February 2011 Epidemics and AIDS Update

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Computer Model System Helps Clinicians Select Best Antiretroviral Drug Combo

SUMMARY: The HIV Treatment Response Prediction System (HIV-TRePS)—a free web-based tool developed by compiling treatment data from thousands of HIV patients around the world—can help clinicians predict which combination antiretroviral therapy (ART) regimens are likely to work for a specific individual, according to research reported in the January 8, 2011, issue of AIDS Patient Care and STDs. In 2 studies, the system helped select regimens that produced greater viral suppression with fewer pills.

Below is a press release issued by the HIV Resistance Response Database Initiative (RDI), the collaboration that developed the prediction system, describing the study findings.

Clinical Studies By Expert HIV Clinicians Suggest that HIV-TRePS May Have Clinical and Economic Benefits

London, UK—January 18, 2011—Two multinational clinical studies indicate that the RDI’s system for predicting how HIV and AIDS patients will respond to different drugs could be a useful tool with potential clinical and economic benefits. The studies, published in the January issue of AIDS Patient Care and STDs, involved highly experienced physicians in the USA, Canada and Italy who used the system to help them select the optimum combination of HIV drugs for patients whose therapy was failing. mm³

The HIV Treatment Response Prediction System (HIV-TRePS) harnesses the power of complex computer models that have been trained with data from thousands of patients around the world. In these studies, physicians entered their patient’s data and their selection of the next combination of HIV drugs, via the Internet. A prototype version of HIV-TRePS predicted how the patient would respond to hundreds of alternative combinations of HIV drugs. Within seconds, the physician received a report listing the drug combinations that the models predicted were most likely to work. Having reviewed the report, the physicians recorded their final treatment decision and completed an online evaluation.

The results demonstrated that use of the system was associated with a change of treatment decision in one-third of cases to combinations with fewer drugs overall, which were predicted to result in better virological responses. Evaluations indicated that the physicians found the system to be easy and useful. Based on these findings, use of the system could potentially improve patient outcomes and reduce the overall number—and therefore cost—of drugs used. An improved version of HIV-TRePS is now available free of charge over the Internet (via the RDI web site) as an experimental tool.

"HIV-TRePS is an innovative and important tool to improve the health of people living with HIV, and the BC Centre for Excellence in HIV/AIDS (BC-CfE) is proud to contribute to its development," commented Dr. Julio Montaner, Past President of the International AIDS Society and Director of the BC-CfE, based in Vancouver, Canada. "These promising results are the first to be published from a clinical evaluation of such a system. I would encourage people to try the system and enter follow-up data and evaluations to help the RDI to continue to refine and improve the system."

Selecting and changing treatments for patients with HIV and AIDS in order to keep the virus suppressed is complex and challenging. There are approximately 25 HIV drugs available, from which physicians normally choose a combination of three or more to suppress the virus. However, mutations occurring in the viral genetic code can cause resistance to the drugs used against it. The physician then has to select a new combination of drugs to overcome this resistant strain.

The computational models within HIV-TRePS, called "Random Forests," base their predictions on a range of more than 80 different variables including mutations in the viral genetic code, the drugs used to treat the patient in the past, CD4 cell counts (a type of white blood cell that is attacked by HIV) and the
amount of virus in the bloodstream. The models estimate the probability of each combination of drugs reducing the amount of virus to below the limit of detection in the blood (50 copies HIV RNA/ml) based on what the system has 'learnt' during its training with thousands of real clinical cases. The system’s overall accuracy during development and testing was approximately 80%.

"We are very pleased to see the results of these studies published," said Dr Brendan Larder, Scientific Chair of the HIV Resistance Response Database Initiative (RDI). "It is gratifying to see evidence that the years of technical development have resulted in a system that is likely to produce clinical benefits and that physicians are keen to use."

The RDI is already working on a version of HIV-TRePS for use in resource-limited settings where there are fewer treatment options and health care workers do not have access to all the information that this initial system requires. The RDI's approach could also have potential benefit in other diseases, most obviously where drug resistance can be a problem such as hepatitis.

The RDI is an independent, not-for-profit research group set-up in 2002 with the mission to improve the clinical management of HIV infection through the application of bioinformatics to HIV drug resistance and treatment outcome data. Over the eight years since its inception, the RDI has worked with many of the leading clinicians and scientists in the world to develop the world’s largest database of HIV drug resistance and treatment outcome data, containing information from approximately 70,000 patients in more than 15 countries.

**Note:** HIV-TRePS is an experimental system intended for research use only. The predictions of the system are not intended to replace professional medical care and attention by a qualified medical practitioner and consequently the RDI does not accept any responsibility for the selection of drugs, the patient’s response to treatment or differences between the predictions and patients’ responses. More information can be found at: [http://www.hivrdi.org](http://www.hivrdi.org)  2/1/11

**Reference**


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### Tuberculosis Coinfection Increases Risk of Mother-to-Child HIV Transmission

**SUMMARY:** HIV positive women coinfected with tuberculosis (TB) are more likely to transmit HIV to their babies during pregnancy, according to a study described in the February 1, 2011, *Journal of Infectious Diseases*. These findings underline the importance of TB treatment and use of antiretroviral therapy (ART) to prevent HIV transmission.

**By Liz Highleyman**

Amita Gupta and fellow investigators with the Six Week Extended-Dose Nevirapine (SWEN) India Study Team looked at risk factors for mother-to-child HIV transmission among nearly 800 HIV positive women.

Maternal HIV viral load, CD4 Tell count, breast-feeding, use of antiretroviral drugs, and coinfection with malaria are well-established factors associated with vertical HIV transmission, the study authors noted as background, but the impact of tuberculosis has not been well established.

The SWEN study was designed to compare extended nevirapine (Viramune) for 6 weeks versus single-dose nevirapine to reduce mother-to-child HIV transmission among breast-fed infants.

The present analysis included 783 HIV positive Indian women and their infants, who were randomly assigned to the 2 dosing schedules. The researchers assessed the impact of maternal TB occurring during pregnancy and the first year after delivery on vertical HIV transmission.

**Results**

- Among 783 mothers, 3 had existing TB at study entry and 30 developed new TB by 12 months after delivery.
- Among the 33 mothers with TB, 10 (30%) transmitted HIV to their infants, compared with 87 of 750 (12%) mothers without TB (odds ratio 3.31, or more than 3 times the risk).
- A majority of infants with HIV were identified at birth, indicating infection in the womb, rather than during delivery or through breast-feeding.
- In a multivariate analysis, maternal TB was associated with 2.51-fold increased risk of mother-to-child HIV transmission, after adjusting for other maternal factors (viral load, CD4 count, ART) and infant factors (breast-feeding duration, nevirapine use, gestational age, and birth weight) (P=0.04).
"Maternal TB is associated with increased [mother-to-child transmission] of HIV," the study authors wrote. "Prevention of TB among HIV-infected mothers should be a high priority for communities with significant HIV/TB burden."

In an accompanying editorial, Ben Marais from Stellenbosch University in South Africa noted that TB is the most important infectious cause of disease and death among HIV positive women in areas with endemic TB such as sub-Saharan Africa and Asia.

Pregnant women may be more vulnerable to developing TB due to immune system changes (Th-1 down-regulation) during gestation, he suggested. "The strong Th-1 stimulus provided by TB may increase placental inflammation, explaining some of the adverse fetal outcomes observed and the increased risk of in utero HIV [mother-to-child transmission]."

Increased HIV viral load due to TB-related immune stimulation accounted for some of the increased risk, but excess risk remained after adjusting for viral load.

This study "demonstrates that prevention of TB among HIV-infected mothers should be considered as part of a well-functioning prevention of HIV [mother-to-child transmission] program," Marais recommended. 2/1/11

References

Researchers Identify Novel HIV Replication Strategy in Macrophages

**SUMMARY:** HIV appears to use a previously unrecognized strategy to reproduce in macrophages, according to research published in the December 10, 2010, Journal of Biological Chemistry. This mechanism allows the virus to hide out in these long-lived immune cells and continue replicating, even in the absence of its usual genetic building blocks, and offers a potential new target for anti-HIV therapy.

Below is a press release issued by the University of Rochester Medical Center explaining the research and its findings.

**Unexpected Find Opens Up New Front in Effort to Stop HIV**

Rochester, NY—January 21, 2011—HIV adapts in a surprising way to survive and thrive in its hiding spot within the human immune system, scientists have learned. While the finding helps explain why HIV remains such a formidable foe after three decades of research—more than 30 million people worldwide are infected with HIV—it also offers scientists a new, unexpected way to try to stop the virus.

The work by researchers at the University of Rochester Medical Center and Emory University was published Dec. 10 in the Journal of Biological Chemistry.

It's thanks largely to its ability to hide out in the body that HIV is able to survive for decades and ultimately win out against the body's relentless immune assault. One of the virus's favorite hiding spots is an immune cell called a macrophage, whose job is to chew up and destroy foreign invaders and cellular debris.

For more than 15 years, Baek Kim, PhD, has been fascinated by HIV's ability to take cover in a cell whose very job is to kill foreign cells. In the last couple of years Kim, professor of Microbiology and Immunology at the University of Rochester Medical Center, has teamed with Emory scientist Raymond F. Schinazi, PhD, DSc, director of the Laboratory of Biochemical Pharmacology at Emory's Center for AIDS Research, to test whether the virus is somehow able to sidestep its usual way of replicating when it's in the macrophage.

The pair found that when HIV faces a shortage of the molecular machinery needed to copy itself within the macrophage, the virus adapts by bypassing one of the molecules it usually uses and instead tapping another molecule that is available.
Normally, the virus uses dNTP (deoxynucleoside triphosphate, the building blocks for making the viral genetic machinery) to get the job done, but dNTP is hardly present in macrophages—macrophages don't need it, since they don't replicate. But macrophages do have high levels of a closely related molecule called rNTP (ribonucleoside triphosphate), which is more versatile and is used in cells in a variety of ways. The team found that HIV uses primarily rNTP instead of dNTP to replicate inside macrophages.

"The virus would normally just use dNTP, but it's simply not available in great quantities in the macrophage. So HIV begins to use rNTP, which is quite similar from a chemical perspective. This is a surprise," said Kim. "The virus just wants to finish replicating, and it will utilize any resource it can to do so."

When the team blocked the ability of the virus to interact with rNTP, HIV’s ability to replicate in macrophages was slashed by more than 90 percent.

The work opens up a new front in the battle against HIV. Current drugs generally target dNTP, not rNTP, and take aim at the infection in immune cells known at CD4+ T cells. The new research opens up the possibility of targeting the virus in macrophages—where the virus is out of reach of most of today’s drugs.

"The first cells that HIV infects in the genital tract are non-dividing target cell types such as macrophages and resting T cells" said Kim. "Current drugs were developed to be effective only when the infection has already moved beyond these cells. Perhaps we can use this information to help create a microbiode to stop the virus or limit its activity much earlier."

Kim notes that a compound that targets rNTP already exists. Cordycepin in an experimental compound, derived from wild mushrooms, that is currently being tested as an anti-cancer drug. The team plans to test similar compounds for anti-HIV activity.

"This significant breakthrough was unappreciated prior to our paper. We are now exploiting new anti-HIV drugs jointly based on this novel approach that are essentially not toxic and that can be used to treat and prevent HIV infections," said Schinazi, who has developed several of the drugs currently used to treat HIV patients.

Reference

Specific Populations of Gut Bacteria Linked to Fatty Liver
ScienceDaily (Jan. 31, 2011) — The more we learn about biology, the closer we get to being able to treat disease—and the more complicated our understanding of disease itself becomes.

A new research finding showing a strong relationship between complex microbial ecologies in human intestines and the common but serious medical condition known as fatty liver illustrates this paradox.

From past genomic studies, we have learned that a mind-boggling multitude of different kinds of benign bacteria inhabit our intestines and that these populations can vary almost infinitely from one human being to the next. We know that the kind of food we eat is important to our health and we know that having the right bacteria in our intestines is important in digesting our food properly, but we still do not know how our individual variations in gut bacteria might influence more specific health issues. In particular, we do not know how these bacteria influence how the substances we eat affect our organ systems.

In the condition known as fatty liver, fat deposits build up in the liver, with potentially serious health consequences for nearly a third of the American population. Fatty liver can be caused by alcohol abuse, obesity, hormonal changes and/or diabetes. Recent work has suggested that diet is also important with strong indications that deficiencies in the essential nutrient choline might be partially involved in some incidences of the condition. Choline deficiency also implicates genetics, since many people lack the genes to efficiently make choline internally.

Now, a new bioinformatics finding shows that the abundance or scarcity of certain types of bacteria in the gut may also help predict susceptibility to non-alcoholic fatty liver. The implication of the finding is that these groups of bacteria may be influencing the body’s ability to properly use the choline available in food, though the study does not examine the specific metabolic activity of the bacteria involved.

In a metagenomic analysis of the microbial communities living in the intestinal tracts of 15 female patients participating in a study of the effects on liver condition from a choline-depleted diet, bioinformaticians researchers at the University of North Carolina at Charlotte found a strong correlation
between the relative abundances of two specific classes of bacteria and the development of fatty liver. A report on the finding appears in the current issue of the journal *Gastroenterology*.

"Certain bacterial populations correlated very strongly with increased fat in the liver during a restricted choline diet," said Melanie Spencer, a doctoral student in bioinformatics at the University of North Carolina at Charlotte and the lead author on the paper. "To us, it's an amazing result because you just don't see this clear a correlation in biological experiments in humans very often."

Using a metagenomic technique that compares versions of a ribosomal RNA gene known to vary between bacterial groups, the researchers analyzed the genomes of the patients' gut bacteria before, during and after the patients were put on a choline deficient diet. Because all patients consumed identical diets during the study, the researchers predicted that the initially distinct and complex communities of microbes in the patients' intestinal tracts would react by becoming less distinct from each other. The researchers found instead that, though each of the patients' bacterial communities did change a bit, each individual's community still remained distinctive throughout the study.

"What we expected we might find would be that when we put the patients on exactly the same diets, everyone's gut microbe mixture would begin to look similar, with the microbial communities converging. It did not happen—everybody was clearly individual throughout the entire study," Spencer noted.

"So we also looked at how the patients' microbes actually changed in pattern, even though they remained distinct from each other," she said. "The patterns of change were very interesting. Some of the patterns were very distinct in themselves."

The researchers noticed that among the numerous classes of bacteria present in each patient, variations in the populations of two particular groups seemed to correspond with variations between patients in the degree to which they developed a fatty liver during the period of dietary choline depletion.

"Those patients with the highest abundance of *Gammaproteobacteria* at the beginning of the study seemed to have the lowest fatty liver development. The ones with the least developed the most fatty liver," Spencer noted. "Erysipelotrichi showed exactly the opposite association, though this relationship was not quite as strong. So there seemed to be change going on in opposite directions."

When the trends of *Gammaproteobacteria* abundance and *Erysiptoltrichi* scarcity were combined and related to fatty liver development, the relationship became even stronger.

Finally, the researchers factored in individual genetic variations that affect internal production of the nutrient choline and that should explain why some patients developed fatty liver and others did not. Surprisingly, the results showed that each person's genetics did not entirely account for their fatty liver outcome. When the researchers modified the analysis to include the abundances of the two bacterial groups and each individual's genetics, the correlation between fatty liver development and these three factors was nearly perfect. Further mathematical tests were performed to show that the correlations were not likely to be an artificial result of some bias hidden in the analysis.

"There was some concern that we were 'over-fitting' the model," Spencer noted, "so we tested it out and ran a million permutations, altering the bug abundance and subject association, to see if we could identify how many actually showed a higher correlation by chance. What we found is that the p values still held up. We can have a lot of confidence in the result."

The big question that remains for the team is why the two bacterial populations correlate so strongly to the development of fatty liver. Anthony Fodor, UNC Charlotte assistant professor of bioinformatics and the project's director, sees a possible explanation, while warning against drawing specific conclusions without further study.

"We cannot yet assign cause and effect, but it implies that some bacteria are doing something that is making it easier for people to deal with a choline deficiency and for the liver to metabolize fat."

Conversely, the bacteria whose high population levels correlate with disease may be somehow removing available forms of choline from digested food. Fodor explains that further study will be needed to answer these questions.

"We're debating what the next step is," he said. "In some ways, this is a very specialized experiment because we are inducing fatty liver in a very specific way. In the general population, fatty liver is induced in many, many ways and not everyone who has fatty liver has low choline.

"It's probably like Alzheimer's or cancer, where there are many different causes for a disease that displays a common phenotype. More research will be required to determine the extent to which bacterial populations play a role in fatty liver development in the general population, but our results strongly suggest that there may be a link in some people."
Unlocking the Secrets of DNA

ScienceDaily (Jan. 28, 2011) — Neutron scattering has been used to investigate the structure of fibre DNA during the melting transition. This is the range of temperatures over which the bonds between base pairs break, or denature, causing the two strands of DNA to separate. (Credit: Copyright Santiago Cuesta)

Neutron scattering gives information about the correlation between base pairs during denaturation, which is not possible using other techniques. This is used to measure the characteristic size of the denatured regions as the temperature is changed, and these sizes can be compared with those predicted by the theoretical model.

The Peyrard-Bishop-Dauxois (PBD) model predicted that fibre DNA denaturation due to temperature would happen in patches along the molecule, rather than 'unzipping' from one end to another. This experiment, the first to investigate the model, strongly supported the model's predictions for the first part of the transition, as the molecule is heated. The experiment could only measure the first stage because when the strands become 50% denatured they are too floppy to remain ordered and the fibre structure is no longer stable—the DNA sample literally falls to pieces.
“This is an important verification of the validity of model and the associated theory, so it can be applied with more confidence to predict the behaviour and properties of DNA,” says Andrew Wildes, an instrument scientist at ILL. “This will help to understand biological processes such as gene transcription and cell reproduction, and is also a step toward technological applications such as using DNA as nanoscale tweezers or as computer components.”

“There’s been a lot of research producing good data—eg nice melting curves—about the transition point, but these couldn’t tell us how it was happening. For example at 50% melted are half the DNA molecules totally denatured and the other half still firmly joined? Or are the strands of each molecule partially separated? Neutron scattering has enabled us to get structural information on the melting process to answer this kind of question,” says Michel Peyrard Professor of Physics at Ecole Normale Supérieure de Lyon, and co-developer of the PBD model. “As well as implications for technological development it could also help biological applications, such as predicting where genes might be located on long stretches of DNA sequences.”

The experiment follows from the pioneering work of Rosalind Franklin, who showed that x-ray scattering from DNA fibres would give structural information. Based on her work, James Watson and Francis Crick deduced the well-known double helix structure of DNA in 1953. DNA is a dynamic molecule that undergoes large structural changes during normal biological processes. For example, DNA inside the cell nucleus is usually ‘bundled up’ into chromosomes, but when the genetic information is being copied it must be unravelled and the strands separated to allow the code to be read.

Journal Reference:

In Amsterdam, Gay Men Have More Risky Sex

A new long-term study of Amsterdam men who have sex with men (MSM) shows the need for targeted HIV prevention messages, say researchers.

Dr. Iralice A.V. Jansen, of the Public Health Service of Amsterdam, and colleagues followed 1,642 MSM for up to 25 years. The team found that from 1984 to 1988, the percentage of men who reported unprotected anal sex in the last six months declined from 78 percent to 33 percent. The rate slowly ticked up to 38 percent in 1995; by 2009, it had reached 55 percent.

When the researchers looked at yearly rates of new HIV infections, they found a significant drop during the study’s earlier period, from 8.6 percent of MSM in 1985 to 1.3 percent in 1992. But beginning in 1996, a small increase was detected, reaching 2 percent in 2009.

According to the findings, the biggest HIV risk factor was unprotected sex with a casual partner. MSM who reported unprotected receptive sex with a casual partner in the six months prior were six times more likely to become HIV-positive during the study. “There is no doubt that prevention should continue to focus on their sexual behavior with casual partners,” said the team.

In addition, MSM should be cautious with steady partners as well. One-quarter of all HIV infections during the study period were likely transmitted from a steady partner. A growing proportion of infections among men in their 40s and 50s was associated with steady partners; why is not clear, the team said. It could be that older men were more likely to be in long-term relationships and had fewer casual partners compared to younger MSM.

“Targeted prevention messages should continue to focus on sexual behavior with casual partners, but also on sexual behavior within steady relationships,” the authors concluded.

The study, “Ongoing HIV-1 Transmission Among Men Who Have Sex with Men in Amsterdam: A 25-Year Prospective Cohort Study,” was published in AIDS (2011;doi:10.1097/QAD.0b013e328342f6e9).

Banning Prostitution Not the Way to Reduce AIDS in Indonesia, Minister Says

Regional governments need to support a scheme to centralize prostitution in order to better monitor it and push down the number of HIV/AIDS infections in the country, the coordinating minister for people’s welfare, Agung Laksono, said on Monday.

“Some regional governments have pushed through regulations that shut down some of the red-light districts in their districts,” Agung said.
“That is counterproductive because prostitution will only go underground where there are no health guidelines for either the prostitutes or their customers.”

Limiting prostitution to one clearly delineated area would not only help control and monitor the activities but also provide the appropriate health guidance and services, he said.

Nafsiah Mboi, the secretary general of the National AIDS Prevention Commission (KPA), called on regional governments to reassess their regulations on prostitution.

“The idea of shutting down red-light districts is actually very dangerous because there is no control over reproductive health, no condom distribution and also no regular health checks,” Nafsiah said.

She said that the banning of prostitution only pushed it out of sight, with places like ports — of which there are more than 2,000 in Java and Sumatra — and bus terminals becoming centers for the illicit trade.

Gamawan Fauzi, the minister of home affairs, said poverty was the driving force behind prostitution and the rising number of HIV/AIDS case.

Agung called on all political parties and civilian organizations not to politicize the issue of centralizing prostitution or distributing free condoms because they were main keys to combating the spread of the HIV virus in the country.

Unfortunately, he said, there were many who did not support these methods, saying they were “not in accordance with cultural and religious values.”

The official number of people with HIV/AIDS in the country as of December 2010 was 79,979 in 32 provinces, 24,131 of which had full-blown AIDS, Ministry of Health data showed.

The data also showed that the main cause of transmission was unsafe sexual activity among heterosexuals at 52.7 percent, followed by drug injection at 38 percent and homosexual encounters at 3 percent.

Agung said prevention was the only option as there was no cure for the disease.

“Giving away free condoms to those who engage in high-risk sexual activities will help reduce the number of HIV/AIDS cases, as will providing sex education to people in 15 to 24 age bracket,” the minister said.

Agung also honored 10 governors, including Jakarta’s Fauzi Bowo, for their commitment to combating the spread of the disease. The other governors were from Riau Islands, Riau, Bangka-Belitung, Central Java, Yogyakarta, South Kalimantan, South Sulawesi, North Sulawesi and East Nusa Tenggara.

“I hope this award will prompt all provincial leaders to produce the same efforts as those 10 governors,” Agung said, adding the award was based on three criteria — leadership, concern for the HIV/AIDS population and support for the regional AIDS Eradication Commissions.

**Condom Gap “Quite Disturbing” According to PEPFAR**

By David Bryden · February 2, 2011 · Post a comment

There is a pervasive pattern of stockouts of condoms, both male and female condoms, in African countries confronting HIV/AIDS, according to Carolyn Ryan, M.D., M.P.H, the Director of Technical Leadership at the Office of the Global AIDS Coordinator.

She called the condom gap “really quite disturbing,” given that condoms are a crucial tool for HIV prevention. While HIV incidence has fallen in recent years, in 2009 there were an estimated 2.6 million people newly infected with HIV, meaning that about 7000 people are acquiring the infection each day.

She made her comments at the January 6–7, 2011 meeting of PEPFAR’s Scientific Advisory Board. Many of the slides delivered at this meeting have now been made public on the PEPFAR website, including the presentation by Dr. Ryan on prevention and one by Dr. Charles Holmes on care and treatment, including PMTCT.

Dr. Ryan said that OGAC surveyed a number of high HIV prevalence African countries and found that in 9 out of 10 there were persistent, sector-wide stock-outs of condoms during 2008-2010 and that it was common for these stock-outs to last more than 2 months.

She said the median availability of male condoms is only 9.65 condoms per man per year, with large variations from country to country. In 2008 Ethiopia, Cote d’Ivoire and Zambia received the fewest condoms per man from donors among the countries surveyed.

Uganda has had a history of such stockouts, and Ryan’s presentation shows that in 2008 donors shipped only 7.9 condoms per man. A news report from last month indicates that in some northern districts in Uganda, health facilities have no condoms in stock for free distribution. HIV prevalence in the northern-central region of the country is about 8.2 percent, compared with the national average of 6.4 percent.
OGAC is working to understand the complex reasons behind the stockouts, and in a forthcoming report the agency will address how the US intends to respond. Ryan listed a number of factors leading to the shortages:

- Insufficient donor support for both condom provision and demand creation
- Ineffective funding mechanisms, such as ineffective basket funding
- Confusion over the US Government position on condoms
- Lack of prioritization of condoms by host governments
- Weak public sector supply chain systems
- Unfavorable regulatory policies – including import taxes and unnecessary post-shipment testing

Ryan also noted that similar issues led to insufficient supplies of female condoms. The Center for Health and Gender Equity states that the U.S. has dramatically increased its distribution of female condoms in recent years, with shipments growing from 1.1 million in 2003 to 14.6 million in 2009. However, the Center notes that female condoms still represented just 3.2 percent of total U.S. condom shipments in 2009 and that “U.S. government investment in female condom procurement falls short.” In addition, the Center, which will be releasing a new report on access to female condoms, states that the US is “not investing enough in programming to see the product really succeed.”

Ryan’s presentation listed a number of overall gaps in HIV prevention:

- Gap 1 – prevention efforts do not reach those who most need them
- Gap 2 – structural and human rights factors increase risk and vulnerability
- Gap 3 – fragmented interventions miss opportunities to interrupt transmission
- Gap 4 – prevention efforts lack resources and remain limited in scope

Condoms are an essential component in the fight against HIV/AIDS. Increased condom use is considered to have played a role in the decline in HIV incidence in Africa since 2001. According to the latest UNAIDS report, young people in a large number of African countries are reporting more condom use, as well as declines in sex before 15 and in multiple partners.

Yet, tracking US spending on condoms is difficult. One study has shown a decline in US support for condom provision between 2005 and 2008, however, it is unclear if the analysis considered all US government funding sources, including PEPFAR. In FY 2009, PEPFAR spent $272.5 million, including headquarters spending, in the budget category that includes condoms, “Other Prevention”, primarily through USAID, up from $229 million in FY 2008, according to PEPFAR’s Operational Plans.

Insufficient donor support and a history of mixed signals on condoms have been top concerns of HIV/AIDS advocates. Concerns are also growing that the momentum for foreign aid cuts in the US Congress will affect funding for HIV programs, including resources for purchase and distribution of condoms.

Notwithstanding objections to condom distribution by some conservatives, there is evidence that Americans from a wide variety of backgrounds, including Christian Evangelicals and Catholics, strongly support condoms for HIV prevention, and advocates hope that a strong message for prevention funding will lead to greater support in the Congress.

**When HIV Is Acquired Affects Pregnancy Rates**

By Michael Smith, North American Correspondent, MedPage Today, February 02, 2011

**Today Action Points**

- Note that this study demonstrates important differences in pregnancy rates and outcomes depending on when women are infected with HIV.
- Note that behaviorally infected women had significantly higher rates and vertically infected patients were much more likely to terminate a pregnancy.

**Review**

Young women infected with HIV at birth appear to be significantly less likely to get pregnant compared with those who acquired the virus as a result of risky behavior, according to a retrospective study.

The study, which looked at the medical records of more than 180 HIV-positive women, also found that those infected at birth were more than six times as likely to terminate the pregnancy, according to Kelly Gebo, MD, MPH, of Johns Hopkins University in Baltimore, Md., and colleagues.

On the other hand, there were no differences in adverse outcomes of pregnancy, such as premature birth and spontaneous abortion, Gebo and colleagues reported in the Feb. 2 issue of the *Journal of the American Medical Association.*
Females infected with HIV at birth—or vertically infected—are now reaching child-bearing age, thanks to highly active anti-retroviral therapy, the authors noted. But it's possible that pregnancy incidence and adverse outcomes differ between those young women and women who have acquired the virus behaviorally, they said.

To investigate the issue, Gebo's group examined records of 181 young women treated between January 1997 and May 2009 at four academic pediatric clinics in the HIV Research Network. The 130 vertically infected women, ages 13 to 24, were followed for a median of 8.9 years. The 51 behaviorally infected patients were followed from their clinic enrollment to age 24, for a median of 1.6 years.

Gebo and colleagues found:

- 66 of the participants had a total of 96 pregnancies, including 34 pregnancies among the 130 vertically infected women and 62 among the 51 behaviorally infected patients.
- 28 vertically infected patients (or 21.5%) had at least one pregnancy, compared with 38 behaviorally infected patients (or 74.5%), a difference that was significant at $P<0.001$.
- There were 52.3 pregnancies per 1,000 patient-years among vertically infected patients and 372.9 per 1,000 patient-years among behaviorally infected patients, which was again significant at $P<0.001$.
- Behaviorally infected women were more likely to have more than one pregnancy compared with vertically infected patients—36.8% compared with 14.3%, which was significant at $P=0.04$.
- Vertically infected women were also more likely to terminate a pregnancy—the odds ratio was 6.5, with a 95% confidence interval from 2.2 to 19.2.
- There were no significant differences in the rates of spontaneous abortion, stillbirth, or prematurity.

The authors noted that the rates of pregnancy among behaviorally infected young women were higher than those seen in the general population—five times higher for those ages 15 through 19 and 2.5 times higher for women ages 20 to 24, respectively.

Compared with national data for young women, they also had higher rates of premature births and spontaneous abortions—34.4% versus 21.5% and 13.5% versus 8.9%, respectively.

Gebo and colleagues cautioned that the findings might not apply to all clinics caring for HIV-positive young women. In addition, they noted that the study was limited by its retrospective nature, small numbers, and shorter follow-up time for behaviorally infected women.

Primary source: Journal of the American Medical Association

**Girls Opting Out of HPV Shots**

*London Free Press (Ontario)*, (01.28.2011) Kelly Pedro

In 2009-10, about 45 percent of local eighth-grade schoolgirls received the necessary three doses of Gardasil vaccine against human papillomavirus, according to the Middlesex-London Health Unit (MLHU). That is slightly down from 48 percent uptake of the federally subsidized, school-based HPV vaccine program in 2008-09. However, the rate is still above the 39 percent uptake for 2007-08, when the health unit began the program.

"We'd like to be higher, obviously," said Dr. Bryna Warshawsky, MLHU's associate medical officer of health. "We'd like to be more toward 70 percent," she said, with 100 percent uptake the ultimate goal.

Gardasil protects against two HPV strains responsible for about 70 percent of cervical cancer cases and two other strains that cause about 90 percent of genital warts.

"Cervical cancer is extremely, extremely uncommon," said Patricia Armstrong, a mother in Rodney who refused consent to have her daughter vaccinated, fearing Gardasil is unsafe. "It's one of the most treatable cancers out there. The chances of getting it are so slim." Armstrong counsels her daughter to get annual Pap smears and to avoid sexual contact, through which HPV is spread.

Cervical cancer is the second most common cancer in women ages 20-44, MLHU says. Every year, 390 women in Canada die from cervical cancer, and about 1,400 women are newly diagnosed with it.

"There were no safety concerns when the vaccine was authorized for use and there continues to be no safety concerns," Warshawsky said.
Researchers have engineered an RNA molecule to block freely circulating HIV as well as replication inside infected cells. Tests in mice engineered to be susceptible to HIV showed the chimeric RNAs reduced HIV-1 replication by several orders and staved off viral-induced CD4+ T-cell declines, say researchers.

One part of the RNA molecule has a high binding affinity to the gp120 protein found on the surface of HIV’s envelope and on HIV-infected cells. It is designed to neutralize free-floating HIV in the blood and attach to and deliver into infected cells a small interfering RNA (siRNA) “that triggers sequence-specific degradation of HIV RNAs,” the study authors wrote.

“You’re only targeting what has to be targeted,” said co-author John Rossi, a molecular biologist at the City of Hope’s Beckman Research Institute in Duarte, Calif., who likened the molecule to a “smart bomb.”

The molecule could someday figure into combination or stand-alone therapy, Rossi said. The antiviral effect of the chimera lasts about a week, so any treatment would require regular injections.

“They do see quite dramatic inhibition” of HIV, said Ben Berkhout, a retrovirologist at the University of Amsterdam. But most seems traceable to the anti-gp120 aptamer, or binding affinity, rather than the work of the siRNA, he said. “I haven’t seen the double action of this combination,” he said.

Rossi and colleagues found that in comparison to the aptamer alone, its combination with siRNA provided more extensive inhibition. The team found siRNA in the lymphocytes of treated mice, and measurements of the two targeted sequences—tat and rev—in such cells were 75 percent to 90 percent lower after treatment. Tat and rev genes also were cut in the right spots, indicating the molecule worked.


Bacteria in the Gut May Influence Brain Development

One type of bacteria normally found in the gut is E. coli. E. coli bacteria serve the useful task of keeping other bacterial organisms in check (however, the O157:H7 E. coli strain produces a potent toxin). (Credit: CDC/ Berenice Thomason)

ScienceDaily (Feb. 1, 2011) — A team of scientists from around the globe have found that gut bacteria may influence mammalian brain development and adult behavior. The study is published in the scientific...
journal *PNAS*, and is the result of an ongoing collaboration between scientists at Karolinska Institutet in Sweden and the Genome Institute of Singapore.

The research team compared behavior and gene expression in two groups of mice—those raised with normal microorganisms, and those raised in the absence of microorganisms (or germ-free mice). The scientists observed that adult germ-free mice displayed different behavior from mice with normal microbiota, suggesting that gut bacteria may have a significant effect on the development of the brain in mammals.

The adult germ-free mice were observed to be more active and engaged in more 'risky' behavior than mice raised with normal microorganisms. When germ-free mice were exposed to normal microorganisms very early in life, as adults they developed the behavioral characteristics of those exposed to microorganisms from birth. In contrast, colonizing adult germ-free mice with bacteria did not influence their behavior.

Subsequent gene profiling in the brain identified genes and signaling pathways involved in learning, memory and motor control that were affected by the absence of gut bacteria, highlighting the profound changes in the mice that developed in the absence of microorganisms. This suggests that, over the course of evolution, colonization of the gut by microorganisms (in total 1.5 kilograms) in early infancy became integrated into early brain development.

"The data suggests that there is a critical period early in life when gut microorganisms affect the brain and change the behavior in later life," says Dr. Rochellys Diaz Heijtz, first author of the study.

"Not only are signal substances like serotonin and dopamine subject to regulation by bacteria, synapse function also appears to be regulated by colonizing bacteria," continues Prof. Sven Pettersson, coordinator of the study. "However, it is important to note that this new knowledge can be applied only to mice, and that it is too early to say anything about the effect of gut bacteria on the human brain."

**Journal Reference:**

**Gilead Says FDA Won't Accept Filing for AIDS Pill**
*Bloomberg News*, (01.25.2011) Rob Waters
The Food and Drug Administration wants additional information on Gilead Sciences Inc.’s proposed once-daily AIDS drug combination, the drug maker said. FDA had originally agreed to complete a priority review of the combination, Gilead’s Truvada with Johnson & Johnson’s (J&J) experimental drug TMC278, in six months. Since FDA decided not to accept the application, the clock is not ticking, said Norbert Bischofberger, Gilead’s executive vice president for research and development and chief scientific officer.

FDA wants more details on the chemistry and manufacturing of the combination treatment. During testing of the proposed drug, Gilead discovered a “degradation product” was present in the medicine at a level that requires evaluation, the drugmaker said. “The impurities have to be qualified to be sure they don’t pose a risk,” said Bischofberger.

Gilead said it will give FDA the requested information by the end of March. “I am confident this will result in only a minor delay in bringing this important new treatment to patients,” said John Martin, Gilead’s CEO.

Tibotec, a unit of J&J, submitted a marketing application to FDA for TMC278 following the completion of two large clinical trials. According to Gilead, the application for Truvada-TMC278 is supported by a bioequivalence study showing the drugs combined reached the same levels in the bloodstream as each drug separately.

The combination drug could attract patients seeking to avoid the side effects of Gilead’s Atripla, which includes Bristol-Myers Squibb Co.’s Sustiva. Data presented at the July International AIDS Conference in Vienna showed TMC278 suppressed HIV as well as Sustiva, said Michael Saag of the University of Alabama-Birmingham. That study also showed that Sustiva kept 4.8 percent of patients’ viruses from rebounding, compared to 9 percent for TMC278.

**Schools HIV Test Program on Track**
*Independent Online*, (01.29.2011) Sipokazi Fokazi; Cape Argus
If everything goes as planned, South Africa could roll out a voluntary HIV counseling and testing (HCT) campaign in schools this February.
The health and education departments are working in consultation on campaign logistics and “special measures” to guarantee the confidentiality and support of the children. Implementation of the program will not be rushed at the expense of the students’ benefit, said Fidel Hadebe, a Department of Health spokesperson.

“The needs of learners for child-specific support and follow-up requires the HCT campaign to adopt extra preparatory measures to ensure the best interests of the children involved,” said Hadebe.

To avoid disrupting school instruction, the Western Cape Education Department will provide testing only on weekends and school holidays. Faiza Steyn, a spokesperson for the provincial health department, said the campaign would be carried out in the province as part of a wellness day targeting high schools. All testing, which requires parental consent, will be done in private spaces at the schools. The participation of parents, teachers, and others will be encouraged to minimize any teasing of participants.

According to Hadebe, in addition to encouraging young people to know their HIV status, HCT would also bring services to students who spend most of their time in classes, and have less time to go to clinics to be tested.

“The message we are trying to bring across to learners,” said Hadebe, “is, if you are negative please stay negative. But, to those that might test positive, we are saying that we will give them the necessary support in terms of counseling and treatment.”

Yale scientists identify a deadly tool in Salmonella’s bag of tricks
The potentially deadly bacterium Salmonella possesses a molecular machine that marshals the proteins it needs to hijack cellular mechanisms and infect millions worldwide.

In a paper published Feb. 3 online in Science Express, Yale University researchers describe in detail how Salmonella, a major cause of food poisoning and typhoid fever, is able to make these proteins line up in just the right sequence to invade host cells.

“These mechanisms present us with novel targets that might form the basis for the development of an entirely new class of antimicrobials,” said Jorge Galan, senior author of the paper and the Lucille P. Markey Professor of Microbial Pathogenesis and chair of the Section of Microbial Pathogenesis at Yale.

Galan’s lab has been in the forefront of investigating the intricate mechanisms that microbes such as Salmonella use to infect foreign cells. In the new study, Galan and colleagues identify what they call a bacterial sorting platform, which attracts needed proteins and lines them up in a specific order. If the proteins do not line up properly, Salmonella, as well as many other bacterial pathogens, cannot “inject” them into host cells to commandeer host cell functions, the lab has found.

Understanding how this machine works raises the possibility that new therapies can be developed which disable this protein delivery machine and therefore thwart the ability of the bacterium to become pathogenic. This process would not kill the bacteria as most antibiotics do, but would cripple its ability to do harm.

In theory, this means that bacteria such as Salmonella might not develop resistance to new therapies as quickly as they usually do to conventional antibiotics. Salmonella sickens at least 40,000 people annually in the United States and kills about 400 people, according to the Centers for Disease Control.

Boosting body’s immune response may hold key to HIV cure
Australian scientists have successfully cleared a HIV-like infection from mice by boosting the function of cells vital to the immune response.

A team led by Dr Marc Pellegrini from the Walter and Eliza Hall Institute showed that a cell signaling hormone called interleukin-7 (IL-7) reinvigorates the immune response to chronic viral infection, allowing the host to completely clear virus. Their findings were released in today’s edition of the journal Cell.
Dr Pellegrini, from the institute's Infection and Immunity division, said the finding could lead to a cure for chronic viral infections such as HIV, hepatitis B and C, and bacterial infections such as tuberculosis, which are significant economic and global health burdens.

Current approaches to curing chronic infections tend to focus on generating a long-lived immune response to a specific disease. Dr Pellegrini, working with colleagues Mr Simon Preston and Mr Jesse Toe, and collaborators Professors Pamela Ohashi and Tak Mak from the Ontario Cancer Institute, argues that long-lived immune responses to chronic diseases are not always effective, and has instead concentrated on how the immune response can be manipulated to better fight infection.

"Viruses such as HIV and hepatitis B and C overwhelm the immune system, leading to establishment of chronic infections that are lifelong and incurable," Dr Pellegrini said. "Despite tremendous efforts, long-lived immune responses for some of these viruses are ineffective, because the body is so overrun by virus that the immune system, in particular T cells, just give up trying to battle the infection. Some people have coined the phrase 'immune exhaustion' to explain the phenomenon. Our approach is to discover some of the mechanisms that cause this immune exhaustion, and manipulate host genes to see if we can boost the natural immune response in order to beat infection."

The team investigated the role of IL-7, a naturally-occurring immune hormone, in a mouse model of HIV infection. IL-7 is a cytokine (cell signalling hormone) that plays a critical role in immune system development and maintenance. "We found that IL-7 boosted the immune response in a pretty profound fashion, such that animals were able to gradually clear the virus without too much collateral tissue damage," Dr Pellegrini said.

Further investigations revealed that, at the molecular level, IL-7 switched off a gene called SOCS-3.

"In an overwhelming infection, SOCS-3 becomes highly activated and suppresses the immune response, probably as a natural precaution to prevent 'out-of-control' responses that cause collateral damage to body tissue," Dr Pellegrini said. "In the case of these overwhelming infections, the immune system effectively slams on the brakes too early, and the infection persists."

Mr Preston, who worked on the SOCS-3 studies, said that switching off the SOCS-3 gene boosted the immune system and helped the animals to completely eliminate the infection.

"The key for us was figuring out that turning off SOCS-3 only really worked when it was within T cells," Mr Preston said. "It allowed the immune response to boost the number of virus-specific T cells and have an immune response good enough to eliminate the virus without initiating an immune response that was too large and would make the animal sick."

Dr Pellegrini said the research had provided excellent ideas for new therapies that could target and boost host immune cells to fight disease, rather than targeting the disease itself.

"The findings could help to develop drugs that target some of these host molecules, such as SOCS-3, and turn them off for very short, defined periods of time to reinvigorate the T cells, allowing them to regroup to fight infection," he said.

**New Clue to Lupus: Failed Autoimmune Suppression Mechanism**

ScienceDaily (Feb. 3, 2011) — Researchers at Dana-Farber Cancer Institute in Cambridge, Mass., in collaboration with Jackson Laboratory scientists, have identified a regulatory defect that drives lupus.

Correcting the defect "may represent an effective therapeutic approach to systemic lupus erythematosus-like autoimmune disease," the researchers state in their research paper, published in the *Proceedings of the National Academy of Sciences*. The research team was led by Harvey Cantor, M.D.,
chair of the department of cancer immunology and AIDS at Dana-Farber, in collaboration with the laboratory of Jackson Professor Derry Roopenian, Ph.D.

Autoimmune diseases develop when the immune system, which is supposed to identify and vanquish potentially dangerous infectious agents, instead attacks the individual's own body. Most autoimmune diseases strike specific organs, such as the pancreas in type 1 diabetes. Lupus, however, is a systemic disease in which abnormal antibodies are produced throughout the body, inflaming a variety of tissues and organs, including the skin, heart, lungs, kidneys and brain.

Folicular T helper (TFH) cells fuel B cells to produce antibodies, which can be useful in fighting infections. But in lupus, TFH fuel B cells that produce dangerous antibodies that attack normal tissues (autoantibodies). CD8+ T cells ("killer T cells"), on the other hand, normally attack and destroy only infected cells. Cantor and colleagues discovered that a small, but critically important, population of CD8+ T regulatory, or Treg, cells are specially equipped to destroy TFH cells, and by doing so, prevent lupus from developing.

Using a mouse model for systemic lupus erythematosus in humans that was originally discovered at 30 years ago by Edwin Murphy at The Jackson Laboratory, the Dana-Farber researchers, working with Roopenian's laboratory, found defects in CD8+ Treg activity.

The new paper, Roopenian explains, is the first to demonstrate the potential breakdown of this suppression mechanism in lupus. "Overcoming this defect," he says, "offers a potential approach prevent lupus."

Journal Reference:

NYTimes, February 3, 2011
Close Look at a Flu Outbreak Upends Some Common Wisdom
By NICHOLAS BAKALAR
If you or your child came down with influenza during the H1N1, or swine flu, outbreak in 2009, it may not have happened the way you thought it did.

A new study of a 2009 epidemic at a school in Pennsylvania has found that children most likely did not catch it by sitting near an infected classmate, and that adults who got sick were probably not infected by their own children.

Closing the school after the epidemic was under way did little to slow the rate of transmission, the study found, and the most common way the disease spread was a through child’s network of friends.

Researchers learned all this when they studied an outbreak of H1N1 at an elementary school in a semirural community in spring 2009. They collected data in real time, while the epidemic was going on.

With this information on exactly who got sick and when, plus data on seating charts, activities and social networks, they were able to use statistical techniques to trace the spread of the disease from one victim to the next. Their report appears online in the Proceedings of the National Academy of Sciences.

The scientists collected data on 370 students from 295 households. Almost 35 percent of the students and more than 15 percent of their household contacts came down with flu. The most detailed information was gathered from fourth-graders, the group most affected by the outbreak.

The class and grade structure had a significant effect on transmission rates. Transmission was 25 times as intensive among classmates as between children in different grades. And yet sitting next to a student who was infected did not increase the chances of catching flu.

Social networks were apparently a more significant means of transmission than seating arrangements. Students were four times as likely to play with children of the same sex as with those of the opposite sex, and following this pattern, boys were more likely to catch the flu from other boys, and girls from other girls.

The progress of the disease from day to day followed these social interactions: from May 7 to 9, the illness spread mostly among boys; from May 10 to 13 mostly among girls.

“Our social networks shape disease spread,” said Simon Cauchemez, the lead author. “And we can quantify the role of social networks.”

Thirty-eight percent of children 6 to 10 were infected, compared with 23 percent of 11- to 18-year-olds and 13 percent of those older than 18. Adults were only about half as susceptible as children, but when they got sick they were just as likely to transmit the virus to others.
The school closed from May 14 to 18, but there was no indication that this slowed transmission. It may already have been too late — May 14 was the 18th day of the outbreak, and 27 percent of the students already had symptoms.

The scientists found no difference in transmission rates during the closure and during the rest of the outbreak. This, they write, confirms earlier studies showing that a school has to be closed quite early in an epidemic to have any effect on disease transmission.

Only 1 in 5 adults caught the illness from their own children, and this goes against one of the most common arguments for closing schools: that it will prevent the disease from moving from the school to households.

“Here we find that most of the infected adults were not infected by one of the children in their household,” said Dr. Cauchemez, a research fellow at Imperial College London. “This information could be used to understand whether it might be better to close a school, or to close individual classes or grades.”

Other experts were impressed with the work. “I think it’s a nice step,” said Ira M. Longini Jr., a professor of biostatistics at the Fred Hutchinson Cancer Research Center in Seattle. “It’s a beautiful analysis of an important dataset. This virus spreads very fast among school-age children, so the topic is important.”

Super Bowl a Magnet for Under-Age Sex Trade

 Reuters, (01.31.2011)

“The Super Bowl is one of the biggest human-trafficking events in the United States,” said Texas Attorney General Greg Abbott at a January trafficking-prevention meeting. On Sunday, Dallas will play host to this year’s Super Bowl.

As many as 300,000 girls aged 11 to 17 are lured into the US sex industry annually, according to data from a 2007 report sponsored by the Department of Justice and written by the non-profit Shared Hope International. One section of the report referring to Atlanta estimates that 90 percent of runaways and children whose parents force them to leave home fall into the sex trade.

Jerry Strickland, communications director in the Texas attorney general’s office, estimates that up to 10,000 adult and under-age girls have come to previous Super Bowls for sex work. “The statistics are a moving target. They can’t be counted in turnstiles like ticket holders,” said Strickland.

Deena Graves, executive director of the child advocacy group Traffick911, noted law enforcement agencies and advocacy groups rescued approximately 50 girls during the previous two Super Bowls. Six were registered on the Center for Missing and Exploited Children website — one from as far away as Hawaii.

To combat the trade, authorities, child welfare advocates and the airline industry are supporting Traffick911’s “I’m Not Buying It!” campaign. Nancy Rivard, president of Airline Ambassadors International, is working with 100 flight crews to distribute the group’s materials on flights. In addition, representatives from American Airlines, Delta, United, Quantas and American Eagle are holding trainings to help spot signs of trafficking.

The “I’m Not Buying It!” petition on www.change.org has amassed some 67,000 signatures, and the campaign is garnering the support of 60 non-profits and faith-based groups, as well as celebrities such as Dallas Cowboy Jay Ratliff. The father of two daughters is recruiting other NFL players for the effort.

“You hear of sex trafficking overseas,” said Ratliff. “But you never imagine it is happening in the United States.”

Disparities in Diagnoses of HIV Infection Between Blacks/African Americans and Other Racial/Ethnic Populations — 37 States, 2005-2008

Morbidity and Mortality Weekly Report Vol. 60; No. 4: P. 93-98, (02.04.2011) B. Laffoon; A. Satcher Johnson, MPH; S. Cohen, MPH; X. Hu, MS; R.L. Shouse, MD

Since early in the HIV epidemic, blacks/African Americans have been disproportionately affected, the report authors noted. Drawing on data from the National HIV Surveillance System, they estimated numbers, percentages and rates of HIV diagnoses in blacks/African Americans during 2005-08 and described the results of those analyses.

During 2005-08, blacks/African Americans accounted for 50.3 percent of HIV diagnoses in 37 states with mature HIV surveillance systems, despite representing just 13.6 percent of the population in these
states. By comparison, whites accounted for 67.9 percent of the population and 29.4 percent of diagnoses, while Hispanics/Latinos accounted for 13.4 percent of the population and 17.8 percent of diagnoses.

Among males, black/African Americans represented the largest proportion (44.8 percent) of HIV diagnoses during 2005-08. Among females, black/African Americans accounted for most (65.9 percent) diagnoses, including a majority for the South (70.9 percent), Midwest (60.9 percent) and Northeast (60.0 percent). Blacks/African Americans comprised the largest proportion of HIV diagnoses in every age group.

By transmission category, among black/African-American males, male-to-male sexual contact was most frequently reported (61.1 percent), followed by heterosexual contact (23.1 percent), injection drug use (11.9 percent) and both IDU and male-to-male (3.6 percent). Among black/African-American females, most were exposed through heterosexual contact (85.2 percent), followed by IDU (14 percent).

Males ages 13-24 accounted for the largest proportion (30.9 percent) of HIV diagnoses among black/African-American males with infection attributed to male-to-male sexual contact, followed by males ages 25-34 (28.7 percent) and 35-44 (23.7 percent). Among black/African-American female diagnoses, the largest percentages were in those ages 35-44.

For more information about CDC efforts to address these disparities, visit: www.cdc.gov/hiv/aaa and www.nineandahalfminutes.org.

**Johns Hopkins researchers capture jumping genes**

**RIPs are alive and well—and moving—in the human genome**

An ambitious hunt by Johns Hopkins scientists for actively "jumping genes" in humans has yielded compelling new evidence that the genome, anything but static, contains numerous pesky mobile elements that may help to explain why people have such a variety of physical traits and disease risks.

Using bioinformatics to compare the standard assembly of genetic elements as outlined in the reference human genome to raw whole-genome data from 310 individuals recently made available by the 1000 Genomes Project, the team revealed 1,016 new insertions of RIPs, or retrotransposon insertion polymorphisms, thereby expanding the catalog of insertions that are present in some individuals and absent in others. Their results appeared online October 27 in Genome Research.

Retrotransposons are travelling bits of DNA that replicate by copying and pasting themselves at new locations in the genome. Having duplicated themselves and accumulated over evolutionary history, transposable elements now make up about half of the human genome. However, only a tiny subfamily of these insertions known as LINE-1 (L1) is still active in humans. Line 1 insertions are able to mobilize not only themselves but also other pieces of DNA.

"In any individual, only between 80 to 100 retrotransposons are actively copying and inserting into new sites," says Haig Kazazian, M.D., professor of human genetics, McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine. "We're not only discovering where they are and who has which ones, but also finding out that they insert with a remarkable frequency: On the order of one in every 50 individuals has a brand-new insertion that wasn't in their parents."

The researchers recognized L1 retrotransposons — distinguishing them from the vast amount of fixed "fossil" transposable elements that litter the genome — because these actively jumping genes are human specific and almost exactly the same in sequence from one person to another.

"Our genome contains around half a million interspersed L1 sequences that have accumulated over evolutionary history, along with over a million more repeats, most of which were mobilized by L1 elements," explains Adam D. Ewing, Ph.D., a postdoctoral fellow in Kazazian's lab. "Since the vast majority of these are ancestral and therefore common to all humans and even some of our primate relatives, we can ignore them and focus on L1s that contain human-specific characters in their sequences. Those are the actively mobilized elements responsible for considerable genomic diversity among human individuals."

The high frequency of these L1 insertions gives us a better idea about the extent of human diversity, according to Kazazian, whose 22-year focus on retrotransposons seeks to reveal how they alter the expression of human genes.

Just as the structural variants known as single nucleotide polymorphisms (or SNPs, pronounced "snips") serve as markers for various diseases, the hope is that RIPs — which are up to 6,000 times bigger than SNPs, and therefore may have a stronger effect on gene expression — will correlate with disease phenotypes.
"In that same way that someone had to go out and find the SNPs, this study was about finding RIPs that remain active and continue to produce new insertions," Kazazian says. "Now we have the background necessary to begin studies that may correlate these L1 insertions with everything from autism to cancer."

**Discovery of Jumping Gene Cluster Tangles Tree of Life**

ScienceDaily (Feb. 5, 2011) — Since the days of Darwin, the "tree of life" has been the preeminent metaphor for the process of evolution, reflecting the gradual branching and changing of individual species.

The discovery that a large cluster of genes appears to have jumped directly from one species of fungus to another, however, significantly strengthens the argument that a different metaphor, such as a mosaic, may be more appropriate.

"The fungi are telling us something important about evolution ... something we didn't know," said Antonis Rokas, assistant professor of biological sciences at Vanderbilt. He and research associate Jason Slot reported their discovery in the Jan. 25 issue of the journal *Current Biology*.

Rokas and Slot discovered that millions of years ago, a cluster of 23 genes jumped from one strain of mold commonly found on starchy foods like bread and potatoes, *Aspergillus*, to another strain of mold that lives in herbivore dung and specializes in breaking down plant fibers, *Podospora*.

The findings came as a major surprise, as there are only a handful of cases in recent evolutionary history where this type of gene transfer between organisms, known as horizontal gene transfer, has been reported in complex cells like those found in plants, animals and fungi.

"Because most people didn't believe that such large gene clusters could be transferred horizontally, they haven't looked for them and they haven't been found," Rokas said.

Rokas and Slot detected the unprecedented gene cluster transfer during a detailed comparison of the entire genomes of nearly 100 species of fungi. The primary goal of their research is to identify the most reliable methods for determining the evolutionary relationships of species of all kinds. In the course of their analysis, they discovered the 23-gene capture.

The jumping gene cluster codes for a toxic compound called sterigmatocystin. Cells produce this type of compound to attack competing organisms or to protect themselves from attacks. As a result, these types of compounds are the source of a number of important drugs, like penicillin and cyclosporin, as well as a number of natural poisons.

"Fungi produce an astonishing variety of drugs and poisons. Our discovery that one of the largest gene clusters responsible for making such a poison moved intact between species suggests that horizontal transfers of wholesale pathways may have contributed significantly to the generation of this diversity," Rokas said.

In the past, evolutionary research has focused on the passage of genes from parent to child, known as vertical gene transfer. This process, acted out over the eons of geological time, gives rise to the branching structure of the tree of life.

Since the 1980's, however, evolutionary scientists have become increasingly aware that horizontal or lateral gene transfer also plays a major role in evolution. In vertical gene transfer, all the genetic material in each new species come from a single ancestral species. In horizontal gene transfer, by contrast, species that receive bits of genetic material from its neighbors are directly related to a number of often unrelated species.

Horizontal gene transfer was first discovered in bacteria, and has been recognized as largely responsible for the problem of drug resistance. If one bacterium evolves a method for surviving a drug, this ability can spread rapidly to other unrelated microorganisms via horizontal gene transfer, substantially reducing the drug's effectiveness.

Though researchers now generally agree that horizontal gene transfer is relatively common among simple organisms like bacteria, they have continued to assume that it remained relatively rare among complex organisms like plants and animals.

"The thinking has been that there is very little horizontal gene transfer among plants and animals except for a few big, ancient events and maybe the occasional transfer of a single gene here or there," Slot said. "Our discovery suggests that the horizontal transfer of gene clusters may have been a big player not only in the evolution of bacteria but also in more complex organisms."

**Journal Reference:**

How the Body’s Frontline Defense Mechanism Determines If a Substance Is a Microbe

ScienceDaily (Feb. 5, 2011) — The Proceedings of the National Academy of Sciences has just published an article describing how the first line of defense of the human immune system distinguishes between microbes and the body’s own structures. The basis of this recognition mechanism has been unclear since the key protein components were discovered over 30 years ago—and has now finally been cracked by researchers at the University of Helsinki, Finland.

When a microbe has infected us, the first defense mechanism that attacks it is a protein-based marking and destruction system called complement. It usually suffices that foreign targets are marked as enemy while our own targets are left untouched, so that white blood cells attack only foreign targets like bacteria, viruses and parasites.

Researchers at the Haartman Institute and the Institute of Biotechnology at the University of Helsinki have, as a result of years of work, been able to show how complement distinguishes foreign structures from our own structures—all days before antibodies have a chance to develop. The key to unlocking the problem was when the groups of Sakari Jokiranta and Adrian Goldman in Helsinki, along with David Isenman’s group in Canada, were able to solve the structure of two components of the system at atomic resolution. The structure revealed a stunning unexpected arrangement: factor H bound two of the C3bs, which mark foreign targets, in two different ways. Laboratory tests showed that this actually happened: to recognize our own cells, factor H binds not only C3b but also the cell surface at the same. Thus, the system marks only foreign structures for destruction by the white blood cells.

This new understanding of how host and foreign structures are distinguished by the front-line defense mechanism also explains how the severe and often fatal form of disease "Hemolytic Uremic Syndrome" (HUS) starts. This rare disease often occurs in children and can be caused by genetic defects in factor H or in C3b, or else by the disruption of factor H activity by antibodies. Some of these patients have had to have complete liver-kidney transplants because of the severity of the disease.

The research’s surprising and wide-reaching result will be important not only in terms of advancing basic immunological research but also in the diagnosis and treatment of very sick children.

Journal Reference:

Bionor Will Conduct Further Trials of HIV Vaccine After Early Test Failure

By Frances Schwartzkopff—Feb 4, 2011 6:20 AM ET Fri Feb 04 11:20:03 GMT 2011

Bionor Pharma ASA is proceeding with development of its experimental HIV vaccine even after it failed to keep patients off antiviral drugs in an early trial.

Buoyed by subsequent findings that the vaccine reduces the amount of virus that causes AIDS, Bionor is planning tests that it can finance on its own to confirm the results, and more extensive ones if it finds a partner, Chief Executive Officer Henrik Lund said yesterday in a telephone interview.

“We are looking for both private and public partners,” said Lund, who became CEO of the Oslo-based drugmaker in September. Lund spent the previous five years as head of research and development operations in Europe, Asia and Latin America for London-based AstraZeneca PLC.

The company’s shares fell 81 percent Oct. 1, when the results of the trial were first released. Bionor has since climbed almost fourfold in the past three months, making it the biggest gainer among Nordic drugmakers. Bionor in December secured funding through the first quarter of 2013 after selling trademarks for some nutrition products for 110 million kroner ($19 million), putting it in a “healthy financial situation,” Lund said.

Researchers have been looking for a vaccine that can harness the body’s own natural defenses to prevent and kill HIV infections. The search started about a quarter of a century ago, with the first trial beginning in 1988 at the Bethesda, Maryland-based National Institutes of Health. The virus’ ability to mutate and hide has slowed progress.

“What they’re trying to do is not easy,” said Gary Nabel, director of NIH’s Vaccine Research Center and one of the scientists who last year discovered an antibody that kills more than 90 percent of HIV strains.
‘Some Potential’
“This is a product that has some potential and needs further testing,” Nabel said in a Jan. 26 phone interview. “It’s really a toss of the coin as to whether the study will replicate the effect and whether the effect will be clinically significant.”

In its October trial, Bionor sought to test whether its vaccine would strengthen the body’s immune system enough so patients could stay off anti-retroviral therapy, typically a combination of several drugs with side effects ranging from headaches and rashes to vomiting and fever. Results showed patients were just as likely to resume ART treatment.

Bionor, which has posted losses in 11 of the past 12 years, is designing another trial that, like the failed one, likely will test the vaccine’s effectiveness against a placebo in several treatment centers across several countries, Lund said. Unlike the first trial, the second will test to what extent virus levels fall in patients taking the treatment, he said.

Preliminary Discussions
Preliminary discussions with potential private investors and public partners also have begun, Lund said.

The initial trial may have failed because too few people took part, Richard Pollard, that study’s lead investigator and head of the infectious diseases division at the University of California, Davis’ Health System, said in an e-mail.

“All approaches to control viral replication are needed and should be pursued,” Pollard said in a Jan. 12 e-mail. “There are still multiple attempts going on to enhance immunity to one’s own virus, and it is only through continued exploration that we will get needed results.”

Other companies testing HIV vaccines include Novartis AG, Inovio Pharmaceutical Inc., Profectus BioSciences Inc., and GlaxoSmithKline Plc. Merck & Co. discontinued development of its vaccine V520 in 2007 after an early-stage trial failed.

Health Information Remains High on the List of Popular Uses for the Internet
Washington Post, (02.01.2011) Nancy Szokan
The Pew Internet Project, which has been tracking web usage since 2000, reports health information as the third most-prevalent activity among US Internet users. Eight out of 10 users report going online for health information, even if only occasionally, Pew said in a report issued Feb. 1. “Health care information is there when they need it,” said Pew’s Susannah Fox.

According to the report, the two most common activities were exchanging e-mail and using search engines. For health information, people most often look up diseases, treatments, and physicians.

“We were really struck by the depth of feeling that people expressed” about how online searching helped them with health care, said Fox. “In many ways, the Internet has become the de facto second opinion. People go online to prepare for a doctor’s appointment—or recover from [it].”

However, the study found fewer than half of adults in the following groups use the Internet for health care information: African Americans, Latinos, people age 65 and older, disabled persons, and those living in households with an annual income below $30,000. But Pew noted some of those figures are in flux, since African Americans and Latinos are increasingly accessing information from smart phones and other mobile devices.

“Yahoo, for example, reports that ‘pregnancy,’ ‘herpes’ and ‘STD’ (sexually transmitted disease) are among the top five searches performed on the mobile version of their site,” the study noted. “These topics do not appear at all among the top five health searches for the non-mobile versions of either Yahoo or Google.”


Researchers Criticize AIDS Spending, Stigma
Associated Press, (02.03.2011) Donna Bryson
“Despite a more than 53-fold increase in AIDS funding in barely over a decade, the epidemic continues to outpace the rate at which programs are delivering,” according to a new UNAIDS-commissioned report.

Published as a book, “AIDS: Taking a Long-Term View” was presented Thursday in Johannesburg at the office of the Nelson Mandela Foundation. The former South African president publicly acknowledged in 2005 that AIDS killed his son, and he has campaigned to raise AIDS awareness in the country.

Collectively known as the aids2031 Consortium, the report’s two-dozen authors were asked to review progress on how the world has tackled HIV/AIDS. They were then to determine changes needed to
radically reduce the number of infections and deaths by 2031—50 years since the AIDS virus was first reported.

According to the researchers, scarce resources are being misspent, while laws making homosexual sex illegal and the harassment of intravenous drug users are preventing the most vulnerable from seeking help. In the wake of a worldwide recession and donor fatigue hurting spending on AIDS, the authors said it is “fair to ask whether the AIDS effort has always achieved good value for its money.”

The consortium called for a new focus on prevention and criticized governments for ignoring research with implementable findings. They noted the more than 7,000 daily HIV infections worldwide are roughly double the number of new patients accessing treatment in poor countries, making lifetime treatment for millions of HIV-infected people in poor countries unsustainable. When South African Health Minister Dr. Aaron Motsoaledi took over in 2009, he cut drug costs by more than half by asking more companies to bid for the government’s antiretroviral program and demanding they provide cost breakdowns.

'Do It Yourself' Sexual Health Care: The User Experience
Sexual Health Vol. 8; No. 1: P. 23-29, (01..2011) Paula Baraitser; Kirsty Collander Brown; Zachary Gleisner; Vikki Pearce; Usha Kumar; Michael Brady
In the current study, the team sought to describe “client experience of self-management within a busy walk-in sexual health service.” In this context, self-management refers to self-registration and take-home pregnancy kits, chlamydia and gonorrhea tests, or condoms received from a free vending machine. The study comprised 24 in-depth, semi-structured interviews with users; 19 structured written reports from “mystery shoppers” paid to visit the service and report their experience; demographic details of persons using the self-management option from the clinic database; and 40 hours of recorded observation in the clinic waiting room.

Between Sept. 2, 2008, and Sept. 1, 2009, 18,657 people made 28,545 clinic visits. A total of 1,845 (6.5 percent) visits were self-managed by 1,555 patients (8.3 percent of all clients). Among those who self-managed, 646 (35 percent) obtained a chlamydia and gonorrhea test only; 597 (32 percent) obtained condoms only; and 488 (27 percent) obtained a pregnancy test only.

Clinic visitors appreciated the self-management option “because of the reduced waiting times, autonomy, and privacy that such a service offers,” the authors reported. “Some prefer the additional support offered within a clinical consultation. Users made personalized decisions about self-management based on time pressure, need for additional services, and preferred source of support. Users often required help and advice from client support workers to complete the self-management process. This created problems with confidentiality.”

The team concluded that self-management “is an acceptable option within sexual health services if informal support is available. Self-management options in clinical services could mean that 8 percent of clients at 6 percent of visits do not need to see a clinician, thus freeing up clinical capacity.”

Ocular Syphilis Among HIV-Infected Patients: A Systematic Analysis of the Literature
Sexually Transmitted Infections Vol. 87: P. 4-8, (02..2011) Joseph D. Tucker; Jonathan Z. Li; Gregory K. Robbins; Benjamin T. Davis; Ann-Marie Lobo; Jan Kunkel; George N. Papaliudis; Marlene L. Durand; Donna Felsenstein
In the era of highly active antiretroviral therapy (HAART), ocular syphilis among HIV-infected patients “continues to be a problem,” wrote the authors. “However, outside of case reports or small case series, little is known about the clinical, laboratory, and treatment outcomes of these patients.” The team undertook the current study to examine the literature on HIV-infected patients and determine the results of treatment.

The researchers conducted a systematic review of cases series and case reports among HIV-infected patients with ocular syphilis. They excluded reviews, reports in languages other than English, and reports before 1980. They evaluated the effect of CD4 count and virological suppression on clinical manifestations and diagnostic laboratory values.

The literature review identified 101 HIV-positive individuals. In 52 percent of cases, ocular syphilis led to the HIV diagnosis, including patients with CD4 cell counts above 200 cells/mm³. Posterior uveitis was significantly more common in patients with CD4 counts below 200 cells/mm³ (P=0.002). Three individuals with confirmed ocular syphilis tested negative on non-treponemal tests. Following
intravenous treatment with penicillin or ceftriaxone, 97 percent of patients with visual impairment improved.

“Non-treponemal tests may be negative in HIV-infected patients with ocular syphilis,” the authors concluded. “Ocular syphilis remains an important clinical manifestation that can lead to initial HIV diagnosis.”

Sun exposure, vitamin D may lower risk of multiple sclerosis

ST. PAUL, Minn. – People who spend more time in the sun and those with higher vitamin D levels may be less likely to develop multiple sclerosis (MS), according to a study published in the February 8, 2011, print issue of Neurology®, the medical journal of the American Academy of Neurology. MS is a chronic disease of the brain and spinal cord, usually with recurrent flare-ups of symptoms. It is often preceded by a first episode (or event) of similar symptoms lasting days to weeks.

"Previous studies have found similar results, but this is the first study to look at people who have just had the first symptoms of MS and haven't even been diagnosed with the disease yet," said study author Robyn Lucas, PhD, of Australian National University in Canberra. "Other studies have looked at people who already have MS—then it's hard to know whether having the disease led them to change their habits in the sun or in their diet."

The multi-site study involved 216 people age 18 to 59 who had a first event with symptoms of the type seen in MS. Those people were matched with 395 people with no symptoms of possible MS who were of similar ages, of the same sex and from the same regions of Australia.

The participants reported how much sun they were exposed to during different periods of their lives, and researchers also measured the amount of skin damage participants had from sun exposure and the amount of melanin in their skin. Vitamin D levels (from sun exposure, diet and supplement use) were measured by blood tests.

The risk of having a first event, diagnosed by a doctor, ranged from approximately two to nine new cases for every 100,000 people per year in this study. The reported UV light exposure of participants ranged from about 500 to over 6,000 kilojoules per meter squared. The researchers found that the risk of having a diagnosed first event decreased by 30 percent for each UV increase of 1,000 kilojoules. They also found that people with most evidence of skin damage from sun exposure were 60 percent less likely to develop a first event than the people with the least damage. People with the highest levels of vitamin D also were less likely to have a diagnosed first event than people with the lowest levels.

Studies have shown that MS is more common in latitudes further away from the equator, and this has been confirmed in Australia.

"Added together, the differences in sun exposure, vitamin D levels and skin type accounted for a 32-percent increase in a diagnosed first event from the low to the high latitude regions of Australia," Lucas said.

Lucas noted that the effects of sun exposure and vitamin D acted independently of each other on the risk of first event. "Further research should evaluate both sun exposure and vitamin D for the prevention of MS," Lucas said.

Lucas also stated that people should continue to limit their sun exposure due to skin cancer risks. She also noted that the risks of tanning beds far outweigh any possible protective effect against MS. Exposure to the sun has not been shown to benefit people who already have MS.

Can breastfeeding transmit yellow fever after maternal vaccination?

A five-week old infant most likely contracted a vaccine strain of yellow fever virus through breastfeeding, according to a case report published in CMAJ (Canadian Medical Association Journal) (pre-embargo link only) http://www.cmaj.ca/embargo/cmaj100619.pdf

"Until recently, avoidance of vaccination of breastfeeding women with yellow fever vaccine had been based on theoretical grounds only," writes Dr. Susan Kuhn, with coauthors. "We report the probable transmission of vaccine strain of yellow fever virus from a mother to her infant through breastfeeding," which supports current recommendations for breastfeeding mothers to avoid the vaccine.

The yellow fever vaccine is a live-virus vaccine that has been used since the 1940s.

When the infant was 10 days old the mother received pre-travel advice and travel vaccinations, including one for yellow fever. Subsequently, they traveled to Venezuela for one week and breastfeeding was continued. The infant did not receive vaccinations.
"The previously healthy five-week old infant male presented to the hospital with a two-day history of fever and irritability," write the authors. "The day before his admission, he had been noted to have focal seizures on alternating sides." Testing of the spinal fluid revealed evidence of recent infection with the yellow fever virus. Given that the travellers elected to stay in urban Venezuela where yellow fever is not known to be a risk, the authors concluded that the likely explanation was transmission of the yellow fever vaccine strain through breastfeeding.

The baby showed no sign of insect bites, had not been in contact with sick people, was not exposed to animals in Canada or elsewhere, had no history of herpes infections in family members and had not had any vaccinations prior to his symptoms.

"This probable case of yellow fever virus further supports the current recommendations for avoidance of yellow fever vaccination in lactating mothers of infants under nine months of age," write the authors. "While there may be situations in which the mother will have unavoidable and significant risk of yellow fever exposure, the risk to the infant due to maternal vaccination must be weighed against the risk of wild-type virus infection."

The authors conclude that travelling women should adjust their plans to reduce or limit their risk of exposure or postpone their trip entirely until their infant is no longer breastfeeding or is old enough to be vaccinated.

**Unappreciated dynamism of blood cell production**

The bone marrow stem cells responsible for generating new blood cells are less fixed and more flexible than previously thought, according to a paper published online on February 7 in the *Journal of Experimental Medicine* (www.jem.org).

Some earlier studies suggested that these hematopoietic stem cells (HSCs) come in two distinct varieties: those that remain dormant during times of health but possess the ability to regenerate the whole blood system after trauma such as irradiation or chemotherapy, and those that divide frequently and contribute to new blood production during times of health but lack the capability of restoring the whole blood system after trauma.

Using a new technique to label and track mouse HSCs, Markus Manz and colleagues find that at any given time, cells harboring the capacity to restore a wiped-out blood system can actually be found in both rapidly dividing and dormant HSC populations. In fact, with age, HSCs tend to shift status from rapidly dividing to dormant. Yet upon encounter with life-threatening bacteria, dormant HSCs quickly awake, divide and replicate themselves.

These findings suggest that the burden of blood cell production may be more equally shared than previously realized among all HSCs. Whether human HSCs exhibit similar on-demand adaptability remains to be determined.

**Mubarak’s AIDS Legacy: Torture, Deportation and Arrest for HIV-Positive People**
Would a new government mean more rights for people with HIV?

In Egypt, the victims of Hosni Mubarak’s 30-year autocratic rule haven’t just been government dissenters—they’ve also been people living with HIV.

While receiving a hefty amount of U.S. foreign aid, Egypt has conducted mass deportations of HIV-positive foreigners and arrested, tortured and convicted HIV-positive people based on their status.

“Police have blanket authority to intimidate certain populations,” said Joe Amon, director of the HIV/AIDS program at Human Rights Watch. “There’s a lot of homophobia, and police have targeted the communities, arrested gay men, gone through their address books [and] conducted forceful anal exams.”

Egypt’s National AIDS Program reports that there were 1,155 people living with HIV/AIDS in Egypt in 2007. UNAIDS, however, put the number much higher—at 5,300—in 2005.

Between 1986 and 2006, Egypt deported more than 700 foreigners with HIV, nearly all of whom were of African descent. All foreigners who apply for a work or residency visa must test for HIV, and those who test positive are immediately expelled.

**Government crackdown**

The government frequently uses charges designed to criminalize homosexuality to also criminalize HIV-seropositivity.

In 2007 and 2008, the government launched a crackdown on people living with HIV, arresting at least twelve men suspected of being HIV-positive, calling them a public health threat. Police beat several of them, later subjecting the arrested individuals to anal examinations to “prove” they had engaged in homosexual conduct. Authorities charged them with “habitual debauchery,” a term Human Rights Watch says Egypt uses to punish homosexuality, which is not specifically penalized in the country’s legal code.

Some were chained to their beds for days in a Cairo hospital. Authorities gave all of the men HIV tests without consent—those who tested positive were convicted to a maximum of three years in jail. “People like you should be burnt alive,” a prosecutor reportedly told one of the men, when informing him that he was HIV-positive. “You do not deserve to live.”

**Omitting the facts**

While Egypt is considered a low-HIV prevalence country, its own National AIDS Program warned in a 2009 report that “unless concerted efforts are made, this status might not prevail.” Indeed, Mubarak’s Egypt presents a number of troublesome risk factors that could foment a wider epidemic, including rising poverty, low condom use and an increasing number of people engaging in premarital sex. AIDS education is sparse: Less than five percent of females ages 15 to 24 have comprehensive knowledge of HIV, according to the government survey.

Not surprisingly, however, the 21-page piece says nothing about how government-sanctioned brutality against homosexuals and HIV-positive people contributes to the spread of the virus. The government also left out large pieces of information, such as the percentage of people who have had sex with more than one partner in the last year. That information, the report says, “is not relevant to country epidemic status.”

**Changes ahead?**

It’s unclear what a new government in Egypt would look like: It could be more repressive, which might mean continued attacks on HIV-positive people. If it’s one bent on expanding human rights, however, a measure of relief could be in sight.

“The issue of police brutality in Egypt is larger than just the experience of men who have sex with men and of people with HIV,” said Amon. “Hopefully this pressure on the government and these protests bring real reform to the kinds of abuses that were taking place to a wide range of individuals that the government saw as dangerous or deviant or a threat to Egyptian society.”

**Gay times, bad times**

Farrah Tomazin

*February 8, 2011*

Young homosexuals are suffering more abuse than ever, particularly in schools.

JIMMY Yan was only 16 when he had his first real experience of homophobia. It happened two years ago at a highly sought-after government school in Melbourne’s eastern suburbs, but he remembers it like it was yesterday.

At the time, Yan was in year 11, putting up posters in the school library, publicising a national day of action in support of gay marriage. A teacher approached, read the material, and spat out the words that still make him burn with indignation: "You don’t know what marriage is, faggot boy."
The library was packed with students, many of whom heard the exchange and looked up in dismay. News of the teacher's comments quickly spread around the campus, and it wasn't long before students organised a snap rally outside his office, demanding an apology.

Hannah Williams (left) was banned from bringing her girlfriend, Savannah Supski, to the Ivanhoe Girls' Grammar school formal last year.

The teacher eventually resigned, but for a young bloke who was still coming to terms with his sexuality, the damage was done.

"I was shocked and outraged because you'd never think a teacher, who is meant to be a role model to young kids, would say something like that," says Yan.

"But unfortunately you get these characters everywhere. It doesn't just happen at backward religious schools—the most supposedly progressive ones are some of the most dangerous places for lesbian and gay youth. They can be real cesspools for bigotry, so whenever instances like this come up, they need to be taken seriously, they need to be dealt with and they need to be confronted."

Few could argue with the sentiment, but research suggests that despite years of law reform, changing values and millions of dollars spent on pilot programs and initiatives, homophobic abuse against young people is getting worse, particularly in Australian schools.

A national study into the experiences of thousands of gay youth paints a startling picture. Based on a survey of 3134 people aged between 14 and 21, the La Trobe University study found that 79 per cent of students attracted to the same sex had been physically assaulted or verbally abused.

About one in four of those cases took place in the home, by parents unable to cope with the fact their child was gay. But the majority of homophobic abuse—80 per cent—occurred in schools, up from 69 per cent in 1998 when the study first began.

In one incident, a 17-year-old female student reported being "beaten, stripped and left in a park at night" by schoolyard bullies; in another, a 15-year-old girl had her hair cut in class. Her hair was then set on fire.

One 20-year-old former student reported being the victim of at least 10 schoolyard bashings and an attempted rape, while another wrote of being put in hospital by her own parents: "I got three broken ribs, a broken collarbone, a punctured lung, my jaw broken in two different places and seven of my teeth got punched out when my father found out I was a homosexual."

La Trobe University expert Lynne Hillier, who co-wrote the Writing Themselves In report, says the findings should be a wake-up call for governments, educators and policy makers. Gay and bisexual youths are more likely to have a sexually transmitted infection, are less likely to use a condom and twice as likely to become pregnant compared with their heterosexual peers, partly because they tend to be sexually active earlier and partly because of a lack of relevant sex education.

Almost 70 per cent of participants were sexually active, with young women more likely to have sex than men. But among the women surveyed, one-fifth continued to have sex exclusively with men despite being attracted to other women. This reflects an attempt to suppress their feelings, or a belief that this is what society expected of them.

Perhaps the most worrying sign, however, is that about one in six people who had experienced homophobic bullying had attempted suicide at least once, while a further one in three had tried to harm themselves as they struggled to cope with the torment they felt. But the research also shows a strong correlation between the support offered to gay youth and their well-being.

"The message from the research is clear: where there are policies and support for same-sex-attracted young people, they are less likely to be abused, they're less likely to self-harm and they're less likely to attempt suicide," she says.

While some inroads have been made over the past decade in tackling homophobia, experts argue that there is still a long way to go. As the study shows, more than half the people surveyed said they attended schools with no social or support structures for gay students, and more than one in three described their schools as "homophobic" or "very homophobic".

The irony is that young people are more likely to disclose their sexuality now than they were 10 years ago, and the cultural values have certainly changed—just think of the public outcry last year when former Ivanhoe Girls' Grammar school girl Hannah Williams was banned from bringing her girlfriend Savannah Supski to her high school formal; or the ongoing federal push for same-sex marriage.

"But while more young people are more likely to be out and proud, the level of abuse has gone up—and schools as the place for that abuse has become more common," says Hillier.

"These are huge problems that really have to be owned up to and faced by schools if they care about the well-being of students. And it's an issue for governments, too. I don't think any government would
want to think they could have higher rates of suicide in student populations because they didn’t do enough
to make kids feel safe.”

However, there have been some attempts to address this. The Victorian Education Department, for
example, provides some guidance to teachers in its Supporting Sexual Diversity in Schools policy, while
the Baillieu government recently announced a $4 million plan to develop suicide prevention strategies for
the gay youth.

And last year, in an Australian first, a new Safe Schools Coalition of “gay friendly” schools was set up
to promote tolerance of sexual diversity. Under the program, schools are encouraged to set up
“gay/straight student alliances”, share resources and provide teacher training that identifies, and seeks to
stamp out, homophobia in the classroom.

Students and teachers get access to gay and lesbian health networks and are encouraged to create
posters, newsletters or forums that promote sexual diversity in schools. The hope is that all students — gay
or straight — are comfortable to be themselves.

When the program was launched by the Brumby government in the lead-up to last November’s state
election, 11 schools had signed up. Now, 22 public and private schools are on board — including Methodist
Ladies College, the King David School and Northcote High School — and The Age understands about five
more are considering joining.

Victoria’s Education Minister, Martin Dixon, says he’s yet to be briefed on the success of the program,
and has refused to be drawn on whether the new government would continue to fund the scheme when its
contract expires in July.

But Dixon, a former school principal, says the extent of youth homophobia is troubling, and agrees
that the curriculum should be more inclusive of gay issues, and teachers better trained to identify and
tackle homophobia. However, schools aren’t the only ones responsible, he says.

“This is a community-wide problem. One of the key issues here is about respect for any minority
group or any group of individuals, and what we’re seeing is a loss of that respect throughout the
community,” says Dixon. “We’ve seen increasing violence on the streets, more vandalism and crime and
this is just another manifestation of that growing lack of respect for others. That’s something that we want
to tackle across the whole of government.”

While initiatives like the Safe Schools Coalition have the backing of the government, psychologists
and gay groups, not everyone agrees with the concept. When the program was launched last year,
Victoria’s powerful Christian lobby warned that the program could “normalise” homosexuality in schools
and “promote homosexual or lesbian behaviour, rather than allowing children the time to work these
things out for themselves”.

“Are they going to suggest that children who might be homosexual attend these schools?” Rob Ward,
the Victorian director of the Australian Christians Lobby, said at the time. “Are we creating a homosexual
ghetto?”

David Warner, principal of Eltham College of Education, one of the first schools to join the coalition,
certainly doesn’t think so. Last Sunday, for the first time, the college had a contingent of students, parents
and teachers marching at the annual gay and lesbian pride march in St Kilda. Earlier this month it
conducted a workshop to teach staff how to deal with homophobia in the classroom. Asked why his
prestigious private school decided to join the coalition, Warner replies: “All young people need to feel safe
in school. They can’t learn if they can’t feel safe.”

A few kilometres down the road at Eltham High School, year 12 student Sean Miles couldn’t agree
more. Miles first "came out" in year 8, firstly to a few close friends, and eventually to his family. But he
knows he’s one of the lucky ones — Eltham High has long and proud history of being a gay-friendly school:
students march at Pride every year, and according to principal Vincent Sicari, it’s "the sort of place where
two boys could hold hands and no one would bat an eyelid”.

Miles reckons being educated in this sort of environment can make a huge difference. "I have some
friends from other schools in the region, and they didn’t come out until after they left because they would
have felt like the odd one out, they might have been subject to bullying, or they were just afraid," he says.
"I’m very thankful I’m at this school, because of how comfortable it feels to be gay here.”

Other schools have also sniffed the wind. Two years ago, Melbourne High School student Jordan
Boulter and a friend convinced teachers to allow them to set up a gay support group at the school, known
as SOFA (the Same-sex attracted, Other, Friends of, Alliance). Boulter was questioning his sexuality at the
time, so the idea was to start a group for other like-minded students to chat, seek advice, get health
resources and condoms, or listen to guest speakers.
"It was my second year at Melbourne High School when we started the group," says Boulter, who graduated last year. "I had found the first year really difficult because I never felt like I was "one of the boys" so having this group was really helpful. I could meet like-minded people, learn about [homosexuality] and I began to feel more confident and comfortable. To be able to come out to my peers at school like that was really beneficial, and I earned a lot of respect for it."

Anne Mitchell, director of Gay and Lesbian Health Victoria, says programs like the Safe Schools Coalition are critical, and disagrees with suggestions that they "encourage" homosexual behaviour among young people. "This isn't about gay recruiting," she says. "This is a serious health problem."

Recent events also suggest the consequences of inaction can be fatal. Last year in the US, school officials were forced to rethink their efforts against bullying after a spate of teen suicides was linked to anti-gay harassment. One was the death of Tyler Clementi, who jumped off the George Washington Bridge after his roommate allegedly posted on the internet video of him having sex with another man. In the UK, a 15-year-old student from South Wales, Jonathan Reynolds, lay in front of train after being called a "faggot" and a "poof" at school.

Australia may not have had the spate of tragic cases seen in the US, but experts agree more needs to be done, and the report makes a range of recommendations: introduce police programs that liaise with the gay community and make it easier for young people to report homophobic abuse. Schools should have specific policies on gay bullying, including protection for gay students; a rethink of sex education to include more information about homosexuality; and better training for teachers and health professionals.

"But what we're really talking about here is social change," says La Trobe's Lynne Hillier. "And social change never happens without a struggle."

**Nigerian Church Ordered to Stop Faith Healing Ads**

*Agence France Presse*, (02.03.2011)

South Africa’s advertising authority has ordered Christ Embassy, a charismatic church based in Nigeria, to stop making claims on national television that it can treat diseases such as AIDS through faith healing.

The ruling came after the Treatment Action Campaign (TAC), South Africa’s main HIV/AIDS lobby group, filed a complaint against the church, which has paid programming on the private e.tv channel featuring people recounting how they have been cured by Christ Embassy. The church was ordered to withdraw the advertisement from the station immediately.

“The message that is communicated to the e.tv audiences/viewers is that joining the Christ Embassy or its Healing School, or associating with it or attending its ‘faith healing sessions’ will lead to its pastor(s) transferring God’s healing powers to anyone who suffers from the list of diseases that are read out or announced in the program,” said the authority in its ruling.

According to TAC, it lodged a complaint after receiving a report that a woman with extensively drug-resistant tuberculosis (XDR TB), who had made significant progress on her medical treatment, gave it up because she believed Christ Embassy had cured her. “She consequently became ill with XDR TB again and died, but only after transmitting the disease to her children,” said TAC.

“Faith-based organizations can and do play an important role in supporting HIV-infected people in accessing and taking such treatments,” said the Southern African HIV Clinicians Society. “However, organizations that offer miracle cures seek to mislead people that are sick and vulnerable down a path that often costs them their lives, and potentially leads to the infection of others.”

**Chlamydia Trachomatis Age-Specific Prevalence in Women Who Used an Internet-Based Self-Screening Program Compared to Women Who Were Screened in Family Planning Clinics**

*Sexually Transmitted Diseases Vol. 38; No. 2: P. 74-78*, (02..2011) Charlotte A. Gaydos; Mathilda Barnes; Bulbul Aumakhan; Nicole Quinn; Catherine Wright; Patricia Agreda; Pamela Whittle; Terry Hogan

The aim of the current study was to learn whether women who test for chlamydia using self-collected vaginal swabs at home demonstrated a higher positivity than women who tested in family planning clinics.

The vaginal swab collection kits were requested using the Internet; the specimens were collected at home and mailed to a laboratory for testing. In addition, the women completed questionnaires detailing acceptability and sexual risk history. Those women found to be infected were treated at participating...
clinics. The team compared the age-specific prevalence rates of these women to those using family planning clinics.

Among the 1,171 females who mailed in swabs, chlamydia positivity was 10.3 percent. Among the women in the family planning setting, prevalence ranged from 3.3 percent to 5.5 percent. “Positivity for Internet age groups was much higher than those for family planning age groups,” the authors reported.

For Internet participants, positivity ranged from a low of 4.4 percent in Baltimore in 2005 to a high of 15.2 percent in Baltimore for 2007. Prevalence among family planning participants in Baltimore and Maryland ranged from a low of 3.3 percent in Baltimore in 2006 to a high of 5.5 percent in Baltimore in 2008.

“The median age for all years for Internet users in Baltimore and Maryland combined was 23 years; the median age for all years for attendees to family planning clinics who had chlamydia testing performed was 23 years,” the authors reported. “Internet-recruited women demonstrated higher positivity of chlamydia than those in family planning, providing new options for chlamydia screening programs.”

**Researchers Turn Salmonella Into Antiviral Gene Therapy Agent**

ScienceDaily (Feb. 7, 2011) — New experiments at the University of California, Berkeley, may one day lead to anti-viral treatments that involve swallowing *Salmonella* bacteria, effectively using one bug to stop another.

Researchers at UC Berkeley’s School of Public Health have reprogrammed *Salmonella*, the same foodborne pathogen that can cause diarrhea, fever and abdominal cramps, to safely transport virus-stopping enzymes into cells without causing disease. Not only did this technique effectively treat mice infected with cytomegalovirus, it worked as an oral solution that was swallowed instead of injected.

Virologist Fenyong Liu teamed up with bacteriologist Sangwei Lu to develop the innovative technique, which is described in a study to be published online the week of Feb. 7 in the journal *Proceedings of the National Academy of Sciences*.

"A number of vaccines, including those for polio and smallpox, use live but weakened viruses to build up the immune system. But this is the first time anyone has successfully engineered bacteria for treatment of a viral infection," said Liu, a UC Berkeley professor at the Division of Infectious Diseases & Vaccinology.

The researchers said *Salmonella* was particularly appealing because it has evolved to survive the human digestive system, allowing it to be swallowed instead of injected or inhaled.

"This is the first gene therapy treatment for viral infection that can be taken by mouth, which is far more convenient to administer than an injection," said Lu, a UC Berkeley associate adjunct professor at the Division of Infectious Diseases & Vaccinology. "Moreover, there is already an attenuated strain of *Salmonella* with a decent track record for safety in humans since it is now used in the vaccine for typhoid (a disease caused by *Salmonella typhi*)."

Researchers know that ribozymes, enzymes that are able to target and cut specific RNA molecules, can be used to inactivate a pathogen’s genes. But to do their work, ribozymes need to first get into the cells, and for that they need help.

It so happens that *Salmonella* is very good at invading cells, so the researchers found a way to use the bacterium as a vector for the RNase P ribozyme that could stop the gene activity of cytomegalovirus, or CMV.

CMV is in the same family of herpes viruses that causes cold sores, mononucleosis and chickenpox. CMV infections are generally mild among healthy individuals, but they can become deadly for people whose immune systems are compromised and are a leading viral cause of mental retardation in newborns.

Previous research by Liu and Lu showed that *Salmonella* could effectively sneak the anti-viral ribozymes into human cells infected with human cytomegalovirus and reduce the viral load of the cell cultures. This new study put the technique to the test in living mice.

As an added measure of safety, researchers took the attenuated strain of *Salmonella* and further mutated a gene that the bacteria needs to replicate. They tested the new mutant *Salmonella* strain in mice and confirmed that the mice did not get sick.

They then cloned the anti-viral ribozymes into a plasmid, or DNA molecules within the bacteria that can replicate. Among mice that had been infected with cytomegalovirus, those that had been given oral doses of the ribozyme-carrying *Salmonella* survived much better than mice that had not been treated or mice that had been given *Salmonella* carrying a defective version of the ribozyme. The treated mice lived
at least 50 days after infection, whereas the mice in the other two groups died within 25 days after infection.

Moreover, the researchers found that the viral load of mice treated with the ribozyme-carrying *Salmonella* was 400- to 600-times lower than the viral load for mice given the defective ribozymes and for mice that were untreated.

The researchers pointed out that using bacteria instead of viruses as gene-therapy vectors has a number of advantages.

"Viruses can't replicate on their own; they must be grown in host cells," said Lu. "It is more challenging to grow host cells in a lab, and there is always the risk that those cells can be contaminated with unknown viruses. To grow bacteria, you only need to add some bacteria to a simple medium, and the next day you can have 100 billion bacteria ready to go. It's safer, easier and cheaper as a vector for gene therapy."

The researchers pointed to the potential for developing this technique into a range of gene-targeting therapeutic strategies. "This study focused on the use of *Salmonella* and ribozymes to fight infections, but with more research, this method could eventually be used to treat other conditions as well, including cancer," said Liu.

Other UC Berkeley authors on the paper include lead author Yong Bai and Hao Gong, both post-doctoral researchers in infectious diseases; Hongjian Li, a former post-doctoral researcher in infectious diseases; and Gia-Phong Vu, a graduate student in comparative biochemistry.

**Journal Reference:**

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**Little evidence of transmission of virus that's resistant to newer anti-HIV drugs**
Michael Carter
Published: 09 February 2011

Italian investigators have found evidence of the transmission of HIV that is resistant to the fusion inhibitor T-20 (enfuvirtide, *Fuzeon*).

However, there is as yet no evidence that virus is being transmitted that is resistant to the integrase inhibitor raltegravir (*Isentress*). The investigators report these findings in the February 1st edition of the *Journal of Acquired Immune Deficiency Syndromes*.

HIV can become resistant to antiretroviral drugs, and this resistant virus can be transmitted. Surveillance suggests that between 6-16% of patients newly infected with HIV in Europe have contracted virus that is resistant to one or more anti-HIV drugs in the NRTI, NNRTI or protease inhibitor classes.

It is currently recommended that all patients newly diagnosed with HIV should have a test to see if they are infected with resistant virus. The results of resistance testing can help select the combination of anti-HIV drugs that are most likely to achieve long-term suppression of HIV.

Improvements in HIV treatment and care have in recent years been accompanied by falls in rates of transmitted resistance. Important new classes of antiretrovirals have been introduced, including the fusion inhibitor T-20 and the integrase inhibitor raltegravir. The use of these drugs has largely been reserved for patients with extensive experience of antiretrovirals and resistance to drugs in the older classes.

Little is known about the prevalence of resistance to newer classes of antiretroviral drugs in patients recently infected with HIV. Therefore between 2008 and 2010 a team of investigators in Milan tested all newly diagnosed patients for resistance to NRTIs, NNRTIs, protease inhibitors, and the newer drugs T-20 and raltegravir.

A total of 79 patients were included in the study, most of who (77%) were gay men.

Overall 18% of patients had transmitted drug resistance. This included 11% who had reduced susceptibility to NNRTIs, 9% with some resistance to NRTIs, and 4% with protease inhibitor resistance.

In addition, resistance to T-20 was detected in one patient.

T-20 was approved in 2003, and the investigators note that other studies have found evidence of the transmission of strains of the virus with resistance to this drug.

Initially, many patients taking T-20 were unable to assemble a combination of drugs to suppress their viral load to undetectable levels, leading to the development of strains of virus that were resistant to T-20. However, the advent of powerful drugs with high barriers to resistance means that an undetectable viral load is now achievable by most patients, even those with extensive resistance to older drugs.
This could explain why the investigators found no evidence of the transmission of virus that was resistance to raltegravir. The investigators note, "raltegravir was approved for clinical use in Italy in late 2007, and the prevalence of patients experiencing virologic failure is still low."

Reference

Huge decline in HIV rates in Zimbabwe driven by fear of infection
Keith Alcorn
Published: 09 February 2011

The big drop in the numbers of people infected with HIV in Zimbabwe is because of mass social change, driven by fear of infection, according to an international study reported today in the journal PLoS Medicine.

A major investigation of the reasons why HIV prevalence in Zimbabwe has fallen from 29% in 1997 to 16% in 2007 was carried out by epidemiologists at Imperial College, London, and Harvard University School of Public Health, Boston, in partnership with the Zimbabwean Ministry of Health, the UN Population Fund and UNAIDS.

The research included extensive analysis of epidemiological data, together with focus groups and key informant interviews, to test different explanations for the dramatic decline of prevalence. Although HIV prevalence remains high even by African standards, the fall in HIV prevalence that has taken place in Zimbabwe is the largest seen anywhere in sub-Saharan Africa.

HIV incidence – the number of new infections taking place each year – also fell markedly, especially after 2000, falling from 5 infections per 100 persons per year to less than 2 infections per 100 persons per year in 2010.

Professor Simon Gregson, from the School of Public Health at Imperial College London, and senior investigator on the study, said: "Given the continuing, and worrying, trend for high HIV/AIDS infection rates in many sub-Saharan African countries, we felt it was important to understand why the disease has taken a such a dramatic downturn in Zimbabwe. Very few other countries around the world have seen reductions in HIV infection, and of all African nations, Zimbabwe was thought least likely to see such a turnaround. This is why there was such an urgent need to understand its direct and underlying causes."

Past speculation that the economic crisis in Zimbabwe and consequent migration out of the country might have contributed to the decline in HIV prevalence is dismissed as an explanation by the researchers. They point out that the financial crisis did not begin to bite until after 2002, when changes in behaviour were well underway.

For migration to explain the big fall in prevalence, they say, the majority of emigrants would need to be HIV-infected, yet in the UK, HIV prevalence among pregnant women from Zimbabwe peaked in the early 2000s at 12%, less than half the level recorded among women still living in Zimbabwe.

Condom use does not appear to have risen substantially after 1999 (Zimbabwe already had a high level of condom use by the mid-1990s), and continued to be low in regular partnerships.

What drove the change, researchers now agree, was the big increase in AIDS deaths after the mid-1990s. Deaths peaked between 2000 and 2005 in Zimbabwe, and focus groups agreed that the critical factor in changing individual behaviour had been seeing someone die of AIDS. This made people fearful of contracting HIV, and led to a reduction in the number of casual partners.

For example, focus groups told researchers that major changes in norms of sexual behaviour began to take place in Zimbabwe from the late 1990s, such that visiting sex workers or getting a sexually transmitted infection was considered shameful rather than a badge of masculine pride.

This is backed up by evidence from a number of surveys showing a decline in multiple sexual partners between 1998 and 2005, together with a decline in the number of men who reported paying for sex.

The decline in HIV prevalence may have been greater in Zimbabwe than in other countries of the region because of high levels of both education and marriage, especially among urban men, who exhibited the greatest degree of behaviour change. Sixty per cent of urban men aged 17-43 were married in Zimbabwe in 2005, compared to less than 20% in Namibia, Mozambique and Botswana in surveys between 2000 and 2003.

Similarly, over 80% of Zimbabwean men aged 17-43 had received some secondary education, compared with 50% in Malawi and around 60% in Botswana and Zambia. Education helped people understand and accept messages about HIV transmission and prevention, while marriage helped people
to act on the "be faithful" messages included in prevention campaigns. Zimbabwe has a higher rate of marriage than most neighbouring countries.

The comprehensive nature of prevention activities may also have helped, the researchers suggest. Although respondents failed to identify a specific prevention activity that influenced their behaviour, the researchers speculate that the combination of activities resulted in a "tipping point" that encouraged widespread change. Messages about HIV were widespread in popular culture in the late 1990s.

Home-based care for people with AIDS promoted by the government may also have influenced society, because more people saw relatives or neighbours die at home as a result. In contrast people with AIDS in Botswana received hospital care.

The researchers say that partner reduction played a crucial role and needs to play a central part in prevention campaigns. In Zimbabwe public and private sector prevention activities are now giving stronger warnings about multiple and concurrent partners, and this model has been followed in Swaziland.

Dr Timothy Hallett, also from the School of Public Health at Imperial College London and an investigator on the study, said: "The HIV epidemic is still very large, with more than one in ten adults infected today. We hope that Zimbabwe—and other countries in southern Africa—can learn from these lessons and strengthen programs to drive infections down even further."

Reference

HIV Drugs Grow Rarer, Costlier as States Falter: Financial Crises Hurt Care for the Poor in Illinois, Elsewhere in US
Chicago Tribune, (02.09.2011) Bruce Japsen
Illinois is among several states wrestling with unprecedented deficits, and its AIDS Drug Assistance Program (ADAP) for low-income patients is being challenged by increasing demand and high drug costs.

The state has seen a 14 percent spike in the number of patients enrolled in ADAP over the past year, in part because of persistently high unemployment. While Illinois has so far been able to avoid instituting a waiting list for the program, it has limited the number of available medicines, capped clients’ drug expenses, and tightened enrollment. Nationwide, some 6,000 patients in at least 10 states were on waiting lists for HIV/AIDS medicines as of Feb. 3, according to the National Alliance of State & Territorial AIDS Directors.

AIDS advocates say ADAPs need approximately an additional $126 million from the federal government. The programs receive federal funds, which are then matched and administered by state governments at varying levels and structures.

A US Department of Health and Human Services spokesperson noted the federal ADAP allocation in fiscal year 2010 was $835 million, a figure that has risen during the last three years. The "[FY] 2011 amended budget totals $50 million over the [FY] 2010 enacted level for ADAP," the spokesperson said.

Illinois officials say its ADAP is one of just six nationwide that enrolls patients who have an income of up to 500 percent of the poverty level, or $54,150 for an individual. And they defend the state’s $2,000 monthly cap on patients’ access, citing the average per-person cost of $1,050.

Can a Mediterranean Diet Reduce the Effects of Lipodystrophy Syndrome in People Living with HIV? A Pilot Randomized Controlled Trial
Sexual Health Vol. 8; No. 1: P. 43-51, (01..2011) Geraldine Wai Bik Ng; Una Man Shu Chan; Patrick Chung Ki Li; William C.W. Wong
HIV infection and the highly active antiretroviral therapies that fight it both are associated with changes in patients’ lipid profile and fat distribution (lipodystrophy). A pilot study was carried out for a randomized controlled trial to determine whether lipodystrophy in HIV patients can be controlled by adopting a low-fat and low-cholesterol diet or a modified Mediterranean diet.

The participants, 48 HIV patients, were randomized into two diet groups. The one-year study involved regular dietetic consultations during which lipid levels, weight, body mass index, and fat distribution were recorded. Of participants, 36 (75 percent) completed the study.

In the low-fat group, undesirable body fat changes included decreases in tricep skinfold (from 19.9 mm to 15.4 mm (P=0.03)) and hip circumference (from 93.6 cm to 91.7 cm (P=0.01)), but a significant increase in waist-to-hip ratio (from 0.87 to 0.89 (P=0.003)). Serum cholesterol increased significantly at
nine and 12 months (from 4.6 to 5.06 mmol L\(^{-1}\) (P=0.03) and 5.12 mmol L\(^{-1}\) (P=0.01)) in the Mediterranean diet group, with no obvious change in the low-fat diet group. While serum triglyceride levels remained the same in the Mediterranean diet group, they increased from 1.9 to 3.22 mmol L\(^{-1}\) (P=0.07) in the low-fat group.

“A Mediterranean diet seems to have an advantage over the low-fat diet in maintaining serum triglyceride levels and avoiding lipodystrophy, but this advantage was offset by a rise in cholesterol level,” the authors concluded. “Several procedural and methodological issues were identified which must be rectified before a similar large-scale trial taking place.”

Older People Account for Majority of San Francisco AIDS Cases

*Bay Area Reporter (San Francisco)*, (02.03.2011)  Matthew S. Bajko
People in their 50s and beyond comprise the majority of San Franciscans living with AIDS for the first time since the start of the epidemic. In 2010, 53 percent of AIDS cases in the city were among people 50 and older, up from 49 percent in 2009. Of the 9,734 people with AIDS in the city last year, 5,153 were in the 50-and-over age group.

“I think it is a continuing trend,” said Susan Scheer, PhD, MPH, director of the HIV Epidemiology Section (HES) at the city’s Department of Public Health. “It reflects improved treatment so that is the good news. People who were diagnosed a longer time ago and have been able to get good care and treatment are surviving longer.”

HES data show that people in their 40s accounted for 36 percent of the AIDS population in 2010, at 3,516 cases. Men comprise 92 percent of all the city’s AIDS cases.

Despite the graying of San Francisco’s AIDS population, funding for programs targeting older patients has not kept pace. A June report by the HIV Health Services Planning Council and the Mayor’s Long Term Care Coordinating Council noted that while “a few support groups” for older AIDS patients exist, it concluded that “the number is inadequate and limited in that these groups primarily targeted older gay men. No services from any funding stream targeting other demographics were identified.”

Scheer said that thanks to the report’s findings, the issue is garnering more attention. “It is the fastest-growing population of people with AIDS,” she said. “There does need to be a focus on making sure this population has the health services and prevention services that they need.”

Uninfected Infants Born to HIV Positive Mothers May Have Impaired Immune Function

**SUMMARY:** Infants born to mothers with HIV appear to be more susceptible to certain bacterial infections even if they are not HIV-infected themselves, according to research from South Africa published in the February 9, 2011 *Journal of the American Medical Association*. HIV-exposed children get fewer antibodies from their mothers through the placenta during gestation, but they show robust responses to vaccination, indicating that their own immune function is not impaired.

*Bellow is the edited text of a press release issued by Imperial College London describing the study and its findings.*

**Study Suggests Why HIV-Uninfected Babies of Mothers with HIV Might Be More Prone to Infections**

Babies whose mothers have HIV, but who are not HIV-infected themselves, are born with lower levels of specific proteins in their blood called antibodies, which fight infection, compared with babies not exposed to HIV, a new study has found. The finding, published today in the Journal of the American Medical Association, might explain in part why uninfected babies born to women with HIV have a higher risk of illness and death early in life.

Major programs using antiretroviral drugs have successfully reduced the rate of mother-to-child transmission of HIV from 20-30 percent to around five percent in some areas of South Africa and to less than one percent in developed countries. However, HIV-uninfected infants born to HIV-infected mothers in Africa are more prone to infections such as pneumonia and meningitis, and up to four times more likely to die before their first birthday, compared with babies born to HIV-negative women. Socioeconomic factors are thought to account partially for this discrepancy but differences in the babies’ immune systems might also be important.

The new study, by scientists from Imperial College London and Stellenbosch University in South Africa, found that babies born to HIV-infected mothers had significantly lower levels at birth of antibodies against a range of bacterial infections (Hib, pertussis, pneumococcus and tetanus).
Antibodies, which bind to specific pathogens and direct immune cells to attack them, are transferred from mother to child through the placenta late in pregnancy. The study found lower levels of some specific antibodies in mothers with HIV, but also that less antibody is transferred from mother to child across the placenta.

Despite their low antibody levels at birth, the babies in the study responded well to vaccination: they produced similar levels of antibody to some vaccines and higher levels to other vaccines.

"It's likely that lower antibody levels in these babies contributes to lower protection against infection before the babies have received their vaccines," said Dr Christine Jones from the Department of Pediatrics at Imperial College London, the study's first author. "Although they appear more vulnerable in the first few months of life, the good news is that these babies respond well to vaccination. We might be able to protect them even better against infections, either by vaccinating them earlier or by vaccinating the mother in pregnancy. More research will be needed to establish what the best way of protecting these babies might be."

The study involved 109 HIV-infected and uninfected mothers in a community health centre in Khayelitsha, a rapidly-growing township in Cape Town, South Africa. The researchers measured antibody levels in the mothers at delivery and the infants at birth. They also assessed how the babies responded to routine vaccination by measuring the babies' antibody levels at four months, after they had received their routine vaccines.

Amongst the HIV-negative women in the study, a third also had low antibody levels, showing that protection against infection in their babies might also not be optimal in some women, who are otherwise perfectly healthy.

Dr Beate Kampmann, Reader in Pediatric Infection and Immunity at Imperial and the senior author of the study, said: "Around six million children under five die every year from infectious diseases, and a lot of these deaths are preventable by using existing vaccines. Studies like ours are helping us understand why certain infants might be especially susceptible to infections, and how we might tailor vaccination policies to protect vulnerable babies more effectively."

The Imperial team will soon begin a new project studying antibody levels in babies and mothers with and without HIV, among patient volunteers from Imperial College Healthcare NHS Trust. This work is funded by Imperial's Biomedical Research Centre, which was awarded by the National Institute of Health Research (NIHR).

Reference

Other Sources
1. Imperial College London. Study suggests why HIV-uninfected babies of mothers with HIV might be more prone to infections. Press release. February 8, 2011.

Blacks Continue to Have Highest Rate of HIV Diagnosis in U.S.

**SUMMARY:** In advance of National Black HIV/AIDS Awareness Day this past Monday, the U.S. Centers for Disease Control and Prevention (CDC) published a new report in the February 4, 2011, issue of *Morbidity and Mortality Weekly Report* showing that African Americans are still much more likely to be diagnosed with HIV infection than any other racial/ethnic group. Black men were 8 times more likely and black women were 19 times more likely to receive an HIV diagnosis during 2008 than white men and women.

*By Liz Highleyman*

Blacks/African Americans have been affected disproportionately by HIV since the early years of the epidemic, the report authors noted. While they make up about 14% of the total U.S. population, blacks accounted for half of all HIV diagnoses among adolescents and adults during 2005-2008 in the 37 states with consistent names-based reporting.

The investigators used data from the National HIV Surveillance System to estimate numbers, percentages, and rates of HIV diagnoses among blacks/African Americans during this period in states with "mature" HIV surveillance systems, that is, those in operation since at least January 2005.

**Results**

- During 2008 black men were 8 times more likely to be diagnosed with HIV than white men and twice as likely as Hispanic/Latino men.
Black women were 19 times more likely to be diagnosed than white women and 4 times more likely than Hispanic/Latino women.

Blacks accounted for 50.3% of all 156,812 HIV diagnoses during 2005-2008.

Blacks accounted for 46.4% of diagnoses among people age 25-44 and 55.7% among people in the southern U.S.

The number of new HIV diagnoses (not necessarily new infections) each year among black men increased during 2005-2008.

HIV transmissions among black men were classified most frequently as attributable to male-to-male sexual contact (61.1%), followed by heterosexual contact (23.1%), injection drug use (11.9%), and male-to-male sex/injection drug use together (3.6%).

Young men age 13-24 accounted for the largest percentage—30.9%—of HIV diagnoses among black men who have sex with men.

Most black women diagnosed with HIV were exposed through heterosexual contact (85.2%), followed by injection drug use (14.0%).

The National HIV/AIDS Strategy released this past July identified reducing HIV-related health disparities as one of its 3 key goals.

"Reducing HIV risk behaviors and increasing access to testing and referral to health care can help eliminate disparities between blacks/African Americans and other racial/ethnic populations in the rates at which HIV infection is diagnosed," the report authors concluded.

"The higher rates of diagnoses among blacks/African Americans suggest that adolescents and adults from this population who are at higher risk for HIV infection might benefit from more frequent testing to facilitate earlier diagnosis," according to an accompanying editorial note. "Persons infected with HIV who know their status can be referred to medical care and treatment that can improve the quality and length of their lives and to prevention services that can reduce the risk for further transmission." 2/11/11

Reference

Antiretroviral Treatment Interruption Can Cause Long-term Problems

SUMMARY: Taking breaks from antiretroviral therapy (ART) can lead to long-term adverse outcomes that do not reverse themselves even after treatment is restarted, according to a Swiss study described in the February 20, 2011, issue of AIDS. People who interrupted therapy had poorer CD4 T-cell recovery and were more likely to develop opportunistic illnesses or die than those who stayed on treatment.

By Liz Highleyman
The inconvenience, side effects, and cost of ART lead some people with HIV to interrupt therapy for brief or prolonged periods.

The large SMART study and other research has shown that treatment interruption—especially when a patient's CD4 count is relatively low—has detrimental effects in the short term, increasing the risk of both AIDS-related events and non-AIDS conditions such as cardiovascular disease.

Gilbert Kaufmann and fellow investigators with the Swiss HIV Cohort Study looked at the long-term effects of treatment interruption on CD4 cell recovery and clinical events.

The researchers evaluated immunological and clinical endpoints among 2491 participants in the Swiss cohort who started HIV treatment for the first time between 1996—the advent of effective combination ART—and 2008, following them for an average of about 7 years.

Patients were classified according to treatment consistency:

- Group A: interrupted treatment at least once (n = 1271; 51%);
- Group B: continuous ART but intermittent viral suppression, defined as HIV RNA rising to at least 1000 copies/mL (n = 469; 19%);
- Group C: continuous ART with consistent viral suppression < 1000 copies/mL (n = 751; 30%).

Results
At 8 years, CD4 T-cells levels rose in all groups, but more so in people with the most consistent treatment:

- 427 cells/mm³ in the treatment interruption group;
- 525 cells/mm³ in the continuous therapy but intermittent viral suppression group;
- 645 cells/mm³ in the continuous therapy, consistent suppression group.

Percentages of patients achieving a CD4 count > 350 cells/mm³ in the 3 groups were 63.0%, 76.3%, and 87.3%, respectively.

Percentages reaching > 500 cells/mm³ were 37.2%, 55.8%, and 68.0%, respectively, a significant difference (P < 0.001).

CD4 cell recovery was independently associated with cumulative duration of treatment interruptions; those with the longest interruptions experienced a CD4 cell decline.

Participants in the treatment interruption group had more HIV-related symptoms (CDC class B events) and more AIDS-defining conditions (CDC class C events) than those on continuous therapy.

People who interrupted ART also had an increased risk of death (20 deaths per 1000 person-year for interrupters vs 8 per 1000 person-years for those with continuous ART and consistent viral suppression).

Major risk factors for inability to reach a CD4 count above 500 cells/mm³ included lower baseline CD4 cell count, older age, and hepatitis C virus (HCV) coinfection.

"In persons receiving continuous ART larger CD4 T-cell recovery and a reduced risk for opportunistic complications and death was observed," the study authors concluded. "CD4 T-cell recovery was smaller in persons with treatment interruptions more than 6 months."

"The results strongly support the concept that patients should be discouraged to discontinue antiretroviral therapy," they advised. "If any interruption is required, it should be as short as possible to avoid poor clinical outcomes." 2/11/11

Reference

Advocates Call For Follow-Through On Decade-Old Pledge To Remove Tariffs On Malaria Treatments, Prophylactics In Africa
"Malaria prevention advocates say many lives can be saved by removing taxes and tariffs from essential commodities used to fight the disease," VOA News reports (Schlein, 2/9). A decade ago, African leaders promised to remove tariffs on products used to fight malaria, but only six countries have actually done so, according to the Malaria Taxes and Tariffs Advocacy Project (M-TAP), which held a meeting in Geneva on Wednesday, Reuters reports.

"While progress has been made in removing taxes and tariffs and rolling back import barriers, many countries still have a long way to go," Halima Mwenesi, director of M-TAP, said in a statement after the meeting. Eliminating taxes and tariffs can significantly reduce costs, according to campaigners, who note that most drugs and other malaria products are imported from abroad. Guinea, Kenya, Mauritius, Tanzania, Uganda and the Asian nation of Papua New Guinea "have done away with tariffs on commodities recommended by the World Health Organization (WHO) as essential to effective malaria control," according to M-TAP, which has been collecting data from almost 80 malaria-endemic countries over the past two year (Kelland, 2/10).

"They are imported from the manufacturing countries, which are either in Europe or Asia. By the time they get into the countries and you have markups from the private sector or then you have all the distribution costs, etc.,” Mwenesi said. “Then add on to that the tariffs and taxes, it becomes very difficult for people who are not necessarily making a lot of money to access these commodities,” Mwenesi added, VOA News writes. "The commodities include insecticide-treated mosquito nets, artemisinin-based combination therapies, rapid diagnostic tests, insecticides for indoor residual spraying, and spray pumps," according to the story (2/9).
M-TAP "said it found that taxes and tariffs on anti-malaria products provide only minimal revenues, and these gains are often offset by health costs and lost productivity from preventable malaria illnesses," Reuters writes. "Taxes and tariffs may also prevent the poor from gaining access to malaria treatment, the group said. Anecdotal evidence suggests most people seeking treatment for fever buy their medicines from local chemists and kiosks rather than from local government clinics and hospitals. The average medicine course can cost between $6 and $10 in many African and Asian countries, while three billion people worldwide earn less than $2.50 per day, M-TAP said," the news service writes.

"Private sector providers continue to play a critical role in supplying access to malaria treatment and prevention despite the huge increase in donor commitments over the past five years," said Mwenesi, adding, "We must make every effort to ensure that cost does not pose a significant barrier to access."

Awa Marie Coll-Seck, head of the WHO's Roll Back Malaria Partnership, said African countries are starting to take the lead on this initiative and "she hoped governments in Asia and Latin America would now follow" (2/10).

**Rising Number Of Livestock Diseases Threatens Public Health, Food Security In Developing Countries, Report Says**

"A growing number of livestock, such as cows and pigs, are fuelling new animal epidemics worldwide and posing more severe problems in developing countries as it threatens their food security, according to a report [.pdf] released on Friday" during an international conference in New Delhi, India, on Leveraging Agriculture for Improving Nutrition & Health, Reuters reports (Lyn, 2/11).

"The new assessments from ILRI [International Livestock Research Institute] spell out how livestock diseases present 'double trouble' in poor countries," according to an article on ILRI's website. "First, livestock diseases imperil food security in the developing world (where some 700 million people keep farm animals and up to 40 percent of household income depends on them) by reducing the availability of a critical source of protein. Second, animal diseases also threaten human health directly when viruses such as the bird flu (H5N1), SARS and Nipah viruses 'jump' from their livestock hosts into human populations," the article states.

Although developed countries "are effectively dealing with livestock diseases, ... in Africa and Asia, the capacity of veterinary services to track and control outbreaks is lagging dangerously behind livestock intensification," ILRI Deputy Director John McDermott said, according to the release. "This lack of capacity is particularly dangerous because many poor people in the world still rely on farm animals to feed their families, while rising demand for meat, milk and eggs among urban consumers in the developing world is fueling a rapid intensification of livestock production," he added (2/10).

"Animals seem to be the main source of new infectious disease in man: in general around 60% of human pathogens are transmissible from animals; among new diseases, the rate is about 75%," The Economist writes in an article that examines growing concerns in India over emerging infectious diseases that threaten both livestock and humans alike. "As rural populations in India and elsewhere expand, grow richer and eat more protein, backyards where a few chickens or pigs once scratched have become densely packed smallholdings of several dozen animals. These bring owners more wealth, but also hygiene and veterinary problems. ... Smallholdings near or in urban areas may be especially vulnerable," the magazine writes.

As The Economist writes, "[t]hese worries are not new." However, "researchers in Delhi argue that policymakers and farmers, keen to boost food supply, give too little thought to the threats to public health." McDermott and report co-author "Delia Grace [also of ILRI] ... estimate that the world contains 450m smallholder farmers. Where these are most numerous, notably in Asia, they create 'hot spots', where a huge amount of germs circulate among thriving livestock and human populations, especially near cities," the magazine adds (2/10).

McDermott and Grace also noted the economic cost of zoonotic diseases in their report, Reuters writes. "Epidemics like SARS in 2003, sporadic outbreaks of the H5N1 avian flu since 1997 and the H1N1 swine flu pandemic of 2009 racked up enormous economic costs around the world. ... While SARS cost between $50 billion to $100 billion, the report cited a World Bank estimate in 2010 which pinned the potential costs of an avian flu pandemic at $3 trillion," according to the news service (2/11).

**Kenya Broadcasting Corporation News** adds that the "[r]esearchers are now urging for the establishment of surveillance systems that are able to detect animal disease outbreaks in their earliest stages in order to effectively contain an outbreak" (Akolo, 2/11).
The International Food Policy Research Institute conference drew together experts in agriculture, nutrition and health from around the world to discuss "ways to increase agriculture's contribution to better nutrition and health for the world's most vulnerable people," according to the ILRI article (2/10). The conference website features remarks by Secretary of State Hillary Rodham Clinton delivered by video, where she addressed the U.S.' involvement in addressing world hunger: "The United States is committed to this fight. By investing in drought-tolerant and vitamin-rich crops through our Feed the Future Global Hunger and Food Security Initiative, ... by providing micronutrients to pregnant women and children through our Global Health Initiative and also by helping nutrition champions implement country-led solutions thru the One Thousand Days, a global movement to improve maternal and child nutrition," Clinton said. "We are working closely with our partners, including other countries, multilateral organizations, NGOs, and research centers worldwide," she said (2/11).

**New York Times Examines Factors Contributing To Presence of 'Exotic' Infectious Diseases In New York City**

"When New York City's health department revealed last weekend that three people had contracted cholera [after traveling to the Dominican Republic], it was a reminder that the city is not just a world capital of arts, business and the like – but also of exotic diseases," the New York Times writes in an article that explores how diseases from around the world often make their way to the city through its diverse population of travelers.

For instance, "several people every year are found to have a Biblical disease, leprosy ... In 2002, bubonic plague, more commonly associated with the 14th century, found its way to New York City through two travelers who came from a ranch in New Mexico, where the disease is endemic in flea-bitten wild animals like prairie dogs," the newspaper writes.

"Malaria is a steady presence in New York City, with about 200 cases a year – a far greater incidence than that of another mosquito-borne disease, West Nile, which infected 42 New Yorkers last year. ... As for cholera, New York City receives reports of about one case a year, almost always found in someone who has traveled abroad, so the three cases of last weekend represent a bit of an increase."

The article notes how increased surveillance following the "terrorist attacks of 2001" enabled public health officials to better monitor patterns of disease emergence in the city, and factors that contribute to fluctuations in disease outbreaks. The article also features quotes by Don Weiss, the director of surveillance for New York City's Bureau of Communicable Diseases. Of the malaria cases, Weiss said, "The mosquito that transmitted it doesn't live in this part of the world. ... People going home to Africa pick it up and bring it here" (Hartocollis, 2/10).

**'Simply Controlling Polio' Now Could Have Devastating, Prohibitively Expensive Long-Term Consequences**

In an Atlanta Journal Constitution opinion piece Jon Kim Andrus, deputy director of PAHO, and Ciro A. de Quadros, executive vice president of the Sabin Vaccine Institute, reflect on the debate among health experts about whether "the final push to eradicate polio is possible, or even worth the effort."

"To many, the cost of eradicating polio by 2013 – which experts put at $2 billion – sounds prohibitive, particularly in financially uncertain times," and "[t]o be sure, simply controlling polio – or limiting its reach – would mean lower costs in the short term," Andrus and de Quadros write. "But there is ample evidence to suggest that taking this approach could have devastating – not to mention prohibitively expensive – long-term consequences," including re-emergence of the virus in areas where the disease was once thought to have been eradicated.

"[A]dequate funding to continue the polio eradication initiative is key. ... Renewed financial commitments from donor governments including the United States, and political will from leaders in the developing world, are critical to continue the national immunization days in countries that continue to combat polio or are at high risk of unwittingly 'importing' the disease," they write. "The tools needed to stop polio in its tracks and give children a basic human right to good health are ready and available. We are so close. We must stop polio now" (2/9).

**Study finds even with fetal lung maturity, babies delivered prior to 39 weeks are at risk**

SAN FRANCISCO (February 11, 2011) — In a study to be presented today at the Society for Maternal-Fetal Medicine's (SMFM) annual meeting, The Pregnancy Meeting™, in San Francisco, researchers will
present findings that show that despite fetal pulmonary maturity, babies delivered at between 36 to 38 weeks, still have a significantly increased risk of neonatal morbidities.

The American College of Obstetricians and Gynecologists recommends that fetal pulmonary maturity be documented for scheduled deliveries occurring prior to 39 weeks of gestation in order to prevent neonatal respiratory problems.

"We wanted to do the study because recent evidence suggests that deliveries prior to 39 weeks may result in increased neonatal morbidity," said Yu Ming Victor Fang, M.D., one of the study's authors. "We wanted to examine whether neonates who were delivered at between 36 to 38 completed weeks with confirmed fetal pulmonary maturity would be at increased risk for neonatal morbidities when compared to those that were delivered at 39 weeks or greater."

To compare neonatal outcomes, the team looked at mothers who had positive fetal lung maturity tests at between 36 to 38 completed weeks. They compared the neonatal outcomes from these scheduled deliveries prior to 39 weeks with known fetal lung maturity to the outcomes from scheduled deliveries at 39 weeks to 41 completed weeks.

The study was a retrospective cohort study from a single institution over a 12 year period. Neonatal outcomes of women who were delivered following documented fetal pulmonary maturity at 36, 37, and 38 weeks were compared to women undergoing a scheduled delivery at 39, 40, and 41 weeks. A lamellar body count of ≥36,000, lecitin/sphingomyelin (L/S) ratio >2.0, or a phosphotidyglycerol (PG) of 0.3 were considered mature. Neonate outcomes examined included: neonatal intensive care unit (NICU) admission, length of stay (LOS) in the NICU, total neonatal respiratory morbidity (Tot resp morbid), cases of respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN), other respiratory morbidity (other resp morbid), neonates requiring mechanical ventilation (Vent), proven sepsis (Sepsis), hypoglycemia, and neonatal deaths. Fetuses with major congenital anomalies were excluded. Neonatal outcomes between the two groups were compared using the chi square test.

The study concluded that despite fetal pulmonary maturity, deliveries between 36 0/7 to 38 6/7 weeks are associated with significantly increased neonatal morbidity.

"Patients need to be counseled carefully if they choose to have a scheduled delivery prior to 39 weeks," said Dr. Fang. "Even if tests indicate that their baby's lungs are mature, delivery prior to 39 weeks is not without risks."

**Virus, Parasite May Combine to Increase Harm to Humans**

ScienceDaily (Feb. 11, 2011) — A parasite and a virus may be teaming up in a way that increases the parasite's ability to harm humans, scientists at the University of Lausanne in Switzerland and Washington University School of Medicine in St. Louis recently reported in *Science*.

When the parasite *Leishmania* infects a human, immune system cells known as macrophages respond. However, some *Leishmania* strains are infected with a virus that can trigger a severe response in macrophages, allowing the parasite to do more harm in animal infections. In humans, the parasite's viral infection may be why some strains of *Leishmania* in Central and South America tend to cause a disfiguring form of disease that erodes the soft tissues around the nose and mouth.

"This is the first reported case of a viral infection in a pathogen of this type leading to increased rather than reduced pathogenicity," says Stephen Beverley, PhD, the Marvin M. Brennecke Professor and head of the Department of Molecular Microbiology at Washington University School of Medicine. "It raises a number of important questions, including whether we can use antiviral strategies to reduce the damage caused by forms of *Leishmania* that carry viruses."

*Leishmania* infection, known as leishmaniasis, affects an estimated 12 million people worldwide. It is mainly spread by sand fly bites and is a major public health problem in the Mediterranean basin, Asia, Africa, the Middle East, Central and South America and a potential hazard to travelers and military
personnel. Symptoms include large skin lesions, fever, swelling of the spleen and liver, and, in more serious forms of the disease, disfigurement and death.

The study brought together two different lines of investigation in Europe and the Americas. Nicolas Fasel, PhD, professor of biology and medicine at the University of Lausanne, and Nancy Saravia, PhD, of the International Center for Medical Training and Investigation in Cali, Columbia, have been studying the causes of mucocutaneous leishmaniasis, a particularly harmful form of the disease that destroys the soft tissues of the nose and mouth. This type of infection is frequently associated with Leishmania Viannia, a subgenus of Leishmania strains prevalent in Central and South America.

In tests in mice and hamsters using parasite strains taken from the wild, Fasel and Saravia showed that only some Viannia strains spread rapidly and cause high levels of inflammation and damage similar to that seen in mucocutaneous leishmaniasis.

A breakthrough came when researchers realized that the rapid, highly damaging form of infection relied on an immune system sensor protein called TLR3. This protein is found in intracellular vesicles, which are compartments inside macrophages also known to host the parasite.

"Those vesicles are where the rendezvous between host, parasite and virus takes place," Fasel says. "TLR3 normally helps the immune system fight infections, but when we deleted it in mice and repeated the experiment, infections with virus-infected Leishmania were less harmful."

Researchers sorted the Leishmania into viral-infected and non-infected strains and found that the more serious infections in laboratory animals were much more likely to be caused by viral-infected Leishmania.

Beverley's group has been exploring the role of viral infections of Leishmania in the evolution of the RNA interference pathway, which can help fight viruses.

"Surprisingly many Leishmania species have lost the RNAi interference pathway, and one force contributing to this loss could be the successful infection of the parasite by viruses," he says. "This hints at the possibility of an evolutionary trade-off, suggesting that the loss of RNAi could be balanced if the parasite gained some type of advantage when infected by a virus."

To ensure that genetic differences in the wild strains weren't interfering with the results, Lon-Fye Lye, PhD, staff scientist, and Suzanne Hickerson, senior research technician, both of Beverley's lab, supplied lines of genetically identical Leishmania with and without the virus. As in the prior comparisons, virally-infected Leishmania caused more disease and provoked a stronger response from macrophages.

According to Beverley, the results suggest that some viral infections in Leishmania may be improving the parasite's chances to infect the mammalian host's immune cells. He speculates that this increased pathogenicity may be one evolutionary trade-off that makes losing the RNAi pathway worthwhile for Leishmania and other microbes.

"How the virally increased pathogenicity arises is now a fascinating question in its own right," Beverley says. "It could teach us a great deal about how Leishmania causes a severe form of the disease and potentially offer new opportunities for its cure."

Journal Reference:

New Way to Attack Pathogens: RNA Recycling System Gone Awry Brings MRSA to a Halt

Scanning electron micrograph (SEM) depicted numerous clumps of methicillin-resistant
Scientists have discovered a new way to attack dangerous pathogens, marking a hopeful next step in the ever-escalating battle between man and microbe.

In a paper published online Feb. 10 in the journal *PLoS Pathogens*, scientists demonstrate that by stopping bacteria's ability to degrade RNA—a "housekeeping" process crucial to their ability to thrive—scientists were able to stop methicillin-resistant *Staphylococcus aureus* or MRSA both in the laboratory and in infected mice.

The team, headed by a microbiologist at the University of Rochester Medical Center, is now developing closely related compounds designed to be much more potent than the one discussed in the paper.

The new approach shows promise against the most severe strains of MRSA as well as the toughest type of MRSA infection for antibiotics to infiltrate—bacteria enmeshed in biofilms.

"This offers a whole new way to go on the offensive against some of the world's most dangerous bugs," said the leader of the group, Paul Dunman, Ph.D., associate professor of Microbiology and Immunology at the University of Rochester Medical Center and formerly of the University of Nebraska. "We're hoping our research opens the door to an entirely new class of antibiotics."

Dunman's team discovered that a molecule known as RnpA is central to the degradation process. After nailing down the activity of RnpA, the team tested more than 29,000 compoundsin its search for one that inhibits its activity. The team found one, a small molecule called RNPA1000, that brings MRSA nearly to a standstill.

Throwing a monkey wrench into bacteria's RNA recycling system might harm MRSA in a number of ways. One possibility is that since messenger RNA molecules are not destroyed like they should be, the bacteria are overcome by an array of confusing instructions that should have been turned off. Another possibility is that bacteria are unable to make essential new RNA molecules, since the supply of raw material is not available.

"We believe this basically makes the bacterial cell go haywire. The cell is producing proteins it no longer needs, and it can't produce proteins that it does need," said Dunman.

The team found that RNPA1000 is active against the predominant MRSA types circulating in the United States, vancomycin intermediate susceptible *S. aureus* (VISA) and vancomycin-resistant *S. aureus* (VRSA). The compound also showed significant antimicrobial activity against a host of other bugs tested, including *Staphylococcus epidermidis*, antibiotic-resistant *Streptococcus pneumoniae*, *Streptococcus pyogenes*, and vancomycin-resistant *Enterococcus faecium*.

Especially promising was its activity against MRSA biofilms, whose formation is central to the bacterium's virulence in medical settings. Today's antibiotics have a tough time breaking through MRSA biofilms on equipment like catheters, but RNPA1000 brought the bacteria to a halt even when they were ensconced within biofilms.

The agent does not affect other drugs used to treat MRSA infections, including vancomycin, daptomycin, or rifampicin; it does affect oxacillin, making it more potent. That
find might make it possible to eventually combine an agent like RNPA1000 with other drugs that also target the infection.

The compound was also moderately effective in mice. In an experiment with infected mice, all of the untreated mice died from their infection, but **half the mice survived when treated with a large dose of RNPA1000.** The compound is also somewhat toxic to human cells at the largest doses. Those findings make it unlikely that RNPA1000 itself will end up as an antibiotic and spurred Dunman and colleagues to design safer, more potent alternatives.

"This is a great starting point," said Dunman. "We've identified a compound that is very active against RnpA, and now we can use chemistry to try to increase its potency by hundreds of times, as well as make it less toxic to human cells. We've gotten a lead from the drug screen, and now we're building a better molecule."

Dunman is a leader in the development and use of array technology to study microbes and explore fresh approaches to the development of antibiotics. While microarrays are widely used by scientists to take what amounts to a snapshot of the activity of thousands of genes in a cell, Dunman adds a twist. His team employs the technology constantly to watch what happens to RNA molecules after they've been made, typically taking dozens of snapshots in the span of hours to get an ongoing, intimate look at RNA degradation.

The paper caps a six-year effort that began when the first author, Patrick Olson, was a high school student working as an intern in Dunman's laboratory in Nebraska. Olson is now in graduate school at Washington University in St. Louis, working toward both his medical and doctoral degrees.

**Journal Reference:**

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**28 gay Jamaicans granted asylum in US last year**
Saturday, February 12, 2011

NEW YORK, United States — Immigration Equality, an organisation which works to secure asylum for individuals persecuted in their home country based on their sexual orientation, gender identity or HIV-status, said it won dozens of cases for clients from the Caribbean in 2010.

The organisation said that it won a record 101 cases last year.

"An overwhelming number of the victories, 38, were for clients from the Caribbean, with 28 of those for individuals from Jamaica," it said. There were four successful cases from Grenada.

"Other cases included 24 asylum seekers from Central and South America; 16 from Eastern Europe (including seven Russian clients); nine from the African continent and five from the Middle East."

The organisation, which maintains the largest network of pro bono attorneys, in addition to its in-house legal staff, is dedicated solely to seeking asylum for Lesbians, Gays, Bi-sexual and Transgender (LGBT) asylum seekers.

Immigration Equality said that it has 97 additional cases filed in 2010 which are awaiting a ruling, as well as several cases filed prior to 2010.

"For too many lesbian, gay, bisexual and transgender people, the world remains a dangerous place," said Rachel B. Tiven, the group's executive director.

"In many cases, the clients who turn to Immigration Equality for help are literally running for their lives. They have been mistreated and beaten by authorities in their home country, disowned by their families and ostracized by society. By offering them safe haven, the United States is not only saving their lives, but benefitting from the talent, skills and service these asylees bring to our country. We are proud, and honored, to help them begin life anew here in their adopted homeland."

Since the mid-1990s, the United States has recognised persecution due to sexual orientation and gender identity as a basis for seeking asylum.

In the past five years, Immigration Equality and its partner law firms have represented more than 500 LGBT people fleeing persecution abroad. Clients have hailed from some of the most notoriously homophobic countries in the world, including Uganda, Syria and Egypt.
Light Shed on RNA 'On/Off Switches'

ScienceDaily (Feb. 13, 2011) — Scientists from The Scripps Research Institute have shed new light on a molecular switch that turns genes on or off in response to a cell's energy needs.

The study—published February 13, 2011 in an Advance Online Publication of the journal *Nature Structural and Molecular Biology*—shows these recently discovered RNA "riboswitches" are capable of more complex functions than originally thought. In addition, because riboswitches so far have been found primarily in bacteria, the study may have implications for designing new antibiotics against harmful bacteria.

"The study provides new insights into how a single RNA molecule can integrate both positive and negative signals from a cell," said senior author Martha Fedor, an associate professor and member of the Skaggs Institute for Chemical Biology at Scripps Research. "It extends the known capabilities of riboswitches."

Riboswitches respond to the concentrations of molecules produced by a cell’s metabolism—the process of creating or using energy—to regulate genes’ activities. The new study shows that a particular riboswitch does not respond to just a single metabolite, as had been assumed, but rather to many such compounds.

**Switching Genes On and Off**

Each gene serves as a recipe for building a protein molecule. When a particular protein is needed by the cell, the corresponding gene, made of DNA, is turned "on," or transcribed into a messenger RNA, which then carries the "protein recipe" to the protein-making machinery of the cell.

For many years scientists thought proteins, unlike DNA and RNA, were the only molecules in a cell capable of accomplishing sophisticated tasks, such as regulating the activities of genes or carrying out chemical reactions. But in the past couple of decades, researchers have discovered that certain types of RNA molecules are adept at performing feats worthy of their protein counterparts. Riboswitches are one such example.

Discovered only about eight years ago, riboswitches are short stretches of RNA that reside within the messenger RNAs of proteins involved in a cell's metabolism. These riboswitches bind certain metabolites and, depending on how much binding occurs, the riboswitches turn the production of the corresponding proteins on or off.

Until now, most researchers had assumed a single riboswitch was specific for a single metabolite. But the new study by Fedor’s group shows a riboswitch can incorporate signals from many metabolites at once.

**A Self-Destructing Riboswitch**

Fedor’s group was interested in studying the function of a type of riboswitch that binds to a metabolite called glucosamine-6-phosphate. This amino sugar, a building block for many glycosides and glycans, is required for the cell wall and other vital structures in bacterial cells.

This particular riboswitch resides in the messenger RNA that carries instructions for the enzyme responsible for the production of glucosamine-6-phosphate, called GlmS. It was known that when glucosamine-6-phosphate is abundant in a cell, the riboswitch stops production of the GlmS enzyme by destroying itself and its messenger RNA. This self-destruction functions to shut off any more production of glucosamine-6-phosphate.

On the other hand, when glucosamine-6-phosphate concentrations are low, the glmS riboswitch does not self-destruct, keeping the messenger RNA functioning.

**A Puzzling Observation**

Fedor and graduate student Peter Watson had designed an assay to measure the amounts of the glmS riboswitch in yeast cells as they added increasing concentrations of glucosamine. But the scientists stumbled on a puzzling finding.

If they grew their yeast in energy-rich broth that contained glycerol, a 3-carbon energy source, the riboswitch behaved as they expected, shutting off the glmS messenger RNA in response to increasing glucosamine concentrations. However, if bacteria was grown in a broth containing glucose, a 6-carbon energy source, the riboswitch no longer self-destructed.

"At first we thought something was wrong with our system," said Fedor.

But Fedor and Watson solved the puzzle. They discovered this riboswitch can bind both glucosamine-6-phosphate and glucose-6-phosphate. Each compound, however, produces opposite results. Binding glucosamine-6-phosphate induces self-destruction of the riboswitch and turns the glmS gene off; binding glucose-6-phosphate prevents self-destruction and keeps the glmS gene turned on.
"Scientists had long focused on the ability of riboswitches to recognize a single compound, but we have now found that riboswitches, or at least this one, can recognize multiple ones," said Watson.

**Integrating Signals**

"When glucose concentrations are high in a cell, it means that energy is abundant," explained Watson. "That is when cells would want to grow and divide and make more glucosamine-6-phosphate to build new cell walls. But when glucosamine-6-phosphate concentrations are high, then cells know to stop making more of this compound."

The glmS riboswitch function thus depends upon a balance between these two—and possibly additional—competing signals. "This kind of complex signaling had long thought to be the domain of just proteins," said Fedor. "This is another example of a function thought to belong only to proteins that we now know that RNA can do."

Fedor and Watson are now testing whether other types of riboswitches use this same mechanism. Unlike the glmS riboswitch, which self-destructs, most known riboswitches regulate the activities of their respective messenger RNAs by changing their three-dimensional structures in response to metabolite binding. The new shapes act to prevent the transcription of messenger RNA or translation of messenger RNA into protein.

Although riboswitches have not yet been found in humans, Fedor believes this discovery is just a matter of time. "The great thing about the field of RNA is that we are always coming across unexpected findings," she said.

**Journal Reference:**

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**Gene swap key to evolution**

**Horizontal gene transfer accounts for the majority of prokaryotic protein evolution**

[Published 27th January 2011 10:00 PM GMT]

Microbes evolve predominantly by acquiring genes from other microbes, new research suggests, challenging previous theories that gene duplication is the primary driver of protein evolution in prokaryotes.

The finding, published today (January 27) in *PLoS Genetics*, could change the way scientists study and model biological networks and protein evolution.

"Even at a meeting last summer, there were those that thought that bacteria genomes expanded mostly through duplications and others that argued that it was due to gene acquisition," wrote Howard Ochman, an evolutionary biologist at Yale University who was not involved in the research, in an Email to *The Scientist*. "Now we all have a paper to point to that does a very good job of answering this question," he said. "Their conclusions are really robust."

Prokaryotes, including bacteria and archaea, thrive in diverse conditions thanks to their ability to rapidly modify their repertoire of proteins. This is achieved in two ways: by receiving genes from other prokaryotes, called horizontal gene transfer—the nefarious way that bacteria acquire antibiotic resistance—or by gene duplication, in which an existing gene is copied, taking on a new or enhanced function as mutations accumulate.

Past analyses using few, distantly related genomes estimated that horizontal gene transfer contributes to, at best, 25 percent of the expansion of protein families—that is, the addition of proteins with novel functions or structures. But the recent availability of numerous, closely related prokaryotic genomes tempted Todd Treangen and Eduardo Rocha at the Institut Pasteur in Paris to more accurately test which biological process is the main driver of prokaryote protein evolution. "The genomic data was finally there to do a more in depth study," said Treangen, now a postdoc at the University of Maryland.

The duo analyzed 110 genomes of varying size from 8 clades of prokaryotes, focusing in on 3,190 defined protein families. The results were unambiguous: 80 to 90 percent of protein families had expanded through horizontal gene transfer. In addition, the researchers found that the two processes have different evolutionary roles: transferred genes persist longer in populations while duplicated genes are transient but more highly expressed.
"Overall, the role of gene transfer in protein diversification has been underestimated," said Treangen. Still, he noted, they analyzed only a tiny fraction of the microbes that exist in the world, and further research should be done as more genomes become available.

It would be nice to study the same two processes in eukaryotes, said Patrick Keeling, a molecular evolutionary biologist at the University of British Columbia who was not involved in the research. Yet despite numerous documented cases of horizontal gene transfer in eukaryotes, including plants, it would be hard to test because of the lack of genomic data from enough closely related eukaryotes (which have significantly larger, less manageable genomes than prokaryotes). Still, "it raises some really fascinating questions about whether [eukaryotes] evolve in the same way," said Keeling.


By Katherine Bagley

**Gut microbes influence behavior**

**Mice lacking normal gut bacteria show differences in brain development and behavior**

Gut microbes acquired early in life can impact brain development in mice and subsequent behavior, such as decreasing physical activity and increasing anxiety, according to a study published this week in the *Proceedings of the National Academy of Sciences*.

"This paper opens the door to new studies in at least two directions," Yale University microbiologist Andrew Goodman, who was not involved in the research, told *The Scientist* in an email. "First, determining how differences between complete host-associated microbial communities lead to differences in behavior, and second, exploring the contributions of microbes during specific developmental periods in the host."

Gut microbiota often colonize their hosts early in life, either during pregnancy or following birth, and play an integral role in the health of developing organisms. Previous research has shown that the bacteria affect the development of liver function, the protection epithelial cells afford underlying digestive tissue, gut regulation and the growth of new capillary blood vessels. But this is the first time gut flora have been linked to brain development and behavior.

Harmful microbial infections, on the other hand, have been linked to neurodevelopmental disorders, including autism and schizophrenia. And rodents infected by microbial pathogens before and after birth demonstrated behavioral abnormalities, such as anxiety-like behavior and impaired cognitive function, leading Rochellys Diaz Heijtz, a neurobiologist at the Karolinska Institute in Sweden, and her colleagues to wonder if the gut’s normal microbial residents may similarly influence brain development.

The researchers tested exploratory activity in germ-free mice and mice with normal gut microbiota by tracking their movements across open space. They also tested anxiety of the two groups in two classic rodent behavioral tests—the light-dark box and the elevated maze. Spending more time in lit areas and along unwalled, elevated maze portions equated to less anxiety.

Germ-free mice appeared to be more exploratory than mice with normal microbiota, venturing farther and to more areas of the space provided. Germ-free mice also spent more time in the light and engaged in riskier behavior in the maze, indicating they suffered from less anxiety than their microbe-filled counterparts.

The team then infected germ-free mice with normal gut microbiota when they were born to test whether the gut flora could alter the mice's activity and anxiety levels. Sure enough, the newly infected mice spent less time exploring and engaging in risky behavior, like the normal mice in the initial experiments. The results further supported the argument that the microorganisms can affect brain and behavior when introduced early enough in development.

"These microorganisms communicate in a systemic fashion to the developmental programming of a new individual and can influence fundamental aspects of behavior," said Diaz Heijtz. "We should start to consider the possibility that the microbiome and/or its composition may contribute to psychiatric problems."

Looking more closely at the gut flora's effects on the brain, the researchers found that germ-free mice had lower turnover rates of certain neurotransmitters in the striatum, the part of the brain involved in the regulation of motor and cognitive function, than in mice with normal gut microbiota. There were also differences in the levels of key synaptic-related proteins and signaling molecules involved in central nervous system communication.
"This all means that there has been an evolutionary adaption of host-microbe interactions to the most complex organ in the body, the brain," said coauthor Sven Pettersson, a neuro- and microbiologist at the Karolinska Institute.

The scientists stress that there are still many unanswered questions and further research is needed to understand the broad implications of the research. For example, the study didn't distinguish the effects of maternally inherited microbes from those acquired shortly after birth, Goodman noted. "It is also not clear whether microbes residing in other body habitats are playing a role," he said, such as those located in the nose, ears, mouth or vagina.

Next up, Diaz Heijtz and her colleagues are hoping to pinpoint which gut microbiota are affecting brain development and behavior. They also plan to identify which brain cells are responding, and work out the details of the signaling pathways that allow the microbiota to communicate with the brain.

"The intestinal microbiota influences so many aspects of our biology like metabolism and immune function," Justin Sonnenburg, a microbiologist at Stanford University School of Medicine who did not participate in the study, said in an email. "We should not find these results startling, but rather a nice addition to a small but growing body of literature that connect our intestinal microbiota to neurobiology."


Comment on this news story autism and cur microbes
by Nita Hestevold, [Comment posted 2011-02-15 10:12:38]
Someone should do a study looking into a possible connection between gut microbes and autism. There are so many parents that believe that vaccines are associated with autism’s onset (which has been disproven). But this is an age when children are regularly introduced to new foods (and so new gut microbes). Perhaps this could explain the sudden onset.

**Chinese Government Reiterates Ban on Hepatitis B Tests Due to Discrimination Among Job Seekers**

*Xinhua News Agency*, (02.13.2011)
China’s ministries of Health, Education, Human Resources, and Social Security on Feb. 10 issued a statement calling for the end of widespread hepatitis B testing in health screenings for employment and school enrollment. The health ministry also requested a comprehensive investigation of hepatitis B-related discrimination, promising to punish all violators.

Although the tests may not be given even with examinee consent, they are still part of qualifying health exams for 61 percent of the 180 state-run companies surveyed by the non-profit Beijing Yirenping Center. Moreover, 63 companies admitted they would be reluctant or would never hire an infected person, even though transmission only occurs through contact with blood or other bodily fluids.

According to Yirenping Center Principal Yu Fangqiang, disregard for the ban stems from insubstantial penalties for violations and institutional profit concerns. Whereas a worker would expend an incredible amount of time, energy, and money filing a lawsuit and collecting evidence, companies would only be fined thousands to tens of thousands of yuan if they were ruled against (1,000 yuan=$151.76 US), said the center.

China University of Political Science and Law Associate Professor Liu Xiaonan challenged officials to produce a formal law and establish committees dedicated to investigating discrimination and safeguarding workers’ rights.

**Sex Disease Outbreak Worries Chief Medical Health Officer**

A chlamydia outbreak is the greatest public health challenge facing New Brunswick, said Dr. Paul Van Buynder, its outgoing chief medical health officer. There were 1,800 confirmed cases of the STD last year, marking a 20 percent jump compared to 2009.

"If you are under 30 and you are breathing, you need a chlamydia test," Van Buynder said Friday in his final interview before leaving to head a Vancouver-area health authority. At least 10 percent of women and 5 percent of men ages 20 to 24 in New Brunswick have had chlamydia, and recent figures suggest it is now reaching even younger age groups.

According to Van Buynder, the biggest increase in cases was observed in 17-year-old boys and 16-year-old girls. Educational outreach should begin prior to these ages and extend beyond “wear a rubber” conversations to encompass healthy sexuality discussions inclusive of female empowerment messages, he said.
After a focus group revealed most New Brunswick youths did not comprehend the risks of chlamydia, the Department of Health recently began a public awareness campaign targeting 20- to 24-year-olds. The campaign comprises Facebook and movie theater ads, and posters in the province’s bars and universities.

Although the spike in chlamydia rates was Van Buynder’s main health concern, he also spoke on the region’s general public health. Syphilis cases rose to 40 last year from three cases in 2009, a 600 percent increase. Chronic diseases also threaten to drain resources for government services, said Van Buynder. “The cost to the health care system of people who have chronic diseases, smoke cigarettes, who don’t exercise ... we just cannot afford it.”

**HIV Prevalence and Risk Behaviors Among Men Having Sex with Men in Nigeria**
*Sexually Transmitted Infections Vol. 87: P. 65-70*, (02..2011)  Mike Merrigan and others

In the current study, the authors set out to determine HIV and syphilis prevalence among men who have sex with men in Nigeria and to assess HIV-related risk behaviors and exposure to HIV prevention interventions among the MSM. The researchers’ cross-sectional study used respondent-driving sampling conducted in Lagos, Kano, and Cross River states between July and September 2007.

The participants were 879 MSM, 293 from each state, with a median age of 22 years. No syphilis infections were found. HIV infection was diagnosed among the MSM as follows: in Cross River, eight men (1.1 percent, confidence interval 0.1 percent to 2.2 percent); in Kano, 27 men (9.3 percent, CI 5.7 percent to 15.4 percent); in Lagos, 74 men (17.4 percent, CI 12.3 percent to 23.2 percent).

The MSM reported an average of 4.2 male anal sex partners in the previous six months. Selling sex to other men was reported by 24.4 percent of participants in Lagos and 36 percent in Kano. Sex with a girlfriend was reported by 49.7 percent of the MSM, and at least 6.5 percent reported paying female sex workers for sex.

Reports of consistent condom use during commercial sex with other men in the past six months ranged from 28 percent in Cross River to 34.4 percent in Kano. Reports of consistent condom use during non-commercial sex ranged from 23.9 percent in Kano to 45.8 percent in Lagos.

“Associations with HIV positivity included age in the three states, having been the receptive partner in anal sex in the past six months in Lagos, and in Lagos and Kano feeling at risk of HIV,” the authors found. “Large differentials in HIV prevalence between states, together with high mobility, inconsistent condom use, and behavioral links with female sex partners, have the potential for further HIV transmission within MSM networks, and between MSM and the general population.”

**DPH Plugs Female Condoms for Gay Men**
*Bay Area Reporter (San Francisco)*, (02.10.2011) Matthew S. Bajko

The city Department of Public Health is rolling out the nation’s first social marketing campaign to promote the new female condom (FC2) for use by men as well as women.

“The female condom has been out since the 1990s, and we have been offering the old one at City Clinic for some time now,” said Jacqueline McCright, DPH’s community-based STD services manager. “Gay men ask for it more often than women do. It protects against STDs and HIV when having anal sex.”

The DPH campaign, set to launch on Valentine’s Day, will include promotional posters in local businesses, gay bars and sex clubs, and ads on city buses. The department’s approach is a departure from the stance of the Food and Drug Administration, which has not supported the use of female condoms for anal sex as a way to prevent HIV and other STDs.

Supported by a $100,000 MAC AIDS Fund grant, DPH aims to distribute 80,000 of the female condoms, which are made with a thin synthetic material, nitrile, and a design to improve sensation. The FC2 is cheaper than the original female condom.

The artist behind the city’s Healthy Penis campaign, Scott Metzger, created the new female condom poster illustrations. “Because you don’t necessarily know how to use it, we have made special arrangements to have an illustrator draw out how to use it for anal sex,” McCright said.

Walgreens has agreed to sell the condoms at a reduced price, three for $9.99 instead of $6.49 each. Last year, the AIDS Foundation of Chicago produced a website to help educate gay men on how to use a female condom for anal sex, www.ringonit.org, which includes a video created by health workers in Burkina Faso.

For more information about San Francisco’s campaign, visit: www.fc2sf.org.
Foes Seek to De-Fund, Discredit Planned Parenthood

**Associated Press**, (02.13.2011) David Crary

US Rep. Mike Pence (R-Ind.) has introduced a bill that would deny federal family planning funds to any organization that performs abortions, placing the more than $70 million Planned Parenthood receives annually in jeopardy. Though Title X funds cannot be used directly for abortions, Pence maintains the grants free up other funds such groups use to offer the procedure.

Lending momentum are the recently published, covertly taped videos showing a man posing as a pimp and a woman posing as a prostitute seeking health services for underage sex workers at a half-dozen Planned Parenthood clinics in New Jersey, New York, and Virginia. The tapes were released by the anti-abortion group Live Action. Planned Parenthood officials fired one clinic manager who offered advice to the pair, but said other clinic staffers responded appropriately and reported the visits to their supervisors.

For Planned Parenthood officials, these actions represent the latest attacks on women’s ability to get the reproductive health services they choose. “We are a safe place where people can go and ask difficult questions about sex,” said President Cecile Richards.

Abortions represent only a small fraction of the Planned Parenthood’s services provided. The group primarily offers contraception, STD testing, and cancer screenings, and many of its clients are low-income women who otherwise cannot access non-emergency health care. “We’ve been here for the past 95 years, and we’ll be here for the next 95,” said Richards.

With an annual budget of $1 billion, Planned Parenthood could survive a loss of Title X grants, though it would be forced to shutter some clinics and serve fewer clients, said Richards.

On Thursday, Virginia’s House of Delegates voted to ban not only state but also local government funding of the organization. Del. Robert Marshall, the measure’s sponsor, objects to Planned Parenthood’s role in providing abortions and he holds it responsible for broader phenomena like out-of-wedlock pregnancies and adolescent sex and STDs.

'World's Most Ambitious HIV Testing Campaign' Launched

**Mail & Guardian (Johannesburg)**, (02.14.2011) Vuvu Vena

“First Things First,” a new university-based HIV testing campaign launched Monday, is the latest initiative encouraging South Africans to know their serostatus. The public-private partners who are leading the campaign say behavior changes in young people are needed if the country is to successfully tackle HIV/AIDS.

Students should have their “first HIV test in the first weeks of first-year student life at university,” said Val Beaumont, executive director of Innovative Medicines of South Africa, which joined with the government to develop the campaign. Other partners include the US President’s Emergency Plan for AIDS Relief, the South African National AIDS Council, the Foundation of Professional Development, the Higher Education HIV and AIDS Program, and Higher Education South Africa.

“Knowing your status is not the only prevention strategy, but it is the most important intervention,” Health Minister Aaron Motsoaledi said at the campaign’s launch at Witwatersrand University. “We chose to reach out to students as they are our future leaders who can enable positive change within society.”

Motsoaledi said 250 staffers from participating organizations have been trained to test students on an ongoing basis, “ensuring a lasting legacy of testing in tertiary institutions beyond the life of the campaign.” Those who undergo voluntary testing are asked to sign a pledge that reads: “We, the class of 2011, pledge to know our status, to stop the HIV/AIDS stigma and to contribute to the struggle against HIV/AIDS.” Testers will also view a 30-minute DVD as part of the pre-counseling process.

“First Things First” is part of what Beaumont called “the most ambitious HIV testing campaign in the world”—a nationwide effort to test 15 million South Africans by June 2011.

Test Gets Almost One in Five Syphilis Cases Wrong

**Associated Press**, (02.10.2011) Mike Stobbe

A CDC analysis of data from five US laboratories that used an alternative method of screening for syphilis found it returned a higher number of false-positive results than expected.

Some labs seeking to reduce time and labor required for syphilis screening have adopted a reverse sequence of screening in which the treponemal enzyme and chemiluminescence immunoassays (EIA/CIA) is performed first, followed by testing of reactive sera with a nontreponemal test. CDC recommends screening with a nontreponemal test like the rapid plasma reagin (RPR) or
Venereal Disease Research Laboratory (VDRL) test, followed by confirmation using one of several treponemal tests.

From 2006 to 2010, CDC researchers looked at data on reverse sequence testing in populations with high and low syphilis prevalence. Three sites served patient populations with low syphilis prevalence (large managed care organizations), and two sites served populations with high prevalence (including people with HIV and men who have sex with men).

A total of 140,176 specimens screened with EIA/CIA were included; of these, 4,834 (3.4 percent) had a reactive test result. Among them, 2,743 (56.7 percent) were RPR-nonreactive, with additional confirmatory treponemal testing showing 866 (31.6 percent) were nonreactive, suggesting the initial EIA/CIA result was false-positive.

According to CDC, “Among discordant sera, the rate of nonreactive confirmatory treponemal tests was 2.9 times higher in a population with low prevalence of syphilis, suggesting that the low-prevalence population had a higher percentage of false-positive results.”

Reverse sequence screening does have one advantage: “It doesn’t miss people who are infected,” said Dr. Karen Hoover, a CDC epidemiologist and study co-author.

“CDC continues to recommend that nontreponemal tests be used to screen for syphilis and that treponemal testing be used to confirm syphilis as the cause of nontreponemal reactivity. ... However, if reverse sequence screening is used, CDC recommends that a specimen with reactive EIA/CIA be tested reflexively with a quantitative nontreponemal test (e.g., RPR or VDRL). If test results are discordant, the specimen should be tested reflexively using the [Treponema pallidum particle agglutination] test as a confirmatory treponemal test,” the authors concluded.


Multiple sexual partnerships more common in Uganda than usually thought

Roger Pebody

Published: 16 February 2011

In poor urban neighbourhoods of Kampala, 29% of men and 7% of women report having had more than one sexual partner in the past six months, Phoebe Kajubi reports in an article published online ahead of print in the Journal of Acquired Immune Deficiency Syndromes. The figure for women is considerably higher than the estimate usually given.

As a consequence, HIV prevention strategies which assume that the majority of infections occur in stable heterosexual relationships may be misguided. The data may support calls for prevention programmes which aim to reduce multiple partnerships (concurrency).

It is thought that a substantial decrease in the numbers of Ugandan people engaging in multiple sexual partnerships was an important factor in reductions in HIV rates during the 1990s. In a large household survey conducted across Uganda in 2006 (the Demographic and Health Survey), 29% of men and 2% of women reported having had more than one sexual partner in the past twelve months.

Those figures informed the assumption in the country’s National Strategic Plan that transmission within stable heterosexual couples is the largest contributor to new HIV infections. Emphasis has been placed on HIV testing to identify serodiscordant couples and condom promotion for those couples.

Phoebe Kajubi and colleagues wished to find out if the household surveys figures were underestimates—as some researchers suspected. They conducted a random sample, door-to-door household survey in two poor communities on the fringes of Kampala, Uganda’s capital city. Only adults aged 20 to 39 were interviewed; most had low levels of education and worked in unskilled jobs.

While this may be a group of people at high risk of HIV infection, the sample does not have the same demographic profile as that of the Demographic and Health Survey, which was conducted in both rural and urban settings, and with a wider range of ages.

However Kajubi believes that her study may have some methodological advantages, and as a consequence socially stigmatised behaviours are less likely to be under-reported than in the national survey. The study was conducted after the researchers had built trust in the communities, the interviewers were more experienced, they paid particular attention to privacy, and the questionnaire was kept short. A total of 405 people took part. The number reporting multiple sexual partnerships varied according to the question asked:

- Those having more than one sexual partner in the past six months: 29% of men and 7% of women.
Those who had at least two sexual partners at the time of the interview: 23% of men and 4% of women.
Those who had had another partner during their current relationship: 30% of men and 8% of women.
Those who believed that their partner had had other partners during their current relationship: 22% of men and 32% of women.

The researchers also asked participants whether they agreed with a series of statements concerning the severity of HIV and AIDS. Examples of statements included “People with HIV/AIDS lead a normal life,” “Treatment for HIV/AIDS is available to everyone,” and “AIDS is not as bad as it used to be.” They found that people who rated HIV as being more severe than others were more likely to stick to one sexual partner. However they were not more likely to have had no sex at all in the past six months or to use condoms.

The authors conclude: “These results suggest that many urban Ugandans may be included in one way or another in networks of multiple and concurrent sexual partnerships.”

Confirmation from Rakai

Meanwhile, researchers working in the rural Rakai district of Uganda have released data which suggests that only a limited number of new HIV infections occur in monogamous, sero-discordant couples. Looking at new HIV infections in 2005-2006, 43% occurred in people who were not married or in a stable relationship and 26% occurred in people whose stable partner was HIV negative (and was also taking part in the study), suggesting infection acquired from another person. For 18% of the newly infected, the HIV status of their spouse or stable partner was unknown. Only 14% of people with a new HIV infection were married to (or in stable relationship with) an HIV-positive person.

The researchers comment: “Our data indicate that only a minority of total HIV infections occur to a person in an identifiable stable HIV discordant couple relationship in this generalized HIV epidemic setting... Universal VCT targeted on HIV-discordant couples is unlikely to have a major impact on the epidemic.”

References


LGBT Africans Face Blackmail and Extortion on a Regular Basis

Homophobic Laws and Social Stigma to Blame

(Johannesburg, February 15, 2011) Antiquated laws against same-sex sexual activity as well as deeply ingrained social stigma result in the all-too-frequent targeting of lesbian, gay, bisexual and transgender (LGBT) people in Africa for blackmail and extortion, said the International Gay and Lesbian Human Rights Commission (IGLHRC) in a report launched today.

The report, Nowhere to Turn: Blackmail and Extortion of LGBT People in Sub-Saharan Africa, illustrates how LGBT Africans are made doubly vulnerable by the criminalization of homosexuality and the often-violent stigmatization they face if their sexuality is revealed. Based on research from 2007 to the present, the volume features articles and research by leading African activists and academics on the prevalence, severity and impact of these human rights violations on LGBT people in Cameroon, Ghana, Malawi, Nigeria, and Zimbabwe.

"The tragic reality is that blackmail and extortion are part of the daily lives of many LGBT Africans who are isolated and made vulnerable by homophobic laws and social stigma," says IGLHRC’s Executive Director, Cary Alan Johnson. "The responsibility clearly lies with governments to address these crimes and the underlying social and legal vulnerability of LGBT people."

The report’s authors vividly depict the isolation, humiliation and manipulation to which LGBT people are subjected by blackmailers and extortionists and describe the threats of exposure, theft, assault, and rape, that can damage and even destroy the lives of victims. Vulnerability to these crimes is faced on a regular basis and families and communities are not safe havens. For example, according to research conducted in Cameroon and featured in the report, "the bulk of blackmail and extortion attempts were committed by other members of the community—33.9% by neighbors, 11.8% by family members, 11.5% by classmates, and 14.1% by homosexual friends. Police were often complicit in this—either by ignoring or dismissing it or, in 11.5% of cases, directly perpetrating it."
*Nowhere to Turn* explores the role the State plays in these crimes by ignoring blackmail and extortion carried out by police and other officials by failing to prosecute blackmailers, and by charging LGBT victims under sodomy laws when they do find the courage to report blackmail to the authorities.

IGLHRc urges States to take concrete steps to reduce the incidence of these crimes by decriminalizing same-sex sexual activity, educating officials and communities about blackmail laws, and ensuring that all people are able to access judicial mechanisms without prejudice.

A PDF version of *Nowhere to Turn is available here*. To obtain a hard copy of the volume, email iglhrc@iglhrc.org.

NYTimes, February 15, 2011

**Scientists See Success in Flu Vaccine Made by Faster Method**

By ANDREW POLLACK

A flu vaccine made by a new, faster method works just as well as existing products, researchers reported Tuesday.

The finding clears a hurdle in the government’s effort to move toward a manufacturing process that could allow for a more reliable supply of seasonal flu shots and quicker responses to pandemics.

The new vaccine, which could become available in the United States in the next few years, is made by growing the influenza virus in cultures of animal cells rather than in the chicken eggs that have been used for more than half a century.

Using animal cells could shave weeks off the six months or so that is now required to produce a vaccine for a pandemic. In the 2009 swine flu pandemic, large quantities of vaccine were not ready until after the wave of disease appeared to have crested.

Using animal cells, which are grown in enclosed steel tanks, also reduces the risk of bacterial contamination, which has led to shortages of seasonal vaccines in some years.

“I just think it’s an improvement in vaccine production that has been warranted for a long time,” said Dr. W. Paul Glezen, an influenza expert at the Baylor College of Medicine who wrote a commentary to accompany the report, which was published online Tuesday by The Lancet. “I just feel we’ve been sort of slow in implementing it.”

Dr. Glezen said shorter production times would allow health officials to wait longer before deciding which strains to include in the next winter’s flu vaccine, a decision that now has to be made around February. That would increase the chance that the strains in the vaccine match the strains in circulation.

In addition, Dr. Glezen said, when the virus grows in chicken eggs, it undergoes some changes. “It may not match the circulating virus as much as a vaccine made in mammalian cells,” he said.

In a large clinical trial involving 7,250 healthy adults, the new vaccine was more than 70 percent effective in preventing the seasonal flu, according to researchers from Baxter International, the developer of the new vaccine. That rate is similar to what egg-based vaccines have demonstrated in past studies, the researchers wrote.

The clinical trial was paid for by the Department of Health and Human Services, which awarded $1.3 billion to six companies in 2006 to develop cell-culture flu vaccines, including $242 million to Baxter and its partner, the DynPort Vaccine Company.

The trial is the second to show a cell-culture influenza vaccine to be as effective as conventional ones. In November, a study involving a Novartis vaccine was published in Clinical Infectious Diseases.

Experts say it is no surprise that the vaccines work. Still, proof is needed for them to win regulatory approval.

Baxter began selling the vaccine in parts of Europe last October. The company, which is based in Deerfield, Ill., would not say when it would apply for approval in the United States.

P. Noel Barrett, vice president for research and development in Baxter’s bioscience division, said the company was in discussions with the Food and Drug Administration about what kind of data would be needed for approval.

The main issue, Dr. Barrett said, was that the clinical trial involved healthy volunteers ages 18 to 49 and compared the vaccine with a placebo. Yet children and the elderly are more vulnerable to severe problems from the flu, so for those populations it might be unethical to conduct trials using a placebo.

Baxter therefore wants to show that the vaccine produces antibodies in children and the elderly at levels that correlate with those in the adults.

“We are certainly committed to moving this forward into the U.S. as fast as possible,” Dr. Barrett said.
Novartis won approval for its cell-culture vaccine in Europe in 2007 and plans to start the process leading to F.D.A. approval this year. With help from a nearly $500 million federal contract, the company has built a cell-culture vaccine factory in Holly Springs, N.C.

Robin Robinson, the director of the Biomedical Advanced Research and Development Authority in the Department of Health and Human Services, said cell cultures would never completely supplant egg-based production. Two of the six companies that received the federal cell-culture awards in 2006 have dropped their efforts and given back the money, he said.

Dr. Robinson said cell culture was an “interim solution” until even faster techniques come along that do not require growing the virus at all. Baxter’s flu vaccine is made in so-called Vero cells, derived from the kidneys of African green monkeys. The cells are already used to make other vaccines, including those for polio and rabies.

The clinical trial was conducted in the United States during the flu season of 2008–9. Only 13 people, or 0.4 percent, of those getting the vaccine became infected with a flu virus matching one of the three strains in the vaccine, compared with 60 people, or 1.7 percent, of those getting the placebo. That translates to an effectiveness of 78.5 percent.

Counting all strains of flu, even those not in the vaccine, the infection rates were 0.6 percent with the vaccine and 2.2 percent with the placebo, making the vaccine 71.5 percent effective. Side effects were similar to those of conventional vaccines, the researchers said.

'Sleepy' immune system might fight HIV
16/02/2011 12:41:26 PM
CBC News
A Manitoba AIDS scientist, who has spent 25 years trying to unlock the mystery of HIV-resistant sex workers in Kenya, says a reduced immune system might actually be the best defence against the disease. This insight, if proven, could turn billions of dollars in global HIV vaccine research on its head.
And Dr. Frank Plummer and his research team hope their discovery will lead to the creation of an HIV vaccine gel for millions of women.

When a person becomes infected with HIV, the virus goes after the immune system, breaking it down and infecting the cells.

So Plummer and his team studied what happens if an immune system doesn't fight back, doesn't give the virus anything to feed off. The secret is to make an immune system more "sleepy" to HIV so the deadly virus never takes hold, said Plummer, scientific director of the National Microbiology Laboratory in Winnipeg.

The sex trade workers he's studied in Africa since 1985 do this naturally.
"One of the signature characteristics of these (women) is that they have what we call a quiescent immune, or if you like, a 'sleepy immune' system," Plummer told an audience attending a TedX Manitoba conference in Winnipeg on Tuesday.

Plummer and his team just won a five-year $680,000 federal grant to develop a microbicidal gel that will try to copy this protective effect.

The discovery is the result of years of tracking sex trade workers in Nairobi slums who have defied the odds and avoided HIV. Many of the women live in areas with 50 per cent HIV infection rates, where their sex work exposes their bodies to the virus many times a day, and over many years.

Salome Simon is an example. When she appeared in a CBC News The National documentary in 2006, she had been doing sex work uninfected for more than two decades.
"I was very happy to find out that I am resistant. I have seen many of my friends die, but I thank God that I don't have HIV," Simon told CBC News at the time through a translator.

Plummer believes women like her have a natural protection to HIV because their immune systems are so inactive in response to the virus.

Normally, a women’s immune system reacts to HIV by sending in immune cells to counter the virus and stimulate inflammation in the vagina. This, unfortunately, provides avenues for viral infection. But this wasn’t happening in the Kenyan women.

"What we found is that [the sex trade workers] secrete these specific proteins which counter inflammation. This was counter-intuitive," says Dr. Adam Burgener, a University of Manitoba microbiologist who travels back and forth to Nairobi for the research.
"We would've thought there would be lots of inflammation and that they would mount a very strong response during sex work. But it’s the opposite—they have a very subdued immune system,” says Burgener.

Until now, people involved in vaccine development have focused on "jazzing up" the immune system, making it very active, said Plummer.

"And if our work is correct ... that may not be the best thing to do."

Pharmaceutical giant Merck found out the hard way. It invested heavily in a vaccine to boost immune systems, only to find out in its clinical trials in 2007 that the approach only made HIV infection worse. So, the idea that a Manitoba-grown idea to conquer AIDS has researchers here, like Burgener, losing sleep.

"It's very exciting. I have difficulty sleeping on Sunday nights because I'm excited about the work week and what we have to accomplish in order to get into testing."

February 16, 2011

**Lube Alert**

by David Evans

*A forthcoming research report suggests a number of personal lubricants can damage anal tissue cells and increase HIV replication, potentially heightening the risk of contracting HIV, notably if condoms aren’t used.*

The “personal lubricant” market is a thriving one. One popular website sells 53 different brands, with many boasting several varieties. If you’d like one that tastes like fruit or chocolate, or adds the sensation of heat, you’ve got multiple options to choose from. The same goes for the degree of slipperiness, the type of sex you want to have, the ease of cleanup and, most important, condom compatibility.

What sexual accoutrement retailers can’t tell you is whether a lube will increase, decrease or have no effect on your chance of becoming infected with HIV if the condom breaks or you decide not to use a condom in the first place. Until recently, it wasn’t a question high on the list of researchers’ or manufacturers’ priorities—lubes are intended to keep condoms from tearing during sex, end of story. But for scientists at the **Population Council**, a New York City–based research organization at the forefront of HIV microbicide development efforts, the positive or negative effects of lubricants on HIV transmission has been a nagging issue for years.

New research results from the nonprofit organization suggest there may be reasons for concern. According to laboratory studies the group conducted—on schedule to be published in a forthcoming issue of *AIDS Research and Human Retroviruses* and currently available online—a large number of popular lubes may actually make it easier for HIV to get past the body’s defenses, notably during anal sex without a condom. Even more alarming is the finding that four lubes in particular cause HIV to reproduce up to four times faster than it does in the absence of such products.

The researchers caution that the test tube study results are extremely preliminary and merely suggest a potential problem with several personal lubricants. Further studies, they say, are needed to determine the “real world” implications of these findings, including whether or not these products do in fact increase the risk of HIV transmission. One thing this study makes abundantly clear, however, is that we know very little about one of the main ingredients in the safer-sex recipe.

**Lube 101**

When it comes to anal sex, lubricants are a condom’s best friend, as they help reduce friction and the risk of tears during intercourse. But what about the benefits of lube alone, in the event the condom breaks or a rubber is left out of the equation altogether? In these situations, experts have reckoned, the use of a slippery substance is likely better than nothing.

Sex without lubrication can damage the epithelium—the thin membrane of mucosal cells lining the rectum and anus (as well as the mouth, nose and vagina) that keep the vast majority of unfriendly bacteria, fungi and viruses out of our bodies. So the thinking goes: The wetter the better.

If this tissue is damaged—because of physical tears, chafing, infection or inflammation from irritating substances—the epithelial cells and the chemical bonds that hold them together can fray, causing the protective system to break down. That’s where things can also go wrong with sexual lubricants. Several recent studies suggest that instead of protecting epithelial cells, lubes may actually compromising the integrity of the cells.

Enter Othell Begay and José Fernandez-Romero, PhD, from the HIV/AIDS Division of the Population Council. Begay, Fernandez-Romero and their colleagues, who are particularly interested in developing
microbicide gels capable of blocking sexual transmission of HIV, were intrigued by a set of recent reports documenting problems with some of the most commonly available lubricants.

In one study, researchers partnered with the International Rectal Microbicides Advocates (IRMA) to select six of the most popular lubricants used by men and women who practice anal sex. In the process, they tested how these lubes affected epithelial cells as well as the necessary bacteria that help keep the gut and rectum healthy.

That study found that several of the lubes contain more sugar and salt than is typically found inside cells of the anus or vagina. The imbalance causes the epithelial cells to purge their water content and, as a result, become withered and die—a condition called hyperosmolarity.

The study also found that one of the lubes completely wiped out the population of beneficial bacteria in the rectum, a situation that can allow unfriendly organisms—including HIV—to flourish.

A second study looked specifically at the incidence of gonorrhea and chlamydia in people who used lube for anal sex versus those who didn’t use lube, either with or without a condom. The study found that rates of these two sexually transmitted infections (STIs) were twice as high in those who used lube compared with those who didn’t, again suggesting that lubes were causing the rectum to become vulnerable to infection.

**HIV: Another Possible Risk**

To explore the matter further, Begay and Fernandez-Romero’s team purchased 41 over-the-counter lubricants and pitted them against two substances with known effects on both HIV and epithelial cells. Those two substances were Carraguard, which does not harm epithelial cells and is being studied as an HIV-blocking microbicide, and Gynol II, which contains nonoxynol-9, a substance known to harm epithelial cells and increase the risk of HIV infection. They then posed the same two questions about each of the 41 lubricants: Was the lubricant potentially toxic to cells, and did the lubricant inhibit or accelerate HIV replication?

As to the first question, the researchers found that all of the lubes, compared with Carraguard, damaged epithelial cells in test-tube tissue samples.

The team was also able to test the osmolality of 32 of the 41 candidates—in other words, to what degree the salt and sugar concentrations of the lubes could cause the cells to purge or retain water. Only one of the lubricants, Probe Personal, had a neutral osmolality, similar to Carraguard. All of the others were either hyperosmolar, similar to the IRMA study findings, or hypoosmolar—capable of causing cells to swell up with water, which can cause them to burst.

More striking and surprising was the answer to the team’s second question. While none of the lubricants had HIV-inhibiting qualities that approached that of Carraguard, four Astroglide brand lubricants actually appeared to increase HIV replication in cell cultures by as much as four times, compared with cultures not exposed to lubricants. These results stood in contrast to a previous study documenting anti-HIV activity of Astroglide lubes, and the team sought an explanation.

The Population Council research team analyzed the ingredients of the lubes and found that the four lubes in question—Astroglide Liquid, Astroglide Warming Liquid, Astroglide Glycerin & Paraben Free Liquid and Astroglide Silken Secret—all shared a common ingredient that was not present in the other Astroglide formulations: Polyquaterniums, a class of chemicals commonly found in cosmetic products. Polyquaternium-15, in particular, was in three of the four Astroglide formulations.

Though the specific formulation of polyquaternium-15 is not commercially available, the team tested a very similar chemical (MADQUAT). It too resulted in increases in HIV replication, leading the researchers to suspect that polyquaternium-15 might be the cause.

How is it that we’re only coming upon this potentially important safety information now? “Lubricants are classified by the U.S. Food and Drug Administration as a cosmetic, rather than as a medical device,” Begay explains. Most people would probably assume that because they can buy lubricants in stores then the products must be safe and don’t need further testing, including toxicity testing. Not so. Begay says: “After doing microbicide research and getting all of this knowledge on microbicides and how delicate these epithelial cells are, we discovered that lubricants should be tested.”

Fernandez-Romero adds: “The FDA requires that lubricant manufacturers tests lubricants for vaginal irritation. They might consider adding a similar requirement to assess product safety for rectal use.”

**To Lube or Not to Lube?**

The Population Council’s results are preliminary, and Fernandez-Romero stresses it remains unclear whether any lubricant might increase the risk of HIV transmission. “The bottom line,” he says, “is that more research is needed.”
What the paper implies is that not all lubes act the same in cells and tissues in the anus, which could be an issue with respect to HIV transmission. “I think our paper is good,” adds Fernandez-Romero, “because it is saying, ‘There could be a problem here. We have to investigate more.’”

The results also don’t change the fact that the lubes are well tested for their compatibility with condoms, and it is the condom, much more than the lube, that offers the best protection against HIV transmission. “Ultimately, the use of condoms is the best way to prevent transmission, but using a lubricant will prevent condom breakage,” Fernandez-Romero explains. “Lubricants may be important, but they have to be safe. We need assays, models or methods to tell us how safe a lubricant is.”

That said, the results do mean that assessing risk may have gotten more complicated for people who forgo condoms for one reason or another, which includes significant proportions of the population—young and old, gay and straight, male and female.

Fernandez-Romero says his team continues to collaborate with other groups that remain engaged in the study of lubes and the potential heightened risk of HIV transmission. “We have been participating in conference calls and discussion on the topic with IRMA, but we currently don’t have any funding to look at lubricant safety.” He points out that other researchers, including Charlene Dezzutti, PhD, at the University of Pittsburgh, and Pamina Gorbach, Dr.PH, at the University of California at Los Angeles, “are doing some good work and really trying to find answers.

“More research needs to be done,” concludes Fernandez-Romero, “and we need to find the safest lubricants.”

Search: HIV, transmission, lubes, lubricants, Astrogluide, IRMA, Population Council, Othell Begay, Jose Fernandez-Romero, osmolality, hyperosmolarity, hypoosmolarity, Carraguard, polyquaternium-15

Research predicts future evolution of flu viruses
New research from the University of Pennsylvania is beginning to crack the code of which strain of flu will be prevalent in a given year, with major implications for global public health preparedness. The findings will be published on February 17 in the open-access journal PLoS Genetics.

Joshua Plotkin and Sergey Kryazhimskiy, both at the University of Pennsylvania, conducted the research with colleagues at McMaster University and the Institute for Information Transmission Problems of the Russian Academy of Sciences. Plotkin believes that his group’s computational study of 40 years of flu genomes offers a new way of looking at mutations: by cataloging pairs of genetic changes that have occurred in rapid succession, observing that a mutation in one half of the pair can act as an early warning sign of a mutation about to occur in the other.

Tracking single mutations in a vacuum is not always enough to understand how the flu virus evolves. "Sometimes a mutation is functional or adaptive only if it’s in the context of a certain genetic background – that is, if the protein already has some other mutation," Plotkin said. The influence such combinations have on an organization’s adaptive fitness is known as epistasis.

“If you see a mutation occur in Site A and then very soon after you see a mutation in Site B, and this pattern happens repeatedly, then you have some evidence that A and B influence fitness epistatically,” Plotkin said. "The first mutation might be useless on its own, but it might be a prerequisite for the second mutation to be useful. The first mutation is like giving you a nail, and the second one is like giving you a hammer."

Because the studied mutations generally affect the surface proteins that determine whether the virus can enter and infect human cells, being able to predict what mutations are likely to happen in the near future has lifesaving applications. Tens of thousands of Americans, and hundreds of thousands worldwide, die of seasonal flu complications every year. Flu vaccine production is labor intensive and time consuming; to have enough supplies ready for the flu season, public health groups like the Centers for Disease Control and the World Health Organization must make an educated guess as to which strain is likely to be the most active several months in advance. Observing the leading site of an epistatic pair could give them a head start.

Unraveling how prion proteins move along axons in the brain
Researchers at the University of California, San Diego School of Medicine have identified the motors that move non-infectious prion proteins (PrPC) – found within many mammalian cells – up and down long, neuronal transport pathways. Identifying normal movement mechanisms of PrPC may help researchers understand the spread of infectious prions within and between neurons to reach the brain, and aid in development of therapies to halt the transport.

Their study is published in the February 18 edition of the journal Cell.
The small prion protein is found in the cell membrane of brain neurons. The misfolded or infectious form of this protein (also called "scrapie"), is responsible for "mad cow" disease and has also been implicated in Creutzfeldt-Jakob disease in humans. Non-infectious and scrapie forms interact to produce disease; so, in order to help uncover how the infection is spread within and among neuron cells to the brain, the UCSD scientists studied the movement mechanism of normal PrPC in mouse neuronal cells.

"Our work unraveling the normal mechanism of movement of this prion protein will help us understand how the devastating pathogenic versions found in mad cow disease and other prion diseases are formed and transmitted in the brain. Intriguingly, our work may also shed light on what goes wrong in other neurodegenerative diseases such as Alzheimer's disease," said principal investigator Larry Goldstein, PhD, professor of Cellular and Molecular Medicine, Howard Hughes Medical Institute investigator and director of the UC San Diego Stem Cell Program.

It is known that normal prion proteins and infectious prions need to interact in order for prion pathogenesis to occur, though not how or why these interactions occur. Discovering the transport mechanisms of prions is one key to the puzzle of how the two types of proteins interact, and an important question in transport regulation has been how motor activity is controlled in cells.

The prion protein cargo travels on long microtubule tracks along the peripheral and central nervous system nerves toward the terminus, or synapse, in membrane-bound sacs called vesicles. Intracellular transport is often bi-directional, because cargoes regularly reverse their course en route to their final destinations.

The researchers identified the motors driving these vesicles as anterograde Kinesin-1 – which moves only toward the synapse – and dynein, which is retrograde, moving away from the synapse. These two motor proteins assemble on the PrPC vesicles to "walk" them back and forth along the microtubules.

Secondly, they discovered that the back and forth cargo movement is modulated by regulatory factors, rather than by any structural changes to the motor-cargo associations. The study data show that the activity of Kinesin-1 and dynein are tightly coupled, with PrPC vesicles moving at different velocities and for varied lengths along axons. However, the type and amounts of these motor assemblies remain stably associated with stationary as well as moving vesicles, and normal retrograde transport by Kinesin-1 is independent of dynein-vesicle attachment.

The UCSD study of the mechanisms behind normal vesicle movement along the axons in mouse cells might also shed light on other neurodegenerative disease. While Alzheimer's is not generally considered an infectious disease like mad cow disease, emerging data suggest that Tau, amyloid-beta, and alpha-synuclein – proteins implicated in Alzheimer's and Parkinson's disease – have self-propagating fibril structures with prion-like characteristics.

"Whether these toxic molecules spread along neuronal transport pathways in ways similar to the normal prion protein is unknown," said first author Sandra E. Encalada, PhD, of the UCSD Department of Cellular and Molecular Medicine. "But characterization of these normal mechanisms might lead to a way to control movement of intracellular aggregates, and perhaps to therapies for many neurodegenerative diseases."

**Host Genetics Plays Unexpected Role in Dance With Pathogen**

ScienceDaily (Feb. 17, 2011) — A new study suggests that differences in the host’s genetics can make a big difference in susceptibility bacterial infection. In a study in the February 2011 *Infection and Immunity*, Virginia L. Miller of the University of North Carolina, Chapel Hill, and her collaborators show that the virulence of a strain of *Yersinia pestis*, notable for causing bubonic plague, varies drastically among mice strains with different genetic backgrounds. These findings carry major implications for vaccine development, says Miller.

A number of earlier reports dating back 20 years had suggested that removing this bacterium’s capsule—an envelope of a loose protein gel surrounding the bacterial cell—had no effect on its virulence. Then, Miller and her collaborators performed the same experiment, with opposite results.

Searching for an explanation for the conflicting results, the only difference in the experiments that Miller could find was in the strains of mice, and so it occurred to her that their susceptibilities might be different. Her team tested that hypothesis by infecting two different strains of mice with *Y. pestis* in which the capsule had been removed. In one strain, the bacteria were nearly normally virulent, while in the other, they were relatively impotent.
This research made sense of the earlier experiments, "while highlighting the importance that host genetics can play in the dance between host and pathogen, and how it can influence the phenotype of a potential virulence factor," says Miller.

Moreover, these findings "demonstrate for the first time that the capsule is a Y. pestis virulence factor in a mouse infection model," says James Bliska of Stony Brook University, New York. "It had already been shown that [the capsule] is important for flea transmission, and therefore it was clear why [the capsule] was conserved in Y. pestis."

The research is critical for the development of a vaccine against both bubonic and pneumonic plague, also caused by Y. pestis, because considerable effort has been invested in establishing Caf1, an antigen within the capsule, as a protective antigen in vaccines against plague. But all the papers showing that removing the capsule had no effect on virulence had gradually undermined the case for using the capsule antigen in a vaccine, when it had been a major target for vaccine development. But now, "This paper may revive hope that Caf1 in conjunction with other antigens would be a useful component of a multivalent vaccine," says Eric Krukonis of the University of Michigan, Ann Arbor.

Developing such vaccines is important because "Y. pestis is still a major threat to humans, due to endemic pockets of Y. pestis-infected animals and fleas and potential bioterrorism use," Miller and her collaborators note. "A greater understanding of the requirement of the capsule for Y. pestis to cause disease is required. It is particularly important to investigate if natural capsule mutants are able to cause disease and in what contexts, as the current vaccine potentially would not protect against these strains."

Journal Reference:

Closet homosexuals sink further under the radar after Kato’s death
By JOHN K. ABIMANYI (email the author)
Posted Monday, February 7 2011 at 00:00
He sits at a table with his fingers encircled around the tail of a glass filled with Smirnoff. He is at a Kampala nightspot and has dissolved into the crowd, looking just like any other reveller. What most people at the bar would not know however, is that he, plus a couple of his colleagues at the venue, is homosexual. He demands that his identity is hidden if he is to be quoted in the papers instead; he proposes a pseudonym, Alan Mukasa.

He gives off no signs that he is gay. He’s not dressed in a tight fitting pair of jeans, commonly known as skinnies, his hair is a natural un-treated neatly trimmed black, he has no studs or earrings, wears no make-up or anything that may attract undue attention to him. “It’s a security precaution one has to take,” he says. "The best way to hide is to fit in.

Be as ordinary as everyone else and there will not be many questions to ask, and answers to give,” he adds. There is an ever-present sense of consciousness that runs on autopilot in the Ugandan gay man’s mind, Mukasa says. But that was before the murder of gay rights activist, David Kisule Kato last month, which, as Mukasa says, "Forces you to ask yourself whether you have watched your back well.”

Mukasa and Sam Musiime (also not real name), say the gay Ugandan living in the closet now has to add even more latches and keep the world away from the skeletons. “The aftermath of David Kato Kisule’s death is a strange atmosphere of confusion, fear, sadness, shock, and terror,” Musiime says, adding, "After watching a pastor deliver a less than savoury hate speech at his funeral, all I could think is, ‘they must think we are all mad’.”

Musiime and Mukasa are both in their late 2os and have kept their orientation a secret from many for nearly a decade now. “You tell no one. Only gay people like you ever get to know, and even then, you watch which gay person gets to find out because they too could sell you out, accidentally or not,” Musiime says. “The key is to ease into society as much as possible, behave like everyone else, even flirt with girls to portray the usual boy look,” Musiime says.

Musiime then expounds on how he now has to rethink his security. “After Kato’s death, something is triggered in you and even makes you think somebody you do not want to know already knows. Now I have to recheck my passwords – on my computer and phones so that no one accidentally runs into photos or any material that would raise suspicion. You fear that even if people would not kill you, you would lose the respect that those who don’t know still have for you,” he adds.

For Mukasa, Kato’s death also leads him to cover his tracks, but not through fear. “I’ve always been in fear, not for my life, but of being found out. I realised that living in fear only gives you away, so I live in
confidence instead, knowing nothing is wrong with me,” he says. “Society may not be very accommodative of me, so I still have to be careful, maybe even more careful now that matters are rising to the surface. But I live on. I walk on. I go to work in the morning. I go to the bar in the evening. My life in general has not changed.”

When asked what he will do to keep his orientation a secret, Mukasa says, “I am very conscious of who is watching me and what I do. That doesn’t mean I’m always looking over my back. I don’t feel the need to. However, I am always careful. Things like phone calls, emails, communication, and even friends can be clues to a person’s behaviour. I take appropriate measures,” he says, making an effort not to divulge much. Later, he adds, “Answering this one truthfully is tricky, feels like I’d be giving myself away.”

Musime and Mukasa say they are reaping the fruits of a ripened swelling of homophobia in a society that finds their actions terribly archaic. However, to many Ugandans, the attitude towards homosexuality is not an irrational fear like the word homophobia seems to suggest. It’s seen as a cry to save deeply treasured social norms.

At an anti-gay protest in support of the anti-homosexuality bill, hundreds of shouting protestors carried placards with among other messages, writings like, “Think about our children,”, “Together we kick homosexuality out of Uganda,” and “Homosexuals beware of God’s wrath.” Pastor Martin Ssempa then stepped in with a charge that homosexuals target and indeed rape boys in school, and that some teachers condone it.

Uganda, which has been under international spotlight over an anti-gay bill that ruling party MP, Hon David Bahati had tabled in parliament in 2009, returned into the headlines with even stronger criticism over the Police’s handling of Kato’s murder.

Cases of attacks on or perceived attacks on homosexuals feature highly on the news agenda of international media. Even with the crisis that was erupting in Egypt, Kato’s death got extensive coverage on the BBC World Service for instance. In fact, the news of Kato’s murder was broken to many Ugandans not by local media, but through tweets from online news wires.

On the BBC’s From Our Own Correspondent show that offers analysis and insight into news events, Ana Cavell, the reporter, said, “Homophobia in Uganda is different to homophobia in Europe. It is not just that people do not like homosexuality or that they do not like to consider what homosexuals might do together. Here it is seen as an abomination. Gay people are reviled—a bit like how rapists are in other countries.” The show described Kato as a brave man who carried the air of an intellectual. With such attention, Uganda seems to be coming under increasing international pressure as regards what happens to homosexuals here.

President Barack Obama had a personal message read at Kato’s funeral. A senior researcher for Human Rights Watch in the Africa Division, Ms María Burnett, says, “In the case of this killing, the world happens to be watching. Uganda’s reputation as a country that respects the rule of law and human rights is at stake if the case is not rigorously and impartially investigated”.

Back at the nightspot where Mukasa wined his evening away, he and his gay friends chatted about sports, money, cars and yes, girls too. And when a female friend passed by the table, Mukasa reached out with arms wide open and hugged her tightly, the way a boy longing to feel a girl’s chest would. As Mukasa would say, “the best way for to hide is to fit in. Be as ordinary as everyone else.”

Wikileaks Posts Cables from US Embassy in Uganda Concerning Anti-Homosexuality Bill
Jim Burroway
February 17th, 2011
[Update: As Paul Canning points out, these cables were originally released more than a week ago on the Spanish daily El País.]

The Guardian (UK) today posted cables provided by Wikileaks from the U.S. embassy in Uganda concerning that nation’s consideration of the draconian Anti-Homosexuality Bill. In an accompanying article, The Guardian highlighted murdered LGBT rights advocate David Kato’s reluctant participation in a UN-sponsored debate in December, 2009, in which he was mocked during his speech. According to the cables, (Kato) delivered a well-written speech against the bill, but his words were almost inaudible due to “his evident nervousness”. Throughout his talk a member of the Ugandan Human Rights Commission “openly joked and snickered” with supporters of the bill, the diplomat claimed in the cable.

The Christmas Eve, 2009 cable provide more context:
Bahati’s late arrival delayed the event for more than an hour, and the UHRC failed to seat any representative of those opposed to the legislation at the head table, despite seating Bahati and – for unexplained reasons – Uganda’s most outspoken anti-gay activist Martin Ssempa. A comment by an audience member later prompted the UHRC to correct this imbalance by inviting a clearly hesitant and nervous SMUG leader, David Kato, to sit beside Ssempa on the dais. Ssempa proceeded to shake Kato’s hand while striking absurd poses for the assembled press corps.

Bahati’s remarks mirrored his private statements to PolOффs. Bahati also attacked the White House statement opposing the bill, saying that he admires President Obama, that President Obama ran on a platform of change, and that Uganda’s message to him is that “homosexuality is not a change but rather an evil that we must fight.” At this point the room erupted in loud applause, led by Ssempa pounding his hand on the head table, and Bahati observed that oil revenues will free Uganda of foreign entanglements. At other points in Bahati’s tirade against homosexuality, Ssempa registered his support by issuing audible sounds of disgust.

U.S. diplomat wrote of Bahati’s “isolation” following Saddleback Church pastor Rick Warren’s condemnation of the bill. The diplomat wrote:

Recent condemnations by Warren and other U.S. based individuals have further isolated Bahati. His homophobia, however, is blinding and incurable. Bahati, Buturo, and particularly Ssempa’s ability to channel popular anger over Uganda’s socio-political failings into violent hatred of a previously unpopular but tolerated minority is chilling. xxxxxxxxxx described Ssempa as an anti-homosexuality “extremist.” xxxxxxxxxx said he opposes the legislation not because he favors homosexuality, but because legalizing persecution of homosexuals is the first step toward state sponsored persecution of other minority groups.

It’s not just other minority groups which were concerned, but the political opposition to President Yoweri Museveni’s 25-year rule as well:

In September, Otunnu accused state security services of running a smear campaign about his sexual orientation and HIV status to discredit a potential presidential bid (ref. D). xxxxxxxxxx speculated that Uganda could run a similar smear campaign against Besigye, forcing him to curtail presidential campaign activities.

xxxxxxxxxxx said the opposition FDC fears Uganda will use the anti-homosexuality legislation against Besigye, and recalled government efforts to hobble Besigye’s 2006 presidential campaign by arresting him on spurious charges of rape, terrorism, and treason. xxxxxxxxxx speculated that Uganda could disrupt Besigye’s 2011 campaign with phony homosexuality allegations.

In a second cable dated February 10 and released by The Guardian, the U.S. diplomats in Uganda describe a meeting with local human rights activists whose names are redacted. The White House and the State Department had already by then condemned the bill. Activists expressed concerns that the Anti-Homosexuality Bill was part of a larger effort to tilt tomorrow’s elections in favor of the entrenched ruling party:

xxxxxxxxxxx placed the anti-homosexuality bill in the context of a general trend toward restricted human rights and democratic freedoms in Uganda. He said the anti-homosexuality bill is one of many regressive legislative initiatives that are not in the interests of all Ugandans and are intended to tilt the February 2011 presidential elections in the government’s favor. xxxxxxxxxx cited draft legislation to expand the Security Ministry’s monitoring of electronic communications, expanded and perhaps politically motivated enforcement of the 2002 Anti-Terrorism Act, the recently passed Land Amendment Act (ref. A), reduced press freedoms, and the slow pace of electoral reform as pressing human rights concerns. He encouraged the U.S. to treat these issues in the same manner as the anti-homosexuality bill, and said the anti-homosexuality issue is a government “gimmick” to divert attention away from other assaults on human rights and democratic freedoms that will ultimately undermine the integrity of the 2011 elections. Uganda’s elections will be held tomorrow.

The cables go on to describe some of the fear and intimidation that the proposed legislation aroused in Uganda. The fear and intimidation extends beyond the beleaguered gay community, but goes into the political class as well:

xxxxxxxxxxx said Members of Parliament who privately oppose the bill fear losing their seats if they speak out against the legislation, and therefore support the bill in public and will vote for it should it ever reach the parliamentary floor. xxxxxxxxxx said Bahati is blaming homosexuals for the spread HIV/AIDS, pornography, and increasing incidents of rape and defilement, and that the legislation is a diversionary ploy intended to steer attention away from real issues like corruption and the 2011 elections.
Both xxxxxxxxxxx and xxxxxxxxxxx said local xxxxxxxxxxxx activists are using cellphones, blogs, and the internet to the extent possible, but stressed concerns about government monitoring of electronic communications. xxxxxxxxxxx said one local human rights NGO had to switch its domain name after someone hacked its email address, and xxxxxxxxxxx and xxxxxxxxxxx said they and other activists have been forced to switch telephones and restrict electronic communications to avoid harassment and eavesdropping.

**SOUTH AFRICA: HIV patients go missing before treatment**

JOHANNESBURG, 18 February 2011 (PlusNews)—A study has found that about 55 percent of HIV patients in South Africa who are not eligible for treatment at the time of diagnosis will disappear from clinics within a year of initial monitoring, leaving a serious gap in HIV care and prevention, say researchers.

Most patients in South Africa must have a CD4 count—a measure of the immune system’s strength—of 200 or less to be eligible for antiretrovirals (ARVs), but previous research has shown that about two-thirds of people will not meet ARV treatment criteria at diagnosis.

Published in the 1 March edition of the journal AIDS, the study examined about a year’s worth of CD4 laboratory records for 4,223 HIV patients in South Africa’s KwaZulu-Natal province who were not eligible for ARVs. Conducted by the Africa Centre for Health and Population Studies at South Africa’s University of KwaZulu-Natal, the research found high loss-to-follow-up rates and that patients diagnosed HIV-positive at higher CD4 counts, and who were younger and male, were more likely not to return for CD4 count tests at the recommended six month intervals.

The study also noted that among patients who remained in clinic's outpatient care, the majority returned only once for CD4 monitoring and that their CD4 counts dropped much more quickly than previous South African research has suggested. CD4 level counts dropped by an average of about nine cells per month. However, patients with higher CD4 counts, who were also less likely to adhere to CD4 monitoring, saw drops as much as twice that.

While the study did not include qualitative data on patients’ reasons for discontinuing care, lead author Richard Lessells said the limited medical services available to pre-ARV patients may be partly to blame.

While patients like these can access drugs such as bactrim and co-trimoxazole for opportunistic infections, Lessells said that if patients are sick enough for these drugs, they are usually sick enough to qualify for ARVs.

“As a doctor the most frustrating thing is seeing a patient return with opportunistic infections and finding out that they were diagnosed two years previously with a CD4 count of 300 but had been lost to the system. Now they are presenting sick and require hospital care,” he told IRIN/PlusNews. “It’s frustrating to know that, in theory, this is preventable.”

For Lessells, the study highlights a patient population that has been sidelined in the rush to get those who are eligible on ARVs.

“These patients certainly aren’t the priority,” he told IRIN/PlusNews. “The clinics are already overcapacity just dealing with patients ARVs so there’s very little scope or time even for people who are not in that category.”

**Neglected but important**

With priorities elsewhere, he added that most programmes and the South African Department of Health do not collect data on pre-ARV patients or their access to care, but that these patients represent a key entry point for initiatives looking to reduce AIDS-related mortality and new HIV infections.

With an estimated HIV prevalence of about 18 percent, South Africa currently runs the world’s largest ARV programme with more than one million patients on treatment. In an effort to get more patients on treatment earlier and bolster behavior change, the government is in the midst of a national campaign to voluntarily test 15 million South Africans for HIV by April 2011.

But Lessells cautioned that the high loss-to-follow up of pre-ARV patients jeopardizes these goals.

“The whole point of this testing campaign is to try and get as many people to know their status as possible, based on the assumption that people will change their behaviour, but we need to make sure that there are programmes supporting people, and giving them appropriate care and education about prevention,” he said. “There’s a lot of literature out there about the integration of HIV care and prevention, but at a practical level, this isn’t happening.”
Research needed to inform programme design
While a smaller, Johannesburg-based study published last year in the journal of Tropical Medicine and International Health confirmed high pre-ARV loss-to-follow-up, Lessells said more research was needed into this group, including what programmes could provide in terms of incentives.

“And figuring out what keeps pre-ARV patients away, may mean rethinking programmes. “[Researchers, programme managers] are always looking at what it is about the patients that makes them not come back; there’s always this sense that the patient is to blame,” he told IRIN/PlusNews. “We need to get over that and start thinking what it is about our programmes that are not encouraging people to stay.”

While many studies have shown that the farther patients must travel to a clinic, the less likely they are to return, Lessells’ study found that retention was low despite the fact that about 90 percent of the study population lived within 5km of the nearest clinic.

As government continues to push for the roll-out of isoniazid preventative (IPT) tuberculosis therapy among all HIV patients, Lessells said he hoped research was being undertaken to ascertain whether the addition of this service would provide the kind of incentive needed to retain patients or whether the added stress on clinics and pharmacies would become yet another disincentive to staying in care.

Canada Fails Nunavut in Fighting TB: Journal
Last year, Nunavut recorded the largest TB outbreak in the territory’s 10-year history. At least 100 new active cases were registered in 2010, primarily among adolescents and young adults, suggesting active transmission. The Nunavut TB rate is 62 times the Canadian average.

“This is happening at rates we see in the developing world,” said Dr. Matthew Stanbrook, a respirologist at Toronto Western Hospital and co-author of a new report on the situation. “We are a rich, developed nation that has the resources to solve the problem in Nunavut if we choose to employ them.”

TB has not been eliminated from Inuit communities since arriving with whaling crews in the 19th century. After the Second World War, Inuit were moved from traditional hunting camps to government-provided, one-room houses or cramped shacks, creating a breeding ground for TB, sociologists say. Between 1953 and 1961, 5,240 Inuit were sent south for TB treatment; the entire population of the eastern Arctic was only about 11,500. Many never returned or lost contact with their families, a memory that hinders current treatment efforts, said Stanbrook.

“If you don’t trust the public health officials, you’re not going to disclose symptoms that seem like TB,” Stanbrook said. “That really has frustrated efforts to address this epidemic.”

Substandard housing, poverty, and high rates of smoking and second-hand smoke exposure continue to fuel the epidemic, the editorial said.

Last month, the federal health minister announced $800,000 (US $813,000) for Taima TB, a new door-to-door program to test for latent TB in Nunavut communities. Minister Leona Aglukkaq also announced $100 million (US $102 million) to build 1,000 new housing units.

“When we have the wealth that this country has, there’s no excuse for not using all our resources to cure a curable epidemic disease,” said Stanbrook.


Another HPV Vaccine Benefit Found
St. Petersburg Times, (02.03.2011) Irene Maher
The Gardasil vaccine against human papillomavirus (HPV)—already approved for use in girls to prevent genital warts and cervical cancer, and in boys to prevent genital warts—also protects against anal cancer, according to new research.

“Our study shows it’s a fantastic way to prevent cancer in both men and women with a simple three-dose series of vaccine,” said lead author Dr. Anna Giuliano, a researcher and cancer epidemiology chair at the H. Lee Moffitt Cancer Center in Tampa. Information from the study, funded partially by Merck, the maker of Gardasil, recently led the Food and Drug Administration to expand its approval of the vaccine to include prevention of anal cancer, she said.

Giuliano’s team enrolled 4,065 healthy boys and men ages 16-26 from 18 countries to determine whether Gardasil reduced the incidence of external genital lesions and anogenital HPV infection related to the types the vaccine targets: HPV-6, -11, -16 and -18. The subjects were HPV-free at baseline and half
The study, published by Cell Press in the February issue of the journal Immunity, demonstrates that a vaccine which stimulates production of specific anti-HIV antibodies in the vaginal tissue was sufficient to protect monkeys from exposure to live virus. The results may also help to explain why a few individuals who lack anti-HIV antibodies in the blood are able to resist infection, even when they are repeatedly exposed to HIV.

HIV is most often transmitted by sexual relations when infected body fluids of one individual contact the genital or rectal mucous membranes of another. After initial infection in the mucous membranes, or mucosa, the virus rapidly copies itself and floods the bloodstream. A common HIV-1 vaccine strategy has been to induce HIV antibodies in the blood. However, this approach has not proven effective and alternative strategies are needed. "We designed a vaccine strategy to protect the initial sites of viral entry, especially the female genitals and the rectum, by inducing antibodies within the mucosa itself that hopefully will be able to prevent the establishment of early viral infection," explains lead study author Dr. Morgane Bomsel from the Institut Cochin in Paris.

Dr. Bomsel and colleagues developed a vaccine targeted against gp41, a region of HIV that has shown some promise in studies of mucosal HIV-1 challenge. The vaccine was administered to Macaques through both intranasal and intramuscular routes. Animals were exposed to simian HIV vaginally and tested for infection six months later. Remarkably, five of five vaccinated animals were protected from viral replication in the blood and exhibited vaginal gp41-specific antibodies with various viral neutralizing effects. The mucosal antibodies blocked a pathway that HIV uses to enter the mucosa, while the antibodies in the plasma of these animals completely lacked the ability to neutralize the virus.

Although the authors caution that further work is needed to learn more about the duration of the protective immune response observed here, the findings are significant. "Our results clearly challenge the paradigm that mucosal protection requires significantly high levels of antibodies with virus neutralizing capacity in the blood. Furthermore two classes of vaginal antibodies, IgA and IgG, were induced in the mucosa by the vaccine and exerted complementary antiviral functions to stop the virus very early in its entry at the mucosa," concludes Dr. Bomsel. "These findings may help to explain why a small population of highly exposed, but HIV-negative, women who exhibit gp41-specific IgA in their vaginal secretions are protected from infection. We may have been able to recapitulate in a vaccine what a few individuals do naturally." 2/18/11

**Reference**

European Medicines Agency: d4T to be used only in last resort
Keith Alcorn
Published: 21 February 2011
The European Medicines Agency has issued new guidance on the use of d4T (stavudine, Zerit), saying that the drug should be used only when no other alternative option exists, due to its toxicity.

The agency's Committee for Medicinal Products for Human Use (CHMP) also says that when the drug must be used, it should be used for the shortest time possible.

The decision was taken after a review of safety information as part of a marketing re-authorisation. The drug has several well-established side effects that are either life-threatening or may cause serious long-term harm. These are:

- Lactic acidosis (a build-up of lactic acid in the body), which may lead to death if not treated early enough.
- Peripheral neuropathy (damage to the nerves in the limbs, especially the feet and legs), which may be irreversible in some patients. It leads to pain and difficulty in walking.
- Lipoatrophy (subcutaneous fat loss, especially in the limbs, buttocks and face) which is usually irreversible except through reparative surgery. Patients find the loss of fat highly disfiguring and stigmatising.

Each side-effect is linked to long-term use of d4T, and each side-effect has been known about for at least a decade.

The use of d4T in first-line treatment was abandoned in the United States and Europe after head-to-head comparisons with AZT and with tenofovir-containing regimens showed that patients who received d4T were more likely to suffer lipoatrophy.

The World Health Organization has also issued a series of treatment guideline revisions intended to discourage the use of d4T in resource-limited settings. The drug continues to form part of first-line antiretroviral drug combinations in many countries due to its low cost in comparison to tenofovir.

The agency says that all patients taking the drug in the European Union should be reviewed regularly and switched at the earliest opportunity to another drug.

Circumcision: The Surgical AIDS Vaccine
Circumcision helps prevent HIV infection. Why would AIDS-ravaged San Francisco even think of banning this proven, safe procedure?
By Beryl Lieff Benderly

Voters in San Francisco — the city that has probably suffered from AIDS more grievously than any other in America — may soon vote on whether to ban a safe, one-time procedure that protects against the virus that causes AIDS almost as effectively as the annual flu shot protects against the flu. Millions of dollars and years of research have thus far failed to overcome the diabolical obstacles to making an HIV vaccine. No doubt exists, however, that another treatment provides protection so effective that health experts have called it a “surgical vaccine.” Unlike a flu shot, this protection lasts a lifetime and, at no extra charge, also helps reduce HIV risk for a man’s sexual partners.

By now you may have guessed that this remarkable procedure is male circumcision (the word is Latin for “cutting around”), the ancient operation that removes the foreskin, the sleeve of tissue that sheathes the tip of the penis. Circumcision plays an important role in both the Muslim and Jewish religious traditions as well as in initiation rituals practiced by ethnic groups around the world, particularly in sub-Saharan Africa. Recently, however, retired hotel credit manager Lloyd Schofield, a San Francisco resident who calls himself an “intactivist” and considers circumcision mutilation, has announced that he is gathering signatures to put a referendum on the November city ballot that would ban the procedure. “Just as females are protected from having a drop of blood drawn from their genitals, baby boys deserve the same protection,” Schofield told CNN. To qualify the proposition, proponents would need to gather slightly more than 7,000 signatures by late April.

Schofield is pushing the circumcision ban even though multiple lines of very strong evidence — from epidemiology, physiology, microbiology and three large, internationally recognized “gold standard” clinical trials — converge on the conclusion that removing the foreskin drastically cuts a man’s risk of becoming infected by HIV. It also reduces his risk of other sexually transmitted diseases and cancer of the penis and his female partners’ risk of cervical cancer. Moreover, the operation is safe, takes less than half an hour, heals in weeks and is so common that 80 percent of American men are circumcised. Nor is there
scientific evidence of untoward effects, either immediately after healing or later in life, on men’s health, sexual performance or desire.

The three controlled clinical trials took place in Kenya, South Africa and Uganda, in areas where circumcision rates are low and HIV levels high. More than 11,000 men, most of them young, all of them HIV-negative, uncircumcised and willing to undergo the operation, were randomly assigned either to be circumcised immediately by a doctor, or to be in the control group and wait for circumcision until after the study ended. The three trials were all stopped early, however, because of interim results so strong — a 60 percent reduction in infection risk — that researchers could no longer ethically withhold a procedure shown to be so beneficial. After the South African clinical trial had run for 18 months, for example, 49 of the 1,446 members of the control group had contracted HIV. But just 20 of the 1,431 in the circumcision group had become infected.

Dr. James Shelton, science adviser to the Bureau of Global Health of the U.S. Agency for International Development, believes the true reduction in risk is even larger than 60 percent but was masked by the structure of the experiment. Detailed statistical analysis of the results, he writes, reveals “a protective effect of 76 percent.” That analysis would raise the level of protection into flu-shot range, which begins at 70 percent, according to the Centers for Disease Control and Prevention.

The World Health Organization and UNAIDS, the United Nations’ HIV/AIDS agency, describe the trial results as “compelling.” The two groups now recommend circumcision as “part of a comprehensive HIV prevention package.”

A number of African countries have responded with programs to provide circumcision on a wide scale, particularly to men who already are or are about to become sexually active, because they make the most immediate impact on infection rates. As knowledge of circumcision’s protective effect has spread, uncircumcised men have flocked to have the operation — among other things, women are urging their husbands to go — and parents have increasingly asked to have their sons circumcised. In 2006, a near-riot erupted in Mbabane, the capital of Swaziland, when men waiting outside a clinic learned that they wouldn’t all be getting the appointments they hoped for.

Circumcision’s origins are unknown, but its history goes back at least 4,000 years, as shown by tomb paintings from Egypt’s sixth dynasty depicting men undergoing the procedure. The Hebrews, of course, have practiced it since ancient times, and it was customary among other peoples in the Middle East and East Africa long before the birth of Islam. Circumcision’s ceremonial uses generally involve establishing identity, whether as a member of a community or as an adult. Many scholars argue, however, that the practice first arose out of health concerns, especially to avoid the painful irritations and infections that can result from sand becoming lodged under the foreskins in dry, desert climates. That was the reason, for example, that Australian army doctors during both world wars performed large numbers of circumcisions on soldiers serving in North Africa and the Middle East.

Depending on the ethnic and religious composition of a particular country, the number of circumcised males in Africa ranges from less than 20 percent to more than 80 percent. The large difference in HIV rates between countries with high and low rates of circumcision became obvious more than 20 years ago, alerting scientists to the potential protective effect of the procedure.

Researchers believe that the area between the foreskin and the penis shaft provides a hospitable area for HIV to exist, post-intercourse. And physiological research has identified a likely mechanism for infection there: The foreskin contains a particular type of cell that can provide the HIV virus a direct route into the body. These cells — known as Langerhans cells and discovered by the same German doctor who also found the better-known isles or islets of Langerhans in the pancreas — are plentiful on the underside of the foreskin but absent from the rest of the penis. Like the T cells that are a major target of the HIV virus, Langerhans cells belong to the immune system and are highly susceptible to HIV infection.

The shaft of the penis lacks Langerhans cells but contains a protective material called keratin that helps block entry of the virus. After circumcision, keratin develops in the tip of the penis, rendering it less vulnerable. The HIV protection that circumcision provides is not perfect, and public health authorities emphasize that circumcised men must still practice safe sex to limit risk.

Still, the clinical trials demonstrated the strong protective effect of circumcision in vaginal intercourse, which is important in Africa because the epidemic there has spread largely by heterosexual activity and involves people of both sexes. The logic of the physiology, however, argues that circumcision should also protect men who take the insertive role in sex with other men, although this proposition has not been tested. It is clear, however, that by reducing the number of men who become infected, circumcision also reduces their partners’ exposure to the virus.
“Herd immunity” is the name epidemiologists give to the reduction in risk that people not themselves vaccinated enjoy when a vaccine cuts the amount of an infectious agent that is circulating in a population. With HIV, this type of protection extends not only to circumcised men’s female partners but, by cutting women’s risk, to their babies as well. Fewer men becoming infected with HIV means fewer people of both genders and all ages getting the infection.

In rich countries in recent years, HIV treatment has improved so drastically that being infected no longer constitutes an imminent death warrant. Modern drug therapies now keep HIV-positive people alive for years, but in the United States each year, nearly 60,000 new people still join the more than 1.2 million already living with HIV. And in 5 people with the infection don’t know they have it, which helps it continue to spread. People are still dying, and treatment is costly and complicated.

Any injection offering a 60 percent reduction in the risk of contracting this plague would be received as a miracle in the HIV-ravaged regions of the world — and probably as a Nobel Prize-worthy triumph in the scientific community. Despite all these advantages, of course, some people do not think circumcision appropriate for themselves or their sons. That is certainly their right. But why would anyone — in San Francisco, which has known firsthand the grievous cost of HIV, or anywhere else — want to deprive those who wish this protection of the ability to obtain

**Haiti's Cholera Outbreak Has Plateaued, Death Rate Remains High In Rural Regions, U.N. Says**

The U.N. on Friday said Haiti’s cholera outbreak appears to be waning overall, but high death rates from the virus in rural regions of the country remain a concern, the Associated Press reports. According to figures released by the Haitian government, 231,070 cholera cases and 4,549 deaths from the disease have been reported since the outbreak first emerged in October.

"National mortality rates from cholera are down to 2 percent, from as high as 9 percent earlier, but in some rural areas, more than one-in-ten people who contract the disease die," the news service writes. "In Haiti’s Sud Est region, the mortality rate hit 10.7 percent as of Feb. 9, while in Nippes it was 6.7 percent and in the Grande Anse region, 5.9 percent. The rate should be under 1 percent, according to the World Health Organization," the news service reports. U.N. officials also have expressed concerns that the country’s upcoming Carnival season could lead to an uptick in cholera cases (2/18).

The U.N. on Monday held "a special meeting with donor countries to drum up support for its cholera treatment and control operations in Haiti," according to VOA News (Schlein, 2/21).

The organization "has appealed for 175 million dollars to help treat the outbreak, but donors have so far only given about 45 percent [roughly $80 million] of the funds needed," Deutsche Presse-Agentur/M&C reports. According to the news service, the funding shortage was forcing some NGOs "to shut some of their projects in the country, including programmes providing for the chlorination of drinking-water wells in the capital Port-au-Prince. Cholera is often spread through contaminated water sources" (2/18).

VOA News describes the U.N.‘s efforts to meet the needs on the ground to stop the spread of disease while also encouraging donor countries to help fill the funding gap to treat the cholera outbreak. According to the news service, "WHO spokeswoman Fadela Chaib says her agency is working with the Haitian Ministry of Health to replace NGOs that were running cholera centers,” which she "says ... are increasingly being integrated in the country's overall health-management programs" (2/21).

Chaib is quoted by the AP as saying the U.N. plans to continue its efforts in Haiti until the country’s mortality rate from cholera dips "under 1 percent" (2/18). World Radio Switzerland features an interview with Elisabeth Byrs, a spokeswoman for the Office for the Coordination of Humanitarian Affairs, in which she addresses NGOs leaving Haiti, the need for donor countries to fill the funding gap to boost cholera treatment in the country and the impact of cholera on Haiti’s food security (2/21).

**New face of sleeping sickness epidemiology highlights need for new tools**

Recent developments have rekindled hopes of eliminating human African trypanosomiasis (HAT), more familiarly known as sleeping sickness, as a public health problem in those areas of sub-Saharan Africa where the disease is endemic. In the February 2011 issue of the open-access journal PLoS Neglected Tropical Diseases, Simarro and colleagues at the WHO report in "The Human African Trypanosomiasis Control and Surveillance Programme of the World Health Organization 2000-2009: The Way Forward" that new cases of sleeping sickness fell below the symbolic number of 10,000 in 2009, setting the stage for a possible elimination of sleeping sickness in sub-Saharan Africa – a prospect that was unthinkable a
decade ago. In order to highlight the existing literature that PLoS NTDs authors have contributed to the field, PLoS *Neglected Tropical Diseases* Deputy Editor-in-Chief Serap Aksoy has compiled a collection of articles on HAT with a specific emphasis on potential applications for disease control.

While previous efforts to curb the disease throughout the early twentieth century had met with some success, the subsequent loss of effective control programs in the 1960s resulted in a steep increase in sleeping sickness within endemic countries. According to Dr. Simarro, these more recent encouraging signs are the result of "leadership from the WHO and coordination of control activities in endemic countries, as well as the unaltering commitment and determination of teams of National Sleeping Sickness Control Programmes, research institutions, bilateral cooperation, NGOs and the private sector. In the 2000s the objective was largely to hold sleeping sickness at bay, using systematic screening of at-risk populations and providing early treatment, followed by a decisive phase which focused on shrinking the map of endemic areas. In addition to generous drug donations and continuing research, funding for control activities, training, logistical improvement and infrastructure all contributed in helping to make diagnosis and treatment more accessible, safer and less cumbersome."

In the same issue, Serap Aksoy also elaborates on these findings in her editorial, "Sleeping Sickness Elimination in Sight: Time to Celebrate, Reflect but not Relax," in which she provides a historical perspective to HAT epidemics and emphasizes the need for continued vigilance in preventing future re-emergence of the disease.

Both Drs. Simarro and Aksoy conclude that the future for HAT elimination is promising, but only if donors continue to maintain their commitment to control and research, stressing that a sustainable strategy for elimination must be implemented and that an awareness of the threat of re-emergence of the disease be maintained.

**Natural (Born) Killers: what do they really do?**

Our immune systems contain three fundamentally different types of cell: B-cells, T-cells and the mysteriously named Natural Killer cells (NK cells), which are known to be involved in killing tumour cells and other infected cells. Experiments to investigate the function of NK cells have proven difficult to interpret because the interactions between the various components of the immune system make it almost impossible to isolate effects of individual cell types. This has changed with the development of a mouse in which individual genes can be knocked out (eliminated) only in NK cells, thereby providing scientists with a tool to study the importance of NK cells and indeed of individual pathways in these cells. The mouse was generated in the group of Veronika Sexl, who has recently moved from the Medical University of Vienna to the University of Veterinary Medicine, Vienna. An initial characterization is presented in the current issue of the journal *Blood*.

The development of a tool alone would not normally generate headlines but this case is different: the new mouse can be used to knock out any gene completely and exclusively in NK cells. It thus permits researchers to examine the functions of NK cells in the entire organism or even to investigate the importance of individual genes in this particular cell-type.

Sexl herself has naturally used the tool already. She has been able to show that a particular transcription factor known as Stat5 is essential for the correct development of NK cells – when this factor is eliminated, the cells fail to develop properly. The upshot is a mouse with an immune system that lacks NK cells but is otherwise fully intact. This is the first time it has proven possible to remove this particular cell type without affecting the rest of the animal. Finally, then, it is possible to learn what NK cells actually do in the intact organism.

Sexl and her collaborators have shown that mice lacking NK cells have normal T-cell responses to tumours, although their NK cell-mediated responses are naturally dramatically reduced. This experiment proves conclusively that the mouse can be used to untangle the web of interactions among the various cells of the immune system.

Sexl’s work has immediate implications for the treatment of cancer in humans. As an example, leukemia is sometimes treated by inhibiting the STAT5 protein. Sexl’s findings make it clear that this approach has a real drawback: inhibition of STAT5 will lead to a drop in the number of NK cells and so interfere with one of the body’s own mechanisms for fighting the cancer. It will be important to assess whether NK cells normally play a part in fighting diseases before inhibiting STAT5. For the first time, the newly developed mouse provides a tool to do so. Not surprisingly, it is already attracting a great deal of interest – as Sexl says, “They’ve been going like hot cakes ever since the word got out.”

The paper A novel Ncr1-Cre mouse reveals the essential role of STAT5 for NK cell survival and development by Eva Eckelhart, Wolfgang Warsch, Eva Zebedin, Olivia Simma, Dagmar Stoiber, Thomas Kolbe, Thomas Rückle, Mathias Mueller, Emilio Casanova and Veronika Sexl is published in the journal *Blood* (3 February 2011, Vol. 117, pp. 1565-1573). [The article's abstract online](http://www.bloodjournal.org/content/117/5/1565) [Link 1]
Although Sexl has only just joined the University of Veterinary Medicine, Vienna she has had a long association with the University and her recent work was performed in close collaboration with a number of its scientists as well as with the group of Emilio Casanova at the Ludwig Boltzmann Institute for Cancer Research, Vienna.

How Disordered Proteins Spread from Cell to Cell, Potentially Spreading Disease

ScienceDaily (Feb. 18, 2011) — One bad apple is all it takes to spoil the barrel. And one misfolded protein may be all that’s necessary to corrupt other proteins, forming large aggregations linked to several incurable neurodegenerative diseases such as Huntington’s, Parkinson’s and Alzheimer’s.

Stanford biology Professor Ron Kopito has shown that the mutant, misfolded protein responsible for Huntington’s disease can move from cell to cell, recruiting normal proteins and forming aggregations in each cell it visits.

Knowing that this protein spends part of its time outside cells "opens up the possibility for therapeutics," he said. Kopito studies how such misfolded proteins get across a cell’s membrane and into its cytoplasm, where they can interact with normal proteins. He is also investigating how these proteins move between neuronal cells.

The ability of these proteins to move from one cell to another could explain the way Huntington's disease spreads through the brain after starting in a specific region. Similar mechanisms may be involved in the progress of Parkinson's and Alzheimer's through the brain.

Kopito discussed his research on Feb. 18 at the annual meeting of the American Association for the Advancement of Science in Washington, D.C.

Not all bad

Not all misfolded proteins are bad. The dogma used to be that all our proteins formed neat, well-folded structures, packed together in complexes with a large number of other proteins, Kopito said. But over the past 20 years, researchers have found that as much as 30 percent of our proteins never fold into stable structures. And even ordered proteins appear to have some disordered parts.

Disordered proteins are important for normal cellular functions. Unlike regular proteins, they only interact with one partner at a time. But they are much more dynamic, capable of several quick interactions with many different proteins. This makes them ideal for a lot of the standard communication that happens within a cell for its normal functioning, Kopito said.

But if some of our proteins are always disordered, how do our cells tell which proteins need to be properly folded, and which don’t? "It's a big mystery," said Kopito, and one that he's studying. This question has implications for how people develop neurodegenerative diseases, all of which appear to be age-related.

Huntington's disease is caused by a specific mutated protein. But the body makes this mutant protein all your life, so why do you get the disease in later adulthood? Kopito said it’s because the body's protective mechanisms stop doing their job as we get older. He said his lab hopes to determine what these mechanisms are.

A bad influence

But it’s clear what happens when these mechanisms stop working—misfolded proteins start recruiting normal versions of the same protein and form large aggregations. The presence of these aggregations in neurons has been closely linked with several neurodegenerative diseases.

Kopito found that the mutant protein associated with Huntington's disease can leave one cell and enter another one, stirring up trouble in each new cell as it progresses down the line. The spread of the misfolded protein may explain how Huntington's progresses through the brain.

This disease, like Parkinson's and Alzheimer’s, starts in one area of the brain and spreads to the rest of it. This is also similar to the spread of prions, the self-replicating proteins implicated in mad cow disease.
disease and, in humans, Creutzfeldt-Jakob disease. As the misfolded protein reaches more parts of the brain, it could be responsible for the progressive worsening of these diseases.

Now that we know that these misfolded proteins spend part of their time outside of cells, traveling from one cell to another, new drugs could target them there, Kopito said. This could help prevent or at least block the progression of these diseases.

Kopito is currently working to figure out how misfolded proteins get past cell membranes into cells in the first place. It is only once in the cell’s cytoplasm that these proteins can recruit others. So these studies could help find ways to keep these mischief-makers away from the normal proteins.

He is also collaborating with biology professor Liqun Luo to track these proteins between cells in the well-mapped fruit fly nervous system. In the future, Kopito said he hopes to link his cell biology work to disease pathology in order to understand the role misfolded proteins play in human disease.

Pollution With Antibiotics Leads to Resistant Bacteria, Scientists Find
ScienceDaily (Feb. 22, 2011) — Many of the substances in our most common medicines are manufactured in India. Some of these factories release huge quantities of drugs to the environment. Swedish scientists now show that bacteria in polluted rivers become resistant to a range of antibiotics. International experts fear that this may contribute to the development of untreatable infectious diseases worldwide.

Using a novel method, based on large-scale DNA sequencing, the Swedish scientists show that bacteria residing in Indian rivers are full of resistance genes, protecting them from otherwise effective antibiotics.

"Since we buy medicines from India, we share moral responsibility to reduce the pollution, says Joakim Larsson," associate professor at the Sahlgrenska Academy, University of Gothenburg, one of the scientists behind the study, published online in PLoS ONE.

"If the pollution contributes to resistance development in clinically important bacteria, it becomes our problem also in a very direct way," he says.

"We have combined large-scale DNA sequencing with novel ways to analyze data to be able to search for thousands of different antibiotic resistance genes in parallel," says Erik Kristiansson, assistant professor at Chalmers University of Technology.

"Such an approach may become useful also in hospitals in the future," he points out.

Several international experts, interviewed by the journal Nature, describe the results as worrying."Even if the bacteria found are not dangerous to humans or other animals in the area, they may transfer their resistance genes to bacteria that are," says Dave Ussery, a microbiologist at the Technical University of Denmark.

David Graham at Newcastle University, UK, describes the Indian site.

"In a way, it's sort of like a beaker experiment that tests the worst-case scenario, only this is in a natural system."

Björn Olsen, an infectious-disease specialist at Uppsala University in Sweden compares the resistance with volcano-ash.

"The cloud is going to drop down somewhere else, not just around the sewage plant."

The study was carried out at the Sahlgrenska Academy, University of Gothenburg in collaboration with Chalmers University of Technology and Umeå University, Sweden

Journal Reference:

Dry Copper Kills Bacteria on Contact
ScienceDaily (Feb. 22, 2011) — Metallic copper surfaces kill microbes on contact, decimating their populations, according to a paper in the February 2011 issue of the journal Applied and Environmental Microbiology. They do so literally in minutes, by causing massive membrane damage after about a minute’s exposure, says the study’s corresponding author, Gregor Grass of the University of Nebraska, Lincoln. This is the first study to demonstrate this mechanism of bactericidal.

"When microbes were exposed to copper surfaces, we observed contact killing to take place at the rate of tens to hundreds of millions of bacterial cells within minutes," says Grass. "This means that usually no live microorganisms can be recovered from copper surfaces after exposure."

Thus, such surfaces could provide a critical passive defense against pathogens in hospitals, where hospital-acquired infections are becoming increasingly common and costly, killing 50,000-100,000
Americans annually, and costing more than $8 billion, according to one estimate. Still, Grass cautions that "metallic copper surfaces will never be able to replace other hygiene-improving methods already in effect," although they "will certainly decrease the costs associated with hospital-acquired infections and curb human disease as well as save lives." However, he expects this strategy to be inexpensive, because "the effect does not wear off."

Critically, the researchers provide strong evidence that genotoxicity through mutations and DNA lesions is not a cause of dry copper's antimicrobial properties. This is important, because mutations can cause cancer in animals and humans, and the lack of such mutations in bacteria from copper means that copper does not endanger humans.

The relevant experiment was particularly interesting. The bacterium, *Deinococcus radiodurans*, is unusually resistant to radiation damage, as its DNA repair mechanisms are especially robust. The hypothesis: if metallic copper kills by causing DNA damage, *D. radiodurans* should be immune to copper. It is not.

It is important to note that only dry copper surfaces are amazingly lethal to bacteria. The difference between dry and wet surfaces, such as copper pipes, is that only dry surfaces are inhospitable environments for bacterial growth. Bacteria can easily grow and reproduce in wet environments, and in so doing, they can develop resistance to copper. Resistance has not been observed to develop on dry copper surfaces.

**Journal Reference:**

**Antifungal Compound Found on Tropical Seaweed Has Promising Antimalarial Properties**
ScienceDaily (Feb. 22, 2011) — A group of chemical compounds used by a species of tropical seaweed to ward off fungus attacks may have promising antimalarial properties for humans. The compounds are part of a unique chemical signaling system that seaweeds use to battle enemies—and that may provide a wealth of potential new pharmaceutical compounds.

Using a novel analytical process, researchers at the Georgia Institute of Technology found that the complex antifungal molecules are not distributed evenly across the seaweed surfaces, but instead appear to be concentrated at specific locations—possibly where an injury increases the risk of fungal infection.

A Georgia Tech scientist reports on the class of compounds, known as bromophycolides, at the annual meeting of the American Association for the Advancement of Science (AAAS) Feb. 21, 2011 in Washington, D.C. The research, supported by the National Institutes of Health, is part of a long-term study of chemical signaling among organisms that are part of coral reef communities.

"The language of chemistry in the natural world has been around for billions of years, and it is crucial for the survival of these species," said Julia Kubanek, an associate professor in Georgia Tech’s School of Biology and School of Chemistry and Biochemistry. "We can co-opt these chemical processes for human benefit in the form of new treatments for diseases that affect us."

More than a million people die each year from malaria, which is caused by the parasite *Plasmodium falciparum*. The parasite has developed resistance to many antimalarial drugs and has begun to show resistance to artemisinin—today’s most important antimalarial drug. The stakes are high because half of the world’s population is at risk for the disease.

"These molecules are promising leads for the treatment of malaria, and they operate through an interesting mechanism that we are studying," Kubanek explained. "There are only a couple of drugs left that are effective against malaria in all areas of the world, so we are hopeful that these molecules will continue to show promise as we develop them further as pharmaceutical leads."

In laboratory studies led by Georgia Tech student Paige Stout from Kubanek’s lab—and in collaboration with California scientists—the lead molecule has shown promising activity against malaria, and the next step will be to test it in a mouse model of the disease. As with other potential drug compounds, however, the likelihood that this molecule will have just the right chemistry to be useful in humans is relatively small.

Other Georgia Tech researchers have begun research on synthesizing the compound in the laboratory. Beyond producing quantities sufficient for testing, laboratory synthesis may be able to modify the compound to improve its activity—or to lessen any side effects. Ultimately, yeast or another microorganism may be able to be modified genetically to grow large amounts of bromophycolide.
The researchers found the antifungal compounds associated with light-colored patches on the surface of the *Callophycus serratus* seaweed using a new analytical technique known as desorption electrospray ionization mass spectrometry (DESI-MS). The technique was developed in the laboratory of Facundo Fernandez, an associate professor in Georgia Tech’s School of Chemistry and Biochemistry. DESI-MS allowed researchers for the first time to study the unique chemical activity taking place on the surfaces of the seaweeds.

As part of the project, Georgia Tech scientists have been cataloging and analyzing natural compounds from more than 800 species found in the waters surrounding the Fiji Islands. They were interested in *Callophycus serratus* because it seemed particularly adept at fighting off microbial infections.

Using the DESI-MS technique, researchers Leonard Nyadong and Asiri Galhena analyzed samples of the seaweed and found groups of potent antifungal compounds. In laboratory testing, graduate student Amy Lane found that these bromophycolide compounds effectively inhibited the growth of *Lindra thalassiae*, a common marine fungus.

"The alga is marshalling its defenses and displaying them in a way that blocks the entry points for microbes that might invade and cause disease," Kubanek said. "Seaweeds don’t have immune responses like humans do. But instead, they have some chemical compounds in their tissues to protect them."

Though all the seaweed they studied was from a single species, the researchers were surprised to find two distinct groups of antifungal chemicals. From one seaweed subpopulation, dubbed the "bushy" type for its appearance, 23 different antifungal compounds were identified. In a second group of seaweed, the researchers found 10 different antifungal compounds—all different from the ones seen in the first group.

In the DESI-MS technique, a charged stream of polar solvent is directed at the surface of a sample under study at ambient pressure and temperature. The spray desorbs molecules, which are then ionized and delivered to the mass spectrometer for analysis.

"Our collaborative team of researchers from the Department of Biomedical Engineering and the College of Sciences has worked within the Bioimaging Mass Spectrometry Center at Georgia Tech to better understand the mechanisms of chemical defenses in marine organisms," said Fernandez. "This is an example of cross-cutting interdisciplinary research that characterizes our institute."

Kubanek is hopeful that other useful compounds will emerge from the study of signaling compounds in the coral reef community.

"In the natural world, we have seaweed that is making these molecules and we have fungi that are trying to colonize, infect and perhaps use the seaweed as a substrate for its own growth," Kubanek said. "The seaweed uses these molecules to try to prevent the fungus from doing this, so there is an interaction between the seaweed and the fungus. These molecules function like words in a language, communicating between the seaweed and the fungus."

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**Samples obtained after prostate massage a good guide to HIV load in semen**

Michael Carter  
Published: 23 February 2011

HIV can be successfully measured in urethral fluids and urine that are obtained after prostatic massage, an international team of investigators report in the online edition of *Sexually Transmitted Infections*.

Levels of HIV in fluids and urine after prostatic massage were correlated with those observed in semen samples which were yielded by masturbation.

Most of the study participants found prostatic massage acceptable, and the investigators believe the procedure could be useful for individuals participating in HIV transmission studies who are unable to provide semen samples.

The study also provided some insights into the possible impact of antiretroviral therapy on infectiousness. None of the patients who were taking HIV treatment had detectable virus in either post-massage fluids/urine or semen.

Investigators from Kenya, the US and UK had found previously that levels of HIV in fluids and urine after prostatic massage were correlated with those in semen. They wished to see how acceptable and feasible the collection of samples after prostate massage was in HIV-positive men.

They therefore designed a prospective study involving 47 patients in Kenya. These men had a median age of 31 years, 75% reported that they had sex with other men, with two-thirds also indicating that they had engaged in transactional sex.

Physicians were trained to perform prostate massage and after a maximum of five minutes, fluid was collected from the urethra and then men were asked to provide a urine sample. One week later,
participants provide a semen sample. Individuals were instructed to abstain from any kind of sex for 48 hours before prostate massage and the production of semen.

Blood samples were also collected to see if levels of HIV correlated those observed in fluids/urine/semen.

Computer-assisted questionnaires were used to assess the acceptability of prostate massage and masturbation to provide semen samples.

The patients had quarterly assessments between 2007 and 2009.

Three-quarters of men reported that they abstained from sex for the specified period before prostate massage, with 95% reporting abstinence before the provision of semen samples.

Only 8% of men reported reservations about prostate massage and fluid/urine collection, and 6% said that they had misgivings about masturbating to provide semen samples.

A fifth of men experienced discomfort during prostate massage.

All the men who successfully provided samples after massage said that they would be willing to undergo this procedure again. Sex with other men and transactional sex work were both associated with the successful provision of samples. The performance of the massage by a female clinician was associated with a significantly lower rate of success (p = 0.014).

Pain, embarrassment and discomfort were associated with reluctance to undergo prostate massage. Heterosexual men were more likely than individuals reporting sex with other men to report reservations or discomfort about the procedure. But the investigators note: “the small number of heterosexual participants limited our evaluation of this factor.”

Prostate massage resulted in fluid/urine collection at 64% of visits, significantly lower than the 81% success rate for semen collection (p < 0.01). However, three-quarters of men successfully provided both types of fluid on at least one occasion.

At the initial assessment, HIV was successfully quantified in both post-massage fluid/urine and semen n 28%, in fluid/urine alone in 7% and in semen alone in 17%.

HIV was detectable in paired semen/blood samples for 45% of men.

Ten men were taking antiretroviral therapy, and three had virus detected in their blood. However, none had detectable viral load in either post-massage blood/urine or semen.

There was a high level of concordance between the results of the initial assessment and those obtained at follow-up visits. All the men treated with antiretroviral drugs maintained an undetectable viral load in both post-massage fluid/urine and semen.

For those with detectable virus, HIV levels in fluid/urine, semen and blood were correlated.

“Post-prostatic massage fluid/urine [post-PMF/U] represents a valid alternative approach to assess HIV-1 shedding in semen,” comment the investigators.

They suggest “for men in certain circumstances (e.g., during wound healing after male circumcision, when a painful ulcer is present, in men with low CD4 cell counts, in men with difficulty providing semen), post-PMF/U may represent a valuable alternative to semen collection in research settings requiring genitourinary sampling.”

Reference

**Bill would require alleged rapists to be HIV tested**

BY ROBERT GEHRKE

The Salt Lake Tribune

First published Feb 22 2011 12:29PM

Updated Feb 22, 2011 07:20PM

Victims of sexual assaults could demand their accused attackers get tested for HIV, under a bill approved unanimously Tuesday by a House committee.

Susan Chasson, the statewide sexual assault nurse coordinator, said that sexual assault victims as a precaution typically receive a regimen of drugs to prevent HIV. The monthlong treatment can have numerous side effects.

Rep. Richard Greenwood, R-Roy, said testing alleged attackers once they have been charged could spare the victim from having to go through that regimen. Currently, only convicted attackers can be tested. In many instances, that could take a year or more.
The mother of a young woman assaulted in Utah County — who asked that her name be withheld — told the House Judiciary Committee that her daughter was left with her jaw wired shut and a tracheal tube to breathe.

“We asked if they could test the man who assaulted her,” the mother testified, “and they said that wouldn’t be possible until he was convicted.”

Doctors had to dissolve the pills in water and try to give them to her twice a day through her nose. Because her jaw was wired shut, she couldn’t take the pill if there was a chance she would vomit.

If Greenwood’s HB324 passes, she said, her daughter would know if she had to go through the ordeal. The measure was unanimously approved by the committee and moves to the full House.

In Kato’s Africa, USAID Money Spurred Spread of HIV Criminalization Laws
When police found Ugandan gay rights activist David Kato bludgeoned to death last month in his Kampala home, the news brought renewed public attention to the well-documented U.S. roots of Uganda’s now infamous anti-homosexuality bill.

What’s gone unnoticed in recent years, however, is U.S. patronage of other anti-human rights legislation in Africa that promotes both homophobia and the persecution of people living with HIV. The U.S. Agency for International Development, while publicly denouncing laws that specifically criminalize HIV, has in fact financed their recent rapid dissemination across the African continent.

Millions of dollars in USAID funds have helped spur what the Canadian HIV/AIDS Legal Network is calling a “legislation contagion” that jeopardizes human rights in Africa.

USAID involvement
A decade ago, not a single African country had a law that specifically criminalized HIV exposure. Now, at least 27 African nations punish exposure. These laws open the door for the jailing—or worse—of people with HIV who practice safer sex; mothers who transmit the virus to their children; and even those who have HIV but are undiagnosed.

The spread of such laws is in part the result of a 2004 model law created by Action for West Africa Region-HIV/AIDS, a five-year project funded at just under $35 million by USAID.

“By funding the creation—and wide dissemination—of a ‘model’ HIV-specific law, USAID has sent mixed messages from the United States,” said Edwin Bernard, editor of HIV and the Criminal Law. “On the one hand, the model law supports human rights by criminalizing stigma and discrimination. But by using vague and imprecise language in its HIV criminalization statute it also creates fear, confusion and the further stigmatization of people living with HIV.”

A ‘human rights’ initiative
In 2004, AWARE, a project led by the North Carolina-based global health organization FHI, convened a meeting of African leaders in N’Djamena, Chad. Two other U.S. groups, Population Services International and the Constella Futures Group, provided funds. The goal, according to FHI, was to design a legislative template for West and Central African nations that would protect people living with HIV and those at risk of contracting the virus. But if the law was meant to protect human rights, its conception was hasty and ill-conceived.

“Many informants discussed the speed at which the model law was drafted and disseminated,” said Daniel Grace, a doctoral candidate at the University of Victoria, British Columbia who is writing his thesis about the creation of the legislation.

In three days, the group created a template. At least 14 African countries have adopted laws mimicking the U.S.-funded model.

Abuses ahead
The template contains a number of dangerous provisions.

First, it punishes the “willful transmission” of HIV through “any means.” This phrase opens the door for wide interpretation, allowing governments to incarcerate a person practicing safer sex, regardless of whether he or she informs a partner of his or her status. The template also opens the possibility of punishment for mothers who pass HIV to their children, regardless of precautions taken to stop transmission.

Second, the model law penalizes partners who do not disclose HIV status to a “spouse or regular sexual partner” within six weeks of diagnosis. In countries where HIV-positive status can subject a person to social isolation, exile, physical abuse or even death, this provision has major implications.

Women, said Frederica Stines, Africa program officer at the International Women’s Health Coalition, will be the overwhelming victims of this criminalization creep. They are more likely to know their HIV
status; more likely to be the victims of rape; more likely to be thrown out of their homes because of their status; and less likely to be able to insist on condom use. “Criminalizing is not prevention,” said Stines, who has more than a decade of experience promoting reproductive rights in Africa. “Who wants to know their status if they could be arrested?”

Many governments adapted the model law but altered it in a way that allows for even broader abuses. Togo’s law makes any sex without a condom an illegal act, regardless of HIV status. Benin’s version makes it a crime for a person who knows he or she is infected to engage in “unprotected sexual relations” without disclosing his or her status—no actual transmission of HIV is required. Burundi’s version says that the government can try a “willful” transmitter for murder.

The Kato connection
It looks like Kato’s Uganda could be the next to catch the criminalization contagion.

The country made headlines in 2009 when parliamentarians introduced a law that would execute homosexuals, legislation many said was inspired by U.S. evangelicals. Then, last year, with less media fanfare, members of parliament introduced a bill that, like the USAID-sponsored N’Djamena law, would criminalize HIV transmission. Human Rights Watch denounced the HIV/AIDS Prevention and Control Act, saying it will discourage testing and encourage stigma. Its sponsors soldier on.

“Kato was known for his fight for the removal of laws like this,” said Dr. Cheikh Traoré, senior advisor for sexual diversity at the United Nations Development Programme. He first met Kato three years ago at an African AIDS conference. “For me, the best way for outsiders to honor his memory is to get behind the people who are in the country, the people who are ignored and isolated, but who try to change these laws.”

U.S. government speaks
Robert Clay, director of USAID’s Office of HIV/AIDS, denounced the very provisions included in the law sponsored by his agency. “Criminalization of HIV/AIDS is not supported by the U.S. government,” he said.

When asked to address the discrepancy between the model law and USAID’s stance, he said the U.S. merely funded the AWARE project—and that the model produced at the N’Djamena conference is not representative of the agency. “We know stigmatization, stigma and discrimination, are really a driver of this epidemic,” he said. “And we need to make sure that we don’t have those types of laws on the books.”

No one at FHI would speak on the record about the organization’s involvement.

Follow the leader
Criminalization of HIV/AIDS is, in fact, supported by the U.S. government.

By criminalizing transmission, African nations are simply following their peers in the West. By 1988, at least eight U.S. states had introduced HIV-specific laws, according to HIV and the Criminal Law. Other wealthy nations followed suit.

Since 1998, UNAIDS and the Office of the United Nations High Commissioner for Human Rights have recommended that governments not enact laws that specifically criminalize HIV. But the U.S. has ignored this call. Today, 28 U.S. states have HIV-related criminal or public health laws. Punishment ranges from a $100 fine to imprisonment of up to 30 years in Arkansas.

“Laws do not just happen,” said Grace. “While the purpose of [my] research is not to blame specific legislative drafters, parliamentarians or lawyers, it is important to hold actors accountable and to make visible the processes by which ‘dangerous’ provisions have been passed across the [African] region.”

Medical Library Association’s Trusted Web List
Charlotte Observer, (02.15.2011)
A test of the health literacy of 28 students from two universities reveals that young people who have grown up in the Internet age do not always access the best information.

Kim Smith, an assistant professor of journalism at North Carolina A&T State University-Greensboro, asked students: “If a friend or loved one acquired HIV/AIDS, where would you go on the Internet to find information?” Nearly all the students typed “HIV and AIDS” into Google or Yahoo and were overwhelmed by the results. “They would just sit there in shock, like ‘What the heck do I do with this?’” he said of the roughly 24 million hits that the search returned.

Ninety percent of the students, though confident in their investigational prowess, failed to utilize Google’s clearly marked “advanced search” option to narrow results. “Without the skills to properly search for and evaluate the information, most students chose the top five links that appeared,” said Smith. “Students expressed no concern over whether the information they were reading ... came from
authoritative sources.” Only one of the websites accessed was Medical Library Association (MLA) at www.mlanet.org/resources/userguide.html.

The following list is recommended by MLA for HIV/AIDS-related searches:
*www.cancer.gov — National Cancer Institute
*www.cdc.gov — CDC
*www.familydoctor.org — American Academy of Family Physicians
*www.healthfinder.gov — US Department of Health and Human Services
*http://hivinsite.ucsf.edu/ —University of California-San Francisco AIDS Research Institute
*www.kidshealth.org — Nemours Foundation, Center for Children’s Health Media
*mayoclinic.com — the Mayo Clinic
*www.noah-health.org — New York Online Access to Health

**Oral Sex Linked to Cancer Risk**
*Agence France Presse*, (02.20.2011)

Data supports the connection of oral sex to cancer, announced US scientists during Sunday’s American Association for the Advancement of Science meeting in Washington.

Ohio State University College of Medicine Professor Maura Gillison advocated further research into how human papillomaviruses (HPVs) may have contributed to the 225 percent increase in US oral cancer cases from 1974 to 2007, primarily among young white males. Today, US HPV-related oral cancer surpasses cases linked to tobacco use, still the predominant cause of such cancers worldwide.

“When you compare people who have an oral infection or not … the single greatest factor is the number of partners on whom the person has performed oral sex,” said Gillison. “When the number of partners increases, the risk increases,” she said.

Earlier studies have indicated that people with six or more oral sex partners over a lifetime are eight times more susceptible to HPV-related head or neck cancer than those with less than six partners, according to Gillison.

Unfortunately, young people are often clueless to the risks, said University of California-San Francisco Professor Bonnie Halpern-Felsher. “Health care providers … parents, and other educators … are not talking to teens about oral sex, period,” she said. “Teens really have no idea that oral sex is related to any outcome like [sexually transmitted infections], HPV, chlamydia, and so on.”

The oral cancer field lags behind that of cervical cancer, which has a more widely known link to HPV, observed University of Missouri researcher Diane Harper, who co-presented with Halpern-Felsher at the conference. However, head and neck cancers could benefit from technology already utilized for identifying HPV in cervical cancer, said Harper.

National Cancer Institute data documents upwards of 150 different HPV types, approximately 40 of which are sexually transmitted and linked to genital warts, oral, anal, vaginal, and penile cancers.

**Virus-mimicking nanoparticles can stimulate long lasting immunity**

Vaccine scientists say their “Holy Grail” is to stimulate immunity that lasts for a lifetime. Live viral vaccines such as the smallpox or yellow fever vaccines provide immune protection that lasts several decades, but despite their success, scientists have remained in the dark as to how they induce such long lasting immunity.

Scientists at the Emory Vaccine Center have designed tiny nanoparticles that resemble viruses in size and immunological composition and that induce lifelong immunity in mice. They designed the particles to mimic the immune-stimulating effects of one of the most successful vaccines ever developed – the yellow fever vaccine. The particles, made of biodegradable polymers, have components that activate two different parts of the innate immune system and can be used interchangeably with material from many different bacteria or viruses.

The results are described in this week’s issue of *Nature*.

“These results address a long-standing puzzle in vaccinology: how do successful vaccines induce longlasting immunity?” says senior author Bali Pulendran, PhD, Charles Howard Candler professor of pathology and laboratory medicine at Emory University School of Medicine and a researcher at Yerkes National Primate Research Center.

“These particles could provide an instant way to stretch scarce supplies when access to viral material is limited, such as pandemic flu or during an emerging infection. In addition, there are many diseases,
such as HIV, malaria, tuberculosis and dengue, that still lack effective vaccines, where we anticipate that this type of immunity enhancer could play a role.”

One injection of the live viral yellow fever vaccine, developed in the 1930s by Nobel Prize winner Max Theiler, can protect against disease-causing forms of the virus for decades. Pulendran and his colleagues have been investigating how humans respond to the yellow fever vaccine, in the hopes of imitating it.

Several years ago, they established that the yellow fever vaccine stimulated multiple Toll-like receptors (TLRs) in the innate immune system. TLRs are present in insects as well as mammals, birds and fish. They are molecules expressed by cells that can sense bits of viruses, bacteria and parasites and can activate the immune system. Pulendran’s group demonstrated that the immune system sensed the yellow fever vaccine via multiple TLRs, and that this was required for the immunity induced by the vaccine.

“TLRs are like the sixth sense in our bodies, because they have an exquisite capacity to sense viruses and bacteria, and convey this information to stimulate the immune response,” Pulendran says. “We found that to get the best immune response, you need to hit more than one kind of Toll-like receptor. Our aim was to create a synthetic particle that accomplishes this task.”

Emory postdoctoral fellow Sudhir Pai Kasturi, PhD, created tiny particles studded with molecules that turn on Toll-like receptors. He worked with colleague Niren Murthy, PhD, associate professor in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University.

“We are very excited about building on this platform to design improved vaccines for existing and emerging infectious diseases” says Kasturi, the primary author working in Pulendran’s lab at the Emory Vaccine Center. One of the particles’ components is MPL (monophosphoryl lipid A), a component of bacterial cell walls, and the other is imiquimod, a chemical that mimics the effects of viral RNA. The particles are made of PLGA—poly(lactic acid)-co-(glycolic acid)—a synthetic polymer used for biodegradable grafts and sutures.

All three components are FDA-approved for human use individually. For several decades, the only FDA-approved vaccine additive was alum, until a cervical cancer vaccine containing MPL was approved in 2009. Because of immune system differences between mice and monkeys, the scientists replaced imiquimod with the related chemical resiquimod for monkey experiments.

In mice, the particles can stimulate production of antibodies to proteins from flu virus or anthrax bacteria several orders of magnitude more effectively than alum, the authors found. In addition, the immune cells persist in lymph nodes for at least 18 months, almost the lifetime of a mouse. In experiments with monkeys, nanoparticles with viral protein could induce robust responses greater than five times the response induced by a dose of the same viral protein given by itself, without the nanoparticles.


Old Folk Remedy Revived: How Tansy May Be a Treatment for Herpes

ScienceDaily (Feb. 22, 2011) — For centuries, tansy has been used as a folk remedy, but now scientists from Britain and Spain believe the plant may have medical benefits after all, as a treatment for herpes. The team’s findings, published in Phytotherapy Research, are the result of joint work between two teams to established scientific evidence for traditional medicines.

Tansy, Tanacetum vulgare, is a flowering plant found across mainland Europe and Asia. From the Middle Ages onwards the plant, whose folk names include Golden Buttons and Mugwort, has been used as a remedy for various conditions, from fevers to rheumatism. However, it’s supposed medical benefits have always been questioned.

"Our research focused on the anti-viral properties of tansy, especially the potential treatment it may represent for herpes," said lead author Professor Francisco Parra from the Universidad de Oviedo. "We currently lack an effective vaccine for either HSV-1 or HSV-2 stands of the disease, which can cause long term infections."

Professor Parra’s team which specialises in investigating new antiviral compounds, both through design or by screening natural plant extracts, began joint work on the properties of tansy with the research group led by Dr Solomon Habtemariam from the University of Greenwich, which studies European medicinal plants to establish the scientific evidence for traditional medicines.

Through a mechanistic-based antiherpetic activity study, the teams revealed which constituents of the plant are responsible for antiviral activity.

"Our study revealed that parthenolide is not one of the major anti HSV-1 principles of tansy, as has been suggested. However we found that tansy does contain known antiviral agents including 3,5-dicaffeoylquinic acid (3,5-DCQA) as well as axillarin, which contributes to its antiherpetic effect," said
Parra. “This shows that multiple properties of the plant are responsible for the supposed antiviral activity of tansy.”

The joint study used an established anti-HSV study model on both crude extracts of the aerial parts and roots of tansy, as well as some purified compounds to analyse the plants anti-viral activity.

"Although the precise molecular targets for tansy extract require further research this study reveals the clear potential of tansy to treat the dermatological lesions caused by HSV, concluded Parra. “This shows that systematic pharmacological and phytochemical studies such as this can play pivotal roles in the modernisation of European traditional herbal medicines.”

Journal Reference:
Ángel L. Álvarez, Solomon Habtemariam, Malindra Juan-Badaturuge, Caroline Jackson, Francisco Parra. In vitro anti HSV-1 and HSV-2 activity of Tanacetum vulgare extracts and isolated compounds: An approach to their mechanisms of action. Phytotherapy Research, 2010; DOI: 10.1002/ptr.3382

New vaccine technology shows promise against hepatitis C virus
2011-02-24 10:50:00

University of Copenhagen scientists have succeeded in developing a vaccine, which provides future hope for medical protection from hepatitis C.

In this type of hepatitis the virus hides in the liver and can cause cirrhosis and liver cancer. Since the virus mutates strongly, there is no traditional vaccine to protect against it.

"The hepatitis C virus (HCV) has the same infection pathways as HIV," said Jan Pravsgaard Christensen, Associate Professor of Infection Immunology at the University.

"Approximately one newly infected patient in five has an immune system capable of defeating an acute HCV infection in the first six months. But most cases do not present any symptoms at all and the virus becomes a chronic infection of the liver," he said.

Every year three or four million more people become infected and the most frequent path of infection is needle sharing among drug addicts or tattoo artists with poor hygiene, such as tribal tattoo artists in Africa and Asia.
Fifteen percent of new infections are sexually transmitted, while ten percent come from unscreened blood transfusions.

The new vaccine technology was developed by Peter J. Holst, a former PhD student now a postdoc with the Experimental Virology group, which also includes Professor Allan Randrup Thomsen and Christensen.

The technology works by stimulating and accelerating the immune system, and showing the body’s defence mechanisms of the parts of the virus that are more conserved and do not mutate as fast and as often, such as the molecules on the surface of the HCV.

"We took a dead common cold virus, an adenovirus that is completely harmless and which many of us have met in childhood," Christensen said.

"We hid the gene for one of the HCV’s internal molecules inside it. At the same time we attached a special molecule on the internal molecule so that when the cells of the mouse body tried to take a sample, they would extract a more extensive section.

"The immune defences would then be presented with a larger section of the molecule concerned. You may say that the immune defences were given an entire palm print of the internal genes instead of just a single fingerprint," he said.

This strategy resulted in two discoveries from the team. Firstly, the mice were vaccinated for HCV in a way that meant that protection was independent of variations in the surface molecules of the virus. Secondly, the immune defences of the mice saw such an extensive section of the internal molecule that even though some aspects of it changed, there were still a couple of impressions the immune defences could recognise and respond to.

The finding has been published in the Journal of Immunology. (ANI)

MIT Engineers Design New Nanoparticle That Could Lead To Vaccines For HIV, Malaria, Other Diseases
23 Feb 2011

MIT engineers have designed a new type of nanoparticle that could safely and effectively deliver vaccines for diseases such as HIV and malaria.
The new particles, described in the Feb. 20 issue of Nature Materials, consist of concentric fatty spheres that can carry synthetic versions of proteins normally produced by viruses. These synthetic particles elicit a strong immune response—comparable to that produced by live virus vaccines—but should be much safer, says Darrell Irvine, author of the paper and an associate professor of materials science and engineering and biological engineering.

Such particles could help scientists develop vaccines against cancer as well as infectious diseases. In collaboration with scientists at the Walter Reed Army Institute of Research, Irvine and his students are now testing the nanoparticles' ability to deliver an experimental malaria vaccine in mice.

Vaccines protect the body by exposing it to an infectious agent that primes the immune system to respond quickly when it encounters the pathogen again. In many cases, such as with the polio and smallpox vaccines, a dead or disabled form of the virus is used. Other vaccines, such as the diphtheria vaccine, consist of a synthetic version of a protein or other molecule normally made by the pathogen.

When designing a vaccine, scientists try to provoke at least one of the human body's two major players in the immune response: T cells, which attack body cells that have been infected with a pathogen; or B cells, which secrete antibodies that target viruses or bacteria present in the blood and other body fluids.

For diseases in which the pathogen tends to stay inside cells, such as HIV, a strong response from a type of T cell known as “killer” T cell is required. The best way to provoke these cells into action is to use a killed or disabled virus, but that cannot be done with HIV because it's difficult to render the virus harmless.

To get around the danger of using live viruses, scientists are working on synthetic vaccines for HIV and other viral infections such as hepatitis B. However, these vaccines, while safer, do not elicit a very strong T cell response. Recently, scientists have tried encasing the vaccines in fatty droplets called liposomes, which could help promote T cell responses by packaging the protein in a virus-like particle. However, these liposomes have poor stability in blood and body fluids.

Irvine, who is a member of MIT's David H. Koch Institute for Integrative Cancer Research, decided to build on the liposome approach by packaging many of the droplets together in concentric spheres. Once the liposomes are fused together, adjacent liposome walls are chemically "stapled" to each other, making the structure more stable and less likely to break down too quickly following injection. However, once the nanoparticles are absorbed by a cell, they degrade quickly, releasing the vaccine and provoking a T cell response.

In tests with mice, Irvine and his colleagues used the nanoparticles to deliver a protein called ovalbumin, an egg-white protein commonly used in immunology studies because biochemical tools are available to track the immune response to this molecule. They found that three immunizations of low doses of the vaccine produced a strong T cell response—after immunization, up to 30 percent of all killer T cells in the mice were specific to the vaccine protein.

That is one of the strongest T cell responses generated by a protein vaccine, and comparable to strong viral vaccines, but without the safety concerns of live viruses, says Irvine. Importantly, the particles also elicit a strong antibody response.

In addition to the malaria studies with scientists at Walter Reed, Irvine is also working on developing the nanoparticles to deliver cancer vaccines and HIV vaccines. Translation of this approach to HIV is being done in collaboration with colleagues at the Ragon Institute of MIT, Harvard and Massachusetts General Hospital. The institute, which funded this study along with the Gates Foundation, Department of Defense and National Institutes of Health, was established in 2009 with the goal of developing an HIV vaccine.

Cleaning Vagina Linked to Increased HIV Risk, Study Finds

Los Angeles Times, (02.16.2011) Amina Khan

Data culled from 13 studies of 14,874 sub-Saharan African women, 791 of whom ended up HIV-positive, found that those cleaning, tightening or drying their vaginas using soap, cloth or paper were more at risk for contracting the virus, according to a new study.

When controlled for factors such as age, marital status, and number of sexual partners within the last three months, the study authors discovered women using cloth or paper for intravaginal cleaning were approximately 1.5 times more susceptible to HIV, and 1.25 times more susceptible if they used soap. In addition, those using soap were vulnerable to bacterial vaginosis or a disruption in the ordinarily healthful balance of vaginal microbes that stave off sickness.
Although study authors were unsuccessful delineating an express causal connection between the hygiene habits and the virus, they theorized that the women’s vulnerability to HIV increased when they compromised their vaginas’ safeguarding mucus, triggered inflammation or other harm, or altered the vagina’s acid levels, which all increase its vulnerability to detrimental microorganisms.


**Gonorrhea Has Picked Up Human DNA**

*USA Today*, (02.13.2011) Dan Vergano

Researchers at Northwestern University studying gonorrhea samples found some had DNA identical to human sequences.

Gonorrhea is an STD that only infects people and is curable with antibiotics. H. Steven Seifert and Mark T. Anderson studied gene sequences from gonorrhea samples mapped at the Cambridge, Mass.-based Broad Institute, finding three had DNA matching human sequences. Further analysis revealed that human DNA is present in approximately 11 percent of Neisseria gonorrhoeae bacteria. But human DNA is absent from Neisseria meningitidis, which causes bacterial meningitis, suggesting the gene transfer occurred in recent history.

While bacteria and viruses are known to readily swap genetic sequences, this is believed to be the first instance of bacteria picking up human genes, said the authors. “The bacterium is getting a genetic sequence from the very host it’s infecting,” said Seifert.

“This has evolutionary significance because it shows you can take broad evolutionary steps when you’re able to acquire these pieces of DNA,” Seifert said.


**Advocates Say Ending Violence Against Women Must Be Top Priority For U.N. Women**

Nearly three quarters (72 percent) of women’s rights advocates say ending violence against women must be a top priority for U.N. Women, according to a report released Wednesday at the Commission on the Status of Women (CSW) in New York, Inter Press Service reports. Released a day ahead of the official launch of the new agency, the "Blueprint for U.N. Women" survey, commissioned by the groups Voluntary Service Overseas (VSO) and Oxfam, outlines "the views and efforts, documented in the report, of some 100 civil society organisations working in over 75 countries on human rights, gender equality and social justice," according to the news service (D’Almeida, 2/24).

"Seventy percent of people living in poverty are women, 60% of people living with HIV in sub-Saharan Africa are women and girls, and violence against women continues to be at alarming levels," VSO Chief Executive Officer Marg Mayne said, according to a VSO press release. The report "clearly lays out a direction for U.N. Women from the people that know best and are working on the ground to deliver change for women in developing countries," Mayne said.

"Eighty four percent of respondents said rural women were the group in most need of targeted approach," the press release states. The respondents also highlighted the importance of the agency targeting women with disabilities as well as those who are uneducated (2/23).

Although the U.N. historically has "focused heavily on safeguarding women’s rights in wartime, the survey indicates that women expressed a greater desire for representation in political processes, freedom to determine their own marriages, and access to reliable justice systems than for protection during armed conflict, indicating that the root cause of the problem is not sporadic conflict, but a constant state of systematic inequality and violence," IPS writes. The IPS story provides more information on the specific findings of the report, describes advocates' concerns about funding for U.N. Women, and includes additional comments by Mayne; Farah Karimi, executive director of Oxfam Novib; and Kathy Peach, the head of external affairs for VSO UK (2/24).

"As U.N. Women is officially launched tomorrow, it is still awaiting a funding commitment from both the U.S. and U.K. governments. Having received just 1% of the UN's budget to date – it is at risk of failing before it has even begun," Mayne said, according to the press release (2/23).
Ghana Cholera Outbreak Spreads To Three Regions
"A total of 1,396 cholera cases have been recorded in three regions" of Ghana and have caused the deaths of 34 people, GhanaWeb reports. Addressing the media on Wednesday, Emmanuel Dzotsi of the Diseases Surveillance Unit of Ghana Health Service "said the current trend posed a possibility of the cholera spreading to the other regions if serious control measures were not put in place." During the briefing, Dzotsi highlighted the measures the country was taking to control the outbreak, the news service added (2/23).

Rare HIV-positive individuals shed light on how body could effectively handle infection
Although untreated HIV infection eventually results in immunodeficiency (AIDS), a small group of people infected with the virus, called elite suppressors (0.5 percent of all HIV-infected individuals), are naturally able to control infection in the absence of antiretroviral therapy, or HAART. Elite suppressors and HIV-infected individuals treated with HAART have similar levels of virus in the blood stream. However, levels of HIV integrated into immune cells are much lower in elite suppressors compared to levels in cells from HIV-infected individuals on HAART, according to a study by University of Pennsylvania School of Medicine researchers published in PLoS Pathogens.

Elite suppressors are thought to have a more effective immune response to HIV; specifically, more effective killer T cells, the subgroup of white blood cells that kill cells infected with viruses. HIV is an RNA virus that converts its RNA genome into DNA intermediates in order to replicate. One important step in the HIV life cycle is integration—where HIV DNA inserts into the chromosomes of human helper T cells. Cells that contain the integrated form of HIV DNA and are metabolically less active appear to be resistant to antiretroviral therapy and persist in the host, forming a latent reservoir. It will be important to understand why the HIV reservoir is lower in elite suppressors than in HIV infected individuals on HAART. To begin to address this question, it would be interesting to see if the level of integration would be lower still after placing elite suppressors on HAART. The investigators speculate that therapeutic vaccinations aimed at generating killer T cells similar to those in elite suppressors may be effective against the treatment resistant latent reservoir.

The cohort of elite suppressors was characterized by NIH researchers who also contributed to the study.

Collisions of protein machines cause DNA replication derailment
23 February 2011
Scientists have published results that will forever change the way researchers view the interplay between gene expression, DNA replication and the prevention of DNA damage. DNA damage, if not kept in check, can lead to many problems including cancers. Researchers, funded by the Biotechnology and Biological Sciences Research Council (BBSRC) and the Wellcome Trust and working at The University of Nottingham, have shown that the process of replication is even riskier than originally thought. This new information is published tomorrow (24 February) in the journal Nature.

Lead researcher Panos Soultanas, a Professor of Biological Chemistry from The University of Nottingham School of Chemistry said "Consider DNA as a bi-directional rail track with two types of train: a big fast one like an eight-carriage cross country train and a small slow one like a two-carriage regional train. As it travels, the big train—the DNA replisome—is responsible for copying the DNA e.g. when a cell is preparing to divide. And the small train—the RNA polymerase—makes its journey to deal with the expression of genes contained within the DNA sequence."

Just like trains, collisions between proteins moving along a strand of DNA can be catastrophic and this is one reason why areas of DNA that are being used a lot are particularly prone to damage. Until now it was thought that only head-on collisions between the DNA replisome (the big, fast, cross country train) and the RNA polymerase (the small, slow, regional train) could lead to serious DNA damage. This research shows that collisions between big and small trains running in the same direction can be just as dangerous and hence the problem in areas of high use is exacerbated.

Professor Soultanas said "Until now we thought that if the fast and slow protein-trains meet going in the same direction along the track then the faster DNA replication train just slows down and follows along behind the slower gene expression train until it has finished its job and moved out of the way. Our new research shows that this isn’t the case at all and in fact they do collide quite often causing what, in this analogy, we could only describe as a major derailment!"
When the DNA replisome falls off the DNA there are other proteins—called “restart replication proteins”—that come in to help get it back on track. Although this ensures that DNA replication can continue, it can potentially increase the risk of mistakes occurring during the copying process, particularly if such restart replication proteins are malfunctioning. In some cases these mistakes can lead to problems e.g. if the mistake causes a genetic malfunction that can lead to a cancer developing.

Describing what happens to the DNA replisome in areas of DNA where there are many RNA Polymerases working on genes that are in high use, Professor Soultanas said: "We are now realizing that when there are a lot of slow moving trains close together on the track, the fast moving train is faced with a huge obstacle and any failure to safely negotiate these areas could easily result in significant errors. Therefore, replication restart mechanisms are of vital importance to ensure accurate copying of the genetic material".

Professor Douglas Kell, Chief Executive, BBSRC said "This is exciting news and an excellent achievement. Biological sciences as a discipline is unique because there are a collection of key ideas, tools, techniques and processes that are applied across an enormous range of topics. The interplay between gene expression, DNA replication and the prevention of DNA damage is an example of just such a tenet of biology and so this result has the potential to touch on research right across BBSRC's portfolio and beyond."

**Virus-Mimicking Nanoparticles Can Stimulate Long-Lasting Immunity**

ScienceDaily (Feb. 23, 2011) — Vaccine scientists say their “Holy Grail” is to stimulate immunity that lasts for a lifetime. Live viral vaccines such as the smallpox or yellow fever vaccines provide immune protection that lasts several decades, but despite their success, scientists have remained in the dark as to how they induce such long lasting immunity.
Scientists at the Emory Vaccine Center have designed tiny nanoparticles that resemble viruses in size and immunological composition and that induce lifelong immunity in mice. They designed the particles to mimic the immune-stimulating effects of one of the most successful vaccines ever developed—the yellow fever vaccine. The particles, made of biodegradable polymers, have components that activate two different parts of the innate immune system and can be used interchangeably with material from many different bacteria or viruses.

The results are described in this week's issue of *Nature*.

"These results address a long-standing puzzle in vaccinology: how do successful vaccines induce long-lasting immunity?" says senior author Bali Pulendran, PhD, Charles Howard Candler professor of pathology and laboratory medicine at Emory University School of Medicine and a researcher at Yerkes National Primate Research Center.

"These particles could provide an instant way to stretch scarce supplies when access to viral material is limited, such as pandemic flu or during an emerging infection. In addition, there are many diseases, such as HIV, malaria, tuberculosis and dengue, that still lack effective vaccines, where we anticipate that this type of immunity enhancer could play a role."

One injection of the live viral yellow fever vaccine, developed in the 1930s by Nobel Prize winner Max Theiler, can protect against disease-causing forms of the virus for decades. Pulendran and his colleagues have been investigating how humans respond to the yellow fever vaccine, in the hopes of imitating it.

Several years ago, they established that the yellow fever vaccine stimulated multiple Toll-like receptors (TLRs) in the innate immune system. TLRs are present in insects as well as mammals, birds and fish. They are molecules expressed by cells that can sense bits of viruses, bacteria and parasites and can activate the immune system. Pulendran’s group demonstrated that the immune system sensed the yellow fever vaccine via multiple TLRs, and that this was required for the immunity induced by the vaccine.

"TLRs are like the sixth sense in our bodies, because they have an exquisite capacity to sense viruses and bacteria, and convey this information to stimulate the immune response," Pulendran says. "We found that to get the best immune response, you need to hit more than one kind of Toll-like receptor. Our aim was to create a synthetic particle that accomplishes this task."

Emory postdoctoral fellow Sudhir Pai Kasturi, PhD, created tiny particles studded with molecules that turn on Toll-like receptors. He worked with colleague Niren Murthy, PhD, associate professor in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University.

"We are very excited about building on this platform to design improved vaccines for existing and emerging infectious diseases" says Kasturi, the primary author working in Pulendran’s lab at the Emory Vaccine Center. One of the particles’ components is MPL (monophosphoryl lipid A), a component of bacterial cell walls, and the other is imiquimod, a chemical that mimics the effects of viral RNA. The particles are made of PLGA—poly(lactic acid)-co-(glycolic acid)—a synthetic polymer used for biodegradable grafts and sutures.

All three components are FDA-approved for human use individually. For several decades, the only FDA-approved vaccine additive was alum, until a cervical cancer vaccine containing MPL was approved in 2009. Because of immune system differences between mice and monkeys, the scientists replaced imiquimod with the related chemical resiquimod for monkey experiments.

In mice, the particles can stimulate production of antibodies to proteins from flu virus or anthrax bacteria several orders of magnitude more effectively than alum, the authors found. In addition, the immune cells persist in lymph nodes for at least 18 months, almost the lifetime of a mouse. In experiments with monkeys, nanoparticles with viral protein could induce robust responses greater than five times the response induced by a dose of the same viral protein given by itself, without the nanoparticles.

*Journal Reference:*

**Microbes Help Children Breathe Easily? Bacteria and Fungi May Offer Protection Against Asthma, Study Suggests**

ScienceDaily (Feb. 22, 2011) — Children who grow up on farms are less likely to suffer from asthma than other rural children. An international team of researchers including Dr. Markus Ege and Professor Erika von Mutius at Ludwig-Maximilians-Universitaet (LMU) has published a large-scale study that now
indicates that this may be due to differences in the spectrum of microbes the two groups are likely to encounter. This findings suggest that certain microorganisms may protect against the disease.

The incidence of asthma among children in Europe continues to rise. But not all children are equally at risk. Several studies published over the past few years have shown that children living on farms are significantly less likely to develop asthma than others. An international team of researchers including Dr. Markus Ege and Professor Erika von Mutius of Children's Surgical Clinic in the Dr. von Hauner Children's Hospital (Medical Center of the University of Munich) has just published an epidemiological study that confirms this finding. It shows that the lower susceptibility of farm children to asthma can largely be accounted for by the fact that they are exposed to a greater variety of microorganisms than other children living in the same regions.

The physiological mechanisms underlying the effect remain to be elucidated, but the investigators have identified several species that might be responsible for the reduction in asthma risk. The results have broad implications for the prevention of asthma in other sectors of the population. "We have a long way to go before we can present new preventive measures, but at least we now have candidates for the development of a vaccine," says Ege. (New England Journal of Medicine online, 24 February 2011)

Asthma is among the most prevalent chronic illnesses among children in Europe, and in many cases the condition will remain with them all their lives.

This is why asthma presents such a challenge for health-care systems. The disease results from a combination of genetic and environmental factors, and various studies have shown that farm children have a significantly lower risk of developing the condition than other children. In order to identify the reasons for this difference, LMU researchers selected a group of Bavarian schoolchildren for detailed study. In the context of two large-scale, pan-European, epidemiological projects, named GABRIEL and PARSIFAL, Ege and his colleagues compared children living on farms with others from the same rural districts who had little direct contact with farms.

In the new work, the investigators focused on the microbes present in domestic interiors. They collected household dust from children's bedrooms, and analyzed the bacterial and fungal DNAs in the samples. The results showed that farm children must cope with a much greater range of microorganisms than are children who live in other types of environment. The bacteria and fungi seem to act as guardians of health, for it turned out that the more diverse the microbial population, the lower the risk of asthma.

Exactly how the cells and spores perform this trick is still unclear, but the researchers suggest a couple of possible explanations. "One possibility is that a particular combination of microbial species stimulates the innate immune system and so prevents it from entering a state that promotes the development of asthma," says Ege. Another model proposes that continuous exposure to many different microorganisms makes it more difficult for the species that potentially induce asthma to become the dominant forms in the lower respiratory tract—similarly to the gastrointestinal tract, where a balanced population of microbes is necessary for optimal organ function.

Microbial diversity alone, however, is not enough to prevent asthma. More probably, it takes a particular consortium of species to exert a protective effect. "Within the large spectrum of organisms that we examined, there are some that may be of special interest," reports Ege. "Among these are certain species of bacilli and staphylococci—Staphylococcus sciuri, for instance—as well as fungi of the genus Eurotium."

The next challenge facing the team is to elucidate, at the level of single species, the nature of the link between the microorganisms in household dust and the protective effect, with the long-term goal of identifying candidates that might serve as the basis of a live vaccine against asthma. In addition to the LMU researchers, investigators from the Technical University of Munich, the Universities of Besançon (France), Marseille (France), Ulm, Basel (Switzerland), Utrecht (The Netherlands) and Imperial College London (UK) participated in the study. The work was supported by the European Commission (GABRIEL and PARSIFAL) and by the DFG (Deutsche Forschungsgemeinschaft) as part of its Priority Program Transregio 22.

Journal Reference:
Probiotic Identified to Treat Ulcers
ScienceDaily (Feb. 24, 2011) — Researchers from Spain have identified a strain of probiotic bacteria that may be useful in treating ulcers caused by Helicobacter pylori. They report their findings in the February 2011 issue of the journal Applied and Environmental Microbiology.

"H. pylori is considered one of the major risk factors underlying the development of gastritis and gastric and duodenal ulcers," write the researchers. "Currently, antibiotic-based treatment for H. pylori infection is neither sufficient nor satisfactory, with the most successful treatments reaching 75 to 90% eradication rates. The use of probiotics is a potentially promising tool to prevent H. pylori."

According to an expert consultation conducted by the Food and Agriculture Organization and the World Health Organization probiotics are "live microorganisms which when administered in adequate amounts confer a health benefit to the host." The regular intake of probiotic microorganisms has been demonstrated to prevent several disorders including diarrhea and inflammatory bowel disease.

Among probiotics Bifidobacterium is one of the favorite genera in studies focused on the prevention of gastrointestinal infection and is often used in fermented dairy products or food supplements. Some studies have been done in vitro (in test tubes or petri dishes) showing bifidobacterial activity against H. pylori.

In this study, the researchers tested numerous strains of bifidobacteria isolated from the feces of breast-fed infants for activity against H. pylori. They identified one strain (Bifidobacterium bifidum CECT 7366) that under certain conditions had an inhibition level of nearly 95% in vitro and tested its activity against infection in mice.

After 21 days, mice treated with the potentially probiotic strain developed significantly less ulcers than the control group. Additional tests suggest that treatment partially relieved damage to gastric tissue caused by H. pylori infection. Ingestion of the bacteria did not induce any disease or mortality in both healthy and immunocompromised mice.

"The results presented here confer to strain B. bifidum CECT 7366 the status of a probiotic bacterium with functional activity against H. pylori," write the researchers. "Human clinical trials must be performed before commercialization of this strain can be approved."

Journal Reference:

Entire T-Cell Receptor Repertoire Sequenced Revealing Extensive and Unshared Diversity ****
ScienceDaily (Feb. 23, 2011) — T-cell receptor diversity in blood samples from healthy individuals has been extensively cataloged for the first time in a study published online February 24 in Genome Research, setting the stage for a better understanding of infectious disease, cancer, and immune system disorders.

Adaptive immunity is mediated by T-cells, a white blood cell that identifies and attacks cells that may be infected with viruses or contain cancer-causing mutations. To recognize a wide array of potentially infectious agents or cancer-causing mutations, gene shuffling creates a highly variable and diverse collection of T-cell receptor sequences.

While the diversity of sequences in immune cell repertoires has been investigated previously, no study had yet been able to capture the entire range present in an individual sample. Now, using next-generation sequencing technology, researchers in Canada have identified essentially all T-cell receptor variants in blood samples, identifying more than one million unique sequences.

Dr. Robert Holt of the BC Cancer Agency and Simon Fraser University, senior author of the report, explained that this study is the first to establish that while there is high T-cell diversity in a standard blood sample, it does not give the entire picture. "This is only part of the diversity that would be present within a person's entire body," Holt said, "but now we know that although the diversity is very large, it is ultimately limited, and it is measurable."

The group found that some T-cell receptor sequences are common, some are rare, and the repertoire can change over time. The individual repertoire was then compared to that of two other individuals, showing that only a minority of sequences is shared between them.

Interestingly, they noted that for sequences that were shared, different gene shuffling events had often generated the same sequence. "This shows that certain sequences are more favored than others, most likely because they are more effective in recognizing specific types of infections or mutations," said Holt.
By cataloging the baseline diversity of the immune repertoire in a healthy individual, Holt explained that future studies would be able to then recognize how the repertoire is disturbed in cases of immune challenge, such as infectious disease or organ transplantation, and furthermore, may assist in the development of new vaccines.

**Journal Reference:**

### New Finding in Ribosome Signaling May Lead to Improved Antibiotics

ScienceDaily (Feb. 22, 2011) — Researchers at the University of Illinois at Chicago have discovered a signaling mechanism in the bacterial ribosome that detects proteins that activate genes for antibiotic resistance.

"The ribosome is one of the most complex molecular machines in the cell," said Alexander Mankin, UIC professor and director of the Center for Pharmaceutical Biotechnology. It is responsible for the production of all proteins in the cell, and in bacteria it is one of the major antibiotic targets.

Understanding how signals are generated and transmitted within the ribosome, Mankin said, may one day lead to better antibiotics.

Mankin’s research, funded by the National Science Foundation, has been published in the journal *Molecular Cell*.

The ribosome is responsible for activating some antibiotic resistance genes in the presence of certain proteins. For that to occur, special sensors in the ribosome must recognize cellular cues and the structure of the regulatory protein. Once the signal is detected, it is then transmitted to the functional centers which alter the ribosome’s performance.

Mankin’s latest research has found at least one of the signal pathways in the ribosome. He and his coworkers found that the presence of the regulatory protein as it is made within the ribosome changes the properties of the ribosome’s catalytic center.

Under normal conditions, the ribosome’s catalytic center can accept any of the 20 natural amino acids, which are then added to the growing protein chain.

However, if the ribosome has synthesized the regulatory protein in the presence of an antibiotic, the catalytic center rejects some or even all amino acids. As a result, synthesis of the regulatory protein stops, and the genes of antibiotic resistance are activated.

"This is one of the strategies used by pathogenic bacteria exposed to antibiotics to regulate expression of antibiotic resistance genes," Mankin said.

In previous studies, Mankin and his research team pinpointed some of the ribosomal RNA residues that interact with the growing regulatory peptide, thus serving the function of the peptide sensors.

**Journal Reference:**

### Anaemia more likely in infants exposed to maternal ARVs during pregnancy and breastfeeding

Carole Leach-Lemens
Published: 25 February 2011

HIV-uninfected infants born to mothers in Botswana and exposed during pregnancy to maternal antiretroviral treatment were at increased risk for severe anaemia during the first six months of life compared to infants exposed to short-term zidovudine alone, Scott Dryden-Peterson and colleagues reported in an analysis of the Mashi and Mma Bana PMTCT intervention trials published in the advance online edition of the *Journal of Acquired Immune Deficiency Syndromes*.

Formula-fed infants on short-term zidovudine had the lowest risk for anaemia.

The decreased odds, compared to breastfed infants exposed to maternal ART and for those exposed to short-term zidovudine, were 5.8 fold and 2.2 fold, respectively. Observational studies of large cohorts in the United States and Europe had similar findings.

In a separate report on infants born to mothers participating in the two trials Kathleen M Powis and colleagues reported that while lower birth weight was associated with infant exposure to maternal antiretroviral treatment compared to exposure to short-term zidovudine, rapid weight gain within the first three months brought the infants close to the norm for age and gender.
While this is reassuring low birth weight nonetheless is associated with the potential for early infant mortality and/or morbidity, note the authors.

Their findings were published in the February 1 edition of the *Journal of Acquired Immune Deficiency Syndromes.*

Maternal ART during pregnancy and breastfeeding for the prevention of mother-to-child transmission is an effective public health intervention. The World Health Organization (WHO) now recommends ART for all pregnant women with CD4 cell counts of 350 cells/mm$^3$ or lower and as an MTCT prevention strategy in women with higher CD4 cell counts. This is of particular relevance for women in resource-poor settings where formula-feeding may be neither safe nor feasible.

So it is important to look at the potential toxicity of infant exposure to maternal ART during pregnancy, as well as the short- and long-term growth implications for infants. Evidence is limited, especially in resource-poor settings.

Zidovudine and other nucleoside reverse transcriptase inhibitors (NRTIs) are known to cause anaemia in adults and children. Studies in resource-rich settings suggest ART causes mild but reversible anaemia. However, in resource-poor settings malnutrition and limited access to blood transfusions make the risk for, and adverse effects of severe anaemia of critical clinical significance.

Scott Dryden-Petersen and colleagues compared severe anaemia rates among three groups: infants exposed to maternal ART during pregnancy, breastfeeding and one month of postnatal zidovudine (ART-BF); infants exposed to maternal zidovudine during pregnancy, six months of postnatal zidovudine and breastfeeding (ZDV-BF); and infants exposed to maternal zidovudine during pregnancy, one month of postnatal zidovudine and formula-feeding (ZDV-FF).

Among 1719 infants severe anaemia was found in 7.4% (118). By six months 12.5% of the ART-BF group had severe anaemia compared with 5.3% of the ZDV-BF group and 2.5% in the ZDV-FF group.

The authors note the apparent contradiction between their findings and an earlier analysis (Bae et al) is due to small sample size (178 compared to 1719 infants), inclusion of HIV-infected infants and most importantly use of the 1994 version of the DAIDS toxicity table. Exclusion of the HIV-infected infants and use of the 2004 table in the Bae analysis gave similar results to their study.

The authors suggest that timing of exposure to ART or the combination of zidovudine with other antiretrovirals may help explain why those in the ART-BF group had the most severe anaemia. A study in Malawi suggested exposure to ART during pregnancy increased the risk for anaemia.

The types of anaemia found corresponded to iron-deficiency. All mothers in both the Mashi and Mma Bana studies were given iron supplements as part of antenatal care. So ART may affect the absorption of iron from mother to foetus as well as make the infant vulnerable because of nutrient deficiencies and infections, they add.

Limitations include: most of the ART-exposed infants were breastfed so separation of antiretroviral and feeding effects were not possible. There is no way of knowing the effect of antenatal and postnatal ART exposure on anaemia.

The authors note that while these limitations may underestimate the effect of maternal ART on anaemia, conclusive causality between ART exposure during pregnancy and infant anaemia was not found suggesting the need for further study.

Most anaemias were asymptomatic and improved with iron and vitamin supplements and stopping zidovudine.

It is unknown whether anaemia not caused by iron deficiency affects child development. The authors note this warrants further study of the aetiology of anaemia in ART-exposed infants.

Kathleen M Powis and colleagues undertook the first study to compare early growth patterns of breastfed infants after ART or zidovudine exposure during pregnancy.

Growth patterns of 619 ART-exposed and 440 zidovudine-exposed HIV-uninfected infants were analysed.

ART-exposed and zidovudine-exposed infants had mean birth weights (WAZ) of 3.01 kg and 3.15 kg, p<0.01, respectively. All ART-exposed infants had lower length for age (LAZ) and weight for length (WLZ) scores at birth compared to zidovudine-exposed infants.

However, from birth until two months of age ART-exposed infants showed the greatest improvements in weight for age and weight for length. And, from three to six months of age there was no difference in weight for age between the groups.

In the first 28 days of life a study from Tanzania showed that lower birth weight among HIV-exposed infants presented a higher risk for death than HIV transmission. The authors stress that infants exposed
to maternal ART “may benefit from programmes to optimise growth in the first several months of life in an effort to mitigate morbidity and mortality.”

Length for age was lower in ART-exposed infants. The authors note Mma Bana infants will be followed beyond six months allowing for a re-evaluation of morbidity and mortality outcomes.

Limitation include the difference in protocols: zidovudine-exposed infants got zidovudine throughout the six month breastfeeding period, while ART-exposed infants got zidovudine for four weeks.

The authors conclude “this analysis is the first to provide reassurance that lower birth weight associated with in utero ART-exposed infants does not persist during early infancy. It also highlights [as does the analysis by Dryden-Peterson and colleagues] the importance of early and routinely scheduled health care for ART-exposed HIV-uninfected infants.”

References

Major fraud suspected with HIV drugs *****
Published: 24 Feb 11 08:22 CET
Online: http://www.thelocal.de/national/20110224-33315.html

German federal police and prosecutors are investigating suspected large-scale fraud around HIV medicines, according to public broadcaster NDR. Wholesalers allegedly sold subsidized medicines meant for Africa for huge profits in Germany.

Investigators are probing several pharmaceutical wholesalers, NDR reported on Thursday, who are suspected of repackaging HIV drugs in Africa, bringing them back to Germany and reselling them at local market rates.

According to investigators, the HIV drugs were often in the form of loose pills in cartons and sacks that were destined for HIV patients in South Africa, which has one of the world’s highest rates of HIV infection. After the medicines were repackaged, they were brought to Germany illegally via Belgium and Switzerland.

"Because South Africa, Switzerland and Belgium as well as other countries are involved, this case is surely going to be one of our biggest," Rüdiger Meienburg, the head prosecutor in Flensburg, told NDR.

According to NDR, one wholesaler allegedly made around €6 million in profits from the trade. In addition to Flensburg officials, prosecutors in Trier and Lübeck have launched investigations and Germany’s federal police have also become involved.

This kind of fraud, according to the Flensburg office, can carry jail terms of three months to ten years.

"These medicines were from aid organizations for treatment of South Africans and the wholesalers brought them to Germany although they were not approved here,” the Lower Saxony spokesman for the AOK health insurance company, Oliver Giebel, told NDR. He said health insurers likely lost tens of millions of euros due to the fraud.

Investigators do not think the effectiveness of the medicines was lowered due to their transport and repackaging, although they are looking into whether some had passed their expiration dates.

"In this case, wholesalers were not only enriching themselves through criminal means, but they were hurting the people who were supposed to receive these drugs," said pharmaceutical expert Gerd Glaeske of the University of Bremen.

"That’s especially reprehensible," he added.

Drug R&D costs are less than estimated – so why the high prices?
ANDRE PICARD | Columnist profile | E-mail
From Thursday’s Globe and Mail
Published Wednesday, Feb. 23, 2011 3:26PM EST
Last updated Thursday, Feb. 24, 2011 11:02AM EST
It costs, on average, $1.3-billion (U.S.) in research and development to bring a new drug to market. That level of investment in R&D by Big Pharma justifies the high cost of prescription drugs.
Those statements are repeated so often that they have come to be accepted as fact.
But are they fact or fiction?
An article in the current edition of the journal BioSocieties, a publication of the London School of Economics, argues that the real cost of R&D is, in fact, a fraction of the commonly cited estimate and we are having the wool pulled over our eyes.

The authors – Donald Light, professor of comparative health care at the University of Medicine and Dentistry of New Jersey in Newark, N.J., and Rebecca Warburton, a health economist at the University of Victoria – have returned to the source of the original estimate and deconstructed it.

Here is the Coles Notes version of their detailed analysis.


It concluded that the mean R&D cost for a new drug was $802-million in the year 2000. (The Pharmaceutical Research and Manufacturers of America, or PhRMA, later “updated” this figure to $1.32-billion in 2006 dollars.) Let’s look at how they arrived at the final figure.

The researchers asked 24 large drug companies to submit R&D costs for “self-originated new chemical entities” – essentially new drugs developed in-house. Ten companies did so but on the condition that the data be kept confidential, meaning we don’t know what companies or what drugs were included, or what exactly is included in R&D.

The researchers estimated that the “cost of discovery” – the time from the synthesis of a drug to animal testing – at $120.9-million. The larger cost was clinical trials, testing the safety and effectiveness of a new drug in humans, at $281.9-million. Add the two and you get the total “average out-of-pocket per new drug”: $402.8-million.

Then Dr. DiMasi and his team calculated the “cost of capital” – essentially what this money would have earned if it had been invested in the stock market instead of in R&D. They used an annual return on investment of 11 per cent.

Applied over the time it takes for clinical trials and regulatory review – 72 months and 18 months respectively – that cost of capital brought the total R&D cost to $802-million.

The original paper said that it took an average 11.8 years to get a drug to market, including 52 months of preclinical research and the aforementioned 90 months for trials and regulatory approval.

Now, let’s look at the critique, or what Dr. Light and Dr. Warburton dub “demythologizing the high cost of pharmaceutical research.”

First, they note that drug companies have “tightly controlled access to verifiable facts” so there is no way of independently confirming their numbers. So let’s assume they are essentially correct but analyze them through a prism of publicly available data.

First, there are not many novel drugs developed. Between 1990 and 2000 only 35 per cent of “new drugs” were actually new chemical entities (NCEs), according to the U.S. Office of Technology Assessment. Most new products are reformulations or recombinations of existing drugs – “me too” drugs in common parlance. Only 22 per cent of drugs developed in-house by pharmaceutical companies are NCEs.

That means the $802-million is, at best, an estimate of the R&D cost of the costliest one-fifth of drugs, not all drugs. The cost of “me too” drugs is necessarily a lot less.

The eyebrow-raising aspect of the original cost calculation is the whopping “cost of capital.” While “costs forgone” is a legitimate calculation for accountants, the accepted standard is to assume an annual return on investment of 3 per cent in the United States and 5 per cent in Canada – not the 11 per cent used in the original cost calculation.

The “cost of capital” is massive because of the length of time it takes to get a drug to market. But the new paper suggests those estimates are off too.

According to the U.S. Food and Drug Administration Register, drug trials last, on average, 36 months, not 72 months, while regulatory review takes less than 12 months on average, not 18 months.

(The original study also said clinical trials involved 5,303 patients on average at a cost of $23,572. According to the U.S. National Institutes of Health, the average trial involves half that number at an average cost of $3,861.) Another controversial figure is the 52 months allocated for preclinical research; that number is virtually impossible to calculate – not to mention that basic research is often done in universities and government-sponsored labs. Yet it accounts for fully one-third of the $802-million estimate.

Finally, the new analysis notes that there are generous tax breaks for R&D and those were left out of the cost calculation. “A reasonable guess is that half of corporate R&D expenses are paid for by taxpayers over the long term,” the authors write.
So, what do you get when you crunch all those numbers?
According to Dr. Light and Dr. Warburton, the net median R&D cost of developing a prescription
drugs varies from $13-million to $204-million, depending on the kind of drug.
Over all, they estimate R&D costs $59.4-million for each new drug.
That is a far cry from $802-million or $1.3-billion.
Consumers who use prescription drugs, and the drug plans that are the principal purchasers, need to
start questioning the “facts” and asking some tough questions.
If R&D costs are only a fraction of what is asserted, then what is the justification for high prescription
drug prices?
Somebody got some ‘splainin’ to do.

HIV makes protein that may help virus’s resurgence
Children’s Hospital of Philadelphia study sheds light on how HIV takes over cell cycle
New research enhances the current knowledge of how human immunodeficiency virus type-1 (HIV-1),
which causes AIDS, controls the cell cycle of cells that it infects. The new findings may shed light on how
the virus reactivates after entering a dormant state, called latency.
"As we better understand the biological events that revive HIV from latency, we hope to devise ways
to eventually intervene in this process with better treatments for people with HIV infection," said study
leader Terri H. Finkel, M.D., Ph.D., chief of Rheumatology at The Children’s Hospital of Philadelphia.
Finkel is the senior author of a study published in the Jan. 27 issue of the journal Blood. The first author,
also from Children’s Hospital, is Jiangfang Wang, M.D., Ph.D.
Viral latency is one of the persistent problems in treating HIV infection. Current combinations of anti-
HIV drugs can reduce HIV to undetectable levels, but the virus hides in latently infected cells in a sort of
hibernation. If a patient stops taking medication, or is weakened by a different infection, HIV can make a
resurgence out of its viral reservoirs, often becoming resistant to previously effective drugs.
The current study focused on a protein, Vif (for viral infectivity factor), that HIV-1 produces. Finkel
and colleagues previously discovered that Vif causes HIV-infected cells to stop growing at one phase of the
cell cycle, the G2 phase. The study team has now found that Vif also acts at an earlier stage in the cell
cycle, driving cells out of the G1 phase and into the more active S phase.
This activity may be important, said Finkel, because G1 is a resting phase, and a biological interaction that
"wakes up" a latent infected cell may reactivate the infection. Other viruses that have a latent infectious
state, such as the herpes virus and the Epstein-Barr virus, also express proteins that drive a transition
from G1 to S phase. "By regulating the cell cycle, viruses control their infectivity," said Finkel.
The researchers carried out their work in HeLa cells, a human cell line long used in cell studies, as
well as in human T cells, immune cells found in the blood. They identified two proteins, Brd4 and Cdk9,
which interact with Vif. This interaction was a new discovery, although the proteins were already known
to regulate the progression of the cell cycle.
Identifying Vif’s cellular partners may also implicate them as potential targets for therapy. "If we can
interrupt the activity of Brd4 or Cdk9, we may be able to prevent latent infection from becoming active," said Finkel. "Alternatively, by harnessing Brd4 or Cdk9, we may be able to drive cells out of latency and
make the virus susceptible to anti-HIV drugs." She added that early preclinical testing of inhibitors is getting under way for other conditions, but cautioned that it is too early to foresee whether, or how soon, her research findings will lead to clinical treatments for HIV.

US May Pay for Sex Disease Tests for Elderly
Reuters, (02.24.2011) Susan Heavey
The Centers for Medicare and Medicaid Services (CMS) announced Thursday it is mulling the inclusion of
certain STD tests for seniors and the disabled. Medicare currently covers HIV testing, but may include
screening for diseases like syphilis and hepatitis B in its push toward preventive treatment.
Life expectancy in the United States has increased—approximately 39 million Americans age 65 or
above are insured by Medicare, along with 7.6 million disabled—and studies show larger numbers of the
elderly are sustaining active sex lives.
According to public health officials, early STD detection and prevention lowers costs by circumventing
problems stemming from postponed care, as well as the transmission of disease to others.
CMS has been able to provide preventive coverage since 2009, and already includes pap smears, pelvic exams, and screening for colorectal cancer and diabetes. Most STD tests under consideration are for women and some are particularly for pregnant women, who are included in Medicare’s disabled beneficiaries.

Medicare is deliberating including examinations for:
- chlamydia in sexually active or pregnant women 24 and under, or for older sexually active or pregnant women at higher risk.
- gonorrhea in all sexually active or pregnant women at increased risk.
- hepatitis B in pregnant women.
- syphilis in all males and females at high risk.
- intense behavior modification therapy for sexually active youth and adults at high risk for STDs.

**HIV Infection Can Cause Faster Aging of T-cells**

**SUMMARY:** Chronic HIV infection appears to speed up aging of CD4 T-cells by as much as 20-30 years, according to research published online January 26 in the open access journal *PLoS ONE.* Compared with HIV negative individuals, HIV positive people had shortened telomeres at the ends of T-cell chromosomes, which leads to poor function and cell death. Immune system aging may help explain the higher rates of chronic age-related conditions such as cardiovascular disease seen among people with HIV.

Below is a press release from the University of California at Los Angeles describing the study and its findings.

**Research Suggests HIV Causes Rapid Aging in Key Infection-Fighting Cells**

Los Angeles, CA—January 26, 2011—In the early years of the AIDS epidemic, being infected with the virus that causes the disease was considered a virtual death sentence. But with the development of antiretroviral therapy, many with HIV are now living much longer. In fact, it is estimated that by 2015, about half of all HIV-positive individuals will be older than 50.

Yet those over 50 also progress to AIDS faster than adults in their 20s or 30s. And those in the younger age bracket—even those responding well to antiretroviral therapy—still exhibit illnesses and clinical conditions commonly associated with older people, such as certain cancers and liver diseases. For the most part, the reasons for this have remained a mystery.

But a UCLA AIDS Institute study published Jan. 26 in the online journal PLoS ONE suggests a partial explanation, showing that HIV causes a specific subset of CD4+ "helper" T-cells—which play an important role in the body's response to infection—to age rapidly, by as much as 20 to 30 years over a three-year period.

In the study, researchers witnessed a decline in CD4+ T-cell numbers and, most strikingly, found that in the surviving T-cells, the HIV virus caused rapid and drastic shortening of the ends of chromosomes, called telomeres, which protect the chromosomes and prevent them from fusing together, much like plastic tips keep shoelaces from unraveling. Telomeres become progressively shorter during natural cell division; when they become too short, cells do not function properly.

"Our findings have important implications for the health of both young and old HIV-1-infected adults," said lead investigator Tammy M. Rickabaugh, an assistant research immunologist in the division of hematology and oncology at the David Geffen School of Medicine at UCLA. "They underscore the importance of developing new approaches to boost immune function to complement current treatments, which are exclusively directed against the virus."

The researchers examined two subsets of CD4+ T-cells (CD45RA+ CD31+ and CD45RA+ CD31-), in two groups of individuals—those aged 20-32 and those aged 39-58—who had been infected with HIV for one to three years and who had not previously been treated with antiretroviral therapy. They compared these two groups with samples from age-matched controls who were HIV seronegative.

The researchers specifically focused on "naive" T-cells—those that had not previously encountered any pathogens and thus act as a reserve against future infections and cancers. They found that in individuals infected with HIV-1, these cells underwent unexpectedly rapid aging—the equivalent of 20 to 30 years of aging within three years of infection. They also found that the number of CD31- T-cells, which are more quickly pulled into the fight against new pathogens, had fallen drastically.

The researchers also investigated whether appropriate treatment could reverse this aging effect. They examined cells from HIV-positive individuals who had been on antiretroviral therapy for two years and whose therapy had successfully kept HIV-1 under control. They found that while the therapy kept their
viral loads at undetectable levels, it did not entirely restore their immune systems, suggesting a reason why younger HIV-positive people still become ill with conditions more common to older people.

"Taken together, our results help to explain some of the clinical observations that have been documented in HIV-infected people and emphasize the need for developing therapeutic approaches directed at improving the naive immune cell compartment," said senior investigator Beth D. Jamieson, an associate professor of medicine in the division of hematology and oncology at the David Geffen School of Medicine at UCLA. "This is critically important in light of the demographic shift of HIV-infected persons."

Grants from the National Institute of Allergy and Infectious Diseases; the National Institute on Aging; the National Cancer Institute; the National Heart, Lung and Blood Institute; UCLA's Jonsson Comprehensive Cancer Center; the UCLA AIDS Institute; and the David Geffen School of Medicine at UCLA funded this study.

The UCLA AIDS Institute, established in 1992, is a multidisciplinary think tank drawing on the skills of top-flight researchers in the worldwide fight against HIV and AIDS, the first cases of which were reported in 1981 by UCLA physicians. Institute members include researchers in virology and immunology, genetics, cancer, neurology, ophthalmology, epidemiology, social sciences, public health, nursing and disease prevention. Their findings have led to advances in treating HIV, as well as other diseases, such as hepatitis B and C, influenza and cancer.

Reference

Can Statins Reduce Inflammation in People with HIV?

**SUMMARY:** Statin medications such as atorvastatin (Lipitor), usually used to lower blood cholesterol, may also reduce immune activation in HIV-positive people, according to a small study described in the March 15, 2011, *Journal of Infectious Diseases*. Reducing immune activation and inflammation may decrease the risk of chronic non-AIDS conditions such as cardiovascular disease, but a much larger study will be required to demonstrate clinical benefits.

By Liz Highleyman

There is now substantial evidence that excessive immune activation and chronic low-level inflammation triggered by persistent virus may help explain the higher risk of cardiovascular disease, neurocognitive dysfunction, and other non-AIDS conditions seen in people with HIV, even while CD4+ T-cell counts remain high. Large studies including SMART and FRAM have found that elevated levels of inflammation biomarkers are associated with increased risk of death, progression to AIDS, and non-AIDS conditions.

In the present study, Anuradha Ganesan from the National Naval Medical Center and colleagues conducted a randomized trial to investigate the effects of atorvastatin on viral load and cellular markers of immune activation among HIV-positive people who were not on antiretroviral therapy (ART).

Statins—also known as HMG-CoA reductase inhibitors—were developed and approved for reducing LDL "bad" cholesterol in the blood, but more recent research has shown that they also reduce inflammation throughout the body. A few studies have suggested that statins may suppress HIV replication and lower viral load, but data are conflicting.

Ganesan’s group analyzed 24 participants who were randomly assigned to receive either 80 mg atorvastatin or placebo each day for 8 weeks. Then, after a 4-6 week "washout" period, they switched to the other treatment assignment.

All participants were men, 63% were white, and they were relatively young, with a median age of 30 years. They had CD4+ cell counts above 350 cells/mm³ and none were on ART. Their LDL cholesterol levels were below the usual threshold for using statins (< 130 mg/dL). All but 2 patients completed the study.

The researchers measured HIV RNA levels as well as immune activation, indicated by expression of CD38 and HLA-DR surface markers on CD4+ and CD8+ T-cells. They did not, however, measure inflammation biomarkers such as C-reactive protein.

**Results**

- HIV RNA levels did not change significantly overall during either the atorvastatin or placebo phases of the study.
- People taking atorvastatin showed a significant reduction in proportions of CD4+HLA-DR+, CD8+HLA-DR+, and CD8+HLA-DR+CD38+ T cells (-2.5%, -5%, and -3%, respectively), which was not seen among placebo recipients.
Reductions in immune activation did not correlate with decreases in blood levels of LDL cholesterol.

Participants who had the largest reductions in immune activation, however, also saw the greatest declines in viral load.

Based on these findings, the investigators concluded, "Short-term use of atorvastatin was associated with modest but statistically significant reductions in the proportion of activated T lymphocytes."

While this study was not large enough and not designed to demonstrate a clinical benefit, the authors said that understanding the mechanisms by which statins influence immune activation markers may suggest new approaches for managing inflammation and its detrimental effects in people with HIV. They noted, however, that it will be important to also study the effects of statins in people on ART with undetectable viral load.

In an accompanying editorial, Andrew Carr from St. Vincent’s Hospital in Sydney speculated that other statins besides atorvastatin are unlikely to suppress HIV.

He recommended that this class of drugs should be further assessed in larger and longer trials to evaluate their effects on HIV-related inflammation, but acknowledged that "[a] very large study would probably be required to determine whether the potentially positive effects of statin therapy on inflammatory markers will translate into less HIV disease progression and fewer cases of inflammatory non-AIDS-related illnesses, such as cardiovascular disease and end-stage liver disease."

References

Inflammation Linked to Higher Mortality Even for People with High CD4 Cell Counts

SUMMARY: Inflammation was associated with an increased risk of death among HIV positive participants in the FRAM study, according to a report in the November 1, 2010 Journal of Acquired Immune Deficiency Syndromes Inflammation. People with the highest levels of 2 inflammation biomarkers—fibrinogen and CRP—had more than 2.5-fold higher mortality than those with the lowest levels. Inflammation remained a predictor of mortality even among people with CD4 counts above 500 cells/mm³.

By Liz Highleyman
A growing body of evidence suggests that chronic inflammation triggered by persistent virus may help explain the higher rates of cardiovascular disease, neurocognitive dysfunction, and other chronic conditions seen in people with HIV—even those with high CD4 T-cell counts and well-preserved immune function.

To further explore this issue, Phyllis Tien, Carl Grunfeld, and fellow investigators with the FRAM (Fat Redistribution and Metabolic Change in HIV Infection) study looked at the association between levels of 2 inflammatory markers, fibrinogen and C-reactive protein (CRP), and 5-year mortality risk.

Fibrinogen and CRP are acute-phase proteins released as part of the inflammation and clotting cascade that occurs with development of atherosclerosis, or blood vessel narrowing that can lead to heart attack or stroke.

The analysis included 922 HIV positive FRAM participants. A majority (about 70%) were men, the median age was 42 years, and 40% were current smokers. Most (about 90%) had used antiretroviral therapy (ART), about 80% had undetectable viral load, and the average CD4 cell count was about 350 cells/mm³. Participants were followed for 5 years.

Results
- Participants with fibrinogen levels in the highest tertile or third (> 406 mg/dL) had a 2.6-fold higher risk of death than people with levels in the lowest tertile (< 319 mg/dL).
- Participants with high CRP (> 3 mg/L) had a 2.7-fold higher risk of death than those with CRP < 1 mg/L.
- When stratified according to CD4 count, fibrinogen remained independently associated
with increased mortality, with the greatest effect seen among people with the lowest counts:

- < 200 cells/mm³: odds ratio 1.93, or nearly twice the risk of death;
- 200-350 cells/mm³: odds ratio 1.43;
- 351 to 500 cells/mm³: odds ratio 1.43;
- > 500 cells/mm³: odds ratio 1.30.

Higher CRP remained associated with higher risk of death overall and within each CD4 count subgroup.

Based on these findings, the study authors 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 researchers noted in their discussion that these findings support the observations from the SMART trial, which found that higher levels of the inflammation biomarkers CRP, interleukin 6 (IL-6), and D-dimer were associated with greater risk of death, progression to AIDS, and non-AIDS conditions such as cardiovascular, kidney, and liver disease.

"The strength of our study was the wide spectrum of CD4 levels in our participants, which allowed us to examine the effect of immunosuppression severity on the association of inflammation with mortality," they wrote. "As expected, we found that the [odds ratio] for mortality associated with fibrinogen and CRP was greatest in magnitude for those with CD4 < 200. However, more important is our finding that higher fibrinogen and CRP levels remained associated with increased mortality risk in participants with CD4 > 500."

2/25/11

Reference

**Infecting Mosquitoes With Genetically Altered Fungus Curbs Malaria Parasite**

By Rebecca Boyle  Posted 02.25.2011 at 11:53 am

To combat malaria, why not skip the step of genetically altering mosquitoes and try some transgenic fungus instead? In a new study, researchers sprayed mosquitoes with a fungus that had been modified to deliver compounds that target the malaria parasite. They found the treatment could reduce disease transmission to humans by at least five-fold.

Researchers at the University of Maryland, who were funded by the National Institutes of Health/National Institute of Allergy and Infectious Diseases, say the method could be an effective treatment against malaria, especially as mosquitoes increasingly evolve to resist insecticides. Even better, the fungus modification can be targeted to almost any disease-carrying insect, potentially allowing fungus-based prevention for maladies like Lyme disease or dengue fever. The study was reported today in the journal Science.

The *Metarhizium anisopliae* fungus naturally attacks mosquitoes, and it has already been used to reduce disease transmission — but it only works if the bugs are sprayed with fungus soon after they picked up the malaria-causing *Plasmodium falciparum* parasite. What’s more, the mosquitoes often die before reproducing, leaving fungus-resistant mosquitoes to take over and render the spray useless. So rather than enhance fungi to better kill mosquitoes, entomology professor Raymond St. Leger and colleagues modified the fungi to block the development of *Plasmodium* in the mosquito.
They used genes for a human antibody and a scorpion toxin, both of which specifically target *Plasmodium*, and inserted them into the fungus. They fed some mosquitoes a *Plasmodium*-infected blood meal, and separated them into three groups. One group got a dose of the transgenic fungus, another got a natural fungus and the third was not sprayed at all. Two weeks after the bugs were exposed to the malaria parasite, the researchers checked for its presence in their salivary glands (this is how it’s transmitted to humans).

Spraying mosquitoes with the transgenic fungus significantly reduced parasite development, the team found.

Malaria is found in 106 countries and there are an estimated 225 million malaria cases every year, including 781,000 deaths, mostly in sub-Saharan Africa. Prevention usually involves spraying bed nets and interior walls with pyrethroid insecticide to kill the mosquitoes, but the bugs are evolving to resist it, and there are no promising prospects for a chemical replacement.

Other teams have genetically altered mosquitoes to resist *Plasmodium*, and modified other mosquitoes to be sterile in order to reduce their populations. But transgenic mosquitoes could pose some ecological problems. A fungal treatment can be modified to keep up with mosquitoes’ natural adaptations, St. Leger said.

“Mosquitoes have an incredible ability to evolve and adapt, so there may be no permanent fix. However, our current transgenic combination could translate into additional decades of effective use of fungi as an anti-malarial biopesticide,” he said.

**Five years on from circumcision trial, nine in ten participants are circumcised and HIV incidence is two-thirds lower**

Gus Cairns
Published: 28 February 2011

Five years after the ending of one of the three big randomised controlled trials of male circumcision as an HIV prevention measure, four out of five men who were in the control arm of the trial and thus not circumcised have opted to get circumcised, a follow-up study presented to the 18th Conference on Retroviruses has found.

The study also found that, if anything, the protective effect ascribed to circumcision appears to have strengthened over time.

The post-trial analysis was conducted on the randomised controlled trial of male circumcision as an HIV prevention measure conducted in Rakai, Uganda, in 2005-6 (Gray 2007). In this study 4996 HIV-negative men aged 15 to 49 were randomised either to be immediately circumcised or to be offered circumcision at the end of the trial.

The study was designed to last two years but was terminated early in December 2006 when it was found that HIV infections were just under half as common (efficacy, 51%) in men who had been randomised to be circumcised compared with men in the control group.

Later analyses showed that this efficacy underestimated the true effectiveness of circumcision. The HIV infection rate in men who actually got circumcised was 58-60% lower than in men who remained uncircumcised, and 70% lower in men with high numbers of partners.

Dr Xiangrong Kong of Johns Hopkins University told the conference in Boston that by the end of the fifth year after the study ended just over 80% of the control group, who had not been circumcised during the trial, had opted for circumcision and, out of 2916 men who were uncircumcised at the last scheduled visit during the trial, only 372 men now remained uncircumcised. Including the intervention group and excluding those lost to follow-up, 90% of those who entered the study had been circumcised.
Looking at men who were not circumcised during the trial, HIV incidence in men who got circumcised, in the post-trial period was one infection per 181 men per year after circumcision (0.55%), and in men who remained uncircumcised one infection per 60 men a year (1.67%). Circumcision was thus 68% effective. If the trial period was included this made very little difference and efficacy still stood at 67%.

If the men who got circumcised during the trial were included, then the overall efficacy of circumcision over the whole period from the start of the study was 73%.

There are data on sexual behaviour for the first 2.8 years since the end of the trial. Before the trial, there had been concerns that circumcision might produce behavioural disinhibition in men and an increase in unsafe sex, especially once men knew circumcision worked.

In the original trial, 18% of participants reported consistent condom use during the trial and 52% did not use them at all. During the follow-up period, condom use declined by 4.3% in consistent condom users to 13.5% and the proportion who never used them increased by 6% to 58.2%.

But there was no difference in decreases in condom use between circumcised and uncircumcised men, and in fact condom use levels now are almost exactly what they were at baseline before the start of the study. The declines in condom use therefore probably reflect reduced availability of condoms and safer sex advice post-trial, rather than any disinhibiting effect of circumcision.

There was no change in the number of non-marital sexual partners, and a 9.4% decrease in the number of men who reported alcohol use during sex, again with no difference between circumcised and uncircumcised men.

These findings are remarkably similar to a post-trial analysis 3.5 years after the end of one of the other two circumcision efficacy trials, in Kisumu, Kenya, presented at the 2008 International AIDS Conference, which found a long-term efficacy of 65% for circumcision and no increase in risk behaviour.

References

West Virginia Only State to See Increase in Teen Pregnancy Rate
Charleston Gazette (W.V.), (02.18.2011) Veronica Nett

The US teen birth rate hit a historic low from 2007 to 2009, but during that timeframe West Virginia’s rate increased by 17 percent, CDC data show.

“The data from CDC is a wake-up call,” said Margaret Chapman Pomponio, executive director of the reproductive rights group WV FREE. “Where [West Virginia] falls short is a lack of a comprehensive approach to sex education,” she said. “We know there is no consistency from county to county and even from school to school.”

A 2008 CDC School Health Profile found that one in every four high schools in the state did not offer education on STD and pregnancy prevention; just over 70 percent of middle schools addressed these topics.

Chapman Pomponio said the state’s high teen pregnancy rate places burdens on communities. “Young mothers have the worst birth outcomes of any age group,” she noted. Teen parents are more likely to drop out of school, remain unmarried, and live in poverty, according to the National Campaign to Prevent Teen and Unplanned Pregnancy.

A 2010 study by the Marshall University Center for Business and Economic Research found state costs of teen pregnancy include: $11 million for public health, $14 million for child welfare, $4 million for incarceration, and $16 million in lost tax revenue.

In October, the non-profits Children’s Home Society of West Virginia and Mission West Virginia Inc. received nearly $2 million in federal grants to provide sex education programs. Chapman Pomponio said she supports “common-sense” programs that incorporate abstinence messages with information about pregnancy and STD prevention, and are “realistic about youth behavior.”

“Now is West Virginia’s chance to show that we care about our youths’ future, and we can work together toward a comprehensive approach to education,” said Chapman Pomponio.
AIDS Gel Shown to Protect Anal Tissue from HIV

*Reuters*, (02.28.2011) Deena Beasley

New research presented at the 18th Conference on Retroviruses and Opportunistic Infections (CROI) in Boston, Feb. 27–March 2, shows that a gel containing tenofovir may help prevent HIV when used rectally.

The gel containing Gilead Sciences Inc.’s AIDS drug has been previously shown to sharply reduce HIV infection in women when used vaginally. The HIV transmission risk from unprotected anal sex may be more than 20 times greater than unprotected vaginal sex, partly because the rectal lining is just one-cell thick compared to the vagina’s multiple cell layers. Thus, HIV can more easily reach cells to infect, said researchers from the University of California-Los Angeles (UCLA) and the University of Pittsburgh.

Dr. Peter Anton, director of the Center for Prevention Research at UCLA, and colleagues studied rectal tissue biopsies from HIV-negative men and women who used the tenofovir gel or a placebo gel daily for one week. Tissue samples were sent to a laboratory where they were exposed to HIV. The samples showed HIV was significantly blocked in participants using the tenofovir gel compared to those using the placebo. An oral dose of tenofovir did not appear to provide protection against HIV.

While the tenofovir gel was found to be generally safe, two participants reported severe gastrointestinal side effects, including diarrhea and lower abdominal cramping. In addition, the researchers are reformulating the gel to make it less harmful to the rectum. It is hoped that a formulation that uses less glycerin, an additive common in many gel-like products, will be better tolerated.

Results from a separate, mid-stage study comparing oral and gel forms of tenofovir presented at CROI found daily use of tenofovir gel resulted in a more than 100-times higher concentration of active drug in vaginal tissue compared with the oral drug. However, the daily tablet was associated with a 20-times higher active drug concentration in blood.

That study, led by Dr. Craig Hendrix, a professor of medicine and pharmacology at Johns Hopkins School of Medicine, included US and African women. Most US women in the trial preferred the oral tablet, while African women favored the gel and tablet equally; many reported the gel enhanced sexual pleasure, according to the researchers.

“How the differences between the gel and the tablet will translate in terms of protective effect, we can’t say just yet,” said Hendrix.

Effects of Self-Esteem and Academic Performance on Adolescent Decision-Making: An Examination of Early Sexual Intercourse and Illegal Substance Use

*Journal of Adolescent Health* Vol. 47; No. 6: P. 582-590, (12.2010) Stephanie B. Wheeler, MPH, PhD

The current study sought “to determine whether higher self-esteem and higher academic performance among youths reduce the likelihood of early sexual intercourse and illegal substance use.”

Multivariate logistic regression, stratified by gender and controlling for known covariates, was used to assess data from waves one through three of the National Longitudinal Study of Adolescent Health. Relationships were examined between self-esteem and academic performance and youth decision-making, in particular self-reported initiation of sexual intercourse and use of illegal substances. “Self-esteem was constructed as an ascending scale of 10 Likert-scaled survey items. Academic performance was assessed using the most recent grades from English, Math, Science, and History,” wrote Wheeler.

Among virginal adolescents, higher self-esteem at baseline had no effect on sexual debut in the following year, though a baseline higher self-esteem among females did correspond with a significantly lower likelihood of illegal substance use one year later (odds ratio, .96; p=.003). In terms of academic performance at baseline, girls averaging “A” grades were significantly less likely to initiate sexual intercourse one year later as compared with girls receiving grades “C” or lower (OR, .52; p=.004). In addition, for girls, being an “A” or “B” student was associated with lower odds of illegal substance use, compared with students who averaged “C” grades or lower (p<.01). Self-esteem and academic performance were not significantly predictive of illegal substance use among young males.

“This study suggests that bolstering self-esteem and improving academic performance among young girls may have specific benefits in sexual decision-making and substance-related risk-taking,” Wheeler concluded.

Research opens door to vaccines that can circumvent maternal antibodies

COLUMBUS, Ohio – New research that reveals how maternal antibodies block an immune response to the measles virus is a first step toward improving current childhood vaccination practices, scientists say.
Maternal antibodies are passed to fetuses during pregnancy and to newborns in their mothers’ milk. The antibodies protect infants against disease in the first months of life, but that protection comes at a cost: Their presence also interferes with the generation of a natural immune response to vaccination. As a result, most babies receive measles immunizations at the age of 12 to 15 months, when maternal antibodies are gone.

Years of studies have advanced the theory that maternal antibodies shield the measles virus so that cells that generate an immune response can’t see the pathogen. If that were the case, little could be done to intervene.

But Ohio State University researchers have demonstrated an entirely different mechanism in an animal model, showing that maternal antibodies bind to a specific receptor that sends a message to stop activation of an immune response to vaccination. The scientists also determined that signals to the immune response can be manipulated, and they are already devising ways that vaccines could be designed to circumvent this natural process.

"In effect, we have found how maternal antibodies affect the off-switch in the immune response, and we have found a potential on-switch," said Stefan Niewiesk, associate professor of veterinary biosciences at Ohio State University and senior author of the study.

The research is published in the online First Edition of the journal Blood.

Under current pediatric practices, children receive measles vaccinations at age 12 to 15 months, and again when they are 5 years old. Maternal antibodies can be active in babies for up to nine months; this schedule is designed to offer protection after the decline of maternal antibodies.

"The maternal antibodies are high at birth, and go down over time. By age 1 year, the maternal antibodies are gone. So this vaccine schedule works quite well if protection is not so urgent. But there is a window of opportunity for measles to come in and infect. So we would like to be able to immunize earlier," said Niewiesk, also an investigator in Ohio State’s Center for Microbial Interface Biology.

Niewiesk has been a leader in developing the cotton rat as an animal model for infectious diseases. The animal is susceptible to common human pathogens that affect the respiratory system, and Niewiesk's lab has developed antibodies and other substances that help to evaluate the immune response, which is similar to that found in humans.

As a result, researchers around the world have consulted with Niewiesk for years, using the animals to test vaccine candidates. Often, the experimental vaccines do not work in the presence of maternal antibodies. And even for the one vaccine that did work, the researchers couldn’t explain why at the time.

So Niewiesk changed direction, setting aside vaccine testing and instead studying how the maternal antibodies influence the immune response to an antigen — in this case, the measles virus. With this new information, he and colleagues now have better information to guide the design of a measles vaccine that will be effective even while maternal antibodies are present.

In a normal immune response, white blood cells known as B cells grow and release antibodies that are prepared to fight a specific invader, known as an antigen. The B cells are called to action by B cell receptors on their surface; when the antigen binds to these B cell receptors, the cells get the message to proliferate and then secrete antibodies that are made strictly for the task of fending off the attacking virus.

But the Ohio State researchers determined that when maternal antibodies are active, and then an antigen comes along, their presence triggers a different receptor on the B cell surface — a receptor known as Fc-gamma RIIB. And because this particular receptor's job is to regulate the immune response, preventing it from going out of control, the receptor tells the B cell to stop — don’t grow, and don’t secrete antigen-specific antibodies.

"The problem is that maternal antibodies come in, and will go away, but this Fc receptor doesn't know it. The receptor reacts — 'Hey, there is antibody already, let's not make too much of an immune response.' This binding leads to a negative signal, and it blocks the receptor's positive signal to the B cell," Niewiesk said.

Further investigation of the multiple signals received by B cells suggests that there are ways to work around this effect that the maternal antibodies have on the immune response, said Dhohyung Kim, first author of the paper and a doctoral candidate in Ohio State’s graduate program in Molecular, Cellular and Developmental Biology.

Maternal antibodies are immunoglobulin G (IgG) molecules, a designation based on their structure, and IgG antibodies are among the most potent players in the immune response. In this current work, Kim showed that another type of antibody, an immunoglobulin M molecule, can be used with a measles vaccine and that these IgM antibodies can activate B cells, even when maternal antibodies are present.
The IgM antibodies bind to yet another type of receptor on the B cell surface, Niewiesk explained. "So we are looking at the various ways B cells are being activated, and we already see that we can improve the positive signal to B cells by stimulating them with IgM antibodies," he said.

As part of the study, the researchers disproved the previous theory about how maternal antibodies work — a process called epitope masking. This theory suggested that maternal antibodies would bind to specific areas on the measles virus needed for immune response recognition — called epitopes — and effectively shield the virus so that B cells could neither see the virus nor activate an immune response.

Niewiesk said the scientists knew that the measles virus surface has numerous epitopes, making it highly unlikely that maternal antibodies could block so many different areas of recognition on a single virus. In addition, they showed that suppression of the immune response did not occur if maternal antibody structures were manipulated to prevent them from binding to the Fc-gamma RIIB receptor. That meant that this Fc receptor was key to the mechanism that allowed maternal antibodies to suppress the immune response.

Placebo Effect Works Both Ways: Beliefs About Pain Levels Appear to Override Effects of Potent Pain-Relieving Drug
ScienceDaily (Feb. 27, 2011) — Poor expectations of treatment can override all the effect of a potent pain-relieving drug, a brain imaging study at Oxford University has shown.

In contrast, positive expectations of treatment doubled the natural physiological or biochemical effect of the opioid drug among the healthy volunteers in the study.

The study of the placebo effect—and its opposite the nocebo effect—is published in Science Translational Medicine. The findings suggest that doctors may need to consider dealing with patients' beliefs about the effectiveness of any treatment, as well as determining which drug might be the best for that patient.

'Doctors shouldn't underestimate the significant influence that patients' negative expectations can have on outcome,' says Professor Irene Tracey of the Centre for Functional Magnetic Resonance Imaging of the Brain at Oxford University, who led the research. 'For example, people with chronic pain will often have seen many doctors and tried many drugs that haven't worked for them. They come to see the clinician with all this negative experience, not expecting to receive anything that will work for them. Doctors have almost got to work on that first before any drug will have an effect on their pain.'

The placebo effect describes the improvements seen when patients—unknowingly—are given dummy pills or sham treatments but believe it will do them good. This is a very real physiological effect; it is not just about patients 'feeling' better. The nocebo effect is the opposite: patients see poorer outcomes as the result of doubts about a medical treatment.

Previous studies have investigated the basis of the placebo effect, when using sugar pills or saline injections for example, and confirmed it can elicit a real response.

This new research, funded by the Medical Research Council and German research funders, goes a step further by examining how manipulating participants' expectations can influence their response to an active drug.

The Oxford University team, along with colleagues from the University Medical Center Hamburg-Eppendorf in Germany, Cambridge University, and the Technische Universität München, set out to investigate these effects among 22 healthy adult volunteers by giving them an opioid drug and manipulating their expectations of the pain relief they might receive at different points.

The volunteers were placed in an MRI scanner and heat applied to the leg at a level where it begins to hurt—set so that each individual rated the pain at 70 on a scale of 1 to 100. An intravenous line for administration of a potent opioid drug for pain relief was also introduced.

After an initial control run, unknown to the participants, the team started giving the drug to see what effects there would be in the absence of any knowledge or expectation of treatment. The average initial pain rating of 66 went down to 55.

The volunteers were then told that the drug would start being administered, although no change was actually made and they continued receiving the opioid at the same dose. The average pain ratings dropped further to 39.

Finally, the volunteers were led to believe the drug had been stopped and cautioned that there may be a possible increase in pain. Again, the drug was still being administered in the same way with no change.
Their pain intensity increased to 64. That is, the pain was as great as in the absence of any pain relief at the beginning of the experiment.

The researchers used brain imaging to confirm the participants' reports of pain relief. MRI scans showed that the brain's pain networks responded to different extents according to the volunteers' expectations at each stage, and matching their reports of pain.

This showed the volunteers really did experience different levels of pain when their expectations were changed, although the administration of pain relief remained constant.

Professor Tracey notes that these results have been seen in a small, healthy group of volunteers, and that these are short-term, not sustained, manipulations of the participants' beliefs about the treatment. But she says it's important not to underestimate the strength of the effect of such expectations on any treatment, and that clinicians need to know how to manage that.

Professor Tracey says there may also be lessons for the design of clinical trials. These are often carried out comparing a candidate drug against a dummy pill to see if there is any effect of a drug above and beyond that of the placebo. 'We should control for the effect of people's expectations on the results of any clinical trial. At the very least we should make sure we minimize any negative expectations to make sure we're not masking true efficacy in a trial drug.'

**Journal Reference:**

**Drug to Fight Tumors Also Fights the Flu and Possibly Other Viruses**

ScienceDaily (Feb. 28, 2011) — Ever get a flu shot and still get the flu? If so, there's new hope for flu-free winters in the years to come thanks to a new discovery by researchers who found that a drug called DMXAA, originally developed as anti-tumor agent, enhances the ability of flu vaccines to ward off this deadly virus. A new research report appearing in the March 2011 issue of the *Journal of Leukocyte Biology* suggests that DMXAA could assist flu vaccines by causing the body to produce its own antiviral proteins, called interferons, which interfere with the virus's ability to spread. In addition, DMXAA may be a useful antiviral therapy to treat newly emerging strains of the flu for which a vaccine has not be developed.

"We are hopeful that DMXAA or similar agents can be used ultimately to blunt the impact of yearly influenza outbreaks, and perhaps, for other virus infections as well," said Stefanie Vogel, Ph.D., co-author of the study and Professor of Microbiology and Immunology at the University of Maryland, School of Medicine in Baltimore.

To make this discovery, Vogel and colleagues infected mice with a mouse-adapted influenza strain. When given DMXAA three hours before or after infection and then two days later, the infection was significantly less severe. In addition, they found that DMXAA protected cells from flu strains that are resistant to Tamiflu®, one of the most advanced anti-flu drugs on the market. These discoveries suggest that DMXAA could potentially enhance the efficacy of current flu treatments and vaccines, and perhaps treat other viruses or bacteria. To be sure that DMXAA led to increased production of interferons, the researchers also tested it in mice that lacked a gene needed to produce interferon, and found that these mice received no benefit from DMXAA.

"H1N1 was a wake-up call that the flu remains a very serious disease, regardless of how "common" we may think it is," said John Wherry, Ph.D., Deputy Editor of the *Journal of Leukocyte Biology*. "Every year this virus mutates, and history has shown us that new, very dangerous strains of this virus will continue to emerge. New drugs like this one that can combat this virus—especially drugs that are effective against newly emerging strains—may prove to be lifesaving for millions of people around the world."

**Journal Reference:**