epidemic has been devastating but often on a household level families have adapted and the community as a whole has done better than expected. While there have been so many other crises, drought and crop failure for example, there have been new opportunities as well.

"People have been changing occupations, diversifying, not necessarily because of HIV but because of diseases that have affected their crops and animals and pressures to earn a cash income. They haven’t only had to face HIV/AIDS, they’ve had problems inflicted by drought, pests and other human disease."

However, Prof Seeley stresses that poverty remains, as does the endemic HIV disease, and that the health status of the population is poor and life remains hard.

"The effects of HIV/AIDS are not as apparent with the simple clarity once assumed because so much else is going on in any society. For policymakers this research shows that they cannot focus on one aspect and assume everything can be attributed to that—too often HIV is reduced to a medical issue, but so much of what is going on is to do with social lives and behaviour, not just sexual behaviour. Resources often go to the medical and not the social support.

"The challenge for development policy and implementation continues to be to find ways of addressing the persistent poverty and deprivation, which in part contributed to the particular manifestation of the AIDS epidemic in this region."


Scientists Unveil Mechanisms of Immune Reconstitution Inflammatory Syndrome

ScienceDaily (Nov. 10, 2010) — Newly published research by scientists at the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, sheds light on a poorly understood, acute illness called Immune Reconstitution Inflammatory Syndrome (IRIS) that develops in some HIV-infected individuals soon after they begin antiretroviral therapy.

IRIS affects certain HIV-infected individuals whose immune systems are heavily damaged by the virus and who have a treated or undiagnosed AIDS-associated infection. When these individuals start antiretroviral therapy and their immune cells begin to regenerate, the immune system unexpectedly produces an exaggerated response that unmasks or worsens the symptoms of the co-infection. IRIS has become a notable challenge in treating HIV disease, particularly in resource-limited settings. The scientists hope that better understanding how and why the syndrome occurs will lead to targeted prevention or therapy.

To find immunologic patterns that distinguish individuals who develop IRIS from those who do not, the researchers analyzed blood samples from HIV-infected individuals, focusing their analysis on a group of immune cells called T lymphocytes. Most of the studied patients had an AIDS-associated fungal, viral or bacterial infection before they started antiretroviral therapy.

The analysis showed that the individuals who developed IRIS had a higher proportion of activated T cells before starting antiretroviral therapy compared with those who did not develop IRIS. These activated T cells had the propensity to make a key infection-fighting molecule called interferon gamma both before therapy began and during IRIS episodes, suggesting that the cells may participate in the exaggerated immune response seen during IRIS. In addition, the surface markers expressed by the T cells—some with a stimulatory effect and some restraining in nature—suggested they were highly activated as a result of an encounter with the microbes co-infecting the HIV-infected individuals.

A companion study describes a new animal model that can be used to directly analyze the immunologic mechanisms that cause IRIS. This model employs mice infected with Mycobacterium avium, a pathogen frequently seen in HIV-infected individuals who develop IRIS. To mimic the immunologic condition of IRIS-susceptible HIV-infected individuals, the researchers began with mycobacterium-infected mice that had extremely low numbers of T cells. The scientists found that rebuilding the population of T cells in these mice, as usually occurs during antiretroviral therapy in humans, triggered an IRIS-like disease. In addition, the researchers observed that interferon-gamma production by the repopulating T cells in the mice clearly facilitated the development of experimentally induced IRIS. The study also implicated a type of immune cell known as a macrophage in sparking IRIS in the mice.

Journal References:

New Lines of Attack in HIV Prevention


Clinical trials testing biomedical means to prevent HIV infection during sex are gaining momentum, experts say.

Last year, a South African trial found that a tenofovir-based vaginal gel conferred about 40 percent protection against HIV. Even though only partially effective, it was the first method for preventing HIV that women could use without men knowing—a vital need, since many males refuse to wear condoms.

Other trials are expected to post results next year and in 2012. If successful, a market-ready product could be possible by 2013. In addition, gels could also protect against herpes.

In the coming months, “we’re going to see a cascade of results” from trials of oral pre-exposure prophylaxis, said Mitchell Warren, executive director of AVAC, an HIV prevention advocacy group. In them, people in high-risk groups take one or two of the antiretroviral drugs typically prescribed to those already infected. It is hoped the ARVs will protect participants from sexually acquired HIV. Regulatory approval might be quick for oral PREP, since ARVs taken orally are already approved.

Rectal microbicides also are on the radar, though progress lags about 10 years behind the vaginal microbicide field, said Dr. Ian McGowan, who leads microbicide trials at the University of Pittsburgh. According to some surveys, 95 percent of US men who have sex with men and 40 percent of heterosexual women have had anal sex at least once in their life.
However, it is first crucial to ensure the gels do not inflame the rectal lining, which is weaker than the vaginal lining. HIV targets activated immune cells, so a gel that inflamed tissue could enhance HIV infection. Tests will soon begin on less viscous formulations that do not pull as much water into the rectum, McGowan said. A 2008 British study in monkeys found a rectally applied tenofovir gel was very effective in preventing anal acquisition of simian immunodeficiency virus.

**Study: Girls Take More Chances During First Sex**

CNN.com, (10.11.2010)

Teenage girls are 30 percent more likely than teenage boys to engage in their first sexual encounter without contraception, according to research presented at the annual meeting of the American Public Health Association (APHA).

Because 80 percent of contraception used at first sex is condoms, the use of birth control largely depends upon boys, noted Laura Lindberg, senior research associate at the Guttmacher Institute.

In her APHA poster session, doctoral student Nicole Weller said that whether teens had received some form of sex education, or what type they received, had no bearing on whether they used contraception during their first sexual encounter. The types of sex education were categorized as abstinence-only, information about birth control methods, and information about STDs.

The data from the National Survey on Family Growth described 5,012 boys and girls ages 11 to 19 who reported any sexual activity. Among all respondents, the average age of first sex was 16. Weller reported that African Americans were 40 percent more likely than whites to have unprotected first sex.

Upcoming research will examine whether girls are more likely to forego contraception if they are in a relationship. “My hypothesis is that relationship status will override sexual education. I love my boyfriend. I trust my boyfriend. I’m not worrying about getting an STD from him,” she said.

The research was conducted at the Arizona State Interdisciplinary Research Center, which is funded by a grant from the National Center on Minority Health and Health Disparities.

**Law Banning Discrimination on HIV Fails in China Court**


Chinese authorities have rejected a 22-year-old college graduate’s claim that he was unfairly denied a teaching job because he is HIV-positive. The man will appeal, his lawyers said.

In his ruling, the judge said regulations barring HIV-positive civil servants take precedence over a four-year-old law that states “no institution or individual shall discriminate against people living with HIV, AIDS patients and their relatives.” The law was promulgated by the State Council, the Chinese government’s chief administrative body.

“I’m heartbroken,” said the man who brought the suit, identified in court papers by the alias “Xiao Wu.” The decision defied logic, the man’s lawyer said. “It’s an example of how the legal system enhances and expands discrimination against people who are HIV-positive,” Li Fangping said.

Xiao had passed written tests and an employment interview, but the local education bureau in the eastern city of Anqing rejected his application when a mandatory blood test revealed his HIV status.

AIDS activists had championed Xiao’s cause, hoping for a precedent-setting positive outcome in the case. Inspired by Xiao, another HIV-positive college graduate has filed a similar case in Sichuan Province.

Now, advocates are concerned that Friday’s court decision could have a chilling effect on the rights of HIV-positive citizens.

“This is bad news given that it was the first time an HIV-positive person dared to stand up for his rights,” said activist Yu Fangqiang. His organization, Beijing Yirenping, provided Xiao with no-cost legal representation. “The entire HIV community had high hopes, but now the door appears to be shutting for people who want to use the courts to fight discrimination.”

**Molecular evolution proves source of HIV infection in criminal cases**

HOUSTON—(Nov.15, 2010) – In 2009, a Collins County, Texas, jury sentenced Philippe Padieu to 45 years in prison for aggravated assault with a deadly weapon – having sex with a series of women and not telling them he had HIV. An important part of the evidence that identified him as the source of the women’s infection came from experts at Baylor College of Medicine (www bcm.edu) and The University of Texas at Austin (www.utexas.edu/).

In a report that goes online today in the *Proceedings of the National Academy of Sciences* (www.pnas.org), Dr. Michael Metzker (http://www.bcm.edu/ genetics/?pmid=109477), associate professor
in the BCM Human Genome Sequencing Center (http://www.hgsc.bcm.tmc.edu/), Dr. David Hillis (http://www.biosci.utexas.edu/IB/faculty/hillis.htm) of UT Austin and their colleagues, describe how they identified Padieu and a man in Washington State in two different cases as the sources of HIV infection to multiple female partners.

"We were blinded in the study," said Metzker. That means they did not know which sample came from the men accused in the crimes and which came from the women who had become infected with HIV.

In determining the source of the infection, they relied on the "bottleneck" that occurs during HIV transmission.

"Within a given person, there is not just one strain but a population of strains because HIV mutates all the time when it makes new virions (viral particles)," said Metzker. "During transmission, however, there is a genetic bottleneck in which only one or two viruses get transmitted to the recipient."

"As many as 75 percent of HIV infections results from a single virus," said Metzker. That means that even though HIV changes in the body, there is a single virus that is the "ancestor" or progenitor of all those viruses.

"Phylogenetic analysis allows us to reconstruct the history of the infection events," said Hillis, professor at UT Austin. "We can identify the source in a cluster of infections because some isolates of HIV from the source will be related to HIV isolates in each of the recipients."

In comparing DNA sequences, Metzker and his colleagues looked at two gene regions of the virus. They are known as env and pol. Comparing these sequences in the different case samples and using mathematics to model evolutionary change, they were able to identify in each case that the viral sequences from case samples were related. More important, they could identify which case sample was the source of the infection.

Only after the scientist had done all the sequencing and analysis did the District Attorneys' offices break the code. In each case, the sample that they thought was the source of the infection came from the man accused of transmitting the virus to the unsuspecting women.

"This is the first case study to establish the direction of transmission," said Metzker.

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**Lung disease common in adolescents with HIV in Zimbabwe**

Keith Alcorn  
Published: 13 November 2010

Health care workers treating older children and adolescents with HIV in sub-Saharan Africa should be alert for early symptoms of chronic lung disease in their patients, and do their best to identify and treat HIV infection before it has a significant impact on those who survive beyond the first year of life.

The lung disease, which is not related to tuberculosis, is severely debilitating.

Without antiretroviral treatment around two-thirds of infants perinatally infected with HIV will die before reaching the age of one year, but evidence from southern Africa shows that among the remainder, survival into adolescence is common.

Twenty-eight per cent of infants infected with HIV around the time of birth or during breastfeeding will survive to the age of ten, and those who survive the first year of life have a median survival of 16 years.

Among this group of survivors, late presentation with HIV disease is common. Children often show severe stunting, delayed puberty and severe cutaneous problems before developing opportunistic infections.

"Although the number of younger children with HIV in our hospitals is melting away due to antiretroviral therapy, the number of older children we are seeing is growing," said Dr Rashida Ferrand, presenting findings from a study conducted in Zimbabwe to the 41st Union World Conference on Lung Health.

A large proportion of older children and adolescents presenting for care to health services in Zimbabwe are infected with HIV, Dr Ferrand told the conference. Among adolescents receiving care at hospitals in Zimbabwe HIV prevalence of 28% has been recorded, while 17% of 10-18 year olds attending primary care were HIV-positive in one cross-sectional study.

A survey of all children enrolled in the first year of primary education in one district of Zimbabwe found an HIV prevalence of 2.8%.

In a country like Zimbabwe with a population of 12 million and high HIV prevalence this means there could be around 30,000 older children and adolescents with undiagnosed HIV infection.
But Dr Ferrand said that among patients of this age group in Zimbabwe, one of the most common problems was chronic and progressive lung disease that frequently leaves patients almost unable to function normally.

She carried out a study in order to understand why so many adolescents without significant evidence of lung damage on chest X-ray were so debilitated, using CT scans to look in more detail at their lungs.

She presented results of a cross-sectional survey of 116 consecutive older children and adolescents with HIV presenting for care at two HIV clinics in Zimbabwe. The mean age was 14, and 69% were receiving antiretroviral therapy; the mean CD4 count was 380.

Among these patients 66% had chronic cough, 21% had a restricted ability to exercise as a result of reduced lung function (NYHA scale 2-4). Forty per cent had hypoxia and 44% had a reduced lung function defined as FEV1 <80% of predicted value. Seven per cent had pulmonary hypertension.

High resolution CAT scan showed that in 50% of patients, there was mosaic attenuation (see link for definition and images), which is strongly correlated with bronchiectasis and airflow obstruction – a condition called obliterative bronchiectasis (OB). It is also characterized by daily production of very large amounts of sputum, coughed up from the airways.

The condition is highly prevalent in Zimbabwean adolescents; a survey showed 44% with CD4 counts above 350 had some evidence of chronic lung disease.

The condition is probably not very responsive to ART, said Dr Ferrand, since there was no significant relationship between the duration of ART exposure and the severity of the condition, suggesting that the condition may be irreversible once established.

Dr Ferrand speculated that OB in children with HIV becomes progressive as a result of a cycle of viral and bacterial infections of the respiratory tract, leading to chronic inflammation, small airway damage and an increased risk of mycobacterial infection. Many of the children in the cohort had received multiple courses of presumptive treatment for tuberculosis as a result of their chronic cough.

Dr Ferrand said early diagnosis of HIV infection and prompt initiation of HIV treatment appeared to be the best way of preventing development of the condition, but further research was needed to determine the extent to which ART can prevent or relieve the condition.

Chronic cough in older children should be the trigger for more thorough investigation, said Dr Ferrand, rather than an immediate presumption of TB. “There’s a need to stress that it’s not always TB just because it’s cough and the chest X-ray looks a bit dodgy,” she said.

Although CT scans are not available in many countries outside private hospitals, Dr Liz Corbett of the London School of Hygiene and Tropical Medicine told aidsmap: “Once you know what [OB] is, and what to look for, the tests are straightforward.”

“Measuring oxygen saturation is not difficult, and even measuring lung function, although it’s technically challenging, is not a high cost intervention,” said Dr Ferrand.

Very basic complaints about inability to exercise should trigger suspicion. “Being unable to sing because of the coughing is a common sign; it’s a big social handicap in Zimbabwe,” said Dr Corbett.

Dr Ferrand recommended the investigation of aggressive management of intercurrent respiratory infections in children with HIV, together with the use of prophylactic antibiotics. Use of a combination of antiretroviral therapy, bronchodilators and corticosteroids might relieve the condition or prevent progression, but this approach needs to be tested, especially given the risk of predisposing patients to TB by corticosteroid use, she said.

Reference


November 15, 2010

**Discordant HIV Levels in the Brain and Blood Are More Common Than Expected**

Up to 10 percent of people on antiretroviral (ARV) therapy have active HIV replication in the brain and spinal fluid despite having undetectable HIV levels in the blood, according to a study published online November 4 in _The Journal of Infectious Diseases_. This could explain why low-level inflammation and cognitive decline persist in people being successfully treated with HIV drugs. It may also have implications for treatment recommendations and the ongoing study of different treatment strategies.

A number of studies in recent years have documented two key findings about HIV in the brains of people taking ARVs. First, that HIV reproduction in the brain and central spinal fluid (CSF) is sometimes different from what occurs in the blood; and second, that immune inflammation and cognitive decline are frequently detected in people who otherwise have very good control of their HIV on ARV therapy.
Another key factor that some researchers believe can significantly affect HIV’s activity in the brain and CSF is the ability of individual drugs to cross the blood-brain barrier. Some ARVs cross easily, while others have poor penetration into these compartments.

In an effort to explore the interaction of these three factors—differences in viral replication in blood and brain, signs of immune inflammation, and the brain penetration potential of a person’s regimen—Arvid Edén, MD, from the Sahlgrenska Academy at the University of Gothenburg, in Sweden, and his colleagues examined blood and CSF samples from 69 HIV-positive people taking ARV therapy.

The blood and brain samples were taken between 2002 and 2010. To be included in the study, in which CSF levels were obtained by a lumbar puncture, a person needed to have been on ARVs for at least six months and to have had undetectable HIV levels in the blood for at least three months. All of the people were taking either Sustiva (efavirenz), Norvir (ritonavir)-boosted Reyataz (atazanavir) or Kaletra (ritonavir plus lopinavir). These drugs were combined with either Viread (tenofovir), Ziagen (abacavir) or Retrovir (zidovudine), plus either Emtriva (emtricitabine) or Epivir (lamivudine).

Edén and his colleagues found that 10 percent of the participants had detectable HIV levels in CSF, many more than they expected. When the team compared the characteristics of those with measurable virus in CSF with those who did not have measurable virus in CSF, they found that people with measurable CSF levels were more likely to have been on ARVs longer, to have had periodic increases in HIV in the blood (blips), and to have taken a treatment interruption.

Edén’s team also found that people with measurable CSF HIV levels were more likely to have high levels of brain inflammation, as determined by measuring neopterin levels.

The makeup of the ARV regimen was not statistically meaningful in regards to discordant viral load responses in the blood and brain. However, there was a trend toward an increased risk of HIV replication in the brains of those who took either Viread or Ziagen compared with those who took Retrovir.

Interestingly, a new method of calculating the likelihood of good ARV control of HIV in the brain, called the central nervous system penetration effectiveness (CPE) rank, was not a good predictor of neither discordant blood and brain HIV levels nor the likelihood of brain inflammation.

Though the brain penetration of the regimens did not significantly affect the likelihood of having discordant HIV levels in the blood and brain, other studies have found that it does. In an accompanying editorial, David Clifford, MD, from Washington University in St. Louis, said this issue needs critical attention, as the most commonly used ARVs today often have only minimal to moderate brain penetration. “If these findings are replicated by others, suggesting 10 percent failure rate of current therapy in the critical CNS compartment, this would be a serious shortscoming for present therapy,” he warned.

“This topic also touches on the interaction of HIV with aging, particularly as it affects the brain and cognitive status,” he continued, noting that cognitive decline from HIV replication and activation could hasten or worsen age-related cognitive problems.

“If control of virus in the brain becomes increasingly difficult to maintain over time,” he concluded, “this implies that increasing neurologic symptoms associated with the virus might augment the cognitive decline of aging, resulting in much more serious late-life neurological issues for HIV-infected patients.”

Ultimately, both doctors, along with Edén’s colleagues, emphasize that this is a very important area of exploration that demands larger studies going forward.

Nearly 25% of People with HIV Show Signs of Neurological Problems

By Liz Highleyman
The occurrence of frank AIDS-related dementia has declined during the ART era, and modern antiretroviral drugs are less likely to cause neuropathy (nerve damage) than earlier agents such as stavudine (d4T, Zerit) or didanosine (ddI, Videx). But as HIV positive people live longer, they are prone to neurocognitive problems related to aging, which appear to progress faster in this population.

In the present study, Pornpun Vivithanaporn and Christopher Power from the University of Alberta and colleagues looked at the impact of combination ART on the changing incidence (new cases) and prevalence (total cases) of neurological disorders among people with HIV and AIDS, as well as their effects on mortality.
The analysis included patients receiving care in a regional HIV care program in Canada from 1998—as combination ART with protease inhibitors came into widespread use—through 2008. A total of 1651 HIV positive people were evaluated. Most (about 80%) were men, nearly 70% were white, and the average age was 33 years.

**Results**

- Of the 1651 patients assessed, 404 (24.5%) had 1 or more neurological disorder.
- Among people with an AIDS diagnosis, the rate rose to 41.0%.
- People with AIDS were nearly twice as likely to have neurological problems as HIV positive people who never had an AIDS diagnosis.
- People with lower current and nadir (lowest-ever) CD4 T-cell counts were more likely to have neurological problems.
- The most common problems were a type of peripheral neuropathy known as symptomatic distal sensory polyneuropathy (DSPN) at 10.0%, and HIV-associated neurocognitive disorders (HAND) at 6.2%.
- About half the patients with any neurological problem had 2 or more disorders.
- The incidence rate of neurological disorders dropped by half over the course of the study, from 12.2% in 1998 to 5.7% in 2007, mostly attributable to decreases in DSPN and HAND.
- A total of 171 patients died during 14,134 person-years of follow-up.
- Participants who had at least 1 neurological disorder had a significantly higher mortality rate than people without such disorders (17.6% vs 8.0%, respectively; \(P < 0.0001\)).
- The disparity was particularly apparent for AIDS-related deaths (9.7% vs 3.2%, respectively; \(P < 0.0001\)).
- The highest mortality hazard ratios (HR)—a measure of the magnitude of increased risk of death—were associated with:
  - Opportunistic infections of the central nervous system: HR 5.3, or about 5-fold greater risk of death;
  - HIV-associated neurocognitive disorders: HR 3.1, or about 3 times greater mortality;
  - Presence of any neurological disorders: HR 2.0, or twice the risk.
- Among people with neurological disorders, the risk of AIDS-related death increased according to viral load and CD4 cell count:
  - 39.0% greater risk per 10-fold increase in plasma viral load;
  - 13.3% greater risk per 100 cells/mm³ reduction in CD4 count.

Based on these findings, the researchers concluded, "The burden and type of HIV-related neurologic disease have evolved over the past decade and despite the availability of combination ART, neurologic disorders occur frequently and predict an increased risk of death."

The frequency of neurological problems seen in this HIV positive population with an average age in the mid-30s was similar to that typically seen in HIV negative people in their mid-50s, the study authors noted in their discussion.

A growing body of evidence indicates that chronic immune activation and persistent inflammation associated with HIV infection contributes to non-AIDS conditions including neurocognitive impairment well before the CD4 cell count drops to a dangerous level. This study supports earlier ART to keep viral load low and CD4 count high as long as possible. 11/16/10

**Reference**
New low-cost method to deliver vaccine shows promise

BOSTON (November 16, 2010) — Researchers have developed a promising new approach to vaccination for rotavirus, a common cause of severe diarrheal disease that is responsible for approximately 500,000 deaths among children in the developing world every year. In a study published in the November issue of Clinical and Vaccine Immunology, a vaccine delivered as nasal drops effectively induced an immune response in mice and protected them from rotavirus infection. The new vaccine delivery system has also been tested successfully and found to be heat stable with tetanus and is currently being tested with diphtheria and pertussis.

The team from the Cummings School of Veterinary Medicine at Tufts University and Tufts University School of Medicine collaborated with researchers from Boston and Tulane Universities to test the effectiveness of immunization with harmless bacteria that were engineered to display rotavirus protein.

"The new vaccine, in conjunction with an agent that enhances immunity, induced sufficient antibody formation against rotavirus to protect mice against infection when the mice were exposed to rotavirus three weeks after their third immunization," explained John E. Herrmann, PhD, research professor in the infectious diseases division of the department of biomedical sciences at the Cummings School of Veterinary Medicine at Tufts University and the senior author of the published study.

"We created the rotavirus vaccine using a harmless bacterium called Bacillus subtilis (B. subtilis), which we can modify to display on its surface or in its cytoplasm proteins from infectious bacteria and viruses. When people are exposed to these proteins, they develop antibodies against them and therefore become immune to the bacteria and viruses," said the study’s first author Sangun Lee, PhD, DVM, research associate at the Cummings School. "The B. subtilis bacteria are so harmless that they are part of the normal diet in several Asian countries."

"The vaccine with the Bacillus bacteria is very inexpensive to produce in large quantities and, unlike most traditional vaccines, requires no special purification steps before use. As a result, the cost of vaccine production is unusually low," explained Saul Tzipori, BVSc (DVM), DSc, PhD, Agnes Varis University Chair in Science and Society, distinguished professor of microbiology and infectious diseases, and director of the infectious diseases division of the department of biomedical sciences at the Cummings School. These findings are consistent with the team’s previous studies in which they demonstrated that B. subtilis bacteria displaying a fragment of tetanus toxin protein completely protect mice from tetanus. Tetanus vaccines have been stored for more than a year at 113ºF without any loss of potency, a property that may be common to all B. subtilis vaccines.

"In addition to being heat-stable and low-cost, the B. subtilis vaccines are given in the form of nasal drops or spray. A needle-free approach to vaccination is particularly advantageous in developing countries where clean needles and syringes and trained personnel are not always available," said team leader Abraham L. (Linc) Sonenshein, PhD, professor and acting chair of molecular biology and microbiology at TUSM and member of the genetics and microbiology program faculties at the Sackler School of Graduate Biomedical Sciences at Tufts.

"This vaccine project is still in the developmental stage," he continued. "The next major step for these vaccines is to show that they are safe and work well in humans, and then to extend the rotavirus and tetanus vaccine technology to include diphtheria, pertussis and other infectious diseases. Those diseases cause tens of thousands of deaths, particularly in newborns and in South-East Asia. We are actively looking for partners in the US and around the world to help us pursue our goal of reaching the point where many childhood and adult vaccines can be manufactured in a way that avoids the need for injection or refrigeration. Jerry Keusch of Boston University School of Public Health and I started this project 15 years ago and it has taken a long time to reach the stage where we now have effective needle-free vaccines. The technology has now advanced enough that we can expect to be successful with many other vaccines in a short time frame."
HIV detectable in CSF of 10% of patients taking successful antiretroviral treatment

Michael Carter
Published: 17 November 2010

Ten per cent of patients taking antiretroviral therapy who have an undetectable viral load in their blood have detectable levels of HIV in their cerebrospinal fluids, Swedish and US investigators report in the online edition of the *Journal of Infectious Diseases*.

Detectable viral load— or viral escape—in cerebrospinal fluid (CSF) was associated with evidence of immune activation in the brain, longer duration of antiretroviral therapy and treatment interruptions.

“Previous studies have shown that CSF HIV-1 RNA generally responds well to antiretroviral therapy”, comment the authors. However, they add, “our findings...suggest that viral escape in CSF, even in subjects with successful systemic treatment with contemporary regimens, is a more common occurrence than previously reported.”

The author of an editorial that accompanies the paper “congratulated” the authors on their research, and writes: “It is concerning that this ongoing viral presence represents a serious threat to brain injury over the many years that patients are expected to live.”

Thanks to antiretroviral therapy the prognosis of many HIV-positive patients is excellent. This treatment suppresses HIV replication in the blood to very low levels allowing the immune system to recover and fight infections. Successful therapy also leads to reductions in localised and systemic inflammation.

However, not all anti-HIV drugs cross the blood-brain barrier or blood-CSF barrier, and few studies have looked at the presence of a detectable viral load in CSF in patients who are taking HIV therapy and have an undetectable viral load in their blood.

Therefore investigators in Gothenburg, Sweden, and San Francisco, California, designed a cross-sectional, or snapshot, study involving 67 patients. All the patients were taking modern anti-HIV drugs and had had an undetectable viral load in their blood for at least six months. None had any neurological symptoms. The patients were recruited between 2002 and 2010.

A total of seven (10%) of individuals had detectable HIV in their CSF. The median CSF viral load was 121 copies/ml (range 52-860 copies/ml).

 Detectable CSF was associated with increased inflammation in the brain. Levels of CSF neopterin (a marker of inflammation and macrophage activation) were significantly higher in patients with detectable CSF viral load than those with undetectable CSF viral load (9.2 vs. 5.1 nmol/ml, p = 0.03).

In addition, 71% of individuals with detectable levels of HIV in their CSF had neopterin levels above the “normal” value (5.8 nmol/l) compared to 40% of patients with undetectable CSF viral load.

Blood viral load did not differ significantly between the patients with detectable and undetectable CSF viral load.

Longer duration of HIV treatment had a significant association with detectable viral load in CSF. Individuals with detectable HIV in their CSF had been taking treatment for a median of 77 months, compared to a median of 35 months (p = 0.002) for individuals with undetectable CSF load.

In addition, detectable CSF viral load was associated with a greater number of viral load “blips”—transient increases in blood viral load above 50 copies/ml. Those with detectable HIV in their CSF had a median of 2.5 blips compared to a median of zero for those with fully suppressed CSF viral load (p < 0.01). The investigators suggest that this could be related to adherence.

Treatment interruptions were also more common among those with detectable CSF virus (p < 0.01). The investigators believe that such interruptions were leading to the “intermittent reseeding” of viral load in the brain and CSF.

There was no evidence that any anti-HIV drug was associated with detectable CSF load. Nor was penetration of drugs into CSF and the brain significant.

“We demonstrate that 10% of subjects had CSF HIV-1 RNA >50 copies/ml”, comment the investigators.

They add, “subjects with detectable CSF virus had significantly longer exposure to ART and higher levels of intrathecal immune activation; treatment interruptions were also more common in these subjects”.

The investigators are uncertain of the clinical significance of their findings.

None of the patients with detectable CSF viral load had neurological symptoms, “suggesting that viral escape in CSF may, at least in the short term, be clinically benign or silent in treated individuals.”
Aware of that their study had a cross-sectional design and small sample size, the researchers conclude by calling for larger, longitudinal studies to examine the issues raised by their research.

This call is echoed by the author of the accompanying editorial, who was especially concerned that ongoing HIV replication in the brain could have an impact on the neurocognitive performance of HIV-infected individuals as they age.

**Reference**


**Sexual Crimes Go Unpunished**

By Rosebell Kagumire

**KAMPALA, Nov 17, 2010 (IPS)**—Thousands of women were raped during Uganda’s war but there have been few government efforts to assist them, especially with psychosocial and counseling services.

Anna Grace Nakasi, recently chosen to contest next February’s local council elections for Tubur subcounty, in Soroti district in North Eastern Uganda, contracted HIV when she was raped during the war.

Nakasi was gang raped on three different occasions—first in 1987, then 1988 and 1990—by soldiers who formed a heavy military presence in her village.

"The first time was in 1987 when I met nine soldiers on patrol who gang raped me until I lost consciousness. I later woke up in a hospital bed," she told IPS. "I could tell they were government soldiers."

Nakasi contracted HIV and developed a fistula. She was rejected by her husband and family and lived alone in a forest for many years.

She overcame her trauma with the support of different aid groups that have also supported her in campaigning for women’s economic empowerment and fighting stigma.

She runs paralegal activities, often following up cases of sexual violence in the area and encouraging women to face their offenders. She has a large support base for her candidature for council due to her work with people living with HIV and AIDS.

"I have so far managed to follow-up a case and have a man jailed for rape," she says.

**Little support for victims of war-time rape**

But Nakasi’s story of her rise from victim of sexual gender based violence to survivor and leader is a unique one.

The two-decades long war in northern Uganda between government and the rebel Lord’s Resistance Army (LRA) resulted in the internal displacement of about 1.5 million people and the death of thousands. Women in internally displaced persons (IDP) camps suffered sexual violence from government soldiers and civilians. Although there are no official figures on the numbers of women affected, reports show this was widespread. The rebels are well known for child kidnapping for use as child soldiers and the abduction of girls as sex slaves.

The war affected the north and north-eastern parts of Uganda until 2007 when the LRA rebels were pushed out to DRC after failed peace talks with the government mediated by the government of South Sudan.

A recent government post conflict recovery programme launched last year lacks a component on addressing the effects on victims of sexual violence in the war.

Further, recommendations calling for reparations for victims of sexual violence made by a commission of inquiry into violations of human rights in Uganda, covering the period from independence in 1962 through the second Obote Regime (1980 – 1985), have never been implemented.

**Inadequate penalties**

And according to a Uganda United Nations Security Council (UNSCR) Resolution 1325 monitoring report released on Nov. 9 by the Kampala-based Center for Women in Governance (CEWIGO), many cases of sexual violence in Uganda go unpunished. UNSCR 1325, which last month marked its 10th anniversary,
acknowledged, for the first time, sexual gender based violence in conflict as a war crime and a crime against humanity.

The report, aimed at tracking Uganda’s progress on the implementation of the resolution, found that many cases are not reported. Rape is the least reported sexual offense in Uganda and the Ugandan law still does not recognise marital rape.

Of those cases that are reported, about half are prosecuted and very few carry penalties at the end of the day.

In 2009, Uganda registered and investigated 619 rape cases. Of those, 37 percent (228) were prosecuted and only five percent were penalised. More than seven thousand cases of the rape of children were reported and only 467 of these cases resulted in a penalty. Five hundred and fifty women reported indecent assault and only 79 were penalised.

**An injustice to victims of sexual violence**

Maude Mugisha from CEWIGO says most families cannot afford to take victims for medical examination or to transport the police to the crime scene. As a result, they opt to negotiate with the perpetrator.

Criminal justice in Uganda requires any person who has been a victim of sexual violence to have a medical test, which is pertinent to the success or failure of a case.

However, only authorized police surgeons can carry out the examination. Not only are the police surgeons insufficient but victims must also pay between US$15 and US$25 to be examined.

"This is the greatest injustice that the survivors of sexual violence are subjected to in Uganda," says Judy Kamanyi, a consultant in gender and development issues.

Rebecca Kadaga, the Deputy Speaker of the Parliament concurs. "It cannot only be a police surgeon that can examine a victim if we are to deliver justice. The examination services should be even carried out by midwives so that women stop paying so much money to access justice."

Kamanyi says government should put in place shelters for women whose lives are in danger and also come up with an emergency plan for abused women and children that caters for their safety.

Access to justice for survivors of gender-based violence is also limited by the fact that sexual offenses are only tried at high court level and these are found in only in five regions of the country. Victims travel long distances to access the courts only to find there is no police surgeon present for the hearing. As a result, sexual offenses cases can take years to be heard.

According to CEWIGO, these gaps in delivery of justice to women victims of sexual violence show that Uganda is far from implementing regional and international instruments meant to safeguard women’s lives, especially in the case of war time rapes.

Miria Matembe, a founder member of CEWIGO says women must continue to pressure governments, especially in the Great Lakes Region of Africa, to implement resolution 1325.

"This resolution remains extremely important for us ... We are a continent still infested with conflict with high levels of gender based violence," she says.

The LRA rebels remain active in DRC, Central African Republic and South Sudan where they continue with abductions.

**Cholera Case Confirmed In Dominican Republic; Haitian Protestors Blame U.N. Peacekeeping Troops For Cholera Outbreak**

Officials on Tuesday said they had confirmed the first case of cholera in Haiti's neighbor, the Dominican Republic, the Associated Press/Forbes reports (11/16). Bautista Rojas, the Dominican health minister, said the patient is a 32-year-old Haitian construction worker who recently returned from Haiti, the BBC reports. The patient is receiving treatment in isolation in the eastern town of Higuey, Rojas said (11/16).

"The Dominican Republic had taken precautionary measures such as stepping up border controls and conducting health checks after the Pan American Health Organization issued a 'high risk' warning of cholera spreading to that country, which shares the Caribbean island of Hispanola with Haiti," RTTNews writes (11/17).

On Monday, protests erupted in Haiti among people who believe U.N. troops played a role in importing the cholera outbreak, Reuters reports. "In Haiti's second [largest] city of Cap-Haitien in the North, hundreds of protesters yelling anti-U.N. slogans hurled stones at U.N. peacekeepers, set up burning barricades and torched a police station, Haitian officials said," the news service writes. "The U.N. mission in Haiti, which is helping the poor Caribbean country rebuild after a devastating January 12 earthquake, has denied rumors that latrines close to a river at the Nepalese U.N. camp were the cause of the cholera outbreak" (Delva, 11/15).
The protests, directed at the multinational U.N. peacekeeping force, continued on Tuesday and have left two people dead, the New York Times reports. U.N. peacekeeping troops have been in the country since 2004, and "[s]ome Haitians see the peacekeepers as hard-line occupiers while others support them out of concern that the national police are unable to maintain order," the newspaper writes.

U.N. spokesman Vincent Pugliese "said the protesters were using the escalating cholera epidemic as an excuse to push the troops out and destabilize the country before the Nov. 28 presidential election," the New York Times reports. "These are not genuine demonstrations," Pugliese said, adding, "They are using spoilers paid to create chaos."

Health authorities said they are not aiming to find the cholera outbreak's origin. "We are focused on treating people, getting a handle on this and saving lives," said Daniel Epstein, a spokesman for PAHO. "Jordan Tappero, an epidemiologist with the United States Centers for Disease Control and Prevention, who is leading medical investigators in Haiti, said by telephone that it was unlikely that scientists would pinpoint where the outbreak began, and that he did not think mounting an all-out effort to find the answer 'is a good use of resources,'" according to the newspaper (Archibold, 11/17).

Also on Monday, Nigel Fisher, the U.N. humanitarian coordinator in Haiti, told reporters on a teleconference that the number of cholera cases in the country is expected to go up significantly as data collection improves, VOA News reports. Fisher also said the U.N. is working with the government to contain the outbreak and reduce fatalities.

"We expect to have, once that data comes in, a significant increase in recorded cases. So people should not be surprised at that," he said. "Fisher said emphasis is continuing on educating the public about the disease and making sure they have access to oral rehydration salts and tablets to chlorinate their water. Fisher said plans are also being made to increase the number of cholera treatment centers across the country. 'It is [cholera] spreading and we have to contain, if not [the] number of cases, we have to try to contain the number of deaths,' he said," the news service writes (Besheer, 11/15).

"Fisher confirmed that cases of the disease continued to expand rapidly, with cases reaching every department, or administrative division, as well as the capital," the U.N. News Centre writes. "This has gone far beyond a health or sanitation matter. It's an issue of environmental concern, it's an issue obviously of national security where we have demonstrations starting already, against for example cholera treatment centres," Fisher said (11/15).

"Soap could slow the terrifying cholera outbreak ... But in the squalid slums of Port-au-Prince and the river towns where the cholera outbreak began three weeks ago, many Haitians held up their hands and shook their heads, saying they had no soap to stop an infection that is spread by contaminated food and water and in which vigorous hand-washing, especially after using the toilet, is the No. 1 way to save lives," the Washington Post writes.

"A cake of yellow Haitian soap costs about 50 cents. But many Haitians do not have soap because they cannot afford it. More than half the population lives on less than $1.25 a day," according to the newspaper (Booth, 11/16).

**NIH scientists show how anthrax bacteria impair immune response**

*Studies in mice reveal how bacteria hamper frontline defense cells*

WHAT: Researchers from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, have determined a key mechanism by which *Bacillus anthracis* bacteria initiate anthrax infection despite being greatly outnumbered by immune system scavenger cells. The finding, made by studying genetically modified mice, adds new detail to the picture of early-stage anthrax infection and supports efforts to develop vaccines and drugs that would block this part of the cycle.

To start an infection, anthrax bacteria release a toxin that binds to immune cells through two receptors, TEM8 and CMG2, found on the cell surface. The binding allows two additional bacterial toxins to enter the cells, setting off a chain of events that impairs their ability to ingest and kill the bacteria.

In the new research, NIAID investigators Stephen Leppla, Ph.D., Shihui Liu, M.D., Ph.D., and colleagues bred mice that lacked CMG2 receptors on two kinds of immune cells, neutrophils and macrophages. These usually are the first cells to arrive at the site of an anthrax infection, where they engulf the invading bacteria and try to prevent the spread of infection.

Mice without CMG2 receptors on these immune cells were completely resistant to infection by *B. anthracis* bacteria, experiencing only a temporary swelling at the site of infection, and fully clearing the infection within two weeks. In contrast, in normal mice, the level of anthrax bacteria increased rapidly in the 48 hours following infection, and all the mice died within six days.
The researchers concluded that B. anthracis uses CMG2 receptors to impair the scavenging action of neutrophils and macrophages during early infection, giving the bacteria time to multiply to levels sufficient to overwhelm the body's defenses. Developing drugs and vaccines that block B. anthracis from establishing early infection via binding to the CMG2 receptor, say the study authors, may be crucial to success in treating and preventing anthrax disease.

**Article**: S Liu et al. Anthrax toxin targeting of myeloid cells through the CMG2 receptor is essential for establishment of *Bacillus anthracis* infections in mice. *Cell Host and Microbe*. DOI: 10.1016/j.chom.2010.10.004 (2010).

**Scientists identify antivirus system**

Viruses have led scientists at Washington University School of Medicine in St. Louis to the discovery of a security system in host cells.

Viruses that cause disease in animals beat the security system millennia ago. But now that researchers are aware of it, they can explore the possibility of bringing the system back into play in the fight against diseases such as sudden acute respiratory syndrome (SARS), West Nile virus, dengue and yellow fever.

The findings, published in *Nature*, solve a 35-year-old mystery that began when National Institutes of Health researcher Bernard Moss, MD, PhD, noticed that poxviruses put chemical "caps" on particular spots in every piece of genetic material transcribed from their DNA. That transcribed material is RNA; to reproduce, viruses need to trick the host cell into making viral proteins from this RNA.

Noting evidence that the host cell puts caps on its own RNA in identical positions, Moss theorized that the caps might be a way for cells to distinguish between their RNA and that of an invader. He guessed the caps might serve as a sort of fake identification badge for the virus' RNA, allowing it to bypass host cell security systems primed to attack any RNA lacking the caps.

Since Moss’s study, scientists have learned that some viruses have strategies for stealing RNA caps from host cells and putting them on their own RNA. Several disease-causing viruses have to make their own caps, including:

- poxviruses, which cause smallpox
- flaviviruses, which cause West Nile encephalitis, yellow fever and dengue;
- rhabdoviruses, which cause rabies;
- coronaviruses, which cause SARS;
- reoviruses, which cause mild respiratory distress or diarrhea.

Scientists also learned that one of the chemical caps added to RNA helps stabilize it, preventing the RNA from breaking down. However, despite years of research, the purpose of another cap, added near the beginning of every RNA strand in a position scientists refer to as 2’ (two prime), was a persistent mystery.

The new paper from the laboratory of senior author Michael S. Diamond, MD, PhD, solves that puzzle and confirms Moss’ speculation. The study used a mutant form of the West Nile virus created by Pei-Yong Shi, PhD, now a researcher at the Novartis Institute for Tropical Diseases. The mutant strain can attach the cap that keeps RNA stable but is unable to add the 2’ cap. When Diamond, professor of medicine, pathology and immunology, and molecular microbiology at Washington University School of Medicine, infected mice with this mutant virus, it could not cause disease.

Next, scientists injected the mutant virus into mice lacking the receptors for interferons. These proteins are important players in defensive reactions to invading viruses within the cell, a branch of the immune system known as intrinsic immunity. The mutant virus made these mice sick, suggesting that intrinsic immunity stops the mutant viruses in normal mice, and that the 2’ cap was helping normal viruses evade this part of the immune system.

Researchers recently identified a gene, IFIT2, that is activated by interferons, has mild antiviral effects against West Nile virus and seems to have potential connections to translation of RNA into proteins. When Diamond turned IFIT2 levels up in cell culture and exposed it to the mutant West Nile virus, the mutant virus could barely replicate. Tests of a mutant poxvirus and a mutant coronavirus that could not attach the 2’ cap produced similar results. Knocking out a related gene in mice, IFIT1, allowed the mutant virus to evade intrinsic immunity and cause infection when it was injected into the brain.

"Now that we know what this cap is used for, we can look at the question of whether the human and viral enzymes that put the cap on are sufficiently different," says Diamond. "If they are, we may be able to design inhibitors that prevent viruses from capping their RNA and make it much harder for them to replicate once the intrinsic immune system is activated."
New, Much Faster, More Accurate Diagnostic for Influenza and Respiratory Syncytial Virus

ScienceDaily (Nov. 16, 2010) — A new, fully automated system is much quicker, and more accurate in diagnosing influenza A and B, and respiratory syncytial virus (RSV) A and B than conventional alternatives, according to a paper in the November Journal of Clinical Microbiology. The new technology promises faster and more appropriate treatment of patients.

"Instead of relying on insensitive but rapid influenza tests for diagnosis in the clinic, or waiting 24 hours or more for molecular results to come back, we can now provide molecular level sensitivity in less than three hours," says principal investigator Nathan A. Ledeboer of the Medical College of Wisconsin, and Dynacare Laboratories, Milwaukee.

"This will mean that hospitalized patients with influenza and RSV infections will be isolated faster, which will decrease the risk of transmission to other patients in the hospital," says Ledeboer. The faster turnaround also means that "fewer patients will be placed on empiric therapy, which will decrease costs and decrease the risk of an adverse event caused by medication." In the study, the assay, a microarray, was tested on 720 patient samples collected throughout the US.

The new technology, called Respiratory Virus Nucleic Acid Test SP" (RVNATsp), is 98 percent sensitive (meaning that 98 percent of positive results are accurate) and 96 percent specific, meaning that 96 percent of negative results are accurate). By comparison, the conventional alternative, culture, is nearly 100 percent specific, but only 70 percent sensitive.

Influenza virus infects millions annually. It is typically associated with infections of the upper respiratory tract and can cause mild to severe illness. RSV can cause severe symptoms in infants, young children, and immunocompromised individuals, and is the leading cause of hospitalization of children under five years of age. In the most vulnerable individuals, children less than six months old, people with chronic lung disease, and immunocompromised individuals, RSV can migrate from the initial site of infection in the upper airway to the smaller bronchioles of the lower airway, where it can cause life-threatening bronchiolitis or pneumonia.

Journal Reference:

New 3-D Model of RNA ‘Core Domain’ of Enzyme Telomerase May Offer Clues to Cancer, Aging

ScienceDaily (Nov. 3, 2010) — Telomerase is an enzyme that maintains the DNA at the ends of our chromosomes, known as telomeres. In the absence of telomerase activity, every time our cells divide, our telomeres get shorter. This is part of the natural aging process, as most cells in the human body do not have much active telomerase. Eventually, these DNA-containing telomeres, which act as protective caps at the ends of chromosomes, become so short that the cells die.

But in some cells, such as cancer cells, telomerase, which is composed of RNA and proteins, is highly active and adds telomere DNA, preventing telomere shortening and extending the life of the cell.

UCLA biochemists have now produced a three-dimensional structural model of the RNA “core domain” of the telomerase enzyme. Because telomerase plays a surprisingly important role in cancer and aging, understanding its structure could lead to new approaches for treating disease, the researchers say.

“We still do not know how the RNA and the proteins cooperate to do this magical thing—extend the ends of our telomeres—but we are now one step closer to understanding that,” said Juli Feigon, a UCLA

A model representation of telomerase’s RNA ‘core domain,’ determined by Juli Feigon, Qi Zhang and colleagues in Feigon’s UCLA laboratory. (Credit: Juli Feigon, UCLA Chemistry and Biochemistry/PNAS)
The critical telomerase RNA core domain is essential for telomerase to add telomere repeats onto the ends of chromosomes, the structures that hold our genes. The core domain contains the template that is used to code for the ends of the chromosomes.

"Telomerase is the most amazing complex," said Feigon, who began studying telomere DNA structure in the early 1990s, which led to her interest in telomerase. "Some people think if we activate telomerase, we can live forever. However, we don't want our cells to be able to divide indefinitely. As they get older and older, they accumulate all kinds of DNA damage and defects; that is why we don't want to have a high level of telomerase activity in most of our cells."

Because cancer cells divide rapidly, their telomeres should get shorter more quickly than normal cells. But while telomerase has low activity in most types of healthy cells in our bodies, the high level of telomerase activity in cancer cells helps rebuild the telomeres, Feigon said. These cancer cells, she said, "become immortal" because of their telomerase, which enables the cancer to progress.

"There is so much potential for treating disease if we understand how telomerase works," Feigon said. She and members of her laboratory are studying its structure at a very detailed level, which provides insights into how telomerase functions. However, Feigon emphasized that her laboratory conducts basic scientific research and is not involved in cancer treatment.

The research was federally funded by the National Institutes of Health, with American Recovery and Reinvestment Act funds, and the National Science Foundation.

The core domain consists of three pieces: a "pseudoknot" required for telomerase activity, at whose core three strands of RNA come together to form a triple helix; an "internal bulge loop," which had been largely ignored but turns out to be quite significant; and a "helical extension"—all of which Feigon and her colleagues modeled using a new method they developed.

"We have the first useful model of the core domain of telomerase RNA," said Feigon, who was elected to the National Academy of Sciences in 2009. "We have put the three pieces together to produce a three-dimensional model of the core domain, the first time this has ever been done at a high resolution. This is exciting in terms of learning how telomerase works because it is the first time we have had a useful picture of the shape of this critical part of the RNA."

The new research, she said, could lead to targets for drug intervention.

"If you want to target drugs to telomerase, you need to know what it's doing at every stage of the cell cycle," Feigon said. "If you know the three-dimensional structure of any protein or nucleic acid that is involved in essential activities in the cell, then the ability to target it with small molecules or other pharmaceuticals to either inhibit or activate it is helped tremendously."

There are diseases in which a mutation in telomerase RNA or in a telomerase protein results in inactivation of telomerase.

"We try to see the global picture with structural biology, including learning how telomerase functions and how to make it dysfunctional," said Qi Zhang, a UCLA postdoctoral scholar in Feigon's laboratory and lead author of the PNAS paper. "This is a very large piece that we are reporting."

The scientists who discovered how chromosomes are protected by telomerase won the 2009 Nobel Prize in physiology or medicine. Yet there is still very little known about the structural biology of the enzyme; its overall three-dimensional structure is not known. Almost all of the three-dimensional structural information about vertebrate telomerase's RNA component has come from Feigon's laboratory.

"While much is known of telomerase's biochemistry, little is known about how the RNA component and the protein component interact in the three-dimensional structure," Feigon said.

Feigon and her colleagues put together the three pieces—the pseudoknot, the internal bulge loop and the helical extension—to create a three-dimensional model. They determined the structures using state-of-the-art nuclear magnetic resonance (NMR) spectroscopy.

"We decided to study the internal bulge loop's structure and its dynamics," Feigon said. "What we found when we determined the structure was, first, it is quite unusual, with an unexpected fold that causes a large bend in the RNA. We then did biochemical studies that showed that the bend and its flexibility is important for telomerase activity. The internal bulge loop turns out to be really important in determining the topology of this domain, which was unpredicted."

"We are learning how the internal bulge loop functions, and we have characterized its role in the catalytic activity," said Zhang, who holds a Baltimore Family Fellowship from the Life Sciences Research Foundation.

The structure and dynamics of the internal bulge loop are important for catalytic activity.
"We have found a rare structure," Feigon said. "We studied the database of all the structures of RNA that have been solved, and it turns out that one other structure has the same type of five-nucleotide bulge. The other one is from an RNA domain of the hepatitis C virus. That was a huge surprise for us. And the bigger surprise is that the nucleotide sequence of that bulge is completely different, but the structure is almost identical. That particular bulge is also critical to the function of the virus; if you disrupt that bulge, the hepatitis C virus becomes less infectious."

For telomerase to be active, it needs the telomerase RNA and a protein called human telomerase reverse transcriptase. Chromosomes are composed of strings of bases—nucleotides—represented by the letters A, C, G and T. The 'C' base always binds to 'G,' while 'A' binds to 'T.' The bases combine to make three-letter codes that specify an amino acid; the corresponding amino acids combine to make proteins.

"Within telomerase, there is an RNA template that is used to code for the telomere DNA repeats," Feigon said. "If you have the letter 'A,' it puts in the letter 'T,' and if you have a 'G,' it puts in a 'C.' This method of copying, from RNA to DNA instead of copying DNA to RNA, is called reverse transcription. The core domain includes the template which does this. HIV also has a reverse transcriptase that copies from RNA to DNA.

"Reverse transcriptases normally copy RNA to DNA but do not contain RNA; in this enzyme, the protein requires the RNA component to function."

"Telomerase is unique because the template is part of the enzyme, and it is used to copy one telomere repeat and then starts over and makes another, and another, all attached to one another. That is how telomerase extends the telomeres," she said. "Telomerase has its own internal piece of RNA that is used to copy the DNA, but this 'template' is only approximately 10 of the 451 nucleotides."

Telomerase has been extremely difficult to characterize structurally because of its size and complexity and its low level in normal cells.

Other co-authors on the PNAS paper are Nak-Kyoon Kim, a postdoctoral scholar in Feigon's laboratory; Robert Peterson, a research scientist in Feigon's laboratory; and Zhonghua Wang, a postdoctoral scholar in Feigon's laboratory. This PNAS research is Feigon's inaugural article as a member of the National Academy of Sciences.

Feigon's laboratory studies the 3D structures of DNA and RNA and how proteins and DNA and RNA recognize one another to switch genes on and off in cells. A member of UCLA's faculty since 1985, Feigon was the first UCLA scientist to use NMR to determine DNA and RNA structures. She and her colleagues utilize a range of molecular biological, biochemical and biophysical techniques.

Serendipity often plays a prominent role in science, and this is another example. When Feigon began her research on telomeres and telomerase in the early 1990s, she was not even thinking about cancer. Instead, she was interested in studying DNA structure.

Journal Reference:

Species, Rather Than Diet, Has Greatest Effect on Gut Bacteria Diversity
ScienceDaily (Nov. 16, 2010) — The types of gut bacteria that populate the guts of primates depend on the species of the host as well as where the host lives and what they eat. A study led by Howard Ochman at Yale University examines the gut microbial communities in great apes, showing that a host's species, rather than their diet, has the greatest effect on gut bacteria diversity.

These findings will publish next week in the online, open access journal PLoS Biology.

"Bacteria are crucial to human health. They enhance the immune system, protect against toxins, and assist in the maturation and renewal of intestinal cells," says Ochman. Gut microbes outnumber our own cells by 10 to 1 but little is known about how certain species come to populate our stomachs, which are sterile at birth. What causes this variation within microbial communities has been a matter of debate. Some scientists have argued that diet and habitat play the most prominent roles. However, Ochman and colleagues found that diversity in the composition of these gut communities, not including those occasional transients and unwelcome visitors such as pathogenic bacteria, depends primarily upon the host species.

Using genetic markers, the team measured the diversity and abundance of various microbial species found in fecal matter of five great ape species collected in their native ranges and discovered that bacterial populations assorted to species. Moreover, the relationships of the microbial communities matched that of their host. In other words, not only is it possible to differentiate chimpanzees from humans by
examining the microbial populations within their guts, but these gut microbes have been tracking the evolution of their hosts for millions of years.

**Journal Reference:**

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**US Panel Positive on Merck Vaccine for Anal Cancer**

*Reuters*, (11.17.2010) Lisa Richwine

On Wednesday, most members of a Food and Drug Administration advisory panel said Merck & Co.’s Gardasil human papillomavirus vaccine appears effective in preventing anal cancer. Merck presented the FDA panel with data from tests of Gardasil among men. However, many panelists said they feel confident the vaccine also would prevent HPV-related anal cancer among women.

The advisory panel did not vote on the matter. FDA will consider the panel’s input as it decides whether to approve Gardasil for preventing anal cancer among males and females ages 9-26. FDA also is expected to determine by the end of the year whether to widen Gardasil’s approval for preventing cervical cancer to include women ages 27-45, said Pam Eisele, a Merck spokesperson.

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**New Drugs to Speed TB Treatment**

*Inter Press Service*, (11.15.2010) Tinus De Jager

Researchers are testing a TB treatment modality that could cut the length of therapy, which now can extend for two years, to six months. The approach shows promise in treating both drug sensitive (DS TB) and multidrug-resistant TB (MDR TB).

None of the drugs being tested is known to interfere with HIV treatment.

“This is a good reason to test these new drugs, as some of the old drugs that were used did interfere with the treatment of HIV,” said Dr. Andreas Diacon, coordinator of the trials.

The approach being tested, known as New Combination 1 (NC001), combines the experimental drug PA-824 and moxifloxacin with pyrazinamide, an antibiotic common in TB treatment. The combination will undergo Phase II testing at two sites in South Africa, the Lung Institute at the University of Cape Town and the TASK Research Center in Bellville.

The 68 patients in the trial will receive two weeks of treatment and three months of follow-up to evaluate the drugs’ effectiveness, safety and tolerability. Results are expected in three to four months. Subsequent research will look at the effect of longer exposure to the drugs.

Effective TB treatment requires careful adherence to the therapy regimen, something patients can find difficult over the long course of treatment. Patients who do not strictly follow a prescribed regimen often must restart therapy and run the risk of developing resistance to TB medications.

TB kills about 2 million people every year, and the impact falls disproportionately on Africa and Asia.

“At the moment we are trying to design new trials where new drugs are taken in new combinations from the start, which could shorten the time span in which new drugs become available. Especially in South Africa, we cannot wait for 20 years to have results,” Diacon said.

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**E. coli infection linked to long-term health problems**

People who contract gastroenteritis from drinking water contaminated with *E coli* are at an increased risk of developing high blood pressure, kidney problems and heart disease in later life, finds a study published online in the *British Medical Journal*.

The findings underline the importance of ensuring a safe food and water supply and the need for regular monitoring for those affected.

It is estimated that *E coli O157:H7 infections cause up to 120,000 gastro-enteric illnesses annually in the US alone*, resulting in *over 2,000 hospitalizations and 60 deaths*. However, the long term health effects of *E coli* infection in adults are largely unknown.

A team of researchers from Lawson Health Research Institute (Lawson) and The University of Western Ontario (Western) assessed the risk for hypertension, renal impairment and cardiovascular disease within eight years of gastroenteritis from drinking contaminated water.

The team used data from the Walkerton Health Study, the first study to evaluate long term health after an outbreak of gastroenteritis in May 2000 when a municipal water system became contaminated with *E coli O157:H7* and Campylobacter bacteria.

Study participants were surveyed annually and underwent a physical examination and laboratory assessment to track their long term health.
Of 1,977 adult participants, 1,067 (54%) experienced acute gastroenteritis, of which 378 sought medical attention.

Compared with participants who were not ill or only mildly ill during the outbreak, participants who experienced acute gastroenteritis were 1.3 times more likely to develop hypertension, 3.4 times more likely to develop renal impairment, and 2.1 times more likely to have a cardiovascular event, such as a heart attack or stroke.

"Our findings underline the need for following up individual cases of food or water poisoning by E. coli O157:H7 to prevent or reduce silent progressive vascular injury," says Dr. William Clark, Scientist at Lawson, Nephrologist at London Health Sciences Centre and Professor of Nephrology at Western’s Schulich School of Medicine & Dentistry. "These long term consequences emphasize the importance of ensuring safe food and water supply as a cornerstone of public health."

Upending Conventional Wisdom, Certain Virus Families Are Ancient
ScienceDaily (Nov. 17, 2010) — Certain families of single-stranded DNA virus are more than 40 to 50 million years old, according to investigators from the Institute for Advanced Study, Princeton, NJ, and the Fox Chase Cancer Center, Philadelphia. The investigators found remnants of circoviruses and paroviruses in the genomes of diverse vertebrates from fishes to birds and mammals that had been integrated into their genomes at different times from the recent past to more than 50 million years ago.

The research upends the conventional wisdom that most virus families are of very recent origin, and is published in the December Journal of Virology.

"Until recently, age estimates for all viruses except retroviruses were in the thousands of years, and nobody expected to be able to trace viruses beyond that time frame due to high mutation rates of the most commonly circulating viruses," says Anna Marie Skalka of Fox Chase. "We showed that several families have been around for tens of millions of years, and have barely changed over that time frame."

Viruses have long been speculated to be a source of novel animal genes, yet little evidence, except from retroviruses, has supported this idea. The team's motivation included the desire to search for such evidence in other viruses.

"We first scanned all published vertebrate genomes for traces of single stranded RNA (ssRNA) viruses other than retroviruses," says Skalka. The team then used a variety of techniques to devise a new method for determining the age of DNA sequences, "To our amazement, we discovered ancient fossils [viral sequences] in 10 vertebrate species that are related to certain currently circulating RNA viruses," notably the deadly Ebolaviruses, and the Bornaviruses, she says. These results, published earlier this year, encouraged these investigators to look for ancient fossils derived from ssDNA viruses.

"Once again we were amazed to find sequences from replication (rep) and capsid genes from ancient viruses related to the Parovirus and Circovirus families in 31 of the 49 vertebrate genomes we tested," says Skalka.

While rep proteins from the circoviruses were already known—some of them selectively kill tumor cells—the relevant codes were certainly not known to have existed in vertebrates almost as far back as when the dinosaurs roamed earth. Skalka notes that there is no evidence yet that those coding sequences are expressed. "But should a beneficial role for these integrations be found, such as control of cancer progression, it may explain why these viruses were selected for over millions of years of vertebrate evolution."

One additional notable finding is that the timeframe of the viral fossils' appearance, 40-60 million years ago, was a time of rapid accumulation of exogenous and other elements into the genome, including multiple families of viruses, so-called "short interspersed elements" and pseudogenes. That's a curious phenomenon which merits investigating, says first author Vladimir A. Belyi.

Journal Reference:
High prevalence and incidence of pre-cancerous cervical lesions in HIV-positive South African women
Keith Alcorn
Published: 22 November 2010

There is a high prevalence and incidence of pre-cancerous cervical lesions in HIV-positive South African women, investigators report in the on-line edition of *AIDS*.

“This is the most comprehensive longitudinal report of cytological progression and regression of a large number of HIV-infected women followed prospectively in a high HIV, high HPV [human papilloma virus] setting,” comment the researchers.

The add, “over one-quarter of women with a baseline normal or [low grade] lesions progressed to high grade cervical lesions during follow-up.”

Antiretroviral treatment had a moderately protective effect against progression of lesions.

The authors believe that their findings have implications for cervical screening strategies in South Africa. However, they do not think that annual check-ups would be cost effective. Instead, they recommend that the frequency of screening should be determined by CD4 cell count.

Access to HIV therapy in South Africa is increasing, therefore significantly extending the prognosis of a large proportion of patients. Infection-related malignancies, such as cervical cancer, are an increasingly important cause of illness and death in patients with HIV.

Treatment for cervical cancer is more likely to succeed if pre-cancerous cell changes are detected early. Therefore investigators wished to establish the prevalence and progression of cervical lesions among HIV-positive women in Soweto.

A total of 2325 women had a cervical smear between 2003 and 2009. Only 4% were taking HIV treatment at baseline, but a further 15% initiated therapy during follow-up. The women were followed for a median of 24 months.

At the time of the initial screen, 38% of women had pre-cancerous lesions. Their average age was 32 and their median CD4 cell count 254 cells/mm$^3$, which was significantly lower than the median of 351 cells/mm$^3$ observed in women with normal cervical cytology ($p < 0.0001$).

Each 100 cell/mm$^3$ increase in CD4 cell count reduced the risk of low-grade lesions by 13%, and high-grade lesions by 18%.

In addition, each five year reduction in age reduced the risk of low-grade lesions was 10%.

A subsequent smear was performed on 1193 women. Women who had only one smear were significantly more likely to have abnormal lesions at baseline ($p < 0.001$). They were also more likely to have been lost to follow-up or to have died ($p < 0.001$).

Overall, 11% of women with a normal cytology or low-grade lesions at baseline developed high-grade lesions. This provided an incidence of 9.6 per 100 person years.

Of the 832 women whose first smear results were normal, 22% developed low-grade lesions and 1% high-grade lesions.

However, an improvement in cervical cytology was also observed in many women.

When the investigators looked at the smear results of the 225 women with low grade lesions at baseline, and who had a second smear at least 11.5 months later, they found that the lesions had regressed in 44% of individuals.

Patients with a CD4 cell count below 200 cells/mm$^3$ were almost twice as likely as those with a CD4 cell count above 500 cells/mm$^3$ to experience disease progression ($p < 0.0001$).

Taking HIV treatment reduced the risk of disease progression by 28%. ($p < 0.05$). “We were able to show a protective effect of HAART [highly active antiretroviral therapy] despite short durations of ART,” write the authors.

Only age above 45 was associated with the regression of lesions. This finding surprised the investigators, who commented: “low grade lesions in older women would be expected to be more persistent lesions. The protective effect of age...is unexplained.”

The researchers believe that their findings have implications for cervical screening programmes in South Africa. It is current practice to screen women every ten years, but the authors recommend “shorter screening intervals” for women with a CD4 cell count below 500 cells/mm$^3$.

However, they do not believe that annual screening would be an efficient use of scarce health-care resources, as many abnormalities are “transient” and destined to “resolve with time.”

Instead they believe that the screening interval should be determined by a patient’s CD4 cell count, and that patients with weak immune systems should have the most frequent monitoring.
Reference

Russia tests three new HIV vaccines
Russian vaccine developers will join forces in a bid to produce new, effective HIV vaccines, the head of one of the companies said on Monday.

The first examinations of three vaccines, being developed in Moscow, St. Petersburg and Novosibirsk, showed their safety, said Yevgeny Stavsky, the head of Novosibirsk-based company Vector. Further tests, to be jointly carried out by the three vaccine developers, have to reveal if the vaccines are effective enough, he said.

"The main and most expensive part of work is now to be implemented," he said, adding that a decision by the three vaccine developers to work together would facilitate and speed up the process.

The Russian government allocated 1 billion rubles ($32.15 million) in 2007 for the development of the vaccines, Stavsky said. A decision on future investments is expected by the end of the year, he said.

According to the World Health Organization, there are more than 33 million HIV-infected people in the world, with half of them aged between 15 and 24. Some 25 million HIV-related deaths have been registered in the world, and the number of infections rises by 2.7 million each year, WHO data says.

In Russia, about 570,000 new HIV infections have been registered in the past three years, the deputy head of the Russian Academy of Medical Sciences' Virology Institute said.

Only one HIV vaccine, developed in the United States and tested in Thailand, has proved its relative effectiveness so far, the head of the AIDS department of the Russian Federal Medical-Biological Agency's Immunology Institute was quoted by the Vector company's press service as saying. The U.S. government had spent $160 million on its development, Igor Sidorovich said.

However, the immunity protection level of this "most effective" vaccine is registered at just 30 percent, providing that injections are made six times during a year.

"Even given this quite modest effectiveness, it is possible to save about 1 million lives a year using the vaccine," Sidorovich said. But HIV in Russia has different variations from those registered in the United States and Europe, which means domestic efforts are crucial for protecting Russians against HIV, he added.

Some 500 people have already been selected to participate in the testing of new vaccines, the director of St. Petersburg's Biological Medical Center, Andrei Kozlov, said.

The pope's shift on condoms is the thin end of the wedge
If he now accepts that condoms can prevent the spread of Aids, how else may his teaching change?

As Pope Benedict sat down with the German journalist Peter Seewald at the papacy's summer residence a few months ago, he probably never imagined that his cautious remarks on condoms would spark international excitement. He appears to be constantly surprised that his ruminations should be noticed.

Benedict reiterated the Catholic church's longstanding and dogmatic opposition to artificial birth control, which remains a grave sin – though honoured rather more in the breach than the observance by many of the faithful, certainly in the western world. And, as some Catholic theologians and even several cardinals – including the former archbishop of Westminster, Cardinal Cormac Murphy-O'Connor – have argued in recent years, using a condom to prevent a greater evil, the passing on of a lethal virus, may be licit.

But it is the implication of his statement – and the fact that the pope has made it himself – that changes things. "In certain cases, where the intention is to reduce the risk of infection, [condom use] can nevertheless be a first step on the way to another, more humane, sexuality," he said, adding: "There may be justified individual cases, for example when a male prostitute uses a condom."

For more than 40 years the church hierarchy has tied itself up in rhetorical knots to justify the encyclical Humanae Vitae of 1968, in which Pope Paul VI overturned the advice of his own papal commission to restate the church's opposition to any artificial birth control.

Now, suddenly and maybe grudgingly, Benedict has acknowledged the weight of pragmatic advice and implicitly accepted the medical case that condoms do indeed help to prevent the spread of infection. He even seems to recognise, by the term male prostitute, that people who in his terms should not be having sex at all do so, and therefore need protection, especially if ultimately it helps them see the light.
Welcome – marginally – to the real world. Cardinal Alfonso López Trujillo, who claimed in 2003 that the Aids virus could percolate through little holes in condoms that only he could see, must be turning in his grave. Benedict sidelined Trujillo when he became pope, so perhaps he always had doubts about the Colombian's credibility.

The church’s position on sex has long contained doses of hypocrisy. Even in times of mass religious observance, it has been well aware that its rules have been flouted or ignored. You can dress it up as the dictates of conscience, or pragmatism, or even human sinfulness, but women have always attempted to practise birth control or, if that failed, risked abortions.

A recent US survey found 40% of women seeking abortions were Catholic (and a further 40% belonged to other religious groups) – proportions that have probably scarcely altered, despite all the condemnation, since the mid-19th century, when one in six pregnancies in the US are thought to have been aborted. Even the rhythm method, or natural family planning as the church calls it, is a form of birth control, in that it attempts to avoid procreation.

Perhaps lapsed Catholics like me should welcome the pope’s shuffle. At least it starts to undermine one of the Vatican’s least intellectually coherent positions: the thin end of a very long wedge. If this can change, what else might follow, if not under this ageing pontiff then his successor? We already have some married priests, converted from Anglicanism. What if the next pope, in response to a divine revelation to answer the shortage of vocations, decided that women could be ordained too? Where would Church of England refugees be then?

**Sex Law that Raises Age of Consent to 16 Not Protecting Youth Most at Risk: Study**

*Canadian Press, (11.16.2010) Camille Bains*

In a bid to prevent the sexual exploitation of adolescents by adults, Canada in 2008 raised the minimum age for legal consent to sexual relations from 14 to 16. However, 14- and 15-year-olds are much more likely to have sex with other youths within three years of their own ages—well inside the law’s five-year “close-in-age” exception. Children under 13, on the other hand, are at greatest risk of exploitation by adults, a new study shows.

The analysis was based on the 2008 British Columbia Adolescent Health Survey, which polled more than 29,000 students in grades seven through 12.

“The change in law isn’t going to change anything for them,” as Canadians under 13 years old were already protected, said Elizabeth Saewyc, a professor of nursing and adolescent medicine at the University of British Columbia. Just 2 percent to 3 percent of teens ages 14-15 at sexual debut had partners who were 20 years old or more. Among those who had sex at age 12 and younger, 39 percent had partners age 20 or older.

“We’re not seeing huge numbers of 14-year-olds, compared to 16-year-olds, having sex with adults,” Saewyc said. “The kids who are much more vulnerable to having sex with adults are 13, 12, and even younger. So that’s clearly an issue.”

The proportion of youth surveyed who reported having had sex before age 14 declined, from about 37 percent in 1992 to 19 percent in 2008, Saewyc said. Condom use rose among the sexually active.

The government could have protected youth more by raising awareness about the existing laws and better enforcing them, said Saewyc.

The study by Saewyc and colleagues was accepted for publication in volume 19 of the Canadian Journal of Human Sexuality (2010;19).

**National Institute of Mental Health Multisite Eban HIV/STD Prevention Intervention for African-American HIV Serodiscordant Couples**

*Archives of Internal Medicine Vol. 170; No. 17: P. 1594-1601, (09..2010) Nabila El-Bassel, DSW; John B. Jemmott, PhD; J. Richard Landis, PhD; Willo Pequegnat, PhD; Gina M. Wingood, ScD, MPH; Gail E. Wyatt, PhD; Scarlett L. Bellamy, ScD; for the NIMH Multisite HIV/STD Prevention Trial for African-American Couples Group*

Noting that rates of new HIV infections are seven times higher for African Americans than for white persons, the researchers undertook to determine whether couple-level efforts may be a promising intervention strategy.

A cluster randomized controlled trial (Eban) was conducted in four US cities—New York, Atlanta, Philadelphia, and Los Angeles—to determine if a behavioral intervention can reduce HIV/STD risk behaviors among HIV serodiscordant African-American couples. Eligibility requirements included both
partners being at least 18 years old, being aware of each other’s serostatus, and having had unprotected intercourse in the previous 90 days. In all, 1,070 participants were enrolled. Their mean age was 43; 40 percent of the males were HIV-positive.

The couples were randomized into one of two interventions: the couple-focused Eban HIV/STD risk reduction intervention, or attention-matched individual-focused health promotion comparison. The study’s primary outcomes were the promotion of condom-protected intercourse acts and cumulative incidence of STDs (chlamydia, gonorrhea or trichomonas). Data were collected before and after the intervention, and at six and 12 months.

Data were analyzed for 260 couples in the intervention group and 275 in the comparison group. At 12-month follow-up, 81.9 percent were retained. Generalized estimating equation analyses found the proportion of condom-protected intercourse acts was greater among intervention group couples (0.77) than among the comparison group (0.47; risk ratio, 1.24; 95 percent confidence interval 1.09 to 1.41, P=.006) after adjustment for baseline criterion measure. The adjusted percentage of couples consistently using condoms was higher in the intervention group (63 percent) than in the comparison group (48 percent, RR, 1.45; 95 percent CI, 1.24 to 1.70, P<.001) The adjusted mean number of (log) unprotected intercourse acts was lower in the intervention group than in the comparison group (mean difference, -1.52, 95 percent CI, -2.07 to -0.98; P<.001).

“The overall HIV seroconversion at the 12-month follow-up was five (two in the intervention group, three in the comparison group) of 535 individuals, which translates to 935 per 100,000 population,” the authors noted.

“The findings draw attention to an effective intervention strategy that may be scaled up to curb the magnitude and continued spread of HIV and other STDs,” the authors concluded. “Future studies must explore the generalizability of the findings to couples irrespective of serostatus and in settings where individuals and couples are not aware of their risks for HIV transmission but whose relationships can be supported as they learn to minimize the risks for themselves and each other. Moreover, the approach of engaging couples should be tested elsewhere in the United States and in other parts of the world, including sub-Saharan Africa, where sex-based power imbalances make it especially difficult for women in couples to reduce their risk of heterosexual exposure to HIV and other STDs.”

Anti-HIV drugs prevent HIV infection, trial shows – if you take them
Gus Cairns
Published: 23 November 2010
A randomised controlled trial has found that the HIV infection rate in HIV-negative gay men who were given a daily preventative pill containing two HIV drugs was reduced by 44%, compared with men given a placebo.

The efficacy in subjects who, by self-report and pill count, took the drugs more than 90% of the time was 73%.

The other big finding of the iPrEx (Pre-exposure Prophylaxis Initiative) trial was that while 93% of trial subjects reported taking the pills correctly, on the basis of drug level monitoring in blood tests, only 51% actually did so.

The investigators calculate that if participants had taken their pills every time, the efficacy of the drug regimen would have been at least 92%, compared with placebo.

The trial
The iPrEx trial gave identical pills containing either the antiretroviral (ARV) drugs tenofovir (Viread) plus FTC (emtricitabine, Emtriva), or a dummy placebo pill, to 2499 initially HIV-negative men who have sex with men at high risk of HIV infection, in nine cities in four continents. The men were told to take the pills once a day.

The trial subjects were told there was a 50% chance they might be taking a placebo and were therefore ‘instructed’ to maintain safer sex. The men paid study visits every four weeks during the two-year study. At every study visit they were tested for HIV, asked about their risk behaviour, given adherence and safer-sex counselling, and provided with condoms.

The subjects were followed for an average of 14 months between July 2007 and December 2009: 31% were followed for two years or more.
Who took part
Over 4900 subjects were screened, of whom 2406 were ineligible or never joined the study, 410 (8.5%) because they turned out already to have HIV. Patients with high liver enzyme or creatinine levels, indicating liver or kidney damage, were excluded.

The average age of the men enrolled was 27 and three-quarters classed themselves as Hispanic and/or of mixed race (participants could choose more than one category). Nineteen subjects (1%) classed themselves as female transgenders. Sixty-eight per cent came from Lima or Iquitos in Peru or Guayaquil in Ecuador: iPrEx was initially launched in these two countries and other study sites added later.

At screening the average number of sexual partners reported by trial subjects in the past three months was 18. Sixty per cent reported unprotected anal intercourse (UAI) in the last three months, 77.5% reported UAI with a partner of unknown HIV status in the last six months and 2.5% with a partner known to have HIV. Thirteen per cent tested positive for syphilis and 35% for genital herpes (HSV-2), for which they received treatment, as did all subjects with STIs. A third had already had hepatitis B and were immune and two-thirds were offered hepatitis B vaccine.

One notable finding was a high level of alcohol use in the trial subjects: over half (54%) had more than five alcoholic drinks per day.

Of note, the provision of safer-sex counselling and condoms worked: by the time of trial enrolment participants reported an average of seven partners in the last three months, and during the trial, this went down to two.

Safety
Few side-effects attributable to the study drug were observed. There was a higher level of nausea (9% versus 5%) in the first month in patients who took tenofovir/FTC, and the investigators advance this as a possible contributing factor to low adherence. Trial subjects gained weight, on average (due to maturing age in this young cohort), but in subjects on tenofovir/FTC the weight gain was delayed by three months relative to subjects on placebo. Nausea of grade 2 level or above (stronger or more long-lasting feelings of nausea) was experienced by 2% of the tenofovir/FTC group compared to 1% of the placebo group.

There were twice as many reports of raised creatinine levels in patients taking tenofovir, which is associated with kidney damage in a minority, though reports were rare: 25 (2%) in patients on tenofovir/FTC versus 14 (1%) on placebo. Five patients were taken off tenofovir/FTC due to raised creatinine levels but four of these re-started and creatinine levels did not rise again.

Resistance
During follow-up 110 men tested HIV antibody positive. It was subsequently found, by doing viral load tests on stored blood, that ten of these subjects actually had acute HIV infection at the time of recruitment, which was not detected using HIV antibody tests.

Doctors’ notes showed that at least seven of these ten subjects had symptoms suggestive of acute HIV infection.

Of the ten participants who had acute HIV infection at baseline, three (one taking placebo) had HIV that was resistant to FTC when they were tested at week four of the study. The one taking placebo clearly had transmitted drug resistance (he had AZT and NNRTI resistance too): one appears to have acquired FTC resistance due to taking the PrEP drugs with a lot of HIV in his body (he had a viral load of 10 million at baseline): and one had a very low viral load at enrolment and could not be given a resistance test, so we cannot say if he developed resistance in response to PrEP.

No-one in the trial developed resistance to tenofovir and none of the 100 people who became HIV-positive during the trial developed any drug resistance.

Efficacy
Of the 100 infected during follow-up, 36 infections occurred in men given tenofovir/FTC and 64 in men given placebo, yielding an overall efficacy of 44% (95% confidence interval, 15% to 63%; p = 0.005).

No HIV drug resistance was found in any subject who acquired HIV during follow-up.

On the basis of pill counts and self-reports, study subjects would have been judged as taking their pills at least 86% of the time and on average over 95% of the time.

In subjects reporting greater than 50% adherence, the efficacy of tenofovir/FTC was 50%. Efficacy in subjects reporting unprotected receptive anal intercourse at screening was 58%; in subjects reporting no receptive sex, efficacy was actually negative, indicating that PrEP may only make a significant difference to infection risk in the highest-risk men, namely ones who take the receptive role in unsafe sex.

Efficacy was also significantly greater than placebo in men reporting over 90% adherence (73% efficacy); aged over 25 (59%); with at least secondary education (54%); who took fewer than five alcoholic drinks a day (57%); who were circumcised (77%); and who did not have HSV-2 (54%).

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Adherence and drug levels
A surprise awaited researchers when they tested for drug levels. They did not do this with every trial subject but tested every subject who became infected with HIV and compared them with two uninfected, matched controls.

They found that drug levels were detectable in either the blood or cells of only 9% of subjects who became infected. But they also found that drug levels were detectable in only 51% of the HIV-negative controls, including 54% who reported over 50% adherence.

The drug level assays used could detect drug in the cells up to two weeks after a dose, indicating not only that far fewer subjects than reported were actually taking their pills, but that this was a long-term pattern and not caused by sporadically missing doses.

The investigators calculate on the basis of these figures that if all subjects had taken the study drug exactly as prescribed, the efficacy would be at least 92% and possibly up to 95%.

Why not only the poor efficacy, but the concealment of it? Other HIV prevention trials have shown that trial subjects adhere to their medication considerably less than they report. This may be influenced, the iPrEx investigators speculate, by knowledge that they may be on placebo or by side-effects. However qualitative surveys found that some of the participants found the style of adherence counselling “overbearing”, according to Principal Investigator Bob Grant, and a new non-directive style of adherence counselling will continue into the rollover study.

In pre-exposure prophylaxis, poor adherence is of concern because it might give rise to HIV drug resistance, although in this trial it appears that adherence in those who did acquire HIV was so low this did not happen.

An open-label rollover study, with all participants in the original study who wish to continue PrEP, will start in early 2011 and will report in 2013.

Conclusion
This is the first study to definitively prove that pre-exposure prophylaxis, as a concept, works. Under study conditions, it protected nearly half of a group of high-risk gay men who would otherwise have caught HIV. With good adherence, its likely efficacy would be considerably greater.

As such, especially in conjunction with the result of the CAPRISA 004 microbicide trial, is a major advance in the study of HIV prevention methods and potentially adds new prevention options.

Bob Grant commented: "I hope this will inspire and galvanise an active discussion in people who care about HIV prevention."

"We now have four positive signals on new methods of HIV prevention—circumcision, a vaccine, microbicides and now PrEP; we have the possibility of constructing an active portfolio of prevention methods for individuals, with the support of an engaged community."

"These were mainly young guys in the trials who were finding out who they were. These are the people PrEP will be useful for. We can say 'We want you to develop your own ways to protect yourself, but meanwhile, here's a pill that can maybe protect you while you're doing that.'"

For comments and interpretations of the iPrEx trial, see further reports.

Reference

New Medicare/Medicaid Rule Will Require Equal Hospital Visitation Rights for Same-sex Partners

SUMMARY: The federal Centers for Medicare and Medicaid Services (CMS) last week issued new rules for hospitals participating in Medicare and Medicaid, requiring them to allow patients to choose their own visitors, including same-sex partners. Prior to the rule change, some hospitals limited visitation only to blood relatives and legally married spouses.

Medicare Finalizes New Rules to Require Equal Visitation Rights for All Hospital Patients

New requirements empower patients to designate their own visitors, including a same-sex domestic partner

The Centers for Medicare & Medicaid Services (CMS) today issued new rules for Medicare- and Medicaid-participating hospitals that protect patients' right to choose their own visitors during a hospital stay, including a visitor who is a same-sex domestic partner.

"Basic human rights—such as your ability to choose your own support system in a time of need—must not be checked at the door of America's hospitals," said HHS Secretary Kathleen Sebelius. "Today's rules
help give 'full and equal' rights to all of us to choose whom we want by our bedside when we are sick, and override any objection by a hospital or staffer who may disagree with us for any non-clinical reason.”

The new rules follow from an April 15, 2010 Presidential Memorandum, in which President Obama tasked HHS with developing standards for Medicare- and Medicaid-participating hospitals (including critical access hospitals) that would require them to respect the right of all patients to choose who may visit them when they are an inpatient of a hospital. The President’s memorandum instructed HHS to develop rules that would prohibit hospitals from denying visitation privileges on the basis of race, color, national origin, religion, sex, sexual orientation, gender identity, or disability. It also directed that the rules take into account the need for a hospital to restrict visitation in medically appropriate circumstances.

The rules require hospitals to have written policies and procedures detailing patients' visitation rights, as well as the circumstances under which the hospitals may restrict patient access to visitors based on reasonable clinical needs.

A key provision of the rules specifies that all visitors chosen by the patient (or his or her representative) must be able to enjoy “full and equal” visitation privileges consistent with the wishes of the patient (or his or her representative).

The rules update the Conditions of Participation (CoPs), which are the health and safety standards all Medicare- and Medicaid-participating hospitals and critical access hospitals must meet, and are applicable to all patients of those hospitals regardless of payer source.

Among other things, the rules impose new requirements on hospitals to explain to all patients their right to choose who may visit them during their inpatient stay, regardless of whether the visitor is a family member, a spouse, a domestic partner (including a same-sex domestic partner), or other type of visitor, as well as their right to withdraw such consent to visitation at any time.

“These rules put non-clinical decisions about who can visit a patient out of the hands of those who deliver care and into the hands of those who receive it,” said CMS Administrator Donald Berwick, MD, MPP. "While we still have miles to go in making care more patient-centered, these rules make it easier for hospitals to deliver on some of the fundamental tenets of patient-centered care—care that recognizes and respects the patient as an individual with unique needs, who treated with dignity and granted the power of informed choice."

CMS finalized the rules based on thousands of comments from patient advocates, the hospital community, and other stakeholders. The rules will be effective 60 days after publication. More information about the rules is available on CMS’ website at www.cms.gov/CFCsAndCoPs/06_Hospitals.asp and www.cms.gov/CFCsAndCoPs/03_CAHs.asp.

11/23/10
Source

FDA Panel Recommends Gardasil HPV Vaccine for Preventing Anal Cancer in Men and Women

**SUMMARY:** An advisory panel of the U.S. Food and Drug Administration (FDA) last week recommended approval of Merck’s human papillomavirus (HPV) vaccine, Gardasil—active against HPV types 6, 11, 16, and 18—to prevent anal cancer and precancerous cell changes (anal intraepithelial neoplasia) in men and women. The vaccine is currently approved for prevention of cervical cancer in young women ages 9 to 26, and genital warts in both young women and men. The FDA’s Vaccines and Related Biological Products Advisory Committee based its decision on data from a study of men who have sex with men, concluding that women would likely benefit as well.

Below is an excerpt from a Merck press release announcing the recommendation.

**FDA Advisory Committee Supports Approval of Gardasil for Prevention of Anal Cancer and AIN in both Men and Women**

Whitehouse Station, NJ—November 17, 2010—Merck announced today that the U.S. Food and Drug Administration’s (FDA) Vaccines and Related Biological Products Advisory Committee has advised that the data presented support an indication for Gardasil [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant] for the prevention of anal cancer and anal intraepithelial neoplasia (AIN) in both males and females 9 through 26 years of age.

“We are pleased with the outcome of today’s meeting and look forward to continued discussions with the FDA as it evaluates the data for the proposed indication,” said Elizabeth Garner, MD, MPH, director,
clinical research, Merck Research Laboratories. "Today's discussion brings us closer to being able to also provide Gardasil to men and women for the prevention of anal cancer and AIN."

The Committee's input will be considered by the FDA in its review of the supplemental Biologics License Application (sBLA) that Merck submitted for Gardasil in early 2010. The FDA is not bound by the Committee's guidance, but takes its advice into consideration when reviewing vaccines.

The efficacy of Gardasil against HPV-related anal disease was studied in a population of men who have sex with men because of the known high risk of anal infection and disease that occurs in this group. Merck submitted the sBLA for use of Gardasil in both men and women because anal cancer affects both men and women and the disease is similar in both genders. Up to 90 percent of anal cancers are caused by HPV, with HPV 16 and 18 causing approximately 80 percent of those cases.

Gardasil is approved in the U.S. for use in girls and young women 9 through 26 years of age for the prevention of cervical, vulvar and vaginal cancers caused by HPV types 16 and 18; genital warts (condylomata acuminata) caused by HPV types 6 and 11; and precancerous or dysplastic lesions caused by HPV types 6, 11, 16 and 18. HPV types 16 and 18 account for approximately 75 percent of cervical cancer cases, and HPV types 6 and 11 account for approximately 90 percent of genital warts cases. GARDASIL is also approved in the U.S. for use in boys and men ages 9 through 26 years of age for the prevention of genital warts caused by HPV types 6 and 11.


Source

Vacc-4x Therapeutic Vaccine Significantly Reduces Viral Load after Stopping Antiretroviral Therapy

SUMMARY: Bionor Pharma announced last week that it would continue development of its candidate therapeutic HIV vaccine, known as Vacc-4x, after finding that people who took the vaccine had significantly lower viral loads after interrupting antiretroviral therapy (ART). The company had previously announced that it would halt development because the vaccine did not enable patients to stay off ART or maintain CD4 cell counts off treatment. Further analysis, however, showed that people assigned to receive Vacc-4x had HIV RNA levels 3 times lower than placebo recipients.

Below is an excerpt from a recent press release from Bionor describing the study and its findings.

Vacc-4x Shows Statistically Significant Reduction in Viral Load in Viral Load
Further analysis of Vacc-4x phase IIB study shows a statistically significant reduction in viral load over placebo—Bionor Pharma reverses decision to put Vacc-4x on hold
Oslo—November 18, 2010—After further analyses of the international, randomized, double-blind, placebo-controlled multi-center phase IIB study of Bionor Pharma’s therapeutic HIV-vaccine candidate, Vacc-4x, the company reports an unexpected statistically significant reduction in viral load (amount of HIV virus) at the end of the study period for patients on the vaccine compared to the placebo group.

The study was designed to test HIV-patients’ ability to stay off antiretroviral therapy (ART) after having been immunized with Vacc-4x. Although the study did not meet its primary endpoints, as announced October 1, the findings from the additional analysis discovered that treatment difference with regard to viral load was statistically significant both within the study period and when compared to the viral load prior to ever starting ART. In patients who received immunization, viral load never returned to its pre-ART level, which normally happens when being taken off ART.

Due to the new findings, the company has reversed its decision to stop development of Vacc-4x. Along with upcoming immunological data, these findings are expected to become the basis for the future positioning of Vacc-4x as a viable therapeutic HIV-vaccine.

As announced October 1, the Vacc-4x phase IIB study did not meet its two primary endpoints; i.e. no difference between the two groups with regard to the number of patients that needed resumption of ART nor any difference in immune cell (CD4) counts at the end of the ART-free period.

Still, the effect on viral load is by health authorities and most clinical experts seen as more important clinically for the treatment of HIV-patients than the effect on CD4 counts. Change in viral load between Vacc-4x and placebo during the study period was among the secondary endpoints in the phase IIB study. A statistically significant treatment difference with regard to viral load was found for the whole patient population (p=0.028), and a statistically significant effect was reproduced also in the sub-set of patients that did not resume ART (p=0.0012).
Additional support for the effect of Vacc-4x on viral load has come from a pooled post-hoc analysis including pre-ART viral loads. Pre-ART level is an important set-point since viral load normally migrates back to this level after ART interruption. Company researchers discovered on further review that patients blinded and randomly assigned to Vacc-4x treatment group had a pre-ART viral load three times higher than that of patients assigned to the placebo group. The study showed that viral load in patients who received immunization never returned to its pre-ART level. A statistically significant reduction in viral load from the pre-ART level (0.55 log, p=0.0003) was found in patients treated with Vacc-4x compared to a non-statistically significant reduction in viral load (0.08 log, p=0.89) in patients in the placebo group.

"These follow up findings on viral load reduction in the Vacc-4x arm compared to placebo are positive and very encouraging," says Professor Dr. med. Jurgen Rockstroh, Oberarzt an der Medizinischen Universitatsklinik, Innere-Rheuma-Tropen Ambulanz, Bonn, Germany. "It is therefore important in follow on studies to investigate whether Vacc-4x in combination with ART could reduce the viral set-point and allow extended periods without HIV medicine."

"Patients starting on antiretrovirals see the viral load effectively reduced, but this is dependent on daily treatment, and we know that HIV remains in the reservoirs," said Richard Pollard MD, Division Chief of Infectious Disease, University of California Davis Center for AIDS Research, Education, and Services and the principle investigator in the trial. "A therapeutic HIV vaccine like Vacc-4x reducing the viral load set-point, could have significant implications for future HIV management used in combination with ART. More research is needed to confirm this hypothesis."

"I am pleased to see that immunization with Vacc-4x, a candidate therapeutic vaccine under clinical development, has shown the ability to reduce virus levels in blood of chronically HIV infected patients," said Professor Giuseppe Pantaleo, Professor of Medicine, Chief Division of Immunology and Allergy and Head of the Laboratory of AIDS Pathogenesis, Department of Medicine, Centre Hospitalier Universitaire Vaudois, University of Lausanne, Lausanne, Switzerland. "These results are important since they indicate that better virus control may be achieved through immunological intervention. Vacc-4x through a different antiviral mechanism may represent a novel intervention to complement antiviral therapy."

"The new analysis gives indications that Vacc-4x has an important effect on viral load despite the failure to reach our primary endpoints in the phase Iib study," said Bionor Pharma CEO Henrik Lund. "While post-hoc analyses are subject to statistical limitations, they are commonly used in vaccine trials due to the complex nature of data interpretation."

"The full immunological analysis and long term data will give us a better basis for evaluating the outcome and implications for the positioning of Vacc-4x as a therapeutic product for HIV-patients. A possible application of Vacc-4x is a combination therapy with repeated ART-Vacc-4x together with analytical treatment interruptions in order to establish a functional cure."

Source

Gonorrhea Rate at an All-Time Low, but Syphilis and Chlamydia Rates Continue to Rise
In 2009, new cases of sexually transmitted disease in the United States numbered about 19 million and cost the health care system $16.4 billion, according to CDC's annual summary.

The number of reported cases of gonorrhea, 301,174, produced the lowest rate since CDC began tracking the disease in 1941, 99.1 per 100,000 people. The highest rate was reported in the South. Among men, the highest rates were in those 20-24; among women, the rates were highest among those 15-24.

Chlamydia cases reported to health officials in 2009 totaled 1,244,180, “the largest number of cases ever reported to CDC for any condition,” the report says. Chlamydia diagnoses climbed 3 percent from the previous year and 19 percent from 2006. Increased screening, rather than an increase in actual morbidity, is believed responsible for the jump. CDC estimates that the number of reported cases reflects about half the actual morbidity.

Syphilis is continuing a comeback after the rate dropped in 2000 to the lowest level recorded since 1941, when reporting began. The 13,997 primary and secondary cases reported in 2009 represent an increase of 5 percent from the preceding year and an increase of 59 percent since 2005.
Cases of congenital syphilis have climbed since the historic low of 339 reported in 2005. The 2009 figure reached 427.

Racial and ethnic disparities persist even as progress is being made against STDs:

- The gonorrhea rate among blacks and Hispanics is 20 times and 10 times that of whites, respectively.
- The rate of chlamydia in black men is 12 times that of the rate in white men; among black women, the rate is eight times that of white women.
- Syphilis also shows racial disparities, with a rate among blacks nine times that of whites. However, this gap has narrowed from a 24-fold difference between blacks and whites observed in 1999.

**UN Sees Global AIDS Epidemic Starting to Turn**

*Reuters* (11.23.2010) Kate Kelland

Global HIV incidence fell 19 percent between 1999 and 2009, and the decline exceeded 25 percent in 33 countries, including 22 in sub-Saharan Africa, UNAIDS said in its annual AIDS Epidemic Update. At least 56 countries either have stabilized or significantly reduced HIV incidence, UNAIDS reported.

An estimated 33.3 million people worldwide have HIV, the agency said. In 2009, 5.2 million people with HIV in poorer countries were receiving treatment, or 36 percent of the 15 million developing-world citizens in need of antiretroviral therapy. An additional 1.2 million people began ARVs last year. However, for every person starting antiretroviral therapy, two people were newly infected with HIV.

"Just a few years ago, there were five new infections for every two people starting treatment," said Michel Sidibe, executive director of UNAIDS. "We are closing the gap between prevention and treatment."

The result was fewer AIDS-related deaths last year, about 1.3 million in sub-Saharan Africa, where 1.8 million people became newly infected with HIV. In addition, a trend analysis shows an overall decline in the percentage of people with more than one sexual partner in the last year in sub-Saharan Africa.

Last year, 370,000 mother-to-child HIV transmissions occurred, down 24 percent from five years ago, UNAIDS said. Rapid expansion of mother-to-child HIV prevention programs has been hindered by inadequate access to ante- and post-natal services, reported the agency.


**HIV Inmate Deprived of Care, Suit Says: ACLU Says Case Reflects Pattern of Failure at City Jails**

*St. Louis Post-Dispatch* (11.19.2010) Valerie Schremp Hahn

An HIV-positive inmate received substandard care at a St. Louis jail, including 17 days without his medication, charges a suit filed on his behalf by the American Civil Liberties Union of Eastern Missouri.

The man, known in court documents as John Doe, is in his late 40s. He was arrested in March 2010 and released this month. Prison officials knew of his condition, and the physician who had treated him successfully before incarceration faxed to the jail details about his medication regimen, the suit says.

The suit named as defendants the city, vendor Correctional Medical Services, jail superintendent Eugene Stubblefield, and Drs. Brenda Mallard and Susan Singer of CMS. The current case is indicative of a pattern of poor care at St. Louis' Justice Center downtown and the Medium Security Institution on Hall Street, the suit says.

"It’s inexcusable, and it’s serious," ACLU Legal Director Tony Rothert said.

A spokesperson for the city rejected the premise of the suit. "Contrary to the claims of the ACLU, the records of the inmate in question reflect that he received adequate medical care consistent with his constitutional rights," Deputy City Counselor Nancy Kistler said.

In a 2009 report, the ACLU charged the jails with inmate abuse, providing inadequate medical attention, falsification of reports, and unsanitary conditions.

**Teens Should Teach Adults About Safe Sex**

*USA Today* (11.19.2010) Joyce King

"... An Indiana University study published last month in the Journal of Sexual Medicine examined the habits of almost 6,000 people ages 14 to 94. Forget the ‘teens gone wild’ stereotypical thinking. The statistics that give pause are unmarried adults:

- 91 percent of men older than 50 do not use condoms for sex with a date or casual acquaintance.
- 70 percent of men over 50 do not use condoms when having sex with someone they just met.
- Some men and women over 50 didn’t use condoms even when they knew that they or their partner had an STD. By comparison, 80 percent of sexually active teen boys and 69 percent of teen girls’
partners used condoms during their most recent encounters. Researchers say this proves kids are getting the 'safe sex' message.

"Why such reckless behavior among older people? According to Debra Herbenick, associate director of the Center for Sexual Health Promotion at Indiana University, Boomers didn't come of age with pervasive messages about condoms. ...

"Public campaigns on condom use and safe sex should begin to target older folks. But Herbenick says health care providers can also play a role by asking patients about all aspects of their sexual lives.

"University of Texas psychologists David Buss and Cindy Meston have conducted several studies, including 'Why Women Have Sex,' which looked at the habits of more than 1,000 women ages 18-86 from every racial group. With women over 30 expressing a greater desire for sex, Buss noted it's possible that the onus for increased condom use, as with birth control in the past, may fall disproportionately to women. ...

"... As hard as I've preached to my 18-year-old son Brandon about behavior, condoms, abstinence, and the stigmas associated with STDs, it's a tad awkward these days as he somewhat jokingly returns the advice to his post-divorce mom. Turnabout is fair play, especially when adults aren't taking their own advice."

The author is a freelance writer in Dallas.

**Pope's Male Prostitute Becomes Female in Translation Mix-Up**

*Agence France Presse*, (11.22.2010)

Vatican sources on Monday cleared up some confusion regarding remarks by Pope Benedict XVI concerning HIV and the use of condoms. In a series of interviews published in his native German, Benedict said condom use may be justified in certain cases, “for example when a male prostitute uses a condom.” However, a lexical error in the Italian version switched the gender of the prostitute from male to female. The mistake reportedly was spotted as the first interview extracts were published Saturday in the Vatican's L'Osservatore Romano newspaper. Sources blamed the error on a rush to translate the remarks into Italian. Vatican experts said the mistranslation did not alter the substance of Benedict's remarks, though the issue prompted wide speculation about why the pope had chosen to specify a male prostitute.

Luigi Accattoli of the Corriere della Sera daily said the pontiff's example of a male prostitute was a "nonconformist" move in line with his character.

**Virginia Tech engineers introduce thermotherapy as a chemotherapy alternative**

Using hyperthermia, Virginia Tech engineering researchers and a colleague from India unveiled a new method to target and destroy cancerous cells. The research was presented at the 63rd annual meeting of the American Physical Society Nov. 23 in Long Beach, Calif.

The cancer treatment uses hyperthermia to elevate the temperature of tumor cells, while keeping the surrounding healthy tissue at a lower degree of body heat. The investigators used both in vitro and in vivo experiments to confirm their findings.

The collaborators are Monrudee Liangruksa, a Virginia Tech graduate student in engineering science and mechanics, and her thesis adviser, Ishwar Puri, professor and head of the department, along with Ranjan Ganguly of the department of power engineering at Jadavpur Univesity, Kolkata, India.

Liangruska of Bangkok, Thailand, presented the paper at the meeting.

In an interview prior to the presentation, Puri explained that to further perfect the technique they used ferrofluids to induce the hyperthermia. A ferrofluid is a liquid that becomes strongly magnetized in the presence of a magnetic field. The magnetic nanoparticles are suspended in the non-polar state.

"These fluids can then be magnetically targeted to cancerous tissues after intravenous application," Puri said. "The magnetic nanoparticles, each billionths of a meter in size, seep into the tissue of the tumor cell due to the high permeability of these vessels."

Afterwards, the magnetic nanoparticles are heated by exposing the tumor to a high frequency alternating magnetic field, causing the tissue's death by heating. This process is called magnetic fluid hyperthermia and they have nicknamed it thermotherapy.

"Temperatures in the range of 41 to 45 degrees Celsius are enough to slow or halt the growth of cancerous tissue. However, without the process of magnetic fluid hyperthermia, these temperatures also destroy healthy cells."

"The ideal hyperthermia treatment sufficiently increases the temperature of the tumor cells for about 30 minutes while maintaining the healthy tissue temperature below 41 degrees Celsius," Puri said. "Our
ferrofluid-based thermotherapy can be also accomplished through thermoablation, which typically heats tissues up to 56 degrees C to cause their death, coagulation, or carbonization by exposure to a noninvasive radio frequency, alternating current magnetic field. Local heat transfer from the nanoparticles increases the tissue temperature and ruptures the cell membranes."

Puri added that testing showed iron oxide nanoparticles are "the most biocompatible agents for magnetic fluid hyperthermia." Platinum and nickel also act as magnetic nanoparticles but they "are toxic and vulnerable" when exposed to oxygen.

The researchers plan to test their analytical approach by conducting experiments on various cancer cells in collaboration with Dr. Elankumaran Subbiah of the Virginia-Maryland School of Veterinary Medicine. A senior design team consisting of five engineering science and mechanics undergraduate Virginia Tech students is fabricating an apparatus for these tests.

**Bacteria Help Infants Digest Milk More Effectively Than Adults**

ScienceDaily (Nov. 24, 2010) — Infants are more efficient at digesting and utilizing nutritional components of milk than adults due to a difference in the strains of bacteria that dominate their digestive tracts.

Researchers from the University of California, Davis, and Utah State University report on genomic analysis of these strains in the November 2010 issue of the journal *Applied and Environmental Microbiology* identifying the genes that are most likely responsible for this difference.

"Human milk oligosaccharides (HMOs) are the third-largest solid component of milk. Their structural complexity renders them non-digestible to the host," say the researchers. "*Bifidobacterium longum* strains often predominate the colonic microbiota of exclusively breast-fed infants. Among the three recognized subspecies, *B. longum subsp. infantis* achieves high levels of cell growth on HMOs and is associated with early colonization of the infant gut."

In the study the researchers used whole-genome microarray comparisons to associate genotypic biomarkers among 15 *B. longum* strains exhibiting various HMO utilization patterns. They identified 5 distinct gene clusters on *B. longum* that were conserved (showed little or no variation) across all strains capable of growth on HMOs and have also diverged in strains incapable of growing on HMOs.

The results of this study suggest that *B. longum* has at least 2 distinct subspecies: *B. longum subsp. infantis*, adapted to utilize milk carbon and found primarily in the digestive tract of children, and *B. longum subsp. longum*, specialized for plant-derived carbon metabolism and associated with the adult digestive tract.

"Although early gut colonization is likely dependent on a multitude of dietary and nondietary factors, the delivery of complex oligosaccharides through milk creates an ideal and unique nutrient niche for the establishment of, and colonization by, *B. longum subsp. infantis* strains," say the researchers. "During weaning, a gradual transitioning from milk-based to plant-based diets generates a shift in carbon availability in the gastrointestinal tract favorable for the expansion and formation of an adult-like gastrointestinal tract microbiota."

**Journal Reference:**

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**Haiti cholera spreading faster than predicted, UN says**

The cholera epidemic in Haiti is spreading twice as fast as had been estimated and is likely to result in hundreds of thousands of cases in the coming months, the UN says.

The UN's humanitarian co-ordinator for Haiti, Nigel Fisher, said aid agencies would have to "ratchet up" their response and send more medical staff.

The Haitian government says 1415 people are confirmed to have died.

The epidemic has complicated preparations for elections next Sunday.

Mr Fisher said more than 200,000 cases of infection could be recorded in the first three months instead of six months as first estimated.

"This epidemic is moving faster and we are in unknown territory in Haiti just because this is moving so fast. There is no immunity to it", he said.
Mr Fisher added that the Haitian government would have to increase pressure on local authorities to find places for more treatment centres and to dispose of bodies.

There has been some opposition to the placing of treatment centres from residents who fear they could bring the infection into their neighbourhoods.

The UN under-secretary for humanitarian affairs, Valerie Amos, who is visiting Haiti, told the BBC there was an urgent need to train Haitian health workers, who have no previous experience of dealing with cholera.

"We need to get the message out there to the people that this is something that can be dealt with. We need to make sure they know about hand-washing and proper sanitation, and we need to get supplies in", she said.

‘Whoonga’ Drug: A New Twist in South Africa’s AIDS War

Drug users in South Africa’s KwaZulu-Natal province are diverting antiretroviral pills intended for AIDS patients and mixing them in illicit concoctions to get high, authorities and health experts say. So far, the practice of smoking the ARV-laced mixture called “whoonga” has been limited to the eastern part of the province. AIDS and addiction specialists hope it does not spread.

KwaZulu-Natal police first noticed whoonga two or three years ago, when gangs began stealing ARVs from patients as they left hospitals, said Vincent Ndunge, a police spokesperson. Users initially smoked the crushed ARVs, but later began adding other substances, he said. Marijuana is one preferred component.

Some patients sell their ARVs for use in whoonga, and AIDS clinics also have been robbed, said Carol du Toit of South Africa’s National Council on Alcoholism and Drug Dependence. Staff members of her private organization are seeing an increase in whoonga users, with many testing positive for heroin.

Whoonga users may be getting high from some other ingredient in the mix rather than from the ARVs, suggests Dr. Njabulo Mabaso, an AIDS expert. Drug dealers have been suspected of cutting their whoonga with many substances, including soap powder and rat poison, to stretch their supply. There is no evidence that ARVs are addictive per se or enhance the marijuana high.

“We are seeing the use of whoonga in communities and it’s very widespread,” said Lihle Dlamini of the Treatment Action Campaign advocacy group. Dealers “are taking this treatment that is supposed to assist people living with HIV and abusing it,” she said.

“The main problem is unemployment,” said Thokozani Sokhulu, who founded “Project Whoonga” this year to help rehabilitate users and help them find jobs or training. “It’s when they’re hanging around all day with nothing to do—that’s when they get hooked.”

Treating Prisoners While Jailed Could Stop Disease

More resources for prison medical care would reduce health crises among prisoners and help protect the health of the general population when prisoners are released, researchers said in new study.

“Prisoners act as reservoirs of infection and chronic disease, increasing the public health burden of poor communities,” wrote Seena Fazel, of the University of Oxford, and James Baillargeon, of the University of Texas Medical Branch.

The United States has about one-quarter of the world’s 10 million prisoners and the world’s highest rate of imprisonment, 756 per 100,000 people, compared to 145 per 100,000 worldwide.

The researchers highlighted conditions such as substance abuse and communicable diseases such as HIV and TB, which are far more prevalent in prison populations than in the community as a whole. Key findings include:

- Among 75 low- and middle-income countries, 20 had an HIV prevalence rate greater than 10 percent in their prison populations.
- The proportional share of the US HIV epidemic borne by prisoners dropped 29 percent between 1997 and 2006. Possible explanations include a lower rate of HIV among those entering the prison system, declining HIV infection among intravenous drug users, and more discharge planning programs for HIV-positive prisoners.
- Chronic hepatitis B infects about 1.0 percent to 3.7 percent of US prisoners, compared to 0.4 percent to 0.5 percent of the general population. Hepatitis C among US prisoners is estimated at 23 percent to 34 percent.
• Sexual networks were the predominant means of HIV transmission among one study of US male inmates, though tattooing also was a factor.
• Federal and state prisons in the US had tuberculosis rates of 29.4 and 24.2 cases per 100,000 prisoners, compared to 6.7 cases per 100,000 in the community.

The researchers recommended:
• Increased resources for prison health care
• Transferring responsibility for prison health care from criminal justice systems to public health systems
• Screening prisoners for physical and mental illness
• Making prison health statistics available to the public
• Developing national prison health care guidelines and policies to alleviate unhealthy living conditions
• Improving discharge planning and linkages to community health resources
• Ending policies that exclude prisoners from clinical studies.

"Finally, the medical profession should take the lead in reforming prison health care, even if this reform means refusing to send prisoners who are in hospital back to prison, where they will suffer inhuman and degrading treatment," the authors wrote.

The study, "The Health of Prisoners," was published in the Lancet (2010; doi:10.1016/S0140-6736(10)61053-7).

Researchers Uncover Insulin Resistance Link

Reuters (11.23.2010)
Researchers at St. Louis’ Washington University (WU) may have shed light on how protease inhibitors could contribute to insulin problems seen in some patients.

In mouse studies, researchers at WU’s School of Medicine found that the first-generation protease inhibitor ritonavir appears to inhibit a key mechanism known as glucose transporter 4, a protein that transports glucose to cells that need it. In mice genetically altered to lack the glucose transporter, known as GLUT4, the introduction of ritonavir did not exacerbate the observed glucose intolerance. In control mice, however, ritonavir did impair glucose tolerance.

Similarly, ritonavir reduced peripheral insulin sensitivity in control mice but not in mice lacking GLUT4.

“Now that we’ve identified the main mechanism, we will look to develop new drugs that treat HIV but don’t cause diabetes,” said Paul Hruz, a WU professor of pediatrics and biology who led the team.


Health Inquiry: Negligence Led to Hepatitis B Scare

Charleston Gazette (W.V.) (11.20.2010) Veronica Nett
Negligence helped fuel a hepatitis B outbreak at a free dental clinic last summer that infected five people, West Virginia health officials said last week.

The confirmed cases of three patients and two volunteers were among seven originally linked to the clinic. Health officials this past June notified 1,137 patients and 826 volunteers they may have been exposed to hepatitis B at the Mission of Mercy Dental Clinic in Hedgesville June 26 and 27, 2009.

No new infections have been found since the initial outbreak. After patients and volunteers were notified of their potential exposure, 388 people were tested and 115 vaccinations were administered. Some 181 people participated in a Berkeley County Health Department clinic in June to test for hepatitis B, C, and HIV.

Volunteers at the clinic hailed from Virginia, Pennsylvania, Maryland, Kentucky, Ohio, and Washington, D.C. Dental students from West Virginia University, Marshall University, and Shepherd University also volunteered.

Vicki Hogan, a hepatitis B epidemiologist with the state Bureau of Public Health, told attendees at the 2010 West Virginia Public Health Symposium that intensive investigation did not uncover exactly how the five were infected, but did identify several breaches of protocol:
• Dental workers did not properly document what procedures were performed on patients, by whom and at what station.
• Patients received multiple, back-to-back procedures, although they were supposed to receive only one per day.
In some instances, volunteers would wipe their faces or mouths with their hands and not change their gloves, according to patient reports.

Hand-washing facilities were in short supply, and a suction machine used in people's mouths was found to backflow.

To combat the sweltering temperatures in the school gym where the clinic was held, organizers installed large fans that may have dispersed blood and other fluids through the air.

An Answer to a Longstanding Question: How HIV Infection Kills T Cells

ScienceDaily (Nov. 24, 2010) — Researchers appear to have an explanation for a longstanding question in HIV biology: how it is that the virus kills so many CD4 T cells, despite the fact that most of them appear to be "bystander" cells that are themselves not productively infected. That loss of CD4 T cells marks the progression from HIV infection to full-blown AIDS, explain the researchers who report their findings in studies of human tonsils and spleens in the Nov. 24 issue of Cell, a Cell Press publication.

"In [infected] primary human tonsils and spleens, there is a profound depletion of CD4 T cells," said Warner Greene of the Gladstone institute for Virology and Immunology in San Francisco. "In tonsils, only one to five percent of those cells are directly infected, yet 99 percent of them die."

Lymphoid tissues, including tonsils and spleen, contain the vast majority of the body's CD4 T cells and represent the major site where HIV reproduces itself. And it now appears that those dying T cells aren't bystanders exactly.

The HIV virus apparently does invade those T cells, but the cells somehow block virus replication. It is the byproducts of that aborted infection that trigger an immune response that is ultimately responsible for killing those cells.

More specifically, when the virus enters the CD4 T cells that will later die, it begins to copy its RNA into DNA, Greene and his colleague Gilad Doitsh explain. That process, called reverse transcription, is what normally allows a virus to hijack the machinery of its host cell and begin replicating itself. But in the majority of those cells, the new findings show that the process doesn't come to completion.

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The cells sense partial DNA transcripts as they accumulate and, in a misguided attempt to protect the body, commit a form of suicide. Greene says that completed viral transcripts in cells that are productively infected probably don't provoke the same reaction because they are so rapidly shuttled into the nucleus and integrated into the host's own DNA.

The researchers narrowed down the precise "death window" of those so-called bystander cells by taking advantage of an array of HIV drugs that act at different points in the viral life cycle. Drugs that blocked viral entry or that prevented reverse transcription altogether stopped the CD4 T cell killing, they report. Those drugs that act later in the life cycle to prevent reverse transcription only after it has already begun did not save the cells from their death.

Those cells don't die quietly either, Greene says. The cells produce ingredients that are the hallmarks of inflammation and break open, spilling all of their contents. That may provide a missing link between HIV and the inflammation that tends to go with it. "That inflammation will attract more cells leading to more infection," Greene said. "It's a vicious cycle."

The findings also show that the CD4 T cells' demise is a response designed to be protective of the host. All that goes awry in the case of HIV and "the CD4 T cells just get blown away," compromising the immune system.

Greene said that all the available varieties of anti-HIV drugs will still work to fight the infection by preventing the virus from spreading and reducing the viral load.

The findings may lead to some new treatment strategies, however. For instance, it may be possible to develop drugs that would act on the cell sensor that triggers the immune response, helping to prevent the loss of CD4 T cells. His team plans to explore the identity of that sensor in further studies. They also are interested to find out if the virus has strategies in place to try and prevent the CD4 T cells' death.

"The cell death pathway is really not in the virus's best interest," Greene says. "It precludes the virus from replicating and the virus may have ways to repel it."

Journal Reference:
Mistakes Still Prevalent in Hospital Care, Study Finds

By DENISE GRADY

Efforts to make hospitals safer are falling short, researchers report, in the first large study in a decade to analyze harm from medical care and track it over time.

The study, in 10 North Carolina hospitals, found that harm to patients was common and did not decrease from 2002 to 2007. The most common problems included complications from procedures or drugs, followed by hospital-acquired infections.

“It is unlikely that other regions of the country have fared better,” said Dr. Christopher P. Landrigan, the first author of the study and an assistant professor at the Harvard Medical School.

The study is one of the most rigorous efforts to collect data about patient safety since a landmark report in 1999 stated that medical mistakes caused 44,000 to 98,000 deaths and more than 1 million injuries a year in the United States. The 1999 report, by the Institute of Medicine, sparked a national movement to reduce errors and make hospital stays less hazardous to patients’ health.

Dr. Landrigan’s team focused on North Carolina as the best place to look for improvements because its hospitals, compared with those in other states, have been more involved in programs to increase patient safety.

But instead of improvements the researchers found a high rate of problems, with no change over time. About 18 percent of patients were harmed by medical care, some more than once, and 63.1 percent of the injuries were judged preventable. The most common problems included complications from procedures or drugs, followed by hospital-acquired infections. Most of the problems were temporary and treatable, but some were serious and a few, 2.4 percent, caused or contributed to a patient’s death.

The findings were a disappointment but not a real surprise, Dr. Landrigan said, adding that a major reason for the problems was the failure of many hospitals to use measures proven to avert mistakes and prevent infections from urinary catheters, ventilators and lines inserted into veins and arteries.

“Until there is a more coordinated effort to implement those strategies proven beneficial, I think that progress in patient safety will be very slow,” he said. The study is being published on Thursday in The New England Journal of Medicine.

An expert on hospital safety who was not associated with the study called the findings a wake-up call to the patient safety movement.

“We need to do more, and to do it more quickly,” said the expert, Dr. Robert M. Wachter, the chief of hospital medicine at the University of California, San Francisco.

A recent government report had similar results, finding that in one month, 13.5 percent of Medicare beneficiaries—134,000 patients—experienced “adverse events” during hospital stays, and that extra hospital costs to repair the damage could reach several billion dollars a year. In 1.5 percent of beneficiaries—15,000 patients in one month — adverse events contributed to their deaths. The report, issued earlier this month by the inspector general of the Department of Health and Human Services, was based on an analysis of Medicare patients discharged from hospitals in one month, October 2008.

Dr. Landrigan’s study reviewed the records of 2,341 patients admitted to 10 hospitals — urban, rural, large, small, teaching and non-teaching. (The hospitals were not named.) The researchers used a “trigger tool,” a list of 54 items regarded as red flags in a patient’s record, indicating that something might have gone amiss. Triggers included certain drugs used only to reverse an overdose, for instance, the presence of bedsores or readmission to the hospital within 30 days of being sent home.

The researchers found 588 instances in which a patient was harmed by medical care, or 25.1 injuries per 100 admissions.

Not all the problems were serious. Most were temporary and treatable, like a bout with low blood sugar or a urinary infection from a catheter. But 42.7 percent required extra time in the hospital, like an infected surgical site. In a few cases, 2.9 percent, patients suffered permanent injury — for example, brain damage from a post-operative stroke that could have been prevented. Certain problems (8.5 percent) were life-threatening, like severe bleeding during surgery. A small number, 2.4 percent, caused or contributed to a patient’s death—such as bleeding and organ failure after surgery, or pneumonia caused by inhaling food, saliva or stomach contents.

“A third of the errors in the intensive care unit disappear when residents work 16 hours or less,” Dr. Landrigan said, but noted that senior residents are still allowed to work longer.
Computerized systems for ordering drugs can cut medication errors by 50 percent to 80 percent, by correcting doses and alerting doctors if they request a drug that a particular patient should not take, Dr. Landrigan said—but only 17 percent of hospitals have those computer systems.

For the most part, reporting adverse events is voluntary.

“At a national level, we need a monitoring system that is mandatory,” Dr. Landrigan said. “There has to be some mechanism for federal-level monitoring where hospitals across the country are held to it, and it’s not just a voluntary thing. We don’t have it. Voluntary reporting vastly underestimates the frequency of errors and injuries that occur.”

Dr. Mark R. Chassin, president of the Joint Commission, which accredits hospitals, cautioned that the study was limited by its ability to find only the types of problems on its list of “triggers.” So if a hospital had performed a completely unnecessary operation, but had done it well, the study probably would not have uncovered that, he said. Similarly, he said, the study would not have found areas where many hospitals have made progress, such as in making sure that patients who had heart attacks or heart failure were sent home with the right medicines.

The bottom line, he said, “is that preventable complications are way too frequent in American health care, and it’s not a problem we’re going to get rid of in 6 months or a year.”

Dr. Wachter said: “The study is telling us how hard improving safety really is. Process changes, like a new computer system or the use of a checklist, may help a bit, but if they are not embedded in a system in which the providers are engaged in safety efforts, educated about how to identify safety hazards and fix them, and have a culture of strong communication and teamwork, progress may be painfully slow.”

Leah Binder, the chief executive officer of The Leapfrog Group, which includes large employers trying to improve health care, said that more open reporting was essential.

“Having to be transparent, and to allow yourself to be compared to other hospitals, can have an effect,” Ms. Binder said. “What we know works in a general sense is a competitive open market where consumers can compare providers and services. Right now you ought to be able to know the infection rate of every hospital in your community.”

For hospitals with poor scores, there should be consequences, Ms. Binder said: “And the consequences need to be the feet of the American public.”

Claims that phylogenetic analysis can prove direction of transmission are unfounded, say experts
Edwin J. Bernard
Published: 24 November 2010

A report from the United States published last week in the Proceedings of the National Academy of Sciences claims to show for the first time that direction of HIV transmission from one individual to another for use as evidence in criminal trials can reliably be established by phylogenetic analysis. However, international experts in phylogenetics who have acted as forensic advisors in criminal courts tell aidsmap.com that the report “draws unwarranted conclusions”.

The report, co-authored by Michael Metzker, associate professor at the Baylor College of Medicine Human Genome Sequencing Center and David Hillis, a professor of evolutionary biology at the University of Texas, details the phylogenetic analysis methodology used in two criminal HIV transmission cases in the United States, in Washington State in 2004 and Texas in 2009, respectively.

These cases were only the second and third times that phylogenetic analysis was used as evidence in a criminal prosecution in the United States, despite at least 350 convictions under HIV-specific and/or general criminal laws for HIV non-disclosure, alleged exposure and/or transmission since prosecutions began in the mid-1980s (CHLP, 2010). Of note, both of these cases involved allegations of multiple heterosexual transmissions from a single source. Such allegations are extremely rare in criminal cases.

Phylogenetic analysis requires the use of complex computational tools to create a hypothetical diagram (known as a phylogenetic tree) that estimates how closely related the samples of HIV taken from the complainant(s) and defendant are likely to be in comparison to other samples.

The report refers to several recent studies (including a 2008 study from Keele and colleagues) which suggest to the authors that a “significant genetic bottleneck” may occur during HIV transmission, and that at least three-quarters of infections may result from a single virus. It also notes that since HIV evolves rapidly following initial infection, this results in “increased diversity of HIV sequences within a newly infected individual.”
However, the report argues that if blood samples are taken from the accused and complainant(s) "shortly after a transmission event" the population of viral sequences in one individual would be expected to be more closely related to the population in the other(s) than other populations of viral sequences used for comparison. This is known as a "paraphyletic relationship." The paper then suggests that "paraphyly provides support for the direction of transmission and, in a criminal case, could be used to identify the index case (i.e., source)."

In both cases, the investigators were blinded as to the identity of the accused and the complainants, which was only revealed in court once they had provided their report to the prosecution. Again, in both cases, the sample they identified as being the source of infection was that of the accused. It is unknown how much weight the judge and jury gave to the phylogenetic reports, but it is known that the prosecution provided a great deal of supporting evidence — including, in the Texas case, contact tracing and HIV testing of most of the complainants' prior sexual partners — and that it was the totality of such evidence that led to guilty verdicts and lengthy prison sentences in both cases.

The paper and its assertions have been widely disseminated via a press release and several articles primarily aimed at the scientific community. Such articles include quotes from the investigators that suggest their methods are unquestionably sound and it was this evidence alone that led to the guilty verdicts. "This is the first case study to establish the direction of transmission," Professor Metzker was quoted in an AFP story with the headline 'Lab detectives use science to nab HIV criminals'.

He asserted to the American Statesman that "[our analysis] provided sound scientific evidence of the direction of transmission, and from that we could identify the source." The article also quotes the main prosecutor in the Texas case, who characterises phylogenetic analysis as "good evidence". Of note, the defence attorney in the case is quoted as saying they were unable to find an expert to testify in court against the reliability of Hillis and Metzker's findings.

"It made a lot of difference in trying the case because we couldn't find an expert on our side," he said. However, Professor Metzker's claims and the paper's assertion that he and his colleagues have established that their methodology is both a new and reliable method of proving the direction of transmission has been questioned by several international experts contacted by aidsmap.com. All of the experts have served as witnesses in criminal trials outside of the United States.

These experts all agree that phylogenetic analysis remains an informed but sometimes imperfect estimate of the relationship between viruses. Although there are a variety of methods by which it is possible to increase the confidence that the samples are very closely related in comparison to other samples, there could never be complete confidence that the defendant infected the complainant(s) based on phylogenetic analysis alone.

Anne.Mieke Vandamme, a professor at Leuven Catholic University and Rega Institute in Belgium, has serious reservations regarding the paper's assertions. "This paper draws unwarranted conclusions," she tells aidsmap.com. "There is still the possibility that there is a missing link, a consecutive transmission with an intermediate missing link. I would only use such paraphyletic clustering to exclude a direction of transmission. The elimination of all other possible contacts is something to be done outside the phylogenetic analysis."

Jan Albert, a professor at the Karolinska Institute and Karolinska University Hospital in Sweden, tells aidsmap.com that "the study suggests, but does not prove, transmission between the examined persons. The main reason for the caveat is that the analyses do not exclude the existence of unsampled persons belonging to the same clusters. The paraphyly does not exclude this possibility. In light of this it is surprising that only 20 local controls were investigated in the Washington case and none in the Texas case."

Thomas Leitner, staff scientist at Los Alamos National Laboratory in the United States, tells aidsmap.com that the methodology described in the paper to test the hypothesis of direction of transmission is not, in fact, new, and that along with co-author Walter Fitch he published a paper outlining a similar methodology eleven years ago. (Leitner T, Fitch WM 1999) He adds that his research suggests that even when all persons involved in an alleged transmission chain are sampled, it may still be the case that the two closest samples in a phylogenetic tree are two individuals who may not have ever met.

Professor Vandamme is also lead author of a paper currently in press with The Lancet Infectious Diseases along with several other authors including Professor Albert and Dr Anna Maria Geretti, of University College London Medical School, Royal Free Hospital, in London, which highlights the substantial risk of miscarriages of justice based on a flawed view of the science behind phylogenetic analysis. It concludes, in concurrence with a briefing paper co-authored by Professor Vandamme and Dr Geretti and published by
NAM and NAT in 2007, that the only ‘safe’ use of phylogenetic analysis in criminal HIV transmission cases is to exonerate the accused.

A fuller discussion of how phylogenetic analysis and other evidence can – and cannot – be used to establish the fact of transmission from the accused to complainant(s) in a criminal case can be found in the 'Proof' chapter of NAM's new international resource, HIV and the criminal law.

References

Haiti Cholera Outbreaks: Experts Urge US to Create Emergency Cholera Vaccine Stockpile for Humanitarian Use

ScienceDaily (Nov. 24, 2010) — In the wake of devastating cholera outbreaks in refugee camps in earthquake-wrecked Haiti, a group of leading experts from Harvard Medical School, George Washington University, and the International Vaccine Institute (IVI) has urged the United States to create an emergency stockpile of cholera vaccines for future humanitarian use.

"The costs to the U.S. of creating and maintaining a stockpile of several million doses of cholera vaccine would be low," said the experts in an article published online first on November 24 in The New England Journal of Medicine (NEJM). "But the humanitarian benefits of rapid deployment of cholera vaccines to areas at high risk for major cholera outbreaks—such as earthquake-wrecked Port-au-Prince, the Haitian capital where 1.3 million people live in unsanitary refugee camps—could be enormous."

Prof. Matthew K. Waldor of Harvard Medical School; Prof. Peter J. Hotez of the Department of Microbiology, Immunology and Tropical Medicine, George Washington University in the U.S; and Dr. John D. Clemens, Director General of the IVI in Korea jointly made this suggestion in their NEJM Perspective article entitled "A National Cholera Vaccine Stockpile—a New Humanitarian and Diplomatic Resource."

In addition to the obvious health and humanitarian benefits that a national stockpile of cholera vaccine could yield, deployment of such a vaccine to regions of the world that are at high risk for a cholera epidemic offers numerous other benefits, the experts stated. "Outbreaks of cholera and other diarrheal diseases impede recovery from natural and man-made disasters," said Prof. Hotez. "They also destabilize poor communities, promoting poverty by interfering with agricultural productivity and adversely affecting food security, and thereby potentially igniting new conflicts or exacerbating existing ones. If the vaccine were available now, it could still be delivered to as-yet-unaffected parts of Haiti in time to stabilize the country."

Cholera is a severe and often rapidly fatal diarrheal disease caused by the bacterium Vibrio cholerae. It can be fatal because the pathogen elicits secretion of large quantities of bacteria-laden fluid from the intestine, resulting in extreme dehydration. It is transmitted through the fecal-oral route and if the drinking water or food supply becomes contaminated with V. cholerae, the disease can spread through a population very rapidly.

It is estimated that the annual global burden of cholera is 3 million to 5 million cases and 100,000 to 130,000 deaths. There is no evidence of a global decline despite major efforts to ensure the provision of clean water and adequate sanitation. Cholera is endemic in many parts of South Asia, and can cause epidemics both in areas where it is endemic and in those where it is not, often as a result of man-made or natural disasters. Last year there were reportedly 4,000 deaths during a protracted epidemic in Zimbabwe, and more than 1,400 people have died in refugee camps in the ongoing outbreaks in Haiti. A recent analysis of the global burden of cholera conducted by the IVI, an international organization dedicated to new vaccines for the world’s poor, estimates that approximately 1.5 billion people are at risk for cholera globally.

Treatment of cholera involves replacement of lost fluid with oral or intravenous rehydration solution and antibiotics, which can be lifesaving and can shorten duration of illness. However, these interventions can be difficult to administer when there are inadequate medical facilities, as is often the case in complex humanitarian emergencies. In addition, rapid progression of the disease means that there is only a narrow therapeutic window, making effective treatment a challenge.

Fortunately, three oral cholera vaccines are available. Dukoral® produced by Crucell of Sweden consists of killed V. cholerae cells and recombinant cholera toxin B. Since 1991, Dukoral® has been licensed in more than 60 countries, and is prequalified by the WHO for purchase by United Nations
It has been used in crisis situations in Indonesia, Sudan, and Uganda, as well as in densely populated urban slums in Mozambique. The two other vaccines—Shanchol® produced by Shantha Biotechnics of India, and mORC-VAX® made byVaBiotech in Vietnam—consist of killed V. cholerae cells without the added toxin. Both vaccines were licensed in 2009, and Shanchol is currently awaiting prequalification by the WHO. All three vaccines are administered in a two-dose regimen.

Notably, the licensing in India of Shanchol, which was originally developed by the IVI, has added considerably to the momentum for the use of oral cholera vaccines to control endemic and epidemic cholera due to the numerous advantages it confers. Unlike Dukoral, it does not require administration with a buffer, thereby greatly simplifying its use under field conditions, including refugee camps and other post-crisis situations. In addition, it is a low-cost vaccine, increasing its access to governments and international agencies. Finally, a large efficacy trial in India has shown that the vaccine is more effective and lasts longer in young children (1-5 years old) than Dukoral. Of critical importance, the WHO’s Strategic Advisory Group of Experts (SAGE) issued new updated recommendations for the use of new-generation cholera vaccines in its position paper in March 2010.

Alarmingly, however, fewer than 500,000 total doses of oral cholera vaccines (Dukoral or Shanchol) are presently available for shipment from their manufacturers, making it impossible to consider large-scale vaccination of at-risk populations. "The global shortage of cholera vaccine reinforces the urgency of creating a stockpile," said Dr. Clemens, an international expert in vaccine evaluation for developing countries.

Even though there is no imminent threat of cholera in the U.S., "We believe that our country should stockpile cholera vaccines for rapid deployment to parts of the world that suddenly find themselves at high risk for this disease," Prof. Waldor said. "Until recently, Latin America and the Caribbean region were considered to have a negligible risk of a cholera epidemic. Recent events in Haiti, however, force us to reconsider this belief. Other areas of the world where populations are at great risk include sub-Saharan Africa and South and Southeast Asia."

Moreover, by providing cholera vaccines to countries such as Pakistan with which the U.S. has a troubled relationship, the U.S. could also do its part to promote international stability and peace through vaccine diplomacy, the experts said.

Journal Reference:

Frank Fenner Dies at 95; Tracked End of Smallpox
By WILLIAM GRIMES
Frank Fenner, an Australian scientist who played an important role in the World Health Organization’s decade-long campaign to eradicate smallpox and who made the official announcement, in 1980, that the disease had been conquered once and for all, died Monday in Canberra. He was 95.

His death was announced on the Web site of the Australian National University in Canberra.

Professor Fenner, a virologist and microbiologist who developed an interest in viruses while doing research on malaria during World War II, became a national hero in Australia in the early 1950s, when he helped direct a program to control the spread of the country’s 600 million feral rabbits, which were nibbling their way through the country’s pastureland.

A pilot study to release the myxoma virus, shown to kill more than 99 percent of rabbits not previously exposed to it, caused public alarm when, by coincidence, mosquitoes began spreading encephalitis as well as myxomatosis. To reassure Australians that the myxoma virus would not infect humans, Professor Fenner and two fellow researchers injected themselves with samples potent enough to kill 1,000 rabbits.

They survived and, with panic averted, the government initiated a pest-control campaign using the myxoma virus. The rabbit population shrank to 100 million, although the rabbits developed resistance to the virus over time and by the early 1990s had rebounded to more than 200 million.

In 1969, after doing research on pox viruses, including the variola virus, which causes smallpox, Professor Fenner began advising the World Health Organization on its campaign to eliminate smallpox.

The initiative had begun in 1967, a year in which the disease was reported in 42 countries and killed two million people. The W.H.O. organized a campaign of mass vaccinations that evolved into a more focused approach: infected patients were quarantined, and vaccinations were administered to those with whom they might have had contact.
In 1977, Professor Fenner was named the chairman of the Global Commission for the Certification of Smallpox Eradication. As the campaign neared its goal, he was able to demonstrate that there were no animal carriers of the disease left, an important step in declaring victory over the disease. The last known case of naturally transmitted smallpox was recorded in Somalia in 1977, and Professor Fenner pronounced its epitaph in Geneva on May 8, 1980.

“It was a terrific thrill to be involved in a program which in 10 years removed from the Earth a disease which, at the time we started, was credited with 20 million cases and two million deaths every year,” he said in 2002, on accepting the Prime Minister's Prize for Science in Australia.


In the early 1970s, his interest in epidemiology and population dynamics led him to found the Center for Resource and Environmental Studies at the Australian National University in Canberra (now the Fenner School of Environment and Society). He directed the center until retiring in 1979 and continued working at the university well into his 90s.

Frank Johannes Fenner was born on Dec. 21, 1914, in Ballarat, Victoria, and grew up in Rose Park, a suburb of Adelaide. He attended the University of Adelaide, where he earned degrees in medicine and surgery in 1938. That year, uneasy about Hitler’s rise, he legally changed his middle name to John.

After receiving a diploma in tropical medicine from the University of Sydney, he joined the Royal Australian Army Medical Corps and during World War II served in Palestine, Egypt, New Guinea and Borneo. In 1942, he was granted a doctor of medicine degree from the University of Adelaide.

In New Guinea, he developed methods to control the malaria and other tropical diseases that were decimating Australian troops. In honor of this work, he was made a member of the Order of the British Empire.

In 1944 he married an army nurse, Ellen Roberts, who died in 1995. He is survived by a brother, William; a sister, Winifred; a daughter, Marilyn Marshall of Canberra; two grandchildren; and one great-grandchild.

After leaving the military in 1946, he was recruited by the eminent virologist Frank Macfarlane Burnet to join the Walter and Eliza Hall Institute of Medical Research in Melbourne. There, while working on the genetics of pox viruses and the immune system, he discovered that mousepox, a disease in mice, provided a useful model for investigating the incubation period of infectious diseases like smallpox, measles and chickenpox.

After spending a year studying tropical diseases at the Rockefeller Institute for Medical Research (now Rockefeller University) in New York, he began researching the myxoma virus at the newly created John Curtin School of Medical Research at the Australian National University, where he was the chairman of the microbiology department and, from 1967 to 1973, director of the school.

Professor Fenner’s views on the environment were not cheerful. Sheer numbers and the rapacious consumption of resources, he predicted glumly, would condemn the human species to the same fate as the smallpox virus.

“Homo sapiens will become extinct, perhaps within 100 years,” he told the newspaper The Australian in June. “A lot of other animals will, too. It’s an irreversible situation. I think it’s too late.”

Focus on six risk factors could prevent up to 80% of HIV infections in South African women

Michael Carter
Published: 29 November 2010

Addressing five modifiable risk factors could significantly reduce the number of new HIV infections among South African women, according to a study published in the online edition of AIDS and Behavior.

The researchers found that six risk factors were associated with HIV seroconversion and that five of them could be addressed through prevention initiatives.

“To have a very substantial impact on HIV prevention, a range of risk factors particularly related with unsafe sex need modifying,” comment the investigators. However, socio-economic factors, possibly related to work migration patterns, were associated with HIV seroconversion for older women.

 “[The] majority of cases among women could potentially have been prevented by effective public health interventions,” write the authors.

Age was the only non-modifiable risk factor for seroconversion identified by the investigators.
HIV incidence among South African women is high and unprotected sex is the single most important risk factor for acquiring HIV in the region.

Some risk factors for HIV – such as sexual behaviour – are potentially modifiable, and researchers wanted to see the proportion of new infections that were attributable to risks that could be addressed through public health interventions.

Their study population included 2523 HIV-negative women in Durban. The women participated in three separate community-based prevention studies between 2002 and 2005. All the women were sexually active, were regularly tested for HIV and other sexually transmitted infections, and completed questionnaires about their sexual behaviour. Information was also gathered on the women’s socio-economic circumstances, including their partnership and employment status.

The median age was 28 (range 22 to 36) and 39% were aged 24 or under. The majority – 80% – were not employed, and 58% were either single or not living with a partner. Over two-thirds (69%) of women reported at least instances of sexual intercourse in the previous seven days. In all, 88% of women said that they consistently used condoms, but 12% of women had a sexually transmitted infection at the time of entry to the study, a further 32% were diagnosed with at least one such infection during follow-up and 22% became pregnant.

A total of 211 women seroconverted for HIV, and the overall incidence rate of the infection was 7%. One non-modifiable risk factor – younger age – was associated with seroconversion (age under 24, \( p < 0.001 \); age 25-34, \( p = 0.017 \)).

All the other risks associated with new infections were related to potentially modifiable risks and included:

- Single or not cohabiting, \( p < 0.001 \).
- Frequency or sex (three or more acts in the previous week), \( p = 0.048 \).
- Sexually transmitted infection at baseline, \( p = 0.0185 \).
- Incident sexually transmitted infection during follow-up, \( p < 0.001 \).
- Pregnancy during the study, \( p < 0.001 \).
- Unemployed or insufficient income, \( p = 0.0437 \).

The investigators noted that reported condom use was not identified as a risk factor. However, they write, “generally, since STIs and particularly pregnancy can only occur with unprotected sex, these two risk factors can give hard evidence of inconsistent condom use.”

Information was not gathered on the number of sex partners. But the investigators believed “being single/not cohabiting combined with high frequency of sexual acts gives strong evidence of those women having multiple partners as well as possibly engaging in transactional sex.”

Next the investigators calculated the proportion of new infections that could be attributed to these potentially modifiable factors.

Overall, 82% of infections could potentially have been averted if modifiable risks were effectively addressed in public health and other social interventions.

Being single, not having a partner, and three or more sex acts a week accounted for 64% of new HIV infections. This increased to 71% when sexually transmitted infections were added. Therefore the investigators believe that “measures aimed at reducing the frequency of unprotected sex and aggressive condom counselling with couples” could have a substantial impact of HIV incidence among women.

However, the importance of individual risk factors varied according to age.

Those related to sex were responsible for 81% of infections in aged 25 to 34. But for older women socio-economic factors had the largest impact on incidence, with not having a job/low income the reason underlying 43% of infections.

“Improving socio-economic conditions for women along with low-risk sexual behaviours may reduce...infections considerably”, comment the investigators. They call for employers to “change labour migrating patterns whereby the family unit moves with the job holder.”

They conclude that their research provides “a robust methodology for calculating quantitative epidemiology measures of disease burden that provides policy makers and health service administrators with an important tool to prioritise health service and prevention strategies.”

Reference

The Lesser-Known Complications of HIV/AIDS

At the age of 56, Jules Levin felt pretty invincible, despite being HIV positive. He went to the gym regularly and controlled his disease well by taking his antiretroviral medicines every day.

Then he slipped one day while on vacation and broke his wrist. He underwent an operation to insert pins in his bones and needed to wear a cast for a month, keep his arm elevated, and then do physical therapy for two months to get to the point where he could lift a five pound weight. "It was one of the most difficult things I've ever been through in my life," he said. "I ran, biked, lifted weights and now all of a sudden I couldn't turn the page of a newspaper. It just really got to me."

After a few simple tests, the reason for Levin's fracture became clear: His bones were weak from osteoporosis, a disease that's most commonly seen in older women, but that's also associated with HIV.

"The giddiness of the age of HAART is over," said Levin, referring to highly active antiretroviral therapy, the life-saving drug regimen prescribed to people with HIV. "We should have an aging clinic in every hospital that's serving HIV patients."

Osteoporosis is one of many conditions associated with old age that is now being seen with increasing frequency in people with HIV. Research suggests that long-term exposure to the virus, and to the inflammation it triggers, make people vulnerable to premature aging and to a host of conditions seen with aging, heart and kidney disease, dementia, and osteoporosis.

Additionally, the overall population of people with HIV is getting older, thanks to improved medical therapy. At present, 1 in 4 people with HIV is age 50 or older. The U.S. Senate Special Committee on Aging has predicted that half of all adults with HIV will be older than 50 by the year 2015. Over the past few years, the National Institute of Health has increased its funding for research on HIV and aging, and the White House hosted a conference on October 27 on HIV and aging.

"The evidence is pretty clear," said Levin, who directs The National AIDS Treatment Advocacy Project (NATAP), a New York-based HIV education and advocacy group. "We're going to see early frailty, early senescence and people are going to start dying at earlier ages."

Compared to other conditions associated with HIV and aging, osteoporosis is relatively straightforward to forestall and treat. To maintain bone strength, it's important for all people with HIV to make sure they are consuming an adequate amount of calcium and Vitamin D. A recent article in the journal Clinical Infectious Diseases recommends 1,000 to 1,500 mg of calcium and 800 to 1,000 IUs of Vitamin D daily, as well as at least 30 minutes of weight-bearing exercise, such as jogging or walking, at least three days a week. Calcium is plentiful in dairy products and sardines, and is available in supplements such as calcium carbonate and calcium citrate. The National Institutes of Health has an online information sheet listing ways to get calcium. It's also important to avoid smoking and heavy alcohol use, since these can cause osteoporosis.

HIV is thought to be associated with osteoporosis for a variety of reasons. The infection, itself, causes inflammation, which in turn impacts the cells that maintain bones. Many conditions common in people with HIV, such as Vitamin D deficiency, being underweight and low testosterone, are associated with osteoporosis. Antiretroviral therapy and other medications frequently prescribed to people with HIV, such as Prednisone, also cause bone loss.

Even though many antiretrovirals can cause bone loss, osteoporosis is not a reason to stop taking them. "Antiretroviral therapy is life-saving, and we know that stopping antiretroviral therapy is not a good strategy for preventing complications," said Dr. Todd Brown, an endocrinology specialist at Johns Hopkins University who co-wrote the article in Clinical Infectious Diseases.

Brown and his coauthors recommend that all HIV-positive men older than age 50 and women who are past menopause undergo testing for osteoporosis, since it's a condition that usually doesn't cause symptoms until the person breaks a bone. His own research has found that osteoporosis is "alarmingly" prevalent among African Americans in inner city Baltimore. "Because of the perception that osteoporosis is a white disease, people of color get short shrift for screening," he said. "This concept that African Americans are protected shouldn't be a reason to neglect them."

Once someone is diagnosed with osteoporosis, it's important to take action to prevent falling, such as removing clutter and slippery rugs from the floor. Physical therapy can help improve strength and balance, which also reduce the risk of a fall. The person also should get his or her vision checked and review his or her medication list with a doctor to try to minimize any drug side effects or interactions that might cause drowsiness or unsteadiness.
A class of medicines called bisphosphonates can improve bone strength, but do have some rare risks. "While they do decrease the risk of fracture, they're not totally benign drugs," Brown said. "On the flip side, you shouldn't not use them in the patient who is at high risk of a fracture."

Levin urges all people with HIV to be assertive about discussing osteoporosis and other age-related conditions with their doctor. "My guess is that 90 percent of patients know nothing about any of this and a lot of clinicians and case managers don't know about it either," he said. "Every patient should ask their clinician, 'are you aware, are you monitoring me for heart disease, diabetes, bone disease, cognitive impairment, kidney disease?' This is an important issue for everybody."

**Inner city tweeter finds poster alleging two men are purposely spreading HIV**

Global News: Friday, November 26, 2010

![Poster](https://www.globalnews.ca/trust/images/2010/11/26/081679-1-340x191.jpg)

Police are investigating after a downtown resident found a stack of posters accusing two men of purposely spreading HIV.

**Photo Credit:** Courtesy, Global News

CALGARY – An inner city resident who lives in an area notorious for crime keeps a public online journal documenting everything he sees.

"I just throw it on my twitter account – videos of people doing things on the street, fights, drunk people, police things – I put it up there."

Because of what he witnesses, he chooses not to identify himself, but his latest discovery was particularly disturbing him, prompting him to go to the police.

On his way to work recently, he noticed dozens of stacked flyers on a street corner near his home. They had a clear picture of two men, their names and phone numbers with a warning – that a gay couple was out to infect as many people with HIV as possible.

Our tweeter didn't know what to think.

"Who knows, it could be a joke, it could be someone that hates someone and they want to get back at them – I have no idea."

A question Calgary Police are trying to find an answer to as well. They have launched an investigation into who is responsible for creating the posters.

"A false complaint like this could be very detrimental to someone's life," says Sgt. Lynn MacDonald. "On the other side of this, it's a very serious allegation. The threat of spreading HIV purposely to unknowing individuals – we take it very seriously."

Linda McKay-Panos, a law professor at the University of Calgary, works with youth who are homosexual and dealing with discrimination. She says whatever the motive; something like this only perpetuates stereotypes.

"That seems to me a form of inciting hatred against people on the basis of their sexual orientation or at the minimum leading to discrimination against people," says McKay-Panos.

The men on the poster cannot be reached by the phone numbers posted but their faces are clearly pictured.

Police say any warnings of this kind should be left for them to deal with and that taking matters into your own hands could warrant a charge of harassment.
“Any vigilante action taken towards these individuals will be investigated thoroughly by the Calgary Police Service,” says Sgt. MacDonald. “If you’re a person who comes across something like this, take it down, exercise your own freedom and get rid of it.”

**Poor Governance Major Cause Of Africa’s Water Problems, AfDB Report Says**

A report released by the African Development Bank (AfDB) at a meeting in Addis Ababa, Ethiopia, during the 3rd Africa Water Week, points to poor governance as a major cause of the inadequate water supply that threatens the health of millions living in Africa. 234next.com reports (Abutu, 11/24).

“The report identifies numerous but common governance risks, and shows that these are easily identifiable and preventable. It also finds that substantial gains would be made if government assessments became standard procedure and if governance criteria were introduced in donor project approval procedures,” according to an AfDB press release.

According to the report, “[w]hile local and national institutions have the most visible role to play in governing the water sector, it is the sector’s underlying policies, legislation and regulations that provide the foundation for overall governance,” the release states. The report, presented in two volumes (here and here), suggests targets and guidelines to be used to assess African programs and projects (11/22).

234next.com reports that during the meeting, Ethiopian Water and Energy Minister Ato Alemayehu Tegenu called for leaders to invest more in the water sector. "The main challenges and issues in the water sector are sustainability, capacity and finance. In order to meet the MDGs by 2015, an enormous annual investment is required which could be more than 4 to 5 times current investment rate on the sector," Tegenu said, according to the news service.

"The minister said already, about 350 million Africans do not have access to water while numerous people on the continent were excluded from their right to clean drinking water," according to the news service. The article also details comments made by Ethiopian President Girma Wolde-Giorgis during the conference (11/24).

**Haiti Cholera Death Toll Increases, U.N. Boosts Estimate For Number Of Expected Cases**

"The cholera epidemic in Haiti is gathering pace and some violence is expected when the country holds elections this week, U.N. officials warned Tuesday," Agence France-Presse reports. The official death toll from cholera is now above 1,400, but "experts believe that the real toll is close to 2,000 dead and the number of cases is between 60,000 and 70,000 rather than the 50,000 given by the authorities, Nigel Fisher, the U.N. humanitarian coordinator in Haiti said," according to the news service (11/23).

Previously, the WHO had estimated that there would be 200,000 cholera cases in Haiti over six months, but Fisher said the agency is "now revising that to 200,000 in closer to a three-month period," Reuters reports. "The medical specialists all say that this cholera epidemic will continue through months and maybe a year at least, that we will see literally hundreds of thousands of cases," Fisher continued (Worsnip, 11/23).

Jon Kim Andrus, deputy director of the Pan American Health Organization, said, "Cholera is virtually everywhere in the country," AFP reports in a separate article. "We need to plan for enough supplies to treat as many as 400,000 cholera cases occurring over the next 12 months," Andrus added (11/23).

CNN reports that "[s]hort-term efforts are focusing on the distribution of chlorine tablets and oral rehydration salts, which are key to preventing and treating the disease." Andrus said, "In the long term, we must create the systems and infrastructure to ensure equitable access to these basic services" (11/23).

The U.N. also said on Tuesday "that less than 4 percent of the" funds needed for the cholera outbreak have been pledged, NPR reports (Beaubien, 11/23). "Donors have stumped up only 6.8 million dollars so far out of 164 million dollars sought by the U.N. in an appeal 10 days ago, said Elisabeth Byrs, spokeswoman for the U.N. Office for the Coordination of Humanitarian Affairs," AFP reports in a third article. Brys said, "The funding is much too weak. It's an extremely urgent situation, a question of hours. The epidemic is not waiting and continuing to evolve."

The U.N. stressed the importance of "educating the public about the illness ... as some people, including pregnant women, are refusing to go to hospitals for fear of contracting cholera" (11/23).

The AFP/Montreal Gazette reports that "[f]ear has grown that the disease could spread more quickly in an election environment when people have to move around and congregate to campaign. ... The U.S. ambassador to Haiti, Kenneth Merten ... urged no delay with the polls, telling a video conference call Tuesday that issues surrounding the disease and the election can be avoided “as long as people are
informed ... of how they can protect themselves from cholera and what treatment to seek" (Jourdain, 11/23).

**Superantigens could be behind several illnesses**

Superantigens, the toxins produced by staphylococcus bacteria, are more complex than previously believed, reveals a team of researchers from the University of Gothenburg in an article published today in the scientific journal *Nature Communications*. Their discovery shows that the body's immune system can cause more illnesses than realised.

"Superantigens have a real talent for disrupting the body's immune system," says Karin Lindkvist from the University of Gothenburg's Department of Cell- and Molecular Biology, one of the authors of the article. "If you're infected with bacteria that secrete superantigens, your immune system will respond so strongly that it'll make you ill. Our study shows that superantigens activate the immune system in more ways than previously thought."

We are all exposed daily to various types of foreign organism that can harm us. The human body has therefore developed cells whose role it is to "kill" and remove all foreign invaders that find their way in – the immune system.

Antibiotic-resistant bacteria have become increasingly common with the more widespread use of different types of antibiotics. Yellow staphylococci (*Staphylococcus aureus*) are one of the most common bacteria in the world around us, with most children and adults carrying them at some point. One strain, MRSA (methicillin-resistant *Staphylococcus aureus*), has developed resistance to penicillin and other penicillin-like antibiotics that are normally used to treat infections caused by staphylococci. Staphylococci can cause a variety of conditions such as long-term wound infections and abscesses, and can also lead to food poisoning.

The toxins produced by staphylococci are also known as superantigens. A normal viral infection will trigger the activation of around 0.0001% of the body's natural killer cells (T cells), which is enough to destroy the virus. However, contracting bacteria that secrete superantigens leads to the activation of 5-20% of the body's T cells. Such a strong immune response will often result in illness, which generally involves fever and extreme nausea. Superantigens are also well-known for causing toxic symptoms, as in toxic shock syndrome. There is also some speculation as to whether superantigens can cause autoimmune disorders such as rheumatoid arthritis.

"By investigating how superantigens activate the immune system via its T cells, we've been able to show that they bind to more than one part of the T cell receptor," says Lindkvist. "This is an important discovery for our understanding of superantigens' biological function, and for the future development of a vaccine against superantigens. We haven't yet looked at whether other superantigens can activate T cells in the same complex way, but it's reasonable to assume that they can."

**HIV+ Women Need Annual Cervical Cytology: ACOG Guidelines**

*Reuters Health Medical News*, (11.22.2010)

The American College of Obstetricians and Gynecologists recently issued guidelines for the routine gynecological care of HIV-positive women. “Most of the women living with HIV today in the US are in their prime reproductive years,” noted Dr. Hal C. Lawrence, vice president of practice activities for ACOG.

All women ages 19 to 64 should receive routine HIV screening, the report recommended. While there is no consensus on how often repeat screening should be offered, the guidelines suggested at least annual testing for women at elevated risk, including injection drug users, those whose partners are injection drug users or HIV-positive, and those have had an STD in the previous year.

The guidelines recommend aggressive treatment of STDs, which increase the risk of HIV transmission. CDC recommends annual testing for curable STDs, ACOG noted. HIV-positive women should have cervical screening twice during the first year after HIV diagnosis and annual screening thereafter.

HIV-positive women are at increased risk of bacterial vaginosis and yeast infections, and treatment may take longer than average, the guidelines note. Women with recurrent yeast infections may need long-term medication to forestall future yeast infections, they said.

Condoms, which are recommended for all sexually active HIV-positive persons, plus another method of birth control are recommended to prevent unintended pregnancy among HIV-positive women of child-bearing age. Oral contraceptives are safe for women with HIV, but combined oral contraceptives generally
are not recommended for women taking certain antiretroviral therapy, as the medications can interfere with each other. ACOG notes that IUDs can be a good birth control option for HIV-positive women.

Strategies are available for HIV-positive women who wish to become pregnant to avoid the risk of vertical transmission. They include reducing the virus to undetectable levels before delivery, not breastfeeding, and administering the infant prophylactic antiretrovirals.

HIV-positive women tend to go through menopause about three to four years before other women, according to the guidelines. In the absence of detailed research, the guidelines suggest standard interventions to address the bone loss often seen in menopausal women: increasing physical activity, stopping smoking, and taking vitamin D and calcium supplements.


OraSure HIV Test Inches Closer to FDA Approval

Morning Call (Allentown, PA), (11.23.2010) Spencer Soper

The Food and Drug Administration is in the final stages of reviewing a proposed over-the-counter version of the rapid HIV test available in hospitals and clinics, test-maker OraSure Technologies said recently. To gain approval, OraSure will at a minimum have to prove that consumers untrained in lab testing can correctly use the OraQuick Rapid HIV test. The final review includes an assessment of such unsupervised self-testing. OraSure said it expects the trial “will continue well into 2011.” “We are extremely pleased to have approval to begin the final phase of studies to support our efforts to obtain FDA approval for an over-the-counter offering of our OraQuick HIV test,” said Douglas A.Michels, the company’s president and CEO.

Stabbed for being HIV+

November 30 2010 at 01:15pm
By Heather Mason
Mbabane, Swaziland—One year ago, in the small southern African kingdom of Swaziland, 25-year-old Zanele Mamba was living on the edge.

She and her husband, Mfanziile Dlaminii, were HIV-positive and had already lost two babies to Aids. They lived in a one-room hut in Mkhulamini, 50 kilometres east of the capital Mbabane, surviving on subsistence farming and Dlaminii’s meagre salary as a night watchman.

Dlaminii’s family, who owned the land they lived on, constantly harassed the couple about their HIV status.

“Mfanziile’s family would say horrible things to him,” said Mamba. “I kept telling him, ‘Don’t worry about it. Don’t go to them.’ But then they came to our house and continued with the verbal abuse.”

The couple lived for their 14-month-old daughter, Phiswa, who was HIV-negative, thanks to the prevention services Mamba received at a local clinic. Dlaminii and Mamba also had access to government—supplied anti-Aids medicine—which allowed them to stay relatively healthy.

The situation worsened as the year wore on. Dlaminii’s treatment failed and he became too ill to work. In June 2010, he died. And Mamba realised she was no longer welcome in her home.

“They (Dlaminii’s family) took everything I had. They took the chickens. They took my clothes. It was a sign saying, ‘Just move. We Don’t want you here’. So I decided to pack up and leave.”

On the day of her husband’s funeral, Mamba took her daughter and left. She was six months pregnant with her fourth child.

Swaziland has the world’s highest prevalence of HIV, the virus that causes Aids. More than a quarter of Swazis aged between 15 and 49—26 percent—is infected, yet people who disclose their status are often severely stigmatised.

Phumzile, who asked that her surname not be used, was stabbed by her husband after they both tested HIV-positive. He blamed her for bringing the disease into their home.

“He said he was going to cut my throat and kill himself because he cant stand the humiliation of telling people that he’s HIV-positive. I think he thought I was dead because I was bleeding profusely.”

Phumzile left to live with her parents and lost all her possessions. She eventually recovered from her injuries and now works at a government hospital, counselling other women who test positive for HIV.

According to Zandile Nhleko, community linkages officer for the Elizabeth Glaser Pediatric AIDS Foundation in Swaziland, HIV stigma is still entrenched in rural parts of Swaziland, where more than 75 percent of Swazis live.
“People in urban areas have more access to information—they have the internet, they go out more,” Nhleko said.

And yet access to information alone hasn’t done enough to overcome stigma, as still-high levels of prejudice among health workers and government officials testify.

Nhleko says she has seen nurses refuse to share dishes and food with colleagues who are HIV-positive.

Last year, a Swazi parliamentarian caused outrage when he proposed branding the buttocks of every Swazi who tests positive for HIV.

Some experts blame a lack of leadership at the top.

King Mswati III, Swaziland’s absolute monarch, has 13 wives—despite multiple concurrent sexual partners increasing the risk of infection with HIV.

In 2001, he banned girls under 18 from having sex in an effort to curb the spread of the virus. Soon after he married a 17-year-old girl.

To date, not a single Swazi political leader has openly disclosed his or her HIV status.

And yet, as World Aids Day approaches again, there are glimmers of hope.

Zanele Mamba is now living with her mother, Alice Mamba, in rural Lubombo region.

Alice, 48, makes no secret of the fact that she is HIV-positive. Several of their neighbours have also disclosed their status, suggesting that efforts by non-government organisations to educate Swazis are working and stigma has eased, at least in this particular community.

“I am very very happy here,” says Zanele, who gave birth in September to a baby boy, Nkosingphile (“Gift from God”), who has tested HIV-negative thus far.

Alice feels that people with HIV should take responsibility for defeating stigma in Swaziland.

People living with HIV should not hide their HIV status, but they should just disclose and tell everybody about HIV,” she said.

“It’s very important for everybody to know that if you have HIV you are still a human being.”—Sapa

dpa

Targeted Human Papillomavirus Vaccination of Men Who Have Sex with Men in the USA: A Cost-Effectiveness Modeling Analysis

Lancet Infectious Diseases Vol. 10; No. 12: P. 845-852, (12..2010) Jane J. Kim, PhD

“A vaccine targeting human papillomavirus (HPV) types 16 and 18, which are associated with 80 percent of anal cancers, is efficacious in men. High-risk populations such as men who have sex with men (MSM) might especially benefit from vaccination,” explained the study author, who aimed to estimate the cost-effectiveness of HPV vaccination of US MSM.

Kim constructed decision-analytic models to estimate the direct health and economic outcomes of HPV vaccination (against types 6, 11, 16 and 18) for HPV-related anal cancer and genital wart prevention. Age at vaccination (12 years, 20 years and 26 years), previous exposure to vaccine-targeted HPV types and prevalence of HIV-1 were the model parameters that were varied. Kim used the models to conduct sensitivity analyses, including duration of vaccine protection; vaccine cost; and burden of anal cancer and genital warts.

In the scenario of HPV vaccination of MSM at age 12 without previous HPV exposure, compared with no vaccination, vaccination cost $15,290 per quality-adjusted life-year gained. In scenarios where MSM are vaccinated at age 20 or 26, after HPV exposure, the cost-effectiveness ratios worsened but were less than $50,000 per quality-adjusted life-year under most scenarios. For example, HPV vaccination of MSM at age 26 cost $37,830 per quality-adjusted life-year when assuming 50 percent of MSM previously exposed to all vaccine-targeted HPV types. Outcomes were most sensitive to variations in anal cancer incidence, duration of vaccine protection and HIV prevalence in MSM.

“HPV vaccination of MSM is likely to be a cost-effective intervention for the prevention of genital warts and anal cancer,” Kim concluded.

Comment: We’ve got to change gay men’s attitudes to cut HIV

by Michael Carter

30 November 2010, 6:27pm

It’s almost 30 years since the first cases of AIDS were diagnosed and the HIV epidemic among UK gay men shows no real signs of abating. According to figures released last week, in 2009, a total of 2,760 gay men in the UK learnt that they had the virus.
With the right treatment and care, most of these men will have a more or less normal life expectancy. But at the very least, having HIV will make their lives harder, and for a good number it will involve both physical and psychological pain and suffering.

One of the reasons for this is huge amount of stigma that still surrounds HIV.

Indifference, hostility, contempt and even hatred characterises the response of far too many gay men to their HIV-positive peers. This doesn’t only hurt feelings and blight opportunities: stigma contributes to the continued spread of the virus and it also leads to needless deaths.

Gay men have much to be proud of in the way that they’ve responded to HIV. We cared when no one else did; we helped shape the domestic and international response to the epidemic; and many of us have responded with love, compassion and empathy.

But all too often this isn’t the case. This was clearly demonstrated by a startling report published in 2009. It examined the attitudes of gay men toward the criminalisation of HIV transmission. A clear majority of gay men supported prosecutions for this offence.

But what was most shocking about the report was – to quote its authors – the “fear and loathing with which men characterise those ‘other’ gay men and bisexual men with HIV”. The researchers concluded that the stigmatising of HIV “continues to be the largest underlying challenge to our HIV response”.

Men who’d never been tested for HIV were the group most likely to support prosecutions. These men – and those who believed themselves to be HIV-negative – also expected HIV-positive men to disclose before sex. But the report made clear that the stigma that surrounds having HIV is likely to act a powerful disincentive to disclosure.

The high levels of undiagnosed HIV among gay men in the UK (25 per cent of those with the infection do not know they have it, according to the most recent figures) means that relying on disclosure is a deeply flawed way to try to avoid the virus.

Moreover, undiagnosed men are driving the continued spread of HIV. A study conducted among gay men in Quebec found that half of transmissions originated in men who’d only recently been infected themselves.

By contrast, many men who have been diagnosed are not the vectors of disease that they are often feared to be. Taking HIV treatment can dramatically reduce a person’s infectiousness. Doctors in Brighton recently tried to establish transmission trains between men who’d recently been diagnosed with HIV and those who were already receiving care at their clinics. There was no convincing evidence that any infections originated in a person taking successful HIV treatment.

The precise impact of treatment on infectiousness is hotly debated. But what’s not in doubt is that anti-HIV drugs save lives. Tens of thousands of HIV-positive gay men in the UK are alive and healthy thanks to this treatment.

However, men who have not had been diagnosed cannot take advantage of this treatment and many men put off testing because they fear HIV so much or think that it has nothing to do with them.

The latest figures show that 39 per cent of gay men were diagnosed when their immune systems were so weak that they needed to start HIV treatment immediately. Moreover, 30 per cent of these men were diagnosed so late that they had a real risk of developing a potentially fatal illness. Indeed, late diagnosis is the reason underlying most of the HIV-related mortality that we still see in the UK. With earlier diagnosis these deaths would have been prevented.

But it’s not just negative and untested men who stigmatise – HIV-positive men can be guilty of this too. This is most evident in the attitude of some men towards those who are co-infected with HIV and hepatitis C.

There’s an epidemic of sexually transmitted hepatitis C in HIV-positive gay men. It appears to be spreading in networks of positive men who are “sero-sorting” – selecting men who have the same HIV status. Risky and rougher sex, especially if it involves contact with blood, appears to be the main risk factor, and drug use also appears to have a role.

Ironically, some HIV-positive men are relying on a flawed disclosure strategy as a way of avoiding hepatitis C and ostracising the men whose infection has been diagnosed. All this does is intensify the stigma that surrounds hepatitis C and create an environment that allows the infection to spread.

Gay men should be encouraged and supported to avoid life-affecting and potentially life-limiting infections like HIV and hepatitis C.

But prevention efforts will be fundamentally undermined unless the stigma that characterises the response of so many men to these infections is addressed. All stigma does is cause pain, perpetuate transmissions, and in many cases contributes to tragically early deaths.
Human Protein Tetherin Disables Production of New Infectious HIV

**SUMMARY:** A human cellular protein known as bone marrow stromal cell antigen-2 (BST02)—also called tetherin—can interfere with maturation and release of newly produced HIV viral particles, thereby offering protection against infection of additional cells, according to findings from a Canadian laboratory study reported in the *December 2010 Journal of Virology*.

By Liz Highleyman

Below is the text of a press release describing the research issued by the American Society for Microbiology, which publishes the journal.

**Cellular Protein Hobbles HIV-1**

A cellular protein called BST-2 had already been known to interfere with the spread of human immunodeficiency virus type 1 (HIV-1), by inhibiting the release of its progeny particles from infected cells. Now a team from McGill University, Montreal, shows that in addition, each progeny virion's ability to cause infection is severely impaired.

"BST-2 may exert a more potent inhibition effect on HIV-1 transmission than previously thought," says coauthor Chen Liang. The research is published in the December *Journal of Virology*.

BST-2 appears to attenuate infectivity of progeny particles by interfering with their maturation. Normally, during synthesis of new virus particles, a protein called PR55Gag is cleaved into three major structural proteins of HIV. "This cleavage process transforms HIV-1 from an immature and non-infectious virion into a mature and infectious virion," says Chen. The protease inhibitors, drugs given to AIDS patients to contain the disease, block this step. Similarly, BST-2 seems to interfere with this step, because in the study, its presence was associated with accumulation of uncleaved Gag precursor and intermediate products. The mechanism of that interference has yet to be elucidated.

BST-2 (bone marrow stromal cell antigen-2), also known as tetherin, is a cellular protein which has been shown to restrict production of enveloped viruses besides HIV-1, including HIV-2, simian immunodeficiency virus, Kapoši's sarcoma herpes virus, Lassa virus, Marburg virus, and Ebola virus. It interferes with release of new virus particles by anchoring one end of itself in the plasma membrane of the infected cell while the other end becomes inserted into the viral envelope.

Different viruses have evolved various countermeasures. For example, in the case of HIV-1, the viral protein Vpu downregulates BST-2 from the cell surface, removing it from virus budding sites.

"The antiviral function of BST-2 has been extensively studied by a number of groups besides ours," says Chen. "Our hope is that the results of all of these studies can eventually be used to develop a BST-2 based anti-HIV-1 therapy." 11/30/10

**Reference**


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**USA Today Examines Why Aid For Haiti Goes Unspent**

"Ten months after the magnitude-7 earthquake that killed 230,000 people and destroyed at least 60% of Haiti's capital city, Port-au-Prince, some relief agencies have not spent the bulk of the donations they raised after the disaster. They say they want to use the rest for the country's long-term recovery, but they can't get rolling because roads are torn up, government agencies aren't functioning, and the economy is at a standstill. Agencies are also working to contain a rapid-spreading cholera outbreak," *USA Today* writes in an article examining aid to Haiti since the quake.

According to the article, "World Vision has spent half of the $192 million it raised after the Haitian earthquake in January ... Partners in Health, which provides health care in developing nations, has spent a third of the $86 million it raised after the disaster ... The American Red Cross has spent 39% of the $476 million it raised."

"There's a dynamic tension between empowering Haitians vs. providing immediate assistance as quickly as possible carried out by American and European agencies," according to Michael Wiest, executive vice president of Catholic Relief Services. American Red Cross projects are "subject to regular monitoring," according to Julie Sell, a spokeswoman for the organization. "Progress reports are submitted monthly, quarterly and annually and HQ and field staff coordinate regularly to monitor and ensure that each project is on track to meet its targets," she said. "The Red Cross has made a commitment to Haiti to spend $43 million to build transitional shelters. About 1,460 shelters, each housing an average of five people, have been built, Sell says," the newspaper writes.

Disaster Accountability Project, a watchdog organization, said only six of the 197 aid groups it surveyed in Haiti in July provided detailed, public updates on their projects. "The result, then, is that..."
people base their donations on emotion and not the facts on the ground,” said Ben Smilowitz, founder of the project. As a result, people might give donations to groups that don’t have the capacity for the work or lack the necessary familiarity with local procedures, Smilowitz said.

Randy Strash, World Vision’s strategy director for emergency response; Saundra Schimmelpfennig, creator of The Charity Rater; and Susan Sayers, interim development director for Partners in Health, are also quoted in the article (Bello, 11/30).

In related news, The Daily Beast examines HIV in Haiti, where after the earthquake “destroyed many health facilities,” experts fear “high rates of rape, prostitution, and promiscuity in the camps” might lead to “an explosive increase in the number of new HIV infections.”

The article continues: “Haiti used to be a model for combating AIDS. Experts at first thought the epidemic might wipe out a third of the population. But instead the country became a surprising success story: Thanks to significant financial support from the U.S. President’s Emergency Plan for AIDS Relief as well as the Global Fund to Fight AIDS, Tuberculosis and Malaria prevalence rates fell from 9.4 percent in 1993 to 2.2 percent in 2008.”

The story features an HIV-positive woman displaced by the earthquake and also includes quotes from a UNAIDS representative and a local HIV/AIDS advocate (Armstrong, 11/29).