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Teaching HIV/AIDS Denialism?

An Italian university is investigating whether a professor was right to teach a course denying a causal link between HIV and AIDS.

By Cristina Luiggi | March 20, 2012

Transmission electron micrograph of HIV virions CDC, Maureen Metcalfe and Tom Hodge
A special commission launched by the University of Florence is investigating a faculty member who helped teach a course and supervise student dissertations that deny a causal role for the HIV virus in AIDS. Specifically, the commission will look into whether molecular biologist Marco Ruggiero’s “conduct complies with the institutional guidelines on teaching contents and adherence to the objectives of the official curriculum of biological sciences,” a university spokesman told Nature.

The investigation was announced by the university’s chancellor, Alberto Tesi, on February 29, and comes as a response to a letter sent by an online community dedicated to the discussion of HIV/AIDS known as the HIV forum group. In the letter, the group asks for the “dissociation” of the university from Ruggiero’s “bad science and activities.” A university spokesman told Nature that if the investigation finds any misconduct on behalf of Ruggiero, it would be dealt with internally.

“We believe in the fundamental role of freedom of research and teaching,” they wrote. “But we also believe that, in order not to discredit the value of academic freedom, it is imperative that scientific method will always be rigorously applied, and that it is mandatory to prevent damage to life and health of patients from whoever, misusing that freedom, spreads theories lacking any scientific evidence.”

Ruggiero, along with known HIV/AIDS skeptic Peter Duesberg of the University of California, Berkeley, co-authored a highly controversial paper, published last December in the Italian Journal of...
Anatomy and Embryology (IJAE), that challenged mortality estimates of an HIV-AIDS epidemic in South Africa and the effectiveness of antiretroviral drugs. The paper was met with a mountain of criticism from the scientific community and led to the resignation of two members of the journal’s editorial board.

Read our March 2012 Reading Frames on the devastating effects of conspiracy theories surrounding the global HIV/AIDS epidemic.

comments

areyoufitenough, Full certified Personal Trainer and Internet Marketer Collapse

Why in a magazine that purports to be one of 'science' must you always label the opposing viewpoint of HIV/AIDS as 'denialism'?

Zerozen.org Records

The Group HIVINFORMA disagree with this article. Everyone should face the problem in the best way basing on his knowledge: the approach of Prof. Marco Ruggiero follows the words of Prof. Luc Montagnier (Nobel Prize), that says in a statements "A good immune system will get rid of the virus within few weeks". Here our letter to the Chancellor Prof. Alberto Tesi — http://www.hivinforma.it/download...

Dr.Avnish

I also believe viruses can be defeated by strong immune response. So if IFN gamma and supporting molecules of a person are denying progression of HIV to cause AIDS. The mechanism/pathways must be studied.

riccio003

"HIV/AIDS" Social Worker Shares Scepticism Re: African "AIDS" and E.U. Hetero "HIV Epidemic"

http://www.youtube.com/watch?v=...

julianna kenny

Why did this very limited and inaccurate article finish up with a direction to Conspiracy theories on HIV and AIDS ? Ruggiero does not profess any views of that kind. There are many studies investigating immunotherapies as supportive or adjunctive therapies to Arv's (HAART) and chemo antibiotics. This is an utter nonsense and just another attempt at exciting ignorance and hostility towards creative thinking in developing functional products to support immune function—much of which happens in the Gut. Ruggiero's work is a follow on from Yamamoto.

It is an experiment. He does not say HIV plays no part in the cause of AIDS. He suggests like many other researchers , and many government funded education programs , by the way (do your homework) that there are "co-factors", and that the co factors may play a larger role prior to HIV, in creating the terrain for this syndrome to advance. To label him a Denialist seems an over reaction.

Gut Microbe Redux

The theory that people can largely be divided into three groups based on their dominant gut microbiota species is called into question.

By Hannah Waters | March 23, 2012

Last year, research suggested that, while everyone has gut bacteria, people can be divided into three groups based on their predominant species: Bacteroides, Prevotella, or Ruminococcus. Clinicians hope to use a person’s enterotype—or gut bacteria grouping—to better understand obesity and gastrointestinal disease, and perhaps to develop treatments.

But those groups may not be so well defined, according to scientists presenting at the International Human Microbiome Congress in Paris, reported Nature.

One researcher replicated the analysis in 663 people and, while his enterotypes were similar to the original research, some people had more than one defining bacterial species and, occasionally, groups overlapped.

Meanwhile, another team replicated the study in more than 1,200 adults and found more of a continuum of gut microbiota than any individual groups.

“There’s this great diversity and we all agree that reducing that complexity and linking it to clinical traits is really important,” Rob Knight of the University of Boulder, who was involved in the second study, told Nature. “The disagreement’s about what the actual structure is.”

Many men with undetectable HIV in blood still have low levels in their semen, studies find

Gus Cairns

Published: 02 April 2012

A study of 101 gay men at the Fenway Health HIV clinic in Boston, USA (Politch) has found that a quarter of men with undetectable viral loads in their blood nonetheless had detectable HIV in their semen.

Although seminal viral load in these men was low (media 200 copies/ml), the researchers suggest that this is still enough to be one of the explanations for ongoing transmission in gay men despite a high proportion being on antiretroviral therapy.

There was a very strong association with detectable HIV in semen and having a current sexually transmitted infection (STI). Six of the eight men whose HIV was undetectable in blood but detectable in semen (so-called virally discordant) had a urethral STI. After adjusting for other
Infectiousness of HIV

Factors the researchers concluded that men who **had an STI and/or urethritis were 29 times more likely to have viral discordancy.**

**A quarter of ‘undetectable’ gay men have HIV in semen...**

In the Boston study, participants were on average 43 years old and three-quarters were white. They had all been on antiretroviral therapy (ART) for more than three months and 86% for over a year.

Nearly three-quarters were judged as being at high risk of acquiring an STI because they had had unprotected sex in the last three months. Nine of the men were diagnosed with an STI (gonorrhoea, syphilis, chlamydia or non-gonococcal urethritis) and 24 had leukocytospermia or white cells from the immune system in the sperm, indicative of urethral inflammation.

Eighteen of the 101 men had a detectable viral load in their blood; their median blood plasma viral load was 560 copies/ml and ranged from 80 to 640,000 copies/ml. Nine of these 18 men also had detectable HIV in their semen (50%).

Of the 83 men without detectable HIV in their blood, 21 (25%) had detectable HIV in their semen. The median seminal viral load in these men was 200 copies/ml and ranges from 80 to 2560 copies/ml.

As well as having an STI, in multivariate analysis, two other factors remained strongly associated with having detectable HIV in semen in men without it in blood. High levels of the inflammatory cytokine TNF-α were associated with a 14-fold greater risk of a discordant seminal viral load, and having had unprotected insertive anal sex (being ‘top’), which was associated with a more than sevenfold greater risk.

There were therefore in this study low but detectable levels of HIV in the semen of a quarter of men who would register as being ‘virologically suppressed’ on a viral load blood test. To what extent might this be contributing to ongoing HIV transmission in gay men? This is unknown, but the researchers point out that although a viral load below 1000 had rarely been associated with transmission in heterosexual studies, some infections have occurred and animal models suggest that HIV is five times more transmissible via anal than vaginal sex – so a median viral load of 200 would imply a low but definite risk of transmission.

**A 2008 study from San Francisco** (Butler) found that the median seminal viral load in men transmitting HIV to partners was just 4300 copies/ml and the lowest was 110 copies/ml, while a **2009 study from Brighton in the UK** (Fisher) that linked HIV infections in gay men genetically found that two out of 41 transmissions of HIV (5%) were from men with an apparently undetectable viral load.

However studies of the link between viral load and transmission suffer from it being difficult to pin down transmitters in a cohort of gay men with multiple partners and where viral load may be measured months after the transmission (in the Butler study the average gap between transmission and viral load test was 103 days).

One interesting aspect of this study was the higher risk of seminal viral load associated with unprotected insertive sex. The researchers suggest that urethritis in these HIV-positive gay men could be caused by infections with fecal bacteria acquired during sex or even that the virus detected could be passively-carried virus from other HIV-positive gay men. Either way, this would tend to increase the infectiousness of HIV-positive men if they have insertive sex with negative men.

**...as do one in 16 ‘low-risk’ heterosexual men**

If STIs are implicated in seminal HIV it might be assumed that low-risk men with undetectable blood level of HIV would not have it in their semen. However another study from France (Lambert-Niclot), of HIV-positive heterosexual men in stable relationships who sought sperm-washing, found that 20 out of 304 men (6.6%) had HIV in their semen.

The study was a longitudinal one of 304 heterosexual men who attended a clinic in France seeking sperm-washing for conception between 2001 and 2011. These men between them provided 628 paired blood and semen samples. HIV was detectable in 107 blood samples (17%) and 49 seminal samples (8%). During this time 20 participants (6.6%) provided at least one paired sample where HIV was undetectable in blood (below 40 copies/ml) but detectable in semen. The Seminal viral load ranged from 135 to 2365 copies/ml in these samples.

The proportion of men with a discordant seminal viral load did not vary over time, despite the development of more sophisticated and potent HIV regimens.

Both studies warn that men with undetectable viral load results should not assume they are non-infectious and should be warned that HIV treatment does not appear to reduce the risk of transmitting HIV to zero.

**References**

Breastfeeding, Not Formula, for South Africa's HIV-Positive Mothers

By Lee Middleton

CAPE TOWN, South Africa, Apr 1, 2012 (IPS) – South Africa's nine provinces will begin phasing out provision of free formula to HIV-positive mothers and implement a new policy on breast-feeding from Sunday. But despite the clarity of the policy and its supporting data, vocal critics, including respected individuals from leading medical and academic institutions, have decried the choice.

Since the Aug. 23, 2011 announcement that exclusive breastfeeding (EBF) will be promoted in South Africa from Apr. 1, debate over the Tshwane Declaration's soundness, rather than discussion around implementation, has dominated the conversation.

A simple two-page document, the declaration states unequivocal support for EBF for all infants up to six months, including HIV-exposed infants, who should receive antiretrovirals (ARVs) to prevent mother-to-child transmission (PMTCT), as recommended in the 2010 World Health Organization (WHO) guidelines.

The declaration originated from concern over low exclusive breastfeeding rates—the lowest in the world at eight percent; unacceptably high child mortality rates—the rate for 2010 remained almost level with the 1990 figure, with 58,000 children dying before the age of five; and the fact that formula feeding increases the risk of death from diarrhea and pneumonia, the biggest killers of infants and children in South Africa.

It also commits resources to promoting EBF, including developing legislation for maternity protection and support for workplace breastfeeding. Finally, and perhaps most controversially, it removes provision of formula feeding at public health facilities except by prescription for medical conditions.

An Emotional Debate

"We can increase our EBF rate, but not to the extent that the Health Department believes is possible," said Haroon Saloojee, a professor in the division of community pediatrics at the University of Witwatersrand, and a leading critic. Saloojee's concerns focus on mothers' ability to adhere to infant ARV regimens and the potential for nevirapine (the prophylaxis that HIV-exposed babies would take) shortages in the public health sector.

"The likely scenario is that clinics don’t have nevirapine, and mothers will not be able to give the babies their medication and will continue to breastfeed. The situation in the health service currently makes that a high-risk probability," Saloojee said.

Supporters of the policy argue that adherence rates to ARVs in South Africa are generally excellent, and based on a recent national study in the March 2012 WHO Bulletin titled "Elimination of Mother-to-Child Transmission of HIV: Measuring the Effectiveness of National PMTCT Programmes", presented at the International AIDS Society meeting in Rome in 2011, mothers clearly are adhering. National mother-to-child transmission among infants from four to eight weeks old was 3.5 percent, the study found.

"There’s no way you can get those transmission rates unless you have good and reliable service delivery and good and reliable adherence to those drugs," said Nigel Rollins of the WHO, referring to that study. "To level the argument that women aren’t going to be able to do it flies in the face of the data. I think most women will be prepared to do something good for their children if they have the knowledge... There will certainly be a learning curve, but there is every reason to believe it can be achieved," Rollins added.

Learning Curves

Unfortunately, the learning needs to go beyond adherence to ARVs as infant prophylaxis. Convincing women to breastfeed exclusively will likely be the greater challenge.

"My mom says there’s not enough milk. I’ve heard from other women that they breast and bottle feed at the same time so the baby can get full," said 21-year-old Nicola Daniels of Manenberg, a Cape township. A first-time mother, Daniels planned to breastfeed but remained unsure about whether to do so exclusively.

Ingrid Le Roux, medical director at Philani, a maternal and child health project, agreed that convincing women to commit to EBF poses a serious challenge. "There are a lot of underlying issues:
mothers are alone, stressed, influenced in a big way by advertising. Some cannot believe that anything they have can be better than what they can buy in the shop,” Le Roux said.

“People don’t believe that it’s possible to breastfeed exclusively for six months. Even health workers... many don’t believe. So if you don’t believe as a health worker, than how can you motivate for it?” Le Roux added.

Despite the very real challenges, evidence from studies around the continent show that EBF is possible with proper support. In KwaZulu-Natal, EBF rates were improved to 76 percent at five months, and 40 percent at six months with home-based and clinic support, according to Anna Coutsoudis, a professor in the Department of Paediatrics and Child Health at the University of KwaZulu-Natal.

Prior to the Tshwane Declaration, KwaZulu-Natal’s Department of Health examined child mortality, EBF, problems with stocking formula and the 2010 WHO guidelines, and decided to promote EBF, in part by removing free formula from public health.

"Data showed that formula feeding was not helping in terms of infant survival, it was actually making it worse; and we had very low EBF rates. So we decided that we should follow the WHO guidelines... to follow one feeding option,” Coutsoudis said of the province’s decision.

"In the early days formula feeding was appropriate,” Coutsoudis added, referring to the previous era’s attempt to reduce mother-to-child transmission by discouraging breastfeeding in HIV-positive women.
"But now we know that if we improve EBF and we have nevirapine, we can reduce the breastfeeding transmission to less than one percent."

Rollins further pointed out that the WHO is promoting EBF not to reduce HIV transmission rates (transmission should neither increase nor decrease with EBF if prophylaxis is used), but because it is better. "EBF to HIV-impacted women is not recommended on the basis of ability to reduce transmission, it is there because it is the best thing for the child for every other reason we know about breastfeeding."

Coutsoudis agreed that EBF is about child survival on the whole. "There's no way we're going to improve breastfeeding and therefore child survival in our country while we've got these mixed messages and free formula being given out," she told IPS.

"If people keep running the policy down it undermines the public's confidence. They need to look at the big picture, that is: if we can improve breastfeeding in this country the whole population will benefit," Coutsoudis said.

GSK’s new once-daily HIV drug matches Merck rival
By Ben Hirschler
LONDON | Mon Apr 2, 2012 3:16am EDT
(Reuters)—A new once-daily AIDS drug from GlaxoSmithKline and its partner Shionogi proved just as good as Merck & Co’s twice-daily rival Isentress in a late-stage clinical trial, boosting hopes for the product.

Both GSK’s new drug dolutegravir and Isentress are so-called integrase inhibitors, a novel class of drugs for fighting HIV/AIDS that block the virus causing the disease from entering cells.

Dolutegravir is important for GSK since it could help rejuvenate its HIV/AIDS business—an area of medicine it used to dominate but where it has fallen behind rivals in recent years.

GSK and Shionogi said on Monday that their experimental drug dolutegravir showed non-inferiority to Isentress, or raltegravir, when given for 48 weeks alongside two older types of HIV/AIDS medicines.

In total, 88 percent of study participants on once-daily dolutegravir had their virus suppressed against 85 percent of those on twice-daily Isentress in the Phase III study. Tolerability was similar for both drugs.

Merck’s drug, which had sales of $1.4 billion last year, is currently the only integrase inhibitor approved by regulators, although Gilead also has one in Phase III testing called elvitegravir.

Dolutegravir belongs to Viiv Healthcare, a joint venture formed between GSK and Pfizer in 2009 in which GSK holds an 85 percent stake, and income from the medicine will be shared with Shionogi.

The compound is viewed by analysts as a potential $1 billion-a-year seller, since the once-daily dosing is likely to be attractive to patients. However, the financial gain to GSK will be diluted by the sharing deals with Shionogi and Pfizer.

Results of further Phase III trials are being awaited before GSK is ready to submit dolutegravir to regulators for approval.
The experimental medicine is also being tested in Phase III in different groups of patients, including those who do not respond to Isentress, as well as in a combination product with GSK's Epzicom, which consists of the HIV drugs Ziagen and Epivir.

With results of these other Phase III clinical studies also due in 2012, dolutegravir could potentially be filed for approval with regulators before the end of this year, a company spokesman said.

South Africa: Sanac Fires Staff
By Khopotso Bodibe, 30 March 2012

Just days before the new National Strategic Plan (NSP) on HIV and AIDS, TB and STIs is due to be implemented on the 1st of April, the entire staff of the South African National AIDS Council (SANAC) has been fired, leaving no one in the SANAC Secretariat to deliver on the plan.

Dr Fareed Abdullah, CEO of the South African National AIDS Council (SANAC) for only two months, is reported to have axed all the seven staff members at the organisation tasked with the co-ordination of the country's response to HIV and AIDS, TB and STIs. SANAC staff, who did not want to be named, say the new CEO gave them letters only on Tuesday informing them that their employment would be terminated at the end of March, meaning that today is their last day of work.

The turn of events proves that SANAC has been problematic for a while. Staff members allege that they have been working without proper contracts for the last six months. Many staff members have been working on short-term contracts since May 2010 and have lost all their employment benefits. They also allege that at one point their salaries were not paid for three months. Salaries are often paid late. For instance, January salaries were only paid on the 6th of February. Sometimes people are underpaid.

Two of the staff members that have been fired were employed on five-year contracts in 2009 under the former CEO, Dr Nono Simelela, who is now advisor to the Deputy President Kgalema Motlanthe. Their contracts were due to end in 2014. They have decided to take SANAC and the Department of Health to the Bargaining council to contest their dismissals.

However, SANAC deputy chairperson Mark Heywood, denied that staff has been fired.

Heywood said SANAC had been working on a restructuring plan for more than six months. The restructuring would eventually result in a new organogram that would ensure effective delivery of the new National Strategic Plan on HIV and AIDS, TB and STIs.

He said staff had been told that some posts would be done away with and that people would have to apply for new jobs within SANAC or to re-apply for their old positions. Heywood added that he supported the restructuring as some of the staff has been inefficient. He denied that everyone is losing their jobs, saying that only four people would not be returning to SANAC in April.

But staff sources said that everyone had received a letter of termination. However, they do concede that they were aware of the looming restructuring.

One staff member said the new structure was presented in February and certain positions were not on it.

Several of the staff members applied for posts and underwent an interview process. Two were subsequently given letters of permanent employment in January, with new salary offers.

So, it was shock when they received correspondence notifying them that their employment will be terminated as of today.

"What doesn't make sense is that you give people letters of termination three days before the end of the working month," said one staff member.

Letters to staff, signed by the Health Department Director-General on the 14th of March and were given to staff only on Tuesday, claim that all SANAC employees received a letter in January informing them that all posts at SANAC have been cancelled. But staff members deny having received such a letter.

It is also not clear whether the SANAC has already recruited people under its envisaged new structure. One staff member said: "We don't know his (the new CEO's) plan. He hasn't had a single staff meeting with us ever since he started here in February. He has only had one-on-one introductory meetings with each of us."

CEO of SANAC, Dr Fareed Abdullah, has subsequently issued out a statement simply denying any dismissals.

In it he says, all staff were aware of the restructuring of the SANAC Secretariat and positions were advertised and they were encouraged to apply. Two staff members were successful and have been appointed. The statement further says that three staff members applied and were found not to have the
skills and expertise necessary for the positions for which they applied. The remainder did not apply for any of the positions.

**Potent Anti-Virus Medication May Not Stem HIV Transmission Among Sexually Active Men, Study Finds**

_Boston Globe_, (03.27.2012) Kay Lazar

HIV-positive men who have sex with men may still be at risk of spreading the virus even while taking strong antiretrovirals, says a new report from Boston researchers. According to scientists from the Boston University School of Medicine and Fenway Health, highly active antiretroviral therapy (HAART), the primary treatment for HIV/AIDS, does not fully suppress HIV in the semen of sexually active MSM with the virus.

Of the 101 MSM recruited for the study, all Fenway Health patients, 18 percent had detectable levels of HIV in their blood, and 30 percent had HIV in their semen. Among those men with no detectable HIV in their blood, a quarter still had HIV in their semen—a finding strongly associated with unprotected sex, STDs, and genital inflammation.

"Men who have sex with men, who are at risk for transmitting HIV, may believe that they have a low risk based on incorrect assumptions that HAART eliminates HIV from semen," said study lead author Joseph Politch, a research associate professor in obstetrics and gynecology at Boston University.

Until additional information is available, it would be “prudent” for sexually active HIV-positive MSM "to use condoms and other risk-reduction strategies," Politch advised.

The study, "Highly Active Antiretroviral Therapy Does Not Completely Suppress HIV in Semen of Sexually Active HIV-Infected Men Who Have Sex with Men," was published online in AIDS (2012;doi:10.1097/QAD.0b013e32835b11b).

**Sanofi Teams Up with India to Make Cheap ARVs in South Africa**

_Agence France Presse_, (03.30.2012)

Under an arrangement announced Friday, French drugmaker Sanofi will partner with India’s Hetero to manufacture low-cost antiretrovirals in South Africa. The move represents progress toward South Africa’s goal of buying 80 percent of its ARVs from local sources, said Sanofi CEO Christopher Viehbacher. “There is a continuous supply shortage for critical medicines for HIV/AIDS. Only 50 percent of patients are able to receive treatment, and there is a real need for more locally manufactured and supplied affordable ARVs.” To accommodate increased demand, Sanofi recently upgraded its factory north of Pretoria.

**New York Times Examines Global Response To Haiti’s Cholera Epidemic**

The _New York Times_ examines the global response to Haiti’s cholera epidemic, writing that while “[m]any health officials consider the cholera response 'pretty remarkable,' as John Vertefeuille, the Centers for Disease Control and Prevention's director in Haiti, said ... [o]thers ... believe the bar for success was set too low and more lives could have been saved." The newspaper continues, "[A]s the deaths and continuing caseload indicate, the world’s response to this preventable, treatable scourge has proved inadequate."

"In the 17 months since [the outbreak began], cholera has killed more than 7,050 Haitians and sickened more than 531,000, or five percent of the population," the Times writes, adding, "The world rallied to confront cholera, ... but the mission was muddled by the United Nations' apparent role in igniting the epidemic and its unwillingness to acknowledge it." The newspaper provides a detailed account of the epidemic as well as the global response, and provides links to a video report and an infographic documenting the spread of the disease (Sontag/Paultre, 3/31).

**New Immune Defense Enzyme Discovered**

ScienceDaily (Apr. 2, 2012) — A previously unknown serine protease forms part of the antibacterial defence arsenal of neutrophil granulocytes.

Neutrophil granulocytes comprise important defences for the immune system. When pathogenic bacteria penetrate the body, they are the first on the scene to mobilise other immune cells via signal molecules, thereby containing the risk. To this end, they release serine proteases – enzymes that cut up other proteins to activate signal molecules. Scientists at the Max Planck Institute of Neurobiology in Martinsried have now discovered a new serine protease: neutrophil serine protease 4, or NSP4. This enzyme could provide a new target for the treatment of diseases that involve an overactive immune system, such as rheumatoid arthritis.
The functioning of the immune system is based on the complex interplay of the most diverse cells and mediators. For example, neutrophil granulocytes (a group of specialized white blood cells) react to bacteria by releasing substances called serine proteases. These enzymes are able to activate signal molecules, such as the chemokines, by cleaving them at a specific position on the molecule. The active signal molecules then guide other immune cells to the focus of inflammation in order to destroy the pathogens.

A research team led by Dieter Jenne at the Max Planck Institute of Neurobiology in Martinsried has come across a previously unknown protease in humans: neutrophil serine protease 4, or NSP4. "The special thing about this enzyme is that it cuts proteins that have the amino acid arginine at a particular point", says Dieter Jenne, research group leader at the Martinsried-based Institute. "This is where NSP4 differs from the other three known neutrophil serine proteases, which are similar in molecular structure, but have a different recognition motif." The scientists may be able to harness this difference to develop an active substance that specifically inhibits NSP4, thereby reducing the immune reaction.

However, serine protease activity comes at a cost. The enzymes not only heal inflammations, but sometimes cause them in the first place. If too many immune cells are activated, they can use their arsenal of aggressive chemical weapons against the body's own tissues. A number of chronic inflammatory diseases are based on precisely this effect. As a result, scientists are searching for substances that can block the neutrophil proteases. To date, however, none of the substances tested have been developed into effective drugs.

"So far, we don't know the identity of the NSP4 substrate, but we assume they must be signal molecules", says Dieter Jenne. Activated chemokines can recruit a vast number of neutrophils, and their sheer quantity alone is enough to cause tissue damage. "Proteases sometimes act as accelerants and can even trigger a chronic inflammation quite independently of bacterial intruders. If we dampened down the defences, we could counteract this effect", explains the scientist.

In terms of evolutionary history, NSP4 is the oldest of the four known neutrophil serine proteases. Using gene sequences, scientists have shown that the enzyme has hardly changed through hundreds of millions of years of evolution from bony fish to humans. "That would indicate that NSP4 regulates a fundamental process", says Dieter Jenne.

The fact that the enzyme remained undiscovered until now is because it occurs at a much lower concentration than the other three proteases. The Max Planck scientists came across it while searching the human genome for genes that encode serine proteases. In the process, they noticed a previously unknown gene sequence. Natascha C. Perera, a member of the Martinsried research group and lead author of the study, managed to produce and examine the enzyme in its active, folded state.

If they are to establish NSP4 in the future as a possible target protein for anti-inflammatory drugs, the scientists must now examine its function in living organisms and discover whether blocking the enzyme has adverse effects. The scientists are working with the company Novartis to answer these questions in laboratory mice. "NSP4 inhibitors could be used in diseases like chronic arthritis or inflammatory skin diseases", says Dieter Jenne, "but first we have to test the long-term effects of these substances."

**Journal Reference:**

**Special Class of Natural Fats Stimulates Immune Cells to Fight Diseases**

ScienceDaily (Apr. 2, 2012) — An international research team led by scientists from Singapore Immunology Network (SIgN) under the Agency of Science, Technology and Research (A*STAR) discovered that a special class of fatty molecules is essential for activating a unique group of early-responding immune cells. This study sheds light on how recognition of fatty molecules by immune cells could protect from infection, allergic reactions, autoimmune diseases and cancer. More importantly, it offers new opportunities to exploit the use of these stimulatory fatty molecules in therapeutic interventions, such as the development of new vaccines and drugs targeted for autoimmune diseases.

The early-responding immune cells investigated in this study, called the invariant natural killer T (iNKT) cells, are important as first line of defence against infectious and foreign agents. When stimulated, iNKT cells secrete large amounts of biological chemicals, and are capable of influencing the responses of other immune cells in the body.

It is well established that iNKT cells recognise and are activated by fatty molecules from various sources, including those from diseases-causing bacteria and those that are naturally produced in the thymus. This study identifies for the first time, the actual type of fatty molecules that stimulates the
development of iNKT cells in the thymus. This discovery came about through systematic biochemical and structural analysis of fatty molecules extracted from the thymus.

The team, co-led by Professor Gennaro De Libero and Dr Lucia Mori, Senior Principal Investigators at SIGN, found that the fatty molecules produced in the thymus which were able to stimulate iNKT cells all have the chemical linkage called ether bonds.

To validate the stimulatory activity of these special class of self-generated fatty molecules, the scientists artificially manufactured ether-bonded fatty molecules through synthetic chemistry, and found that they were similarly able to activate iNKT cells, promoting their development in the thymus.

In addition, the scientists uncovered that these ether-bonded fats were the same type of fatty molecules which are produced by the peroxisome, a sub-compartment that specialises in fat metabolism, found within all cells of the body. Using a mouse strain that is lacking in the peroxisomal enzyme, and hence unable to make ether-bonded fatty molecules, the scientists found that such mice could not produce the complete repertoire of fully functional iNKT cells.

Dr Mori said, "We are very excited to have identified the type of fatty self-molecules that stimulates T cells. This discovery sets a new paradigm for understanding the rules that govern development and activation of frontline immune cells of the body."

Professor De Libero added, "With fresh insights from this study, we now have new tools to explore novel therapeutic strategies for autoimmune and inflammatory diseases where such fatty molecules are key to disease development."

**Journal Reference:**
Federica Facciotti, Gundimeda S Ramanjaneyulu, Marco Lepore, Sebastiano Sansano, Marco Cavallari, Magdalena Kistowska, Sonja Forss-Petter, Guanghui Ni, Alessia Colone, Amit Singhal, Johannes Berger, Chengfeng Xia, Lucia Mori, Gennaro De Libero. Peroxisome-derived lipids are self antigens that stimulate invariant natural killer T cells in the thymus. Nature Immunology, 2012; DOI: 10.1038/ni.2245

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**U.N. Reports Increase In Cholera Cases In Haiti As Rains Begin**

In a monthly bulletin (.pdf) on the humanitarian response in Haiti, the U.N. Office for the Coordination of Humanitarian Affairs said that an increase of new cholera cases has been recorded in the western and northern parts of the country and "that Haitian health officials recorded 77 new cases a day for the whole country in early March, when the rains began," the Associated Press/USA Today reports. "The new cholera cases come after a steady decline since June of last year when aid workers saw peaks of more than 1,000 cases on certain days," the news agency writes.

The effectiveness of medical teams working to slow the spread of cholera "has been hampered in part by little coordination and an absence of salaries paid to people working in cholera treatment centers run by Haitian authorities, the U.N. bulletin said," according to the AP (Daniel, 4/3). The bulletin notes that nearly 531,000 people have been infected with cholera, and the disease has killed more than 7,000 people since the outbreak began in October 2010 (4/2).

**National Program In Mauritania Working To End FGM, IPS Reports**

"A multi-pronged strategy to end female genital mutilation [FGM] in Mauritania is making gradual progress, though campaigners acknowledge much remains to be done in a country where more than two-thirds of girls suffer excision," Inter Press Service reports. "The national program, supported by several development partners, includes lobbying for the adoption of a law criminalizing excision, raising awareness of a fatwa (a religious notice) forbidding excision, and the setting up of regional offices to monitor the practice," according to the news service.

"Khatto Mint Jiddou, who heads the campaign against gender-based violence at Mauritania’s Ministry for Social Affairs, Childhood and the Family, told IPS that the initiative involves a wide range of people, including civil society activists, doctors and religious leaders," IPS writes, highlighting the efforts of several individuals advocating against the practice. "We are seeing a positive trend, even if this phenomenon, rooted in socio-cultural considerations, is far from being brought under control," Aziza Mint Meslem, who works with an NGO called the Mauritanian Association for the Health and Development of Women, said, according to IPS (Abderrahmane, 4/3).

**Children: Better Protection from Influenza With Improved Vaccine**

ScienceDaily (Apr. 3, 2012) — An intranasal vaccine that includes four weakened strains of influenza could do a better job in protecting children from the flu than current vaccines, Saint Louis University research shows.
Before each influenza season, scientists predict which strains of flu will be circulating and make a trivalent vaccine that includes three strains of influenza—two of influenza A and one of influenza B.

The ability to add another strain of influenza B without compromising the vaccine's ability to protect against the other three strains will allow scientists make a better vaccine, said Robert Belshe, M.D., professor of infectious diseases at Saint Louis University School of Medicine and the corresponding author of the research article.

"The bottom line is adding another strain to make a quadrivalent vaccine improves our ability to protect against flu and doesn't reduce the body's immune response to the other strains," said Belshe, who also directs Saint Louis University's Center for Vaccine Development.

"It should bring us better protection because there's less guess work than in the standard trivalent vaccine."

Children are more susceptible than adults to influenza from one of the B strains, which change less often than A strain viruses. Some winters, influenza B viruses—Victoria or Yamagata—cause most of the flu in children and significant infection in adults, Belshe said.

Preventing flu in children is key to protecting the entire population. "We think the most important way for flu to spread is through school-aged children," Belshe said.

In the 1980s, influenza B split into the two circulating lineages of virus, which have evolved into viruses that are quite different. Some years both B viruses or the B strain that doesn't match the vaccine circulate, which means the vaccine doesn't protect people from getting the flu.

"There are these two very different strains of influenza B that don't cross protect. Vaccinating against one strain of influenza B does little to protect against the other," Belshe said.

"It has not been possible to predict which strain has circulated. In the last 10 years, we predicted right five times. So you can flip a coin and do as well."

Previously, manufacturers had not had the capacity to produce a vaccine that protects against four strains of flu, but that is no longer the case, Belshe said.

The researchers tested versions of the FluMist vaccine, which is sprayed in the nose and contains live flu viruses that have been attenuated or weakened so they don't cause infection. The intranasal vaccine is made by MedImmune.

The nasal spray vaccine was tested in about 2,300 children between 2 and 19 years of age. The children were randomized to receive one of three vaccines: a vaccine containing four strains of influenza—two of influenza A and two of influenza B, or one of two vaccines that contained both influenza A strains and one of each of the influenza B strains. Researchers looked at the safety and antibody response to both influenza A and B viruses in children of different age groups who were vaccinated.

Those children who receive vaccine containing four strains of flu had as robust of an immune response as those who received the vaccine that contained three strains. In addition, Belshe noted no clinically significant difference the safety of the vaccines, which were well tolerated.

"We saw stuffy noses, which we know is associated with FluMist, and an occasional low grade fever, which is similar to other childhood vaccines," Belshe said.

On Feb. 28, the U.S. Food and Drug Administration approved MedImmune's quadrivalent flu vaccine for use in people between the ages of 2 and 49. The vaccine could be ready for use during the 2013-2014 influenza season, pending a recommendation from the Advisory Committee on Immunization Practices, a group that advises the Centers for Disease Control and Prevention about vaccination issues.

An injected flu vaccine designed to protect against four strains of flu—instead of the current three—also is in the works, Belshe said.

**Journal Reference:**

**Hepatitis C infections now twice as likely in HIV+ gay men as in injecting drug users, Swiss study finds**
Gus Cairns
Published: 06 April 2012

The annual incidence of hepatitis C infection in gay men with HIV is now nearly twice that seen in HIV-positive injecting drug users, according to a Swiss study.

Hepatitis C infections started increasing substantially from 2005 onwards, the study finds, and there is an accelerating trend, with a particularly large increase in infections in the last year.
The Swiss HIV Cohort Study (SHCS) of the largest and most complete cohorts of HIV patients in the world; it includes the majority of HIV-positive people in Switzerland. Annual tests for hepatitis C became routine in 1998.

This survey looked at 6534 patients who were hepatitis C negative at the point they entered the SHCS and who have had at least one other hepatitis C test since then. In terms of the original route-of-exposure group they belonged to when diagnosed with HIV, 3333 patients (51%) were gay men, 3078 (47%) were heterosexual and 123 (2%) were injecting drug users. For the sake of clarity, patients who were both gay and IDU were excluded from the study, as were heterosexuals who started injecting drugs after HIV diagnosis.

Since 1998 there were 167 new cases of hepatitis C infection of which 101 (60%) were in gay men. But half of the cases in gay men happened since 2009; in the last three years 51 out of 65 new cases of hepatitis C (78%) were in gay men.

Incidence rates have changed dramatically since 1998. In that year the annual incidence of hepatitis C in HIV-positive injecting drug users was 13.9% and it fell to 2.2% a year in 2001. In contrast annual hep C incidence in gay men was just 0.2% a year in 1998 and is now 4.1%, an 18-fold increase.

There has also been a less dramatic increase in non-injecting heterosexuals: hepatitis C incidence was under 0.1% a year in 1998 and is now about 0.8%.

In multivariate analysis, three risk factors stood out in gay men, each roughly doubling the risk of hepatitis C infection: inconsistent condom use, a past history of syphilis, and being already infected with hepatitis B.

“These observations underscore the need for improved HCV surveillance and prevention among HIV-infected men who have sex with men,” comment the researchers.

Reference

Nigeria: Suitor Sues Father-in-Law Over HIV Status of Fiancée
5 April 2012
A Farmer, Muhammad Baban Iro of Rigasa Area in Kaduna on Thursday appeared before a Kaduna Sharia Court for refusing to refund N32,000 being the bride price and other expenses allegedly paid on his daughter.

The demand was made by the suitor following the discovery that she had tested positive to HIV.

One Ibrahim Bala of the same area had gone to the court to complain against Baban-Iro for allegedly collecting the money as bride price and other expenses incurred on his daughter for marriage.

Bala said he decided to discontinue with the marriage following the outcome of a hospital test which showed that his fiancée was HIV-positive.

The complainant said although he could have kept quiet if the lady's father had allowed him to swap with the younger sister of his bride-to-be, but the man refused, saying he would rather refund.

However, four months after the promise, Baban-Iro was yet to repay, Bala told the court.

He claimed that he paid N14,000 as bride price, N4,000 for introduction, N10,000 for clothing and another N4,000 for sewing the clothes.

Bala promised to produce witnesses before the court to corroborate his claim.

Baban-Iro, however, denied collecting N32,000 from the complainant, saying that the only money he collected was for bride price and introduction, amounting to N18,000.

He did not, however, deny the HIV status of his daughter.

The Presiding Officer, Ibrahim Inuwa, directed the complainant to present his witnesses to the court, and adjourned the case to April 12.

Sex Education Efforts Lagging in Schools, CDC Says

Philadelphia Inquirer, (04.06.2012) Robert Preidt, HealthDay

CDC said Thursday that efforts to teach more secondary school students about HIV, STD and pregnancy prevention have stalled in recent years.

A new report details the findings from 2008 and 2010 data from 45 states that participate in biennial school health surveys. CDC researchers assessed the percentage of schools that teach topics related to HIV, STD and pregnancy prevention, which may differ by grade level but typically include basic information about disease transmission and diagnosis and pregnancy risk reduction. Condom use is a topic only covered in high schools, CDC said.
The proportion of middle schools that taught all essential topics to grades 6-8 declined in 11 states and did not increase in the other 33 states. The percentage of high schools that taught all topics to grades 9-12 declined in one state and increased in two. The proportion of high schools that taught three condom-related topics dropped in eight states and increased in three.

An editorial accompanying the report noted that HIV and other STD education is essential — particularly for middle schoolers, who most likely have not yet become sexually active. “Families, the media and community organizations, including faith-based organizations, can play a role in providing HIV, other STD, and pregnancy prevention education,” the editorial noted. “However, schools are in a unique position to provide [this education] ... because almost all school-aged youths in the United States attend school.”


Study Shows Artemisinin-Resistant Malaria Parasite Spreading Along Thai-Myanmar Border

A strain of malaria that is resistant to artemisinin combination therapy (ACT) is spreading along the Thai-Myanmar border and has the potential to spread to Africa if efforts to effectively treat and prevent the disease are not undertaken, according to a study published in the Lancet on Friday, Reuters reports (Lyn, 4/5). Since 2008, patients treated with ACT have been slower to clear the parasite than previously, "[a]nd this precursor to resistance seems to be spreading, despite efforts to carefully use artemisinin (by giving it in combination with other drugs) to avoid the emergence of resistance," Scientific American writes.

In a related study published in Science, researchers examined the genomes of parasites collected in Thailand, Cambodia, and Laos, and were able to determine "a small area of the genome" that is responsible for resistance, Timothy Anderson of the Texas Biomedical Research Institute and a co-author on both studies said, according to the news service (Harmon, 4/5). The finding "gives hope that its spread may be monitored and that new drugs might someday be devised to foil resistance," NPR's health blog "Shots" writes. In an editorial accompanying the Lancet study, Anne-Catrin Uhlemann and David Fidock of Columbia University write, "Should these [ACT] regimens fail, no other drugs are ready for deployment, and drug development efforts are not expected to yield new anti-malarials until the end of this decade" and conclude that the international community should "implement all available measures towards malaria elimination while we can," the blog notes (Knox, 4/5).

Manipulating the immune system to develop 'next-gen' vaccines

The discovery of how a vital immune cell recognises dead and damaged body cells could modernise vaccine technology by 'tricking' cells into launching an immune response, leading to next-generation vaccines that are more specific, more effective and have fewer side-effects.

Scientists from the Walter and Eliza Hall Institute have identified, for the first time, how a protein found on the surface of immune cells called dendritic cells recognises dangerous damage and trauma that could signify infection.

Dendritic cells are critical for raising the alarm about the presence of foreign invaders in the body such as viruses, bacteria and parasites as well as tumour cells and other dead or damaged cells. Also known as antigen-presenting cells, they digest and present molecules from damaged cells to other immune cells that recognise foreign invaders and launch an immune response.

The research was a collaborative effort that involved a team of immunologists, protein chemists and structural biologists. The research team was led by Dr Mireille Lahoud, Dr Jian-Guo Zhang, Dr Peter Czabotar and Professor Ken Shortman.

Dr Lahoud said the study, published today in the journal Immunity, demonstrated that the immune system has evolved a very clever way of detecting damaged and dead cells to help promote an immune response.

"Dr Irina Caminschi and I previously identified a protein called Clec9A (C-type lectin domain family 9A) that sits on the surface of specialised types of dendritic cells and responds to damaged and dying cells," Dr Lahoud said. "In this study we discovered that Clec9A recognises and binds to fibres of actin, internal cell proteins that are found in all cells of the body. Actin is only exposed when the cell membrane is damaged or destroyed, so it is an excellent way of finding cells that could harbour potentially dangerous infections and exposing them to the immune system."
Professor Shortman said that exploiting Clec9A could be used to generate a new, more modern class of vaccines that are more effective and have fewer side-effects. "The Clec9A protein is one of the best targets currently known for improving immune responses," he said. "By creating vaccines that bind to Clec9A, we can trick dendritic cells to think they have encountered a damaged cell and help to launch an immune response to the infectious agent of our choice."

Professor Shortman said targeting Clec9A could decrease the amount of vaccine needed by 100 to 1000 times. "Traditional vaccine technology for generating immunity, such as using inactivated whole viruses or parasites for immune recognition, requires large amounts of vaccine in the hopes it will encounter the correct immune cells, and incorporates other substances (adjuvants) that are needed to signal to the immune system that something foreign is happening. We are proposing a new type of vaccine that we know will head directly to the right cell to help stimulate an immune response, and doesn't cause the same side-effects because it is more specific," Professor Shortman said.

Dr Lahoud said that the finding could develop or increase the efficacy of vaccines for diseases that do not currently have good preventive options, such as malaria, or HIV. "There is also the possibility that the system could be used to develop therapeutic vaccines for treating diseases, such as some forms of cancer, as well as for preventing them," she said.

**Study Shows Unified Process of Evolution in Bacteria and Sexual Eukaryotes**

ScienceDaily (Apr. 5, 2012) — Bacteria are the most populous organisms on the planet. They thrive in almost every known environment, adapting to different habitats by means of genetic variations that provide the capabilities essential for survival. These genetic innovations arise from what scientists believe is a random mutation and exchange of genes and other bits of DNA among bacteria that sometimes confers an advantage, and which then becomes an intrinsic part of the genome.

But how an advantageous mutation spreads from a single bacterium to all the other bacteria in a population is an open scientific question. Does the gene containing an advantageous mutation pass from bacterium to bacterium, sweeping through an entire population on its own? Or does a single individual obtain the gene, then replicate its entire genome many times to form a new and better-adapted population of identical clones? Conflicting evidence supports both scenarios.

In a paper appearing in the April 6 issue of *Science*, researchers in MIT's Department of Civil and Environmental Engineering (CEE) provide evidence that advantageous mutations can sweep through populations on their own. The study reconciles the previously conflicting evidence by showing that after these gene sweeps, recombination becomes less frequent between bacterial strains from different populations, yielding a pattern of genetic diversity resembling that of a clonal population.

This indicates that the process of evolution in bacteria is very similar to that of sexual eukaryotes (which do not pass their entire genome intact to their progeny) and suggests a unified method of evolution for Earth’s two major life forms: prokaryotes and eukaryotes. The findings also get to the heart of another scientific question: how to delineate species of bacteria—or determine if the term "species" even applies to bacteria, which are typically identified as ecological populations and not species. If all bacteria in a population are clones from a common ancestor, the idea of species doesn’t apply. But if—as this new study shows—genes randomly shared among individuals can bring about a new, ecologically specialized population, use of the term may be warranted.

"We found that the differentiation between populations was restricted to a few small patches in the genome," says Eric Alm, the Karl Van Tassel (1925) Career Development Associate Professor of Civil and Environmental Engineering and Biological Engineering and an associate member of the Broad Institute.
Professor Martin Polz of CEE, co-principal investigator on the project, adds, “Similar patterns have been observed in animals, but we didn’t expect to see it in bacteria”

The process of ecological differentiation in bacteria, the researchers found, is similar to that in malaria-transmitting mosquitoes: Some populations develop resistance to antimalarial agents by means of a single gene sweep, while other populations sharing the same habitat do not. The stickleback fish has also been shown to follow this pattern of "sympatric speciation" in shared habitats.

"Even though the sources of genetic diversity are quite different between bacteria and sexual eukaryotes, the process by which adaptive diversity spreads and triggers ecological differentiation seems very similar," says first author Jesse Shapiro PhD ’10, a postdoc at Harvard University who did his graduate work in Alm's lab at MIT.

The researchers performed the work using 20 complete genomes of the bacterium Vibrio cyclitrophicus that had recently diverged into two ecological populations adapted to microhabitats containing different types of zooplankton, phytoplankton, and suspended organic particles in seawater. In a previous study based on just a few marker genes, they had predicted that these closely related Vibrio populations were in the process of developing into two distinct habitat-associated populations.

The new study shows that the two populations were frequently mixed by genetic recombination, remaining genetically distinct at just a handful of ecologically adaptive genes, with an increasing trend toward gene-sharing within—rather than between—habitats.

"This is the most sophisticated paper on bacterial speciation to appear yet, all the more so because it uses the dubious word 'species' only once, and that with caution," says W. Ford Doolittle, professor emeritus of biochemistry at Dalhousie University. "The genetic basis of ecological differentiation in bacteria—how genotype maps to ecotype and what processes determine this mapping—is in my mind the biggest issue in modern microbial ecology."

**Journal Reference:**

**Microflora Have Decisive Role With Autoimmune Illnesses, Some Good, Some Bad**

*Psoriasis. When the right microorganisms are at work, immune cells involved in the development of autoimmune illnesses like psoriasis, multiple sclerosis and arthritis, can develop anti-inflammatory properties. Particular fungi activate the immune cells involved in the development of certain illnesses, whereas other microorganisms, in particular bacteria that are found naturally*
ScienceDaily (Apr. 5, 2012) — When the right microorganisms are at work, immune cells involved in the development of autoimmune illnesses like psoriasis, multiple sclerosis and arthritis, can develop anti-inflammatory properties. Scientists at Charité – Universitätsmedizin Berlin and the Institute for Research in Biomedicine, Bellinzona, Switzerland, have now made this discovery. The scientists have demonstrated that particular fungi activate the immune cells involved in the development of certain illnesses, whereas other microorganisms, in particular bacteria that are found naturally on our skin, lend an anti-inflammatory function to them.

"This not only demonstrates that the composition of our microflora has a decisive role in the development of chronic illnesses, but also that the key cells causing illness can develop an anti-inflammatory 'twin'," explained Dr. Christina Zielinski, first author of the study.

Their work is published in the current issue of the scientific journal Nature.

Allergology Clinic at Charité and Berlin-Brandenburg School for Regenerative Therapies, and her colleagues identified the basic signals that contribute to whether or not a pathogenic or anti-inflammatory immune cell develops. It then emerged that interleukin 1β, one of the body's own immune system hormones, works like a molecular switch. Its presence trains immune cells during autoimmune occurrences to function destructively and to release inflammatory messenger substances. Its absence, on the other hand, allows the immune cells to mature into anti-inflammatory counterparts. Interestingly, it is our own body's microorganisms that decide whether interleukin 1β is produced and therefore which mode is selected.

This observation prompted the scientists to also look for patients suffering from an overproduction of interleukin 1β, which is the case in the so-called auto-inflammatory syndromes (e.g. CAPS, Muckle-Wells, or Schnitzler Syndromes). These patients, especially children, suffer from multiple symptoms like fever, arthritis, and skin rashes. The exact development of these diseases is, however, to a large extent unexplained. Researchers tested whether a therapy of antibodies that block interleukin 1β can generate anti-inflammatory potential in the immune cells. In fact, after the introduction of this therapy the immune cells produced inflammation-retardant messengers. They even developed a memory to release the messenger substances over long time periods.

"I am convinced that an imbalance in our microbial microflora has a decisive influence on the development of chronic inflammatory illnesses like rheumatism, Morbus Crohn and psoriasis. Our organism is composed of ten times more microbial cells than our body's own cells. Keeping this in check is not easy. Interleukin 1β is now turning out to be a decisive molecular switch, which the microbes use to dictate between healthy or sick," says Dr. Christina Zielinski. She sees great potential in the therapy of inflammatory diseases by blocking this messenger substance. In contrast to other immune therapies this does not lead to a weakening of the immune system, but rather enables the cells instead to be anti-inflammatory if needed, without losing the ability to fight dangerous pathogens.

Journal Reference:
Christina E. Zielinski, Federico Mele, Dominik Aschenbrenner, David Jarrossay, Francesca Ronchi, Marco Gattorno, Silvia Monticelli, Antonio Lanzavecchia, Federica Sallusto. Pathogen-induced human TH17 cells produce IFN-γ or IL-10 and are regulated by IL-1β. Nature, 2012; DOI: 10.1038/nature10957
Potential for a 'Moderate' New England 'Red Tide' in 2012

Based on computer model simulations using the 2011 cyst map, researchers believe the 2012 bloom will be moderate in geographic extent. A total closure of between 126—250 miles (200 and 400 km) of coastline might occur somewhere along the Northeast coast. The locations of those closures cannot be specified since they depend on short-term episodic weather patterns that cannot be predicted months in advance. Examples of moderate years were 2006 and 2007 (the latter shown above). During those years, toxicity affected much of the Maine and New Hampshire coasts, but there were minimal closures in Massachusetts. (Compiled from information provided by the Maine Department of Marine Resources, New Hampshire Department of Environmental Services, and the Massachusetts Division of Marine Fisheries.) (Credit: Don Anderson lab, Woods Hole Oceanographic Institution)
New England is expected to experience a "moderate" regional "red tide" this spring and summer, report NOAA-funded scientists working in the Gulf of Maine to study the toxic algae that causes the bloom. The algae in the water pose no direct threat to human beings, however the toxins they produce can accumulate in filter-feeding organisms such as mussels and clams—which can cause paralytic shellfish poisoning (PSP) in humans who consume them.

Under a newly developed rating system, a moderate bloom could cause the closure of shellfish beds along an estimated 126—250 miles of coastline.

The 2012 outlook is based on the quantities of the algae *Alexandrium fundyense* in its dormant—or cyst—state detected in Gulf of Maine sediments last fall. These data are combined with computer simulations that model a complex range of meteorological and oceanographic conditions—winds, sunlight, rainfall, tides, and currents—that impact the size of the bloom.

"Our goal over the last ten years has been to develop a system to help the shellfish industry and environmental managers better plan for the annual bloom," said Woods Hole Oceanographic Institution (WHOI) biologist Don Anderson, who has worked with WHOI colleague Dennis McGillicuddy and North Carolina State University (NCSU) Prof. Ruoying He to develop the computer model to help predict the intensity and location of blooms.

Scientists are unable to make a precise forecast of where and when the regional bloom will make landfall because bloom transport depends on episodic weather events and currents that cannot be predicted months in advance. Rather, the scientists use the computer model to produce a range of bloom scenarios—or an "ensemble forecast"—tracking variables like wind direction and water characteristics based on previous years’ conditions. This is similar to the system used to forecast hurricanes.

A number of factors could impact the forecast. For instance, changing characteristics of water in the Gulf of Maine can have a direct effect on the growing conditions for *Alexandrium*.

"The surveys of cyst abundance gives us an indication of the potential extent of the bloom, but whether or not that potential is realized depends on the growing conditions," said McGillicuddy. "In 2010 we forecast a large bloom but we got it wrong. That spring, an unusual mass of warm, fresh water that was low in nutrients changed the growing conditions."

Wind direction imposes another uncertainty to the forecast. For example, strong northeast winds in the spring and early summer drive the bloom inland toward coastal shellfish beds. In contrast, when southwesterlies dominate, the algae tend to stay offshore.

"Each year, we add another set of environmental conditions to our archive of model runs. In the future, a winter that is warmer and drier than normal can be represented by 2012, but right now, we have no similar year in that archive," said Anderson.

In order to protect public health, shellfish beds are closed when toxicities rise above a quarantine level, often during the peak harvesting season. Due to effective monitoring by state agencies, there have been no illnesses from legally harvested shellfish in recent years, despite some severe blooms during that time period. There have been, however, several severe poisonings of individuals who ignored closure signs.

The economic impacts of PSP toxicity are significant in the region. Direct and indirect costs of the extensive *Alexandrium* bloom in 2005 were estimated at nearly $50 million for Massachusetts and $23 million for Maine.

The 2012 designation of a "moderate" bloom now has a specific, quantifiable meaning, thanks to a complementary research effort by Anderson and his colleagues to develop forecast terminology to describe a bloom’s potential impact. As part of that work, Judy Kleindinst, a member of Anderson’s team, analyzed records of harvesting closures due to PSP extending back 35 years, and identified three categories of bloom severity.

The categories—"limited," "moderate," and "extensive"—are equivalent to closures over 0—125, 126—250, and 251—375 miles of coastline. A moderate outbreak might stretch from Maine to northern Massachusetts, although it could be shifted down the coast, covering the same length of coastline, but over a different area.

When combined, the forecast terminology, the annual cyst surveys and the continual improvements and additions to the computer model have developed into a useful management tool.

"Red tide is a chronic problem affecting commercial and recreational harvesting interests throughout the Gulf of Maine," said Chris Nash, shellfish program manager for the New Hampshire Department of Environmental Services. "State agencies are responsible for monitoring toxicity levels in shellfish harvest areas and implementing harvest closures to prevent illness outbreaks. These regional scale, seasonal outlooks help state managers to plan and use limited monitoring resources effectively. Ultimately our
goals are to protect public health and give consumers confidence in the quality of the seafood products they purchase from markets and restaurants, and these forecasts are useful in realizing those goals."

"NOAA is developing a HAB Operational Forecasting System (HAB OFS) in order to provide advanced warnings like this one to help state agencies monitor harmful algal blooms and minimize public health risks," said David Kennedy, assistant NOAA administrator for the National Ocean Service. "The Gulf of Maine is one of several regions for which HAB forecasts are being developed with the intent to operationalize them within NOAA utilizing multiple assets such as those provided by the National Weather Service."

Project researchers regularly share their field observations and models with more than 80 coastal resource and fisheries managers in six states as well as federal agencies like NOAA, the EPA, and the FDA. Real-time forecasts are updated on a weekly basis and additional information will be provided on the "Current Status" page of the Northeast PSP website, particularly as new information becomes available from coastal ocean observing systems such as the Northeastern Regional Association of Coastal Ocean Observing Systems (NERACOOS), EcoMon, and AZMP. The National Weather Service is also providing extended hydrological and meteorological outlooks to accompany the bloom forecasts.

Possible Clues Found to Why HIV Vaccine Showed Modest Protection
ScienceDaily (Apr. 4, 2012) — Insights into how the first vaccine ever reported to modestly prevent HIV infection in people might have worked were recently published online in the New England Journal of Medicine. Scientists have found that among adults who received the experimental HIV vaccine during the landmark RV144 clinical trial, those who produced relatively high levels of a specific antibody after vaccination were less likely to get infected with the virus than those who did not. The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, co-funded the research.

"This analysis has produced some intriguing hints about what types of human immune responses a preventive HIV vaccine may need to induce," said NIAID Director Anthony S. Fauci, M.D. "With further exploration, this new knowledge may bring us a step closer to developing a broadly protective HIV vaccine."

In the RV144 clinical trial, which involved more than 16,000 adult volunteers in Thailand, the group that received the vaccine had a 31 percent lower chance of becoming infected with HIV than the group that received a placebo. Since the study results were reported in 2009, a consortium of more than 100 scientists from 25 institutions has been searching for molecular clues to explain why the vaccine showed a modest protective effect.

The new report describes the researchers' analyses of blood samples taken from a representative subset of study participants: 41 who were vaccinated and later became infected with HIV and 205 vaccinated participants who remained uninfected. The participants who made relatively high levels of one antibody to HIV were significantly less likely to become infected than those who did not. This particular binding antibody attaches to a part of the outer coat of the virus called the first and second variable regions, or V1V2, which may play an important role in HIV infection of human cells. The antibody belongs to a family called immunoglobulin G, or IgG.

Vaccinated study participants who had relatively high levels of a different type of HIV binding antibody, however, appeared to have less protection from the virus than vaccinated participants who had low levels of this protein. The antibody attaches to a part of the virus's outer coat called the first constant region, or C1, and belongs to a family called immunoglobulin A, or IgA. The study team hypothesizes that the C1 IgA antibody either was associated with less benefit from HIV vaccination or directly reduced the benefit of vaccination.

"The remarkable international collaboration to understand the RV144 study results has generated important hypotheses for scientists to investigate," said Barton F. Haynes, M.D., the leader of the new analysis and the director of the NIAID-funded Center for HIV/AIDS Vaccine Immunology based at Duke University in Durham, N.C.

Researchers plan to further evaluate the new findings in studies to be conducted in non-human primates using the RV144 vaccine regimen and other vaccines. Scientists must conduct more tests to determine whether high levels of V1V2 antibodies directly caused the modest protective effect seen in the RV144 study or simply were linked to other, still unidentified factors responsible for the trial's encouraging outcome. Such testing also will determine whether the V1V2 antibody response is merely a marker of HIV exposure or decreased susceptibility to HIV infection.
The study authors note that different vaccine candidates may protect against HIV in different ways. Therefore, more research is needed to understand whether these new findings will be relevant to other types of HIV vaccines or to similar vaccines tested against HIV strains from other regions or against different routes of exposure to the virus, according to the authors.

**Journal References:**


**Children: Better Protection from Influenza With Improved Vaccine**

ScienceDaily (Apr. 3, 2012) — An intranasal vaccine that includes four weakened strains of influenza could do a better job in protecting children from the flu than current vaccines, Saint Louis University research shows.

Before each influenza season, scientists predict which strains of flu will be circulating and make a trivalent vaccine that includes three strains of influenza—two of influenza A and one of influenza B. The ability to add another strain of influenza B without compromising the vaccine’s ability to protect against the other three strains will allow scientists make a better vaccine, said Robert Belshe, M.D., professor of infectious diseases at Saint Louis University School of Medicine and the corresponding author of the research article.

"The bottom line is adding another strain to make a quadrivalent vaccine improves our ability to protect against flu and doesn’t reduce the body's immune response to the other strains,” said Belshe, who also directs Saint Louis University's Center for Vaccine Development.

"It should bring us better protection because there’s less guess work than in the standard trivalent vaccine.”

Children are more susceptible than adults to influenza from one of the B strains, which change less often than A strain viruses. Some winters, influenza B viruses—Victoria or Yamagata—cause most of the flu in children and significant infection in adults, Belhs said.

Preventing flu in children is key to protecting the entire population. "We think the most important way for flu to spread is through school-aged children,” Belhs said.

In the 1980s, influenza B split into the two circulating lineages of virus, which have evolved into viruses that are quite different. Some years both B viruses or the B strain that doesn't match the vaccine circulate, which means the vaccine doesn't protect people from getting the flu.

"There are these two very different strains of influenza B that don’t cross protect. Vaccinating against one strain of influenza B does little to protect against the other,” Belhs said.

"It has not been possible to predict which strain has circulated. In the last 10 years, we predicted right five times. So you can flip a coin and do as well.”

Previously, manufacturers had not had the capacity to produce a vaccine that protects against four strains of flu, but that is no longer the case, Belhs said.

The researchers tested versions of the FluMist vaccine, which is sprayed in the nose and contains live flu viruses that have been attenuated or weakened so they don’t cause infection. The intranasal vaccine is made by MedImmune.

The nasal spray vaccine was tested in about 2,300 children between 2 and 19 years of age. The children were randomized to receive one of three vaccines: a vaccine containing four strains of influenza—two of influenza A and two of influenza B, or one of two vaccines that contained both influenza A strains and one of each of the influenza B strains. Researchers looked at the safety and antibody response to both influenza A and B viruses in children of different age groups who were vaccinated.
Those children who receive vaccine containing four strains of flu had as robust of an immune response as those who received the vaccine that contained three strains. In addition, Belshe noted no clinically significant difference the safety of the vaccines, which were well tolerated.

"We saw stuffy noses, which we know is associated with FluMist, and an occasional low grade fever, which is similar to other childhood vaccines," Belshe said.

On Feb. 28, the U.S. Food and Drug Administration approved MedImmune's quadrivalent flu vaccine for use in people between the ages of 2 and 49. The vaccine could be ready for use during the 2013-2014 influenza season, pending a recommendation from the Advisory Committee on Immunization Practices, a group that advises the Centers for Disease Control and Prevention about vaccination issues.

An injected flu vaccine designed to protect against four strains of flu—instead of the current three—also is in the works, Belshe said.

Journal Reference:
Stan L. Block, Judith Falloon, Jeffrey A. Hirschfield, Leonard R. Krilov, Filip Dubovsky, Tingting Yi, Robert B. Belshe. The Immunogenicity and Safety of a Quadrivalent Live Attenuated Influenza Vaccine in Children. The Pediatric Infectious Disease Journal, 2012; : 1 DOI: 10.1097/INF.0b013e31825687b0

The Long Arm of the Dendritic Cell: A Link Between Atherosclerosis and Autoimmunity

ScienceDaily (Apr. 4, 2012) — Individuals who suffer from autoimmune diseases also display a tendency to develop atherosclerosis—the condition popularly known as hardening of the arteries. Clinical researchers at LMU, in collaboration with colleagues in Würzburg, have now discovered a mechanism which helps to explain the connection between the two types of disorder. The link is provided by a specific class of immune cells called plasmacytoid dendritic cells (pDCs). pDCs respond to DNA released from damaged and dying cells by secreting interferon proteins which stimulate the immune reactions that underlie autoimmune diseases.

The new study shows that stimulation of pDCs by a specific DNA-protein complex contributes to the progression of atherosclerosis. The findings may have implications for new strategies for the treatment of a whole spectrum of conditions that are associated with chronic inflammatory reactions.

Atherosclerosis is a major cause of death in Western societies. The illness is due to the formation of insoluble deposits called atherosclerotic plaques on the walls of major arteries as a consequence of chronic, localized inflammation reactions. By reducing blood flow, the plaques can provoke heart attacks and strokes. A class of immune cells called dendritic cells plays a crucial role in facilitating the development of these plaques. The term refers to a heterogeneous cell population that makes up part of the immune system. Among the cell types represented in this population are the so-called plasmacytid dendritic cells (pDC), but their potential significance for atherosclerosis had not been explored until now.

A group of researchers led by Dr. Yvonne Döring in Professor Christian Weber's department at LMU, together with a team supervised by Privatdozentin Dr. Alma Zernecke of Würzburg University, has now shown how pDCs promote the development of atherosclerosis—and explained why patients with autoimmune disorders, such as psoriasis or systemic lupus erythematoses (SLE), show a predisposition to atherosclerosis.

Using laboratory mice as an experimental model, the researchers were able to show that pDCs contribute to early steps in the formation of atherosclerotic lesions in the blood vessels. Stimulation of pDCs causes them to secrete large amounts of interferons, proteins that strongly stimulate inflammatory processes. The protein that induces the release of interferons is produced by immune cells that accumulate specifically at sites of inflammation, and mice that are unable to produce this protein also have fewer plaques. Stimulation of pDCs in turn leads to an increase in the numbers of macrophages present in plaques. Macrophages normally act as a clean-up crew, removing cell debris and fatty deposits by ingesting and degrading them. However, they can also "overindulge," taking up more fat than they can digest. When this happens, they turn into so-called foam cells that promote rather than combat atherosclerosis. In addition, activated, mature pDCs can initiate an immune response against certain molecules found in atherosclerotic lesions, which further exacerbates the whole process.

The stimulation of pDCs provides the link between atherosclerosis and autoimmune diseases. "The pDCs themselves are stimulated by the self-antigens that set off the autoimmune reactions which result in conditions like psoriasis and SLE," says Döring. Indeed, it is well known that the secretion of interferons by activated pDCs contributes to the genesis of a number of autoimmune diseases.

"The newly discovered involvement of pDCs in the development of atherosclerosis establishes a direct link between this disorder and autoimmune reactions, and reveals why the stimulation of pDC that is...
characteristic of autoimmune diseases contributes to the progression of atherosclerosis," says Weber. "The findings also suggest new approaches to the treatment of chronic inflammation that could be useful for a whole range of diseases."

**Journal Reference:**

**Oral Fluoroquinolones and the Risk of Retinal Detachment**
Mahyar Etminan, PharmD, MSc (epi); Farzin Forooaghan, MD, MSc, FRCSC; James M. Brophy, MD, PhD, FRCP; Steven T. Bird, PharmD; David Maberley, MD, MSc, FRCSC

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**Abstract**

**Context** Fluoroquinolones are commonly prescribed classes of antibiotics. Despite numerous case reports of ocular toxicity, a pharmacoepidemiological study of their ocular safety, particularly retinal detachment, has not been performed.

**Objective** To examine the association between use of oral fluoroquinolones and the risk of developing a retinal detachment.

**Design, Setting, and Patients** Nested case-control study of a cohort of patients in British Columbia, Canada, who had visited an ophthalmologist between January 2000 and December 2007. Retinal detachment cases were defined as a procedure code for retinal repair surgery within 14 days of a physician service code. Ten controls were selected for each case using risk-set sampling, matching on age and the month and year of cohort entry.

**Main Outcome Measure** The association between retinal detachment and current, recent, or past use of an oral fluoroquinolone.

**Results** From a cohort of 989 591 patients, 4384 cases of retinal detachment and 43 840 controls were identified. Current use of fluoroquinolones was associated with a higher risk of developing a retinal detachment (3.3% of cases vs 0.6% of controls; adjusted rate ratio [ARR], 4.50 [95% CI, 3.56-5.70]). Neither recent use (0.3% of cases vs 0.2% of controls; ARR, 0.92 [95% CI, 0.45-1.87]) nor past use (6.6% of cases vs 6.1% of controls; ARR, 1.03 [95% CI, 0.89-1.19]) was associated with a retinal detachment. The absolute increase in the risk of a retinal detachment was 4 per 10 000 person-years (number needed to harm = 2500 computed for any use of fluoroquinolones). There was no evidence of an association between development of a retinal detachment and β-lactam antibiotics (ARR, 0.74 [95% CI, 0.35-1.57]) or short-acting β-agonists (ARR, 0.95 [95% CI, 0.68-1.33]).

**Conclusion** Patients taking oral fluoroquinolones were at a higher risk of developing a retinal detachment compared with nonusers, although the absolute risk for this condition was small.

**Removing Legal Barriers to High-Quality Care for HIV-Infected Patients**

When AIDS emerged in the 1980s, fear and misunderstanding about the disease prevailed. Patients with AIDS faced a grim prognosis, with no effective treatments. They confronted discrimination in the workplace and throughout society and had little legal recourse for combating it. Simply getting tested for human immunodeficiency virus (HIV) could be incriminating. Throughout the United States, AIDS activists, politicians, and physicians joined forces to enact state laws that created special provisions for HIV testing and protecting patients’ privacy. Several states passed laws requiring specific written informed consent for testing and disclosure of results.

Thirty years later, the HIV landscape has completely changed. Progress in HIV treatment since the mid-1990s has converted a rapidly fatal condition into a chronic, treatable disease. Whereas an AIDS diagnosis in the 1980s meant a median survival of 12 to 24 months, life expectancy for a patient newly diagnosed with HIV infection today is measured in decades.
Furthermore, HIV transmission is readily preventable through behavioral changes and treatment, so infected persons are far less likely to pass the virus on to others. In 2006, the Centers for Disease Control and Prevention, faced with the fact that a substantial minority of HIV-positive Americans were unaware of their HIV status, recommended expanding HIV screening and eliminating any requirements for written or oral informed consent beyond what is required for testing for other conditions. Most states have changed their HIV-testing laws to comply with these recommendations, and there is widespread support for changing the testing laws in the remaining states.

In addition to laws in some states requiring written consent for testing, 35 states also include provisions distinguishing the privacy of the HIV test and its results from all other personal health information. A Web search of state laws revealed widely ranging degrees of restrictiveness regarding the disclosure of results by treating physicians. Massachusetts requires written consent to disclose such results, even to other treating physicians. Some states allow for disclosure to protect the health of the patient. And several states allow disclosure to any provider treating that patient. We would argue that in addition to the dramatic improvement in prognosis for HIV-positive patients since 1986, several other important changes have rendered unnecessary any laws that restrict the disclosure of HIV results to treating providers.

One major change is that federal laws now offer all patients protection that was not available in the 1980s. The Health Insurance Portability and Accountability Act of 1996 (HIPAA) requires that all personal health information be kept confidential, regardless of the medical conditions to which it refers. Employees of health care organizations who violate the law face fines, imprisonment, and termination. The Americans with Disabilities Act (ADA) prohibits discrimination based on HIV status. Thus, HIV-positive patients now have the force of two federal laws protecting them.

A second change is that health care delivery has become more centralized, collaborative, and networked. Market forces have sparked the consolidation of physicians and hospitals into larger networks. The need to control health care spending has focused attention on improving the coordination of care within these networks through tighter clinical and financial integration. Clinical integration will be accomplished through the spread of electronic health records (EHRs), funded in part by federal incentives for the “meaningful use” of information technology. Financial integration will come through accountable care organizations under the Affordable Care Act and through similar models in the private sector. Modern health care is becoming more team-based and coordinated as part of efforts to improve care for patients with multiple conditions requiring complex, interacting treatments. These developments put a premium on the rapid, reliable sharing of clinical information among all members of a patient’s care team.

Such information sharing is particularly critical to the successful management of HIV infection. Patients who receive timely treatment can survive long enough to allow the development of a range of coexisting conditions, both related and unrelated to HIV infection. HIV therapy invariably involves a combination of medications, many of which have clinically significant interactions with other drugs. Patients thus frequently require treatment by multiple specialists as well as primary care physicians, all of whom must be kept informed about patients’ ongoing care and state of health.

Another key priority for modern health care providers is the mandate for continuous improvement of quality of care. There is convincing evidence that not all patients are consistently receiving the care they need. Improving quality requires identifying patients who are at risk for receiving suboptimal care or having poor outcomes, implementing improvement strategies, and measuring results. The ability to aggregate accurate clinical data is critical to these efforts. Ensuring that patients with HIV–AIDS are receiving high-quality care requires the collection of data on viral load, CD4 T-cell counts, medications, and other elements of care.

Because of the restrictions that apply in Massachusetts, there are still situations in which fear of violating the laws has hindered good-quality care for people living with HIV in that state. In one case, patients with HIV infection have been excluded from a program that allows community-based primary care physicians’ access to their own patients’ EHRs while their patients are hospitalized. In another instance, the results of HIV tests conducted within a hospital or a community-based health care system that share an EHR cannot be viewed by a patient’s own physician unless he or she works within the walls of the institution that conducted the test. One hospital’s newborn nursery prohibits the inclusion of the mother’s HIV status in the infant’s chart or EHR due to concern about the legality of releasing this information to the child’s pediatrician. One internal quality-improvement program is denied access to a clinic’s HIV-load results, rendering the clinic unable to measure the rate of virologic suppression or to easily identify patients who are not receiving optimal treatment. In all these cases, concern about privacy has trumped patients’ need to receive high-quality, collaborative care.
Worse still, rather than following the lead of other states, in March the Massachusetts Senate passed a bill that could further tighten existing confidentiality restrictions. Although the proposed law makes testing easier by allowing for oral rather than written consent, it imposes stricter regulations on disclosure to a patient’s treating clinicians unless they work within the facility where the test was conducted. The law requires specific, written consent before there can be sharing of any “HIV-related medical information,” including test results, medication lists, or any other information that indicates HIV status. Implicitly excluded by this law would be disclosure in a peer-to-peer consultation across institutions or from community clinic to hospital, even if it occurs at the patient’s request. Such communication would have to be scrubbed of all information pertaining to HIV status unless specific written consent were granted. Since many health systems share EHRs across multiple facilities, the proposed law could complicate the documentation of “HIV-related medical information” in the medical record. It could engender a separate system of documentation for patients with HIV–AIDS, distinct from that for other patients and disconnected from many treating providers. Faced with these barriers to good clinical care, a group of more than 200 clinicians and researchers who specialize in HIV care or investigation formally protested the bill, which is expected to undergo further revision.

Remarkably, HIV infection has made the transition from death sentence to chronic condition in relatively short order. Laws that restrict the ability to collect, analyze, and appropriately share data on HIV-infected patients put them at risk for suboptimal care. HIV-positive patients should be treated in patient-centered, coordinated systems that ensure they receive all needed elements of care, for all their conditions. We believe it is time to remove special provisions for privacy that are based exclusively on HIV testing and diagnosis.

**Antibody Clues to AIDS Vaccine Success**

*Agence France Presse*, (04.05.2012)

Differing levels of antibody responses may help explain the results of a 2009 trial in which an AIDS vaccine candidate was shown to protect 31 percent of participants, according to a new report.

The new analysis of those initial results indicates the IgG antibody, created by the body to stave off infection, was able to attach itself to the surface of the HIV protein — a region referred to as V1V2 — and, in fact, prevent infection in some individuals who received the vaccine versus the placebo.

However, participants demonstrating the highest levels of another antibody, IgA, seemed more vulnerable to HIV than those with lower levels. This led scientists to believe IgA could have hindered the vaccine and rendered it less effective.

“This analysis has produced some intriguing hints about what types of human immune responses a preventive HIV vaccine may need to induce,” said Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases (NIAID).

The data were gleaned from a trial involving 16,395 HIV-negative volunteers in Thailand; it was funded by NIAID, the US Army Medical Research and Materiel Command, and the Bill & Melinda Gates Foundation. Although the study was considered ground-breaking for its 31 percent protection rate, a vaccine must offer at least 50 percent protection to be introduced in the marketplace.

“Different HIV vaccines may protect against HIV in different ways,” said study co-author Nelson Michael, Military HIV Research Program director at Walter Reed Army Institute of Research.

“More research is needed to fully understand these results, and to determine if they can be generalized to other types of HIV vaccines or similar vaccines tested against other regional types of HIV or via different routes of exposure,” Michael added.


**2 genetic deletions in human genome linked to the development of aggressive prostate cancer**

*Discovery of inherited-genetic variations may help assess a patient's risk of life-threatening disease before it strikes*

NEW YORK (April 9, 2012) — An international research team led by Weill Cornell Medical College investigators have discovered two inherited-genetic deletions in the human genome linked to development of aggressive prostate cancer. The findings, published online today in the *Proceedings of the National Academy of Sciences* (PNAS), indicate a man’s risk of developing prostate cancer either triples or quadruples, depending on the genetic variant they inherit.
In the study, one genetic deletion is shown to affect the functioning of a known gene, while the other, found in a non-coding area of the genome once considered to be "junk DNA," seems to be regulating a cascade of genes. According to the lead co-authors, the study is potentially groundbreaking because it demonstrates that so-called copy number variations (CNVs) in either protein coding or non-coding areas of the human genome play a significant role in the development of cancer in general, and in aggressive prostate cancer, specifically.

"We used to think that only genes that made proteins were responsible for disease, but this study shows us that there is inherited information in the non-coding areas of the genome that appear to play a strong role in development of cancer," says study co-author, Dr. Mark A. Rubin, the Homer T. Hirst Professor of Oncology in Pathology at Weill Cornell Medical College. Other researchers have linked CNVs to Alzheimer's and Parkinson's disease, mental retardation, autism, schizophrenia and neuroblastoma, a type of brain cancer. "This study suggests there are other cancers that might be associated with CNVs," says Dr. Rubin. "It's an exciting new field of research."

"The study shows that copy number variations matter in cancer," says co-lead investigator, Dr. Francesca Demichelis, who is now an Assistant Professor at the Center of Integrative Biology at the University of Trento in Italy and an Adjunct Assistant Professor in the Institute for Computational Biomedicine at Weill Cornell Medical College.

The two genetic variants identified by the research team are not the only cause of aggressive prostate cancer, Dr. Demichelis says. "These variants likely collaborate with other factors early in a man's life leading to development of prostate cancer."

Prostate cancer affects one in six men during their lifetime, and family history is the strongest risk factor for prostate cancer. Because of the inheritable nature of the disease, for the study Weill Cornell researchers hunted to find DNA that is either significantly deleted or duplicated in the genome of patients with prostate cancer to compare it to men without the disease.

In this collaboration between Weill Cornell Medical College, the Brigham and Women's Hospital and Innsbruck University Hospital, researchers examined blood samples from a population of men from the Tyrol Early Prostate Cancer Detection Program in Austria. Since 1993, this program has been aggressively screening men, age 45-75, who live in the Tyrol region with prostate specific antigen (PSA) in order to detect prostate cancer as early as possible. The population includes men who developed prostate cancer as well as men with elevated PSA who have no prostate cancer based on a biopsy. In addition, researchers looked at the germline variation in these patients to see if there is a risk factor as to why some men with elevated PSA have prostate cancer and some men do not.

Molecular studies were performed in the U.S. on more than 1900 blood samples from Tyrolean men (867 unrelated cancer patients and 1,036 controls). Researchers discovered two CNVs that were significantly different between Tyrolean individuals with aggressive prostate cancer and those without cancer, and then reproduced that finding in another group of 800 U.S. patients. The researchers then tested the effect of the two variants in laboratory cells and discovered they increase the ability of cancer cells to grow and to invade.

Both of these variants are small deletions in DNA that lead to over-expression of genes, Dr. Demichelis says. She and her colleagues found that one gene that is over-expressed due to the variant deletion is MGAT4C, which leads to the ability of cells to grow and migrate. "A man with the variant is four times more likely to develop prostate cancer if he inherited this variant than if he did not," Dr. Demichelis says. "Interestingly, MGAT4C was found to be significantly over-expressed in metastatic versus localized prostate cancer;" she adds.

The role of the other genetic variant, located in the "junk" region of the human genome, is not yet known, but the researchers believe it activates a cascade of other genes. They calculated a man is three times more likely to develop prostate cancer if he has inherited this variant.

The investigators calculated these two newly identified variants occur at a frequency of between 1.5-3 percent of the overall population, but are found at a significantly higher percentage in men diagnosed with aggressive prostate cancer. "For the gene coding variant, MGAT4C, we were able to analyze metastatic human samples where we observed that the high-risk gene is abundantly present," says Dr. Demichelis.

Now researchers are looking for other variants they hope to be able to build into a comprehensive DNA test to be used as a diagnostic tool to help clinicians identify men whose prostate cancer will likely progress to advanced stages. "We could also potentially use such a DNA test for chemoprevention if risk of developing aggressive prostate cancer is deemed to be high," says Dr. Demichelis. "This is the start of a new strategy. It would not replace PSA, but would identify other risk factors."
"In this new area of research, we are starting to appreciate that the differences in inherited genomic variants account not only for why we look different or respond in various ways to medication, but also for why we develop disease," Dr. Rubin says. "This is the first study to suggest these variants may account for susceptibility to cancer. This new line of research will also allow us to study the biology around prostate cancer initiation."

Immune cells, 'macrophages' become activated by body temperature
Molecular mechanisms involved in the switch-on of the temperature sensor TRPM2 by hydrogen peroxide have been clarified

Macrophages playing an important role in the immune system eat and fight against pathogens and foreign substances in the very beginning of infection. In this condition, macrophages produce reactive oxygen species for sterilization. However, the relation with the temperature sensor was not previously known. Professor Makoto TOMINAGA from National Institute for Physiological Sciences (Okazaki Institute for Integrative Bioscience), National Institutes of Natural Sciences, and his research team member Ms. Makiko KASHIO have identified the mechanism through which TRPM2 is activated by body temperature with hydrogen peroxide (a kind of reactive oxygen species) produced by immune reactions. This research result was reported (online in the week of 9th April, 2012) by *Proceedings of the National Academy of Sciences* of the United States of America.

The research group focused on the relation between hydrogen peroxide and TRPM2. Although TRPM2 is usually activated by high temperature near 48°C in the absence of endogenous ligands, it becomes activated at our normal body temperature with hydrogen peroxide production. It means that hydrogen peroxide works as "a switch" which controls TRPM2 function. In addition, they found that phagocytic activity of macrophages was enhanced in the febrile temperature (38.5°C). Professor TOMINAGA says, "It was also revealed that oxidation of TRPM2 by hydrogen peroxide is involved in the switch-on mechanism and we identified a single amino acid which is oxidized. This newly identified mechanism of TRPM2 regulation may lead to the development of new treatment strategies or drugs for infection. When we are infected with bacteria, we often run a fever, and it is known that body temperature might be important for our immune system. TRPM2 might explain the mechanism through which fever boosts up our immune system."

Inexpensive Female Genital Schistosomiasis Prevention Could Help Reduce Women's Risk Of HIV Infection

In this Huffington Post "Global Motherhood" blog post, Peter Hotez, president of the Sabin Vaccine Institute and dean of the National School of Tropical Medicine at Baylor College of Medicine, describes female genital schistosomiasis (FGS), which affects more than 100 million women and girls in Africa and "causes horrific pain and bleeding in the uterus, cervix and lower genital tract, not to mention social stigma and depression." According to studies, women affected by FGS "have a three- to four-fold increase in the risk of acquiring HIV/AIDS," but a low-cost drug called praziquantel may prevent FGS "and therefore also serve as a low-cost AIDS prevention strategy if it is administered annually to African girls and women beginning in their school-aged years," he notes.

Hotez says Merck Serono has donated 250 million of the eight-cent praziquantel tablets, and private donors, USAID, and the British Department for International Development (DFID) "have begun to support programs of praziquantel mass treatment for schistosomiasis control." He adds that he has "argued that large-scale AIDS treatment programs such as the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) should also embrace annual praziquantel treatments." Hotez says "another added measure would be to develop a true vaccine to prevent schistosomiasis." He concludes, "We may now be at the beginning of the end of this disease, provided we can scale up schistosomiasis control efforts in addition to making a successful schistosomiasis vaccine" (4/9).

Researchers Alarmed by Indiana High School Rape Rates

Associated Press, (04.07.2012)

A CDC-conducted analysis of sexual violence found that 17.3 percent of Indiana high school girls reported forced sexual intercourse, compared with a national rate of 10.5 percent.
Indiana University (IU) researchers who analyzed the findings believe the figures may not accurately reflect the problem since up to 50 percent of sexual assaults are not reported. Furthermore, Indiana, Mississippi, and New Mexico are the only states that do not require law enforcement agencies to report sexual violence to the Federal Bureau of Investigation.

A challenge is determining why the numbers are so high. “There are other more socially conservative states, more provincial states, certainly poorer states,” said Jonathan Plucker, director of IU’s Center for Evaluation & Education Policy. “But the data we have available to us just didn’t allow us to figure out why our figures are so bad.”

Plucker and Julia Heiman, director of the Kinsey Institute for Research in Sex, Gender and Reproduction, called for better ways to create, track, and fund community-wide sex education programs. Schools should develop more effective and age-appropriate programs and boost staff training, they said.

Toby Strout, executive director of the Bloomington-based Middle Way House, which works to end violence against women and children, said at least 80 percent of unwanted sexual activity involves people who know each other. “We’re not talking about people jumping out from behind the bushes,” he said.

**Lack of Information Raises Risk of Cervical Cancer**

*Inter Press Service*, (03.29.2012) Marcela Valente

Argentinean women know little about cervical cancer, and most have a “complete lack of knowledge” that human papillomavirus is one of its leading causes, according to a new study.

Free HPV vaccination is mandatory for 11-year-old girls, yet cervical cancer remains the second-leading cause of cancer deaths in women ages 35-64. Pap tests can detect pre-cancerous lesions and save lives when followed by proper medical treatment. However, Argentina’s Health Ministry reported in 2009 that only 46 percent of northern province women 35-64 were tested within two years of the survey.

Author Dr. Silvina Arrossi, scientific coordinator of the National Cervical Cancer Prevention Program, said the study aimed “to find out about women’s perceptions and knowledge” of cervical cancer to “incorporate their views into prevention strategies.”

The study, “What Women Think: Knowledge and Perceptions About Cervical Cancer and the Pap Test,” focused on women in Buenos Aires (Argentina’s most populous province) and the northern provinces of Jujuy, Salta, Misiones, and Chaco, which have Argentina’s highest cervical cancer mortality rates.

The interviews uncovered a range of misunderstandings, including that cervical cancer can lie dormant until “awakened” by invasive action—including a Pap test; and that older, sexually inactive women who feel fine do not need Pap tests. Most cited TV and radio as information sources, not the health system.

Arrossi’s team’s findings formed the basis of a photo-novella about a daughter who convinces her mother to continue having Pap tests despite her age. Recommendations also were made for health centers to have female personnel onsite to conduct Pap tests to preserve patients’ modesty. Personnel also will be trained to engage women in a dialogue versus just distributing pamphlets.

**Public Health Leaders Criticize Ottawa’s Ideology-Based Drug Policies**

*Canadian Press*, (03.28.2012) Helen Branswell

In its approach to drug use, the federal government is favoring political ideology over scientific evidence, several Canadian public health leaders are saying. The chief medical officers of health for British Columbia, Saskatchewan, and Nova Scotia have published a commentary in the Open Medicine journal addressing the issue.

“There’s some evidence that [the model we use is] very ineffective and creates a whole class of harms which wouldn’t be there if we weren’t dealing with drugs in this particular way,” said Dr. Perry Kendall, British Columbia’s chief medical officer of health.

Speaking for themselves as individuals, Kendall, Dr. Robert Strang of Nova Scotia, and Dr. Moira McKinnon of Saskatchewan co-authored the commentary declaring that Canada’s current approach has not only failed to control drugs, but also has spawned drug violence and the spread of infectious diseases like hepatitis C and HIV. Dr. Evan Wood, of the British Columbia Center for Excellence in HIV/AIDS, was also a co-author. The B.C. Center supports the Vienna Declaration, which debuted at the International AIDS Conference in Austria in 2010. It calls upon governments to develop evidence-based drug policies.

The authors maintain Canada should address drug addiction as a health problem versus a criminal justice issue. Canada, they said, is moving toward mandatory minimum sentences, even as several US
states are abandoning such laws. Although mandatory minimums were a provision of the omnibus federal crime bill given Royal Assent in mid-March, Dr. David McKeown, Toronto’s medical officer of health, believes that “in the modern era” science should outweigh ideology in shaping policy, which should be evidence-based.

The Urban Public Health Network, which represents the chief public health officers in Canada’s 18 largest municipalities, also has announced its support of the Vienna Declaration.

**Patient-Delivered Partner Therapy for Chlamydial Infections: Practices, Attitudes and Knowledge of California Family Planning Providers**

*Sexually Transmitted Diseases*, (02..2012) Sharon Jotblad; and others

A core strategy of chlamydia control is treating patients’ sex partners. While innovations like patient-delivered partner therapy (PDPT) have been shown effective in preventing repeat infection, providers’ PDPT practices and perceptions have not been adequately evaluated. In the current study, the researchers assessed factors associated with routine use of PDPT, and they described providers’ related practices, knowledge, attitudes, and barriers.

A convenience sample of California family planning practitioners was evaluated in 2007 using a cross-sectional, self-administered, Internet-based survey. Multivariate logistic regression determined predictors associated with routine PDPT use.

A total of 286 providers responded: 73 percent reported routine use of PDPT for chlamydia, and 77 percent provided medication to patients for partner(s). Female clients were more likely to be offered PDPT compared to males (73 percent vs. 53 percent, P < 0.0001).

More than 90 percent of respondents agreed that PDPT helped provide better patient care, was well-received, and protected against re-infection. Common PDPT concerns included missed counseling opportunities (51 percent) and incomplete partner care (42 percent). Forty-one percent said lack of reimbursement for PDPT was an important barrier to routine use. Independent predictors of routine PDPT use included affiliation with an agency that received free, prepackaged single-dose medicines for onsite dispensing (adjusted odds ratio = 2.66, 95 percent confidence interval: 1.39-5.10) and support for a clinic’s medical director (AOR = 4.85, 95 percent CI: 1.57-14.96).

“A majority of providers in this sample reported routinely using PDPT for chlamydia-infected clients; provision of prepackaged medication to clinics facilitated use of PDPT,” the researchers concluded.

**Enjoying Disclosure’s Freedom**

*Westside Gazette (Fort Lauderdale)*, (03.08.2012) Nancy Asha Molock

“I had always been a carefree, happy, spiritual, and truthful person. But after I got HIV from my boyfriend 11 years ago, I stopped feeling like myself. I was doing well physically, my CD-4 count was above 1,100 (and rising), and my viral load was undetectable.

“... I was a prisoner of my own fear and shame, and after 10 years I decided that enough was enough. I had done nothing to be ashamed of, and the contribution I could make to ending this epidemic was more important than the guilt I felt. ...

“On National Women and Girls HIV/AIDS Awareness Day in 2011, I publicly disclosed my HIV status in the Philadelphia Daily News newspaper. ... I received all kinds of responses: the good, the bad, and the ugly. Some people were shocked because I was older, a teacher, mother, wife, upstanding member of my community—and HIV-positive. ... I didn’t fit the ill-perceived stereotype of someone who contracts HIV. But the shock factor worked, because many family members and friends asked me to go with them to get tested.

“That day of my public disclosure was also the day I broke free. A heavy load lifted off my spirit, and 10 years of numbness, shame, guilt, and fear seemed to just melt away. It doesn’t matter anymore what people say or think about me. What matters most to me is that I feel good about myself, and I’m standing in my personal truth.

“... I realize that disclosure may not be best for every HIV-positive person; it’s a personal choice, but a necessary one for me. I feel free and light, as if I can finally spread my wings and soar. Yes, I believe I can fly; I believe I can touch the sky.”

The author, a retired teacher, is writing her memoir.
Birthrate for Teens Is Lowest in History

**USA Today**, (04.10.2012) Sharon Jayson

A new analysis of 2010 preliminary data shows the US teen birthrate reached its lowest point since 1946, the National Center for Health Statistics reported Tuesday.

Federal data released in November found a 9 percent drop in the teen birthrate between 2009 and 2010, to a historic low of 34.3 births per 1,000 teens. That reflected a 44 percent decrease from 61.8 in 1991. The record high was 96.3 in 1957.

Sarah Brown, CEO of the National Campaign to Prevent Teen and Unplanned Pregnancy, credits the reduction to increased use of contraception and less sex. “Young people are being more careful,” she said.

The new analysis notes ethnic/racial group rates of 10.9 for Asians, 23.5 for whites, 51.5 for blacks, and 55.7 for Hispanics. “The fact that states with high Hispanic populations still show declines speaks to the more general pattern of increasing contraceptive use and declining teen births,” said Guttmacher Institute Senior Research Associate Laura Lindberg.

Lindberg’s research for a December report noted no change in the percentage of sexually active teen girls, but significant increases in their use of contraception, especially upon sexual debut.

Lindberg also reported a small percentage decrease in teen girls “who said they wanted to get pregnant,” which she maintains speaks “to an underlying shift in attitudes.” Lindberg documented that the proportion of girls who had ever used “morning-after” emergency contraception, 12 percent to 15 percent, held steady from 2006-2008 to 2008-2010.

Although Guttmacher’s abortion data are from 2006, Lindbergh said that “declining abortion rates [are] paralleling declining pregnancy and birth” rates.

Premarital Intercourse Rising, Sex Education, Regulation Questioned

**Xinhua News Agency**, (04.11.2012)

Premarital sex in China has skyrocketed in the last 20 years, according to a survey of people in 31 areas across the country. The results were published last week in an official Community Party magazine.

Among respondents, 71.4 percent indicated engaging in premarital sex, a 30 percent spike from a 1994 study. The findings renewed debate surrounding China’s legal marriageable age (20 for females, 22 for males) and sex education. During the current National People’s Congress legislative session, Huang Xihua, a deputy to the NPC, recommended lowering the age to 18.

Sex education, long a taboo in traditional society, has gained traction among officials. Sex education textbooks were introduced in Shanghai and Beijing in October. Peng Xiaohui, a sexologist at Central China Normal University, heralds the uptake of early-age sex education. Peng notes Chinese children conventionally would not be taught about sex, neither by families nor in school.

Research results noted 24.5 percent of respondents received information on sex from the Internet, including through pornography, which is strictly prohibited and censored by public security departments and the government.

According to Shanghai high school teacher Li Hui, most male college students know how to download porn. Hui believes exposure to information on sex is somewhat helpful, but increasingly strict oversight has made access more difficult.

Yu Dongyan, a medical worker at the Accidental Pregnancy Hotline for Teenagers, asserts many young girls are hurt by their lack of sexual knowledge this time of year. March and April (around two popular romantic festivals―Valentine’s Day and White Day) are peak times for abortions, Yu said.

80 Percent of Women Don’t Report Rape or Sexual Assault, Survey Claims

**The Telegraph (London)**, (03.12.2012) Martin Beckford

A recent poll conducted by the parenting website Mumsnet revealed 83 percent of women who said they were sexually assaulted or raped did not report the crime to police, and 29 percent did not even tell friends or family.

A total of 1,609 females responded to the survey. Of these, 10 percent said they had been raped and 35 percent sexually assaulted. Nearly one-quarter of these victims were assaulted more than once, and two-thirds knew their attacker.

“We simply shouldn’t accept that we live in a country where one in ten women are raped and over one-third sexually assaulted,” said Justine Roberts, Mumsnet’s co-founder. “Things are made worse by
the feeling among many women that they can’t talk about these crimes for fear of being treated unsympathetically, denying them access to practical and emotional support when they need it most.”

Mumsnet is responding with a campaign entitled “We Believe You.” It seeks to dispel myths—including that women may invite rape by the way they dress, and that sexual assault cannot occur within relationships—as well as to support victims.

“We want to see ongoing public campaigns to tackle attitudes to sexual violence, and work with young people in schools to prevent harmful behaviors developing in the first place,” said Holly Dustin, director of the End Violence Against Women Coalition.

Preteens More Likely to Report HPV Vaccine Side Effects

MyFoxAL.com (Birmingham, Alabama). (04.06.2012) HealthDay News

A survey of almost 900 females ages 11-26 within two weeks of receiving the Gardasil human papillomavirus vaccine found that preteen girls were more likely to report side effects from the immunization. Younger patients also were more likely to have been given other vaccinations—including hepatitis A, tetanus and the like—at the same time as Gardasil.

In total, 78 percent of females surveyed reported pain when receiving the vaccine, 17 percent bruising or discoloration, 14 percent swelling at the injection site, and 15 percent dizziness. One percent fainted.

Pain at injection site was reported by 84 percent of girls ages 11-12, compared with 74 percent for women ages 18-26. Dizziness after vaccination was reported by 19 percent of 11- to 12-year-olds, versus 8 percent for 18- to 26-year-old women.

Allison Naleway, lead author of the CDC-funded study and senior investigator with Kaiser Permanente Center for Health Research in Portland, Ore., said better HPV vaccine education is needed.

“Our study found that young girls do have some knowledge about the vaccine, but they need to know more. If these girls and their parents know what to expect, they will likely be less afraid of getting the vaccine,” she said.

While most surveyed knew Gardasil is given in three injections and prevents cervical cancer, many did not know it also can protect against genital warts and abnormal Pap smears.

“Reported Adverse Events in Young Women Following Quadrivalent Human Papillomavirus Vaccination” was published in the Journal of Women’s Health (2012;doi:10.1089/jwh.2011.2895).

Achilles Heel of Dengue Virus Identified: Target for Future Vaccines

ScienceDaily (Apr. 11, 2012) — A team of scientists from the University of North Carolina at Chapel Hill and Vanderbilt University have pinpointed the region on dengue virus that is neutralized in people who overcome infection with the deadly pathogen. The results challenge the current state of dengue vaccine research, which is based on studies in mice and targets a different region of the virus.

"In the past researchers have relied on mouse studies to understand how the immune system kills dengue virus and assumed that the mouse studies would apply to people as well," said senior study author Aravinda M. de Silva, PhD. associate professor of microbiology and immunology at the UNC School of Medicine.

"Our study for the first time shows what region the immune system targets when they are fighting off the virus. The region on the virus targeted by the human immune system is quite different from the region targeted by mice."

The new research, which will appear online during the week of April 11-14, 2012 in the Proceedings of the National Academy of Sciences, was performed using blood cells from local travelers infected with dengue virus.

The global incidence of dengue has grown dramatically in recent decades, putting about half of the world’s population at risk. Creation of a vaccine is complicated by the fact that there are four distinct, but closely related forms of the virus that cause dengue. Once people have recovered from infection with one form of the virus, they have lifelong immunity against that form.

But if they become infected with one of the other three forms of the virus, they increase their chances of developing the severe bleeding and sometimes fatal dengue hemorrhagic fever and dengue shock syndrome. The leading theory to explain why some people develop dengue hemorrhagic fever is that under some conditions the human immune response can actually enhance the virus and disease during a second infection.

"This is a huge issue for vaccine development," said lead study author Ruklanthi de Alwis, a graduate student in de Silva’s lab. "We have to figure out a way to develop dengue vaccines that induce the good
response that protects against infection, at the same time avoiding the bad response that enhances disease."

de Alwis looked at a particular subset of the immune response—specialized molecules called antibodies. UNC investigators identified 7 local individuals who had contracted dengue during travel to an endemic region and sent blood cells from these individuals to Vanderbilt School of Medicine. Drs. Scott Smith and James Crowe at Vanderbilt were able to isolate dengue antibodies from these cells for further study at UNC. The team found that instead of binding to small fragments of the virus—like mouse antibodies do—human antibodies that neutralized the virus bound to a complex structure that was only present on a completely assembled dengue virus.

"Though this is the first time this phenomenon has been shown with dengue, just last year there were a number of studies showing that antibodies recognize similar complex epitopes in both HIV and West Nile Virus," said de Alwis. "New vaccines as well as those already in the pipeline will need to be assessed to see if they bind just a small fragment or the whole virus, which may determine whether or not they work in humans."

Group Says Indiana’s HIV Law Creates Dilemma
By SHAMEKA NEELY
Posted April 11, 2012
The CDC estimates that 1.2 million people in the United States are living with HIV infection. An Indiana University research class from the Department of Social Work gave a presentation at the Monroe County library on Indiana Senate Bill 52 which passed this session.

The bill gives providers the right to test someone with HIV without their consent if they suspect they have HIV.

“I think all of us felt a little conflicted about how we felt about this bill, because as social workers something that we really work towards is dignity and worth of a person,” says Annie Seltzer, a junior social worker. “It’s hard because sort of goes against someone’s privacy and someone saying no they don’t want the test. However, from a global health stand point this was really important.”

The students said to help stop the spread of the disease people need to be tested to know if they are infected. The CDC estimates 1 in 5 individuals are unaware they are positive. Students were required to look at the impact of the bill on populations and come up with solutions.

“It was interesting to see the students struggle with the idea that this testing can be done without consent for some populations and they talked about that a lot in class of whether that fit social work values,” says Bruce McCallister, a lecturer at the IU School of Social Work.

Governor Daniels signed the bill in mid-March.

Better Treatment for HIV-Positive Pregnant Women
Voice of America News, (04.10.2012) Joe DeCapua
Recently released World Health Organization (WHO) guidelines aimed at ending perinatal HIV transmission advocate earlier and lifelong antiretroviral treatment for infected mothers-to-be. Doctors Without Borders (DWB) supports these guidelines.

DWB Medical Aid Coordinator Dr. Nathan Ford said perinatal HIV transmission remains hugely problematic in developing countries. “There are around 2 million HIV-positive children in developing countries, whereas in the United Kingdom, for example, there are just 70. So, we’ve almost got rid of this problem in the West.”

Ford noted that previous recommendations called for placing HIV-positive expectant mothers on antiretrovirals only during pregnancy. Once they delivered, treatment would be discontinued unless the women fell ill, often measured by a CD4 count below 200, or became pregnant again.

Ford maintains that starting and keeping women on “antiretrovirals irrespective of their level of immunity” for life would simplify the process in rural areas, and eliminate the need “to keep restarting and stopping and restarting” treatment, which could lead to drug resistance or a lag time that would compromise the unborn child.

Although this change in course would cost more initially, Ford said, “Treating an HIV-positive child for life is incredibly expensive. So, avoiding those infections is going to be cost-saving in the long run.”

The WHO guidelines effectively align treatment in developing and developed countries, and DWB notes the potential benefits for millions of people.
“Providing treatment earlier is not only good for an individual’s health, but it’s also good for preventing the spread of the virus from one person to another,” said Ford. “And that’s not just pregnant women. That’s any HIV-positive adult.”

When Ignorance Is Lethal

*The Economist*, (04.07.2012)

Romania has come a long way from the dark days of 1980s and 1990s, when an HIV/AIDS epidemic resulting from poor infection controls and questionable medical practices came to light. Most of those infected at that time were young, hospitalized children. Patients who did not die were frequently ostracized.

Now: Antiretroviral treatment is free to people in need; AIDS death rates have plummeted; mother-to-child transmission rates have declined dramatically due to medical management; and patients’ privacy is closely guarded. Romania is often cited as a success story for other poor countries dealing with epidemics.

But a considerable number of Romanians with HIV are unaware of their infection, and many remain ignorant of the basic facts about AIDS. Hard-hit by economic decline, the country has gutted funding for HIV/AIDS education, campaigners say, noting that prevention outreach has always been challenging in the nation due to fear of the disease.

Sexual transmission is the most common route of HIV infection, according to health workers. The silent pool of HIV-positive people who do not realize that they and their sexual partners are at risk is of great concern to these providers.

Mississippi Teen Pregnancy Rate Highest in US: CDC

*Reuters*, (04.10.2012)

CDC’s latest teen pregnancy report, released Tuesday, shows Mississippi with the highest teen birthrate, 55 births per 1,000 teens ages 15-19, more than 60 percent above the overall US figure of 34.3. In contrast, New Hampshire’s rate of 15.7 was less than half the national average. Between 2007 and 2010, the rate fell by 8 percent or more in 47 states and the District of Columbia. Only West Virginia, Montana, and North Dakota registered little decline. While the teen pregnancy rate in the United States has reached a historic low, CDC noted that it remains among the highest seen in industrialized nations.

Sri Lankan Health Officials Report Increase In Number Of Dengue Cases In First Quarter Compared To 2011

Sri Lankan health authorities “have reported a three-fold increase in the number of recorded dengue fever cases in the first quarter of this year,” *IRIN* reports. According to the national Epidemiology Unit, “9,317 dengue cases and 38 deaths were reported in the first three months of 2012, [compared with] 3,103 in the first quarter of 2011,” the news service writes, noting that more than half of the cases were recorded “in the country's Western Province, where most of the island's 20 million inhabitants live.” Intermittent rain, which allows stagnant water to collect and create mosquito breeding grounds, are expected to continue through April, and “[h]ealth officials agree that removing mosquito breeding sites is the most important step in mitigating risk,” according to IRIN. "In May 2010 the government launched a campaign to curb the spread of the disease," and last year the number of cases dropped when compared to 2010, the news service notes (4/11).

Guardian Examines Swaziland’s HIV Epidemic

The *Guardian* examines the HIV epidemic in Swaziland, writing, "While neighboring countries have made inroads against the disease, the mountain kingdom of one million people continues to suffer setbacks, partly due to cultural norms around sexuality being exacerbated by a financial crisis." According to the news service, Swaziland has "the highest HIV rate in the world, with more than one in four adults estimated to be carrying the virus."

"Research has found that, despite government information campaigns, understanding of HIV/AIDS is poor," the Guardian writes, adding, "A campaign funded by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) to encourage men to undergo circumcision—not a tradition in Swaziland—fell well short of its target." However, "circumcision of newborn boys is proving more successful," and "[t]he government has also achieved 78 percent coverage of people who need antiretroviral (ARV) treatment and
can now conduct tests within the country instead of having to send samples to South Africa," the news service notes (Smith, 4/11).

**Discontinuing Antibiotic Used To Prevent Opportunistic Infections Among HIV Patients Could Increase Risk Of Malaria, Diarrhea**

"Abruptly discontinuing co-trimoxazole—an antibiotic used to prevent opportunistic infections in HIV-positive people—can lead to a higher incidence of malaria and diarrhea compared with patients who keep on taking the drug," according to a study conducted by the CDC in eastern Uganda and published by the Oxford Journal of Clinical Infectious Diseases in March, PlusNews reports. "The researchers found that 72 percent of the 315 cases of fever reported by study participants occurred among those who had stopped taking co-trimoxazole prophylaxis, and they were also nearly twice more likely to report diarrhea," the news service notes.

"The findings most likely mean that HIV-infected persons, while on co-trimoxazole, have a lower rate of these infectious diseases, and stopping the drug increases the rate," James Campbell, lead researcher of the study and director of science at CDC Uganda, told IRIN/PlusNews, "the news service writes. "Co-trimoxazole is relatively cheap, but the researchers note that lifetime prophylaxis using the drug may have cost and toxicity implications," PlusNews notes, adding, "Campbell said, 'Important questions include the effect of more frequent malaria and diarrhea episodes on the longer-term outcomes of HIV infection, the longer-term risks of inducing or selecting for resistant micro-organisms, and comparing antimicrobial prophylaxis to other means of reducing the risk of malaria and diarrhea in this population'" (4/11).

**UCLA-engineered stem cells seek out and kill HIV in living organisms**

Expanding on previous research providing proof-of-principal that human stem cells can be genetically engineered into HIV-fighting cells, a team of UCLA researchers have now demonstrated that these cells can actually attack HIV-infected cells in a living organism.

The study, published April 12 in the journal *PLoS Pathogens*, demonstrates for the first time that engineering stem cells to form immune cells that target HIV is effective in suppressing the virus in living tissues in an animal model, said lead investigator Scott G. Kitchen, an assistant professor of medicine in the division of hematology and oncology at the David Geffen School of Medicine at UCLA and a member of the UCLA AIDS Institute.

"We believe that this study lays the groundwork for the potential use of this type of an approach in combating HIV infection in infected individuals, in hopes of eradicating the virus from the body," he said.

In the previous research, the scientists took CD8 cytotoxic T lymphocytes — the "killer" T cells that help fight infection — from an HIV-infected individual and identified the molecule known as the T cell receptor, which guides the T cell in recognizing and killing HIV-infected cells. However, these T cells, while able to destroy HIV-infected cells, do not exist in great enough quantities to clear the virus from the body. So the researchers cloned the receptor and used this to genetically engineer human blood stem cells. They then placed the engineered stem cells into human thymus tissue that had been implanted in mice, allowing them to study the reaction in a living organism.

The engineered stem cells developed into a large population of mature, multi-functional HIV-specific CD8 cells that could specifically target cells containing HIV proteins. The researchers also discovered that HIV-specific T cell receptors have to be matched to an individual in much the same way an organ is matched to a transplant patient.

In this current study, the researchers similarly engineered human blood stem cells and found that they can form mature T cells that can attack HIV in tissues where the virus resides and replicates. They did so by using a surrogate model, the humanized mouse, in which HIV infection closely resembles the disease and its progression in humans.

In a series of tests on the mice's peripheral blood, plasma and organs conducted two weeks and six weeks after introducing the engineered cells, the researchers found that the number of CD4 "helper" T cells — which become depleted as a result of HIV infection — increased, while levels of HIV in the blood decreased. CD4 cells are white blood cells that are an important component of the immune system, helping to fight off infections. These results indicated that the engineered cells were capable of developing and migrating to the organs to fight infection there.

The researchers did note a potential weakness with the study: Human immune cells reconstituted at a lower level in the humanized mice than they would in humans, and as a result, the mice's immune systems were mostly, though not completely, reconstructed. Because of this, HIV may be slower to mutate...
in the mice than in human hosts. So the use of multiple, engineered T cell receptors may be one way to adjust for the higher potential for HIV mutation in humans.

"We believe that this is the first step in developing a more aggressive approach in correcting the defects in the human T cell responses that allow HIV to persist in infected people," Kitchen said. The researchers will now begin making T cell receptors that target different parts of HIV and that could be used in more genetically matched individuals, he said.

**Test links strains of common parasite to severe illness in US newborns**

*NIH-supported research underscores value of screening for toxoplasmosis*

Scientists have identified which strains of the *Toxoplasma gondii* parasite, the cause of toxoplasmosis, are most strongly associated with premature births and severe birth defects in the United States. The researchers used a new blood test developed by scientists at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, to pinpoint *T. gondii* strains that children acquire from their acutely infected mothers while in the womb.

Pregnant women can become infected with *T. gondii* through contact with cat feces that contain infectious forms of the parasite or by eating undercooked meat. Women who become infected while pregnant may miscarry, give birth prematurely, or have babies with eye or brain damage.

“If undetected or untreated, congenital toxoplasmosis can have serious consequences for a child’s quality of life,” noted NIAID Director Anthony S. Fauci, M.D. “The findings from this study support the value of screening for toxoplasmosis to identify patients who could benefit from treatment.”

Currently available blood tests can determine whether a person has ever been infected with any strain of *Toxoplasma* parasite. The experimental test developed at NIAID improves upon the older tests because it can detect the presence of strain-specific antibodies that distinguish infecting strains from one another. The test was developed by Michael Grigg, Ph.D., of NIAID’s Laboratory of Parasitic Diseases, and his colleagues. It was applied to blood samples collected between 1981 and 2009 as part of the National Collaborative Chicago-Based Congenital Toxoplasmosis Study. The study of congenitally infected children was initiated by NIAID grantee Rima McLeod, M.D., of the University of Chicago, who is the first author of the new study, published online in *Clinical Infectious Diseases*.

At least 15 distinct *T. gondii* strain types have been found throughout the world. In France, where research has been done to establish which strains are most common, a strain called type II predominates. Type II parasites can be distinguished from all other strains, which are collectively termed not exclusively type II strains (or NE-II).

Using the new test, the researchers found evidence of either type II or NE-II infections in 183 of the mother-child pairs in the national congenital toxoplasmosis study. Statistical analysis revealed that NE-II parasites were more likely to be associated with premature birth, and infants infected with these strains were more likely to have severe manifestations of disease than infants infected by type II parasites. For example, severe eye damage was seen in 67 percent of NE-II cases (59 out of 88), while such eye damage was present in only 39 percent of type II cases (18 out of 46). The researchers noted, however, that the association is not absolute, and that mild, moderate or severe disease can result regardless of the infecting strain.
“We knew that, in mice, certain parasite strains are clearly associated with severe disease,” said Dr. Grigg. “But we didn’t know if the same association between strain type and disease severity would hold true for people. Until now, we had not systematically determined whether infected people in the United States had European-type strains or other types, and we also hadn’t determined whether strains found here would have more severe disease symptoms associated with them.”

When she helped start the congenital toxoplasmosis study in 1981, optimal drug treatment regimens were unknown, said Dr. McLeod. Now, thanks in part to controlled clinical trials run under the auspices of the study, the condition can be successfully treated and many babies who are diagnosed before or shortly after birth and who are treated suffer few or no ill effects. When the researchers looked at the clinical histories of those children in the long-term study who had been diagnosed with congenital toxoplasmosis during gestation and whose mothers had received drug treatment prior to giving birth, the association between NE-II and severe disease at birth vanished. “Our study demonstrates that outcomes are equally good following postnatal treatment for type II and NE-II parasites, although not all outcomes are favorable for all children,” she said.

In France, all pregnant women are screened for *Toxoplasma* infection. Prompt treatment is offered to any woman who becomes infected while pregnant, thus lessening the chance that the parasite will damage the fetus, Dr. McLeod noted. “In the United States, obstetrical screening for *Toxoplasma* infection is rarely practiced. This new study underscores the value of identifying all patients who will benefit from treatment and suggests that widespread screening and treatment of pregnant women who are infected could prevent infants from suffering eye and brain damage due to congenital toxoplasmosis,” she said.

Unlike in France, where type II is the most common strain detected, the new study found that NE-II parasites predominated (61 percent) in the United States over the three-decade span of the national collaborative study. NE-II parasites were more common than type II along the Gulf Coast, the Pacific coast and in Hawaii. NE-II strains were also more common among lower-income and rural populations.

**Breakthrough Discovery Unveils Master Switches in Colon Cancer**

ScienceDaily (Apr. 12, 2012) — A team of researchers at Case Western Reserve University School of Medicine have identified a new mechanism by which colon cancer develops. By focusing on segments of DNA located between genes, or so-called “junk DNA,” the team has discovered a set of master switches, i.e., gene enhancer elements, that turn "on and off" key genes whose altered expression is defining for colon cancers. They have coined the term Variant Enhancer Loci or "VELs," to describe these master switches.

Importantly, VELs are not mutations in the actual DNA sequence, but rather are changes in proteins that bind to DNA, a type of alteration known as "epigenetic" or "epimutations." This is a critical finding because such epimutations are potentially reversible.

Over the course of three years, the team mapped the locations of hundreds of thousands of gene enhancer elements in DNA from normal and cancerous colon tissues, pinpointing key target VELs that differed between the two types.

"What is particularly interesting is that VELs define a 'molecular signature' of colon cancer. Meaning, they are consistently found across multiple independent colon tumor samples, despite the fact that the tumors arose in different individuals and are at different stages of the disease," says Peter Scacheri, PhD, senior author of the study and assistant professor, Genetics and Genome Sciences, School of Medicine, and member, Case Comprehensive Cancer Center at Case Western Reserve University. "The set of common VELs govern a distinct set of genes that go awry in colon cancer."

"The VELs signature is notable because it cuts through the complexity of the many genes that are changed in colon cancer, to identify genes that are direct targets of alterations on chromosomes," says Sanford Markowitz, MD, PhD, Ingalls Professor of Cancer Genetics in the Division of Hematology-Oncology at the School of Medicine, member, Case Comprehensive Cancer Center, and oncologist at University Hospitals Seidman Cancer Center, whose team collaborated on the study. "The key next step will be to determine whether we can use VELs for 'personalized medicine,' to molecularly define distinct groups of colon cancers that differ in their clinical behavior, and to enable selection of specific drugs that will best treat a given colon tumor."

In addition to finding that VELs are a "signature" of colon cancer, the team showed that genetic variants which predispose individuals to colon cancer are located within VELs. This suggests that individual differences within VELs may play significant roles in determining different individuals' susceptibility to colon cancer.
"Epigenetics has transformed the way we think about genomes. The genetic code isn't just a series of As, Ts, Gs, and Cs strung together. Epigenetic 'marks' on DNA tell genes when, where, and how much to turn on or off to keep cells healthy," says Batool Akhtar-Zaidi, PhD candidate in Dr. Scacheri's lab and lead author of the study. "When this epigenetic machinery is disrupted, as we see with VEL events, this can tip the balance to cancer."

**Journal Reference:**

**How Cells Distinguish Between Disease-Causing and Innocuous Invaders**

ScienceDaily (Apr. 12, 2012) — The specific mechanisms by which humans and other animals are able to discriminate between disease-causing microbes and innocuous ones in order to rapidly respond to infections have long been a mystery to scientists. But a study conducted on roundworms by biologists at UC San Diego has uncovered some important clues to finally answering that question.

In a paper published in this week's early online issue of the journal *Cell Host & Microbe*, the researchers discovered that intestinal cells in the roundworm *C. elegans*, which are similar in structure to those in humans, internalize bacterial toxins that inactivate several host processes. This then triggers an immune response, which results in the body mounting an immediate attack against the disease-causing microbes.

"The human intestine is teeming with trillions of bacteria, most of which are innocuous, or even beneficial," said Emily Troemel, an assistant professor of biology at UC San Diego who headed the study. "However, sometimes microbes cause disease, such as occurs in food poisoning."

The UC San Diego study and two others published this week in the journals *Cell and Cell Host & Microbe* by research teams headed by Frederick Ausubel and Gary Ruvkun at the Massachusetts General Hospital and the Harvard Medical School, show that the way animal cells detect an attack by poisons or disease-causing bacteria is by monitoring the function of their own cells. If those cells detect a deficit in functions, the scientists discovered, they then trigger a variety of antibacterial or antitoxin responses against the invaders.

The roundworms proved to be the ideal laboratory model for these studies. Not only do they have intestinal cells that are similar in structure to human intestinal cells, but they are transparent and easy to maintain and study in lab.

"*C. elegans* provides a wonderful system in which to study questions of how humans and other animals defend themselves against attacks from disease-causing organisms," said Troemel. "It lacks an adaptive immune system and, instead, relies solely on the evolutionarily ancient innate immune system to fight off attacks. Our findings in these roundworms may have uncovered a new 'pathogen-specific' branch of the innate immune system, which could function in humans as well."
Troemel’s team of researchers—who included Tiffany Dunbar, Zhi Yan, Keir Balla and Margery Smelkinson—found in their experiments that a particular genetic system—the “ZIP-2 surveillance pathway”—was used by the roundworm in detecting an infection by the disease-causing bacterium Pseudomonas aeruginosa. The biologists also found that a specific toxin in the bacterium—“Exotoxin A”—blocks protein synthesis in the worm’s intestine.

"Surprisingly, this block leads to increased protein levels of the ZIP-2 transcription factor to ultimately induce expression of defense genes," the scientists conclude in their paper. "Thus, a common form of pathogen attack acts to switch on host defense, allowing discrimination of pathogens from innocuous microbes."

"In addition to P. aeruginosa Exotoxin A," said Troemel, "there are several other bacterial toxins known to block protein synthesis, such as Diphtheria toxin, Ricin toxin and Shiga toxin. These toxins cause substantial impact on public health. For example, a recent epidemic outbreak of Shiga-toxin producing E. coli caused over 3000 cases of food poisoning in Germany leading to 59 deaths. Like Exotoxin A, these toxins can be internalized into the host cell to block protein synthesis. Perhaps the human intestine also monitors disruption of host protein synthesis to detect food poisoning, and induce a response similar to what is found in the C. elegans intestine."

Troemel noted that it makes sense why animals have evolved systems that respond to core cellular dysfunction, rather than directly to specific toxins.

"We live in an environment filled with a wide variety of disease-causing organisms that can attack us using toxins," she said. "While these toxins are diverse in structure, the manner by which they disrupt our cellular machinery can be very similar. Directly monitoring the functioning of our cellular machinery may provide the optimal system for early detection and response to unknown toxins or pathogenic factors."

**Powerful Sequencing Technology Decodes DNA Folding Pattern**

ScienceDaily (Apr. 11, 2012) — Chromosomes are strands of DNA that contain the blueprint of all living organisms. Humans have 23 pairs of chromosomes that instruct how genes are regulated during development of the human body. While scientists have developed an understanding of the one-dimensional structure of DNA, until now, little was known about how different parts of DNA are folded next to each other inside the nucleus.

Using a powerful DNA sequencing methodology, researchers at the Ludwig Institute for Cancer Research have now investigated the three-dimensional structure of DNA folds in the nucleus of a chromosome. The findings published in the April 11 issue of *Nature* provide scientists with a greater understanding about the basic principles of DNA folding and its role in gene regulation.

"In any biology textbook, when you look at a diagram of how genes are depicted, it is invariably a one-dimensional line. In reality, genes are arranged in such a way that two parts of the gene may be distal to each other linearly, but very close in 3-D," said Dr. Bing Ren, Member of the Ludwig Institute for Cancer Research and Professor of Cellular and Molecular Medicine at the University of California, San Diego. "With the knowledge of how DNA folds inside the nucleus, we now have a more complete picture of the regulatory process of genes. That is the primary reason we sought to tackle this problem. The spatial organization is intimately linked to its role in the body."

Ludwig researchers used a sequencing-based method called Hi-C to examine the 3-D structure of chromosomes. "With this technology, we were able to build a map of pair-wise interactions from each chromosome, and from that, extrapolate the basic folding pattern of the DNA. What we learned is that they fold into many local domains termed topological domains, which are on average one million base pairs in size. By way of comparison, the whole human genome is just over three billion base pairs in size," explained lead researcher, Jesse Dixon, a graduate student in Dr. Ren’s lab.

In examining the interaction map, Dr. Ren’s team discovered that topological domains are the basic unit of folding. The team confirmed their findings by comparing it among different cell types. In each type, the folding of DNA into topological domains was constant.

A parallel study by researchers at Institut Curie and the University of Massachusetts Medical School support Ludwig researchers’ findings. By focusing on the mouse X chromosome segment in embryonic stem cells, as well as neuronal cells and fibroblasts, researchers showed that this segment adhered to similar folding patterns as the ones found by Ren’s team. They further showed that this organization could be linked to gene regulation.

"This is just the beginning of a very exciting area of research focused on the understanding of nuclear processes from a three-dimensional point of view. We know that some cancers, including many
leukemias, are caused by the translocation of two genes. It’s not clear how these translocations are regulated or whether they result from random events. It’s possible that the spatial structure of the chromosome can provide clues about how these translocations occur and, more importantly, how we can prevent them or at least mitigate their effect,” concluded Dr. Ren.

**Journal Reference:**
Jesse R. Dixon, Siddarth Selvaraj, Feng Yue, Audrey Kim, Yan Li, Yin Shen, Ming Hu, Jun S. Liu, Bing Ren. Topological domains in mammalian genomes identified by analysis of chromatin interactions. *Nature*, 2012; DOI: [10.1038/nature11082](https://doi.org/10.1038/nature11082)

**Winnipeg man guilty in death of HIV-positive boyfriend**

By Mike McIntyre, Postmedia News

April 12, 2012

A jury has found a Winnipeg man guilty of manslaughter in the death of his boyfriend, which the Crown argued took place after the victim revealed he was HIV-positive.

**Photograph by:** REUTERS/Morteza Nikoubaz

WINNIPEG — A jury has found a Winnipeg man guilty of manslaughter in the death of his boyfriend, which the Crown argued took place after the victim revealed he was HIV-positive.

Following a month-long trial, the jury took less than two hours to convict Michael Pearce, 43. Family members of Stuart Mark, 36, were in tears following the verdict.

Pearce will be sentenced later this year. The Crown says they will seek a "significant penitentiary term" for Pearce.

He will remain free on bail, as he has been for nearly five years.

Pearce admitted to the January 2007 slaying of Mark — who was beaten and stabbed — but later claimed he was coerced into a bogus confession.

Mark was found bludgeoned to death inside his Winnipeg home.

Pearce went to police in July 2007 and took responsibility for the death. He claimed the killing took place after he became upset when Mark revealed he was HIV-positive.

Crown attorney Melinda Murray had told jurors Pearce's statement is the key piece of evidence against him. There are no forensic or eyewitness links to the slaying.

Murray told jurors the Crown believes Pearce hit him in the head with a golf club, then stabbed him in the stomach.

"The argument was as a result of Stuart Mark revealing to him for the first time that he was HIV-positive," Murray said. "(Pearce) admits to being very angry at Stuart Mark."

The homicide went unsolved for several months and resulted in Winnipeg police making a public plea for information.

Pearce was interviewed on several occasions and eventually gave a videotaped confession, which jurors were shown during the trial.

Pearce now says he had attempted suicide just prior to giving his statement to police. He told court the officers "coaxed" him into admitting responsibility.

Jurors also heard during the trial that Pearce volunteered to take a polygraph test five days before he confessed to killing Mark. In the test, Pearce denied any involvement in the slaying and was deemed by police to have been telling the truth.

**Engineering CD8 Cells to Kill HIV in Tissues**

Expanding on previous research providing proof-of-concept that human stem cells can be genetically engineered into HIV-fighting cells, researchers at the University of California at Los Angeles (UCLA) have now demonstrated that these cells can actually attack HIV-infected cells in a living organism.

The study, published April 12 in the journal PLoS Pathogens and highlighted in an accompanying news announcement, demonstrates for the first time that engineering stem cells to form immune cells that target HIV is effective in suppressing the virus in living tissues in an animal model.

“We believe that this study lays the groundwork for the potential use of this type of an approach in combating HIV infection in infected individuals, in hopes of eradicating the virus from the body,” said Scott Kitchen, PhD, of the David Geffen School of Medicine at UCLA and an author of the PLoS Pathogens report, according to an accompanying news announcement.

In the previous research, the scientists took CD8 cytotoxic T lymphocytes—the “killer” T cells that help fight infection—from a person living with HIV and identified the molecule known as the T cell receptor, which guides the T cell in recognizing and killing HIV-infected cells.

While these cells are able to destroy HIV-infected cells, they do not exist in great enough quantities to clear the virus from the body. So the scientists cloned the T cell receptor and used this to genetically
engineer human blood stem cells. They then placed the engineered stem cells into human thymus tissue that had been implanted in mice, allowing them to study the reaction in a living organism.

The engineered stem cells developed into a large population of mature, multi-functional HIV-specific CD8 cells that could specifically target cells containing HIV proteins. The researchers also discovered that HIV-specific T cell receptors have to be matched to an individual in much the same way an organ is matched to a transplant patient.

In this current study, Kitchen and his colleagues similarly engineered human blood stem cells and found that they can form mature T cells that can attack HIV in tissues where the virus resides and replicates. They did so by using a surrogate model—the humanized mouse—in which HIV infection closely resembles the disease and its progression in humans.

In a series of tests on the mice’s peripheral blood, plasma and organs conducted two weeks and six weeks after introducing the engineered cells, the researchers found that the number of CD4 cells increased, while viral load decreased.

The researchers did note a potential weakness with the study: Human immune cells reconstituted at a lower level in the humanized mice than they would in humans, and as a result, the mice’s immune systems were mostly, though not completely, reconstructed. Because of this, HIV may be slower to mutate in the mice than in human hosts. So the use of multiple engineered T cell receptors may be one way to adjust for the higher potential for HIV mutation in humans.

“We believe that this is the first step in developing a more aggressive approach in correcting the defects in the human T cell responses that allow HIV to persist in infected people,” Kitchen said.

Next up, Kitchen and his colleagues say they will begin making T cell receptors that target different parts of HIV and that could be used in more genetically matched individuals.

**CROI: Crofelemer Reduces Diarrhea in People with HIV; FDA Grants Priority Review**

Published on Tuesday, 10 April 2012 00:00
Written by Liz Highleyman

A plant compound known as crofelemer significantly decreased the frequency of secretory diarrhea in HIV positive patients, researchers reported at the 19th Conference on Retroviruses and Opportunistic Infections (CROI 2012) last month in Seattle. The U.S. Food and Drug Administration (FDA) has given crofelemer priority review status and is expected to take action by early June.

Secretory diarrhea caused by infectious pathogens, toxins, or antiretroviral drugs is a problem for many people with HIV. Crofelemer is a proanthocyanidin compound extracted from the sap of an Amazon rainforest plant (*Croton lechleri*) that is used by traditional healers to treat a variety of conditions including diarrhea. It works by inhibiting 2 different mechanisms that regulate secretion of fluid from the intestines.

Rodger MacArthur from Wayne State University in Detroit and colleagues evaluated the safety and efficacy of crofelemer for treatment of chronic secretory diarrhea in people with HIV.

The Phase 3 ADVENT study included 376 HIV positive patients who experienced watery bowel movements on at least 5 of the 7 days prior to enrollment. Participants were on combination antiretroviral therapy (ART) with CD4 cell counts above 100 cells/mm³. They had no evidence of intestinal pathogens. About 85% were men and the average age was approximately 45 years.

Participants in the first stage of the study were randomly assigned to receive crofelemer tablets at doses of 125, 250, or 500 mg twice-daily, or else placebo, for 4 weeks. The 125 mg dose was selected and tested in more patients in the second stage. After the 4-week placebo-controlled periods, all participants received crofelemer for a 5-month extension period.

The researchers looked at weekly response, defined as the proportion of patients with 2 or fewer watery stools per week, and monthly response, defined as the proportion with 2 or fewer watery stools per week for at least 2 out of 4 weeks in a month.

**Results**

- In the first stage of the study, monthly response rates were 20.5% in the crofelemer 125 mg arm, 9.3% in the 250 mg arm, and 19.6% in the 500 mg arm, compared with just 2.0% in the placebo arm.
In the second stage, 16.3% of participants receiving 125 mg crofelemer experienced monthly response, compared with 11.4% of placebo recipients.

Combining the 2 stages, overall monthly response rates were 17.6% in the 125 mg crofelemer group versus 8.0% in the placebo group, a significant treatment difference of 9.6% (P = 0.0096).

Placebo recipients who crossed over to crofelemer during the 5-month extension phase experienced significant benefit after 1 month (36% vs 9% response; P < 0.0001).

In the placebo-controlled phases, crofelemer recipients had lower incidence than placebo recipients of any adverse events (27% vs 33%), serious adverse events (2% vs 3%), and treatment discontinuation due to adverse events (0% vs 3%).

Based on these findings, the researchers concluded, "Crofelemer 125 mg [twice-daily] effectively reduced secretory diarrhea in HIV positive subjects and had a safety profile similar to placebo. These results are consistent with its targeted gut action and minimal systemic absorption."

Crofelemer was discovered by San Francisco-based Napo Pharmaceuticals and was being developed by Salix Pharmaceuticals, but Napo terminated its collaboration agreement with Salix in November 2011, claiming the latter company had failed to meet its obligations to develop and commercialize the product in a timely manner.

According to a press release issued by Napo, the FDA accepted the New Drug Application (NDA) for crofelemer for HIV-related diarrhea with a Priority Review designation. The agency has set June 5, 2012, as the action date for the NDA under the Prescription Drug User Fee Act (PDUFA). The company is also studying crofelemer for irritable bowel syndrome, acute gastrointestinal infections (including cholera), and pediatric diarrhea. 4/3/2012

Reference

Breastfeeding, not Formula, for Country's HIV-Positive Mothers

Inter Press Service (04.01.2012) Lee Middleton

South Africa is phasing out a program that provides free formula to HIV-positive mothers. The move in all nine provinces is in support of the 2011 Tshwane Declaration that exclusive breastfeeding (EBF) be promoted starting The Tshwane Declaration calls for supporting EBF for all infants up to age six months, including those exposed to HIV; these babies should receive antiretrovirals (ARVs) to prevent mother-to-child transmission (MTCT), per World Health Organization (WHO) guidelines.

The declaration stems from concern over: South Africa’s EBF rate, which, at 8 percent, is the world’s lowest; high child mortality rates; and the fact that formula feeding increases the risk of death from diarrhea and pneumonia—the largest killers of the nation’s infants and children. Public health facilities will provide formula only by prescription.

Critics, however, say the declaration is too ambitious. “We can increase our EBF rate, but not to the extent that the Health Department believes is possible,” said Haroon Saloojee, a pediatrics expert at the University of Witwaterstrand. Saloojee said greater concerns are the possibility of MTCT drug shortages in the public health sector, and ensuring that mothers adhere to infant ARV regimens.

“There’s no way you can get those transmission rates unless you have a good and reliable service delivery and good and reliable adherence to those drugs,” said Nigel Rollins of WHO.

Politico Pro Examines Reaction To Melinda Gates's TEDxChange Speech On Family Planning

Politico Pro examines the reaction to a speech delivered by Melinda Gates, co-chair of the Bill & Melinda Gates Foundation, at a TEDxChange conference in Berlin on April 5. "Gates’s speech was primarily focused on explaining why family planning is important in the developing world,” according to the news service. Gates said lack of access to modern contraceptives is "a life and death crisis" because with family planning, the lives of hundreds of thousands of women and children could be saved annually, the news service notes. "But multiple global health experts heard her comments as an intentional effort to push back on the politicization of birth control in the United States following the Obama administration’s new contraception coverage policy, which they fear could spill over into global health policy," the news service writes. However, "Gates Foundation spokesman Chris Williams said Gates was simply reiterating her long-standing support for family planning and that viewing these remarks in light of domestic politics would be ‘using the wrong lens,’" the article notes.
"For better or for worse, the president’s handling of the contraception issue has really ignited a much bigger conversation that Melinda has now taken global," said Tom Sheridan, a long-time political strategist who cut his teeth in the HIV/AIDS movement," the news service writes. "What Melinda Gates is saying from Berlin, interestingly, is speaking to the ... members of Congress who are out of touch with reality in terms of the importance of contraception in women's lives here and the rest of the world,' said Guttmacher Institute Director of Government Affairs Susan Cohen. 'She's also trying to communicate to the rest of the world that notwithstanding about what they may be reading in the newspapers, [birth control] is not controversial among American women or American men," she added, according to Politico Pro. "It was a decision by her and the foundation that this was such an important public health issue ... [that] she wanted to elevate the discussion," Jen Kates, vice president and director of global health and HIV policy for the Kaiser Family Foundation, said, the news service writes. "When they decide to speak about something ... it is noticed," she added, Politico Pro notes (Feder, 4/11).

Cholera Vaccination Pilot Project Begins In Haiti
"A year and a half after cholera first struck Haiti, a tiny portion of the population on Thursday began getting vaccinated against the waterborne disease that has infected more than 530,000 Haitians and killed more than 7,040," the New York Times reports (Sontag, 4/12). The pilot project, which will reach only one percent of Haiti's population, "[aim[s] ... to show that it's possible to give the required two doses over a two-week period to desperately poor and hard-to-reach people," NPR's health blog "Shots" writes. "If it works, the plan is to convince the Haitian government, deep-pocketed donors and international health agencies to support a much bigger campaign to vaccinate millions of Haitians at highest risk of cholera," according to the blog (Knox, 4/12).

The organizers, Partners In Health and GHESKIO, this week received approval from a national bioethics committee to move forward with their plan, the New York Times notes (4/12). A delay in beginning the project, which was planned to begin six weeks ago, "has caused a lot of anxiety," the NPR blog reports. First "Haiti's spring rainy season has begun," which can exacerbate the spread of the cholera bacteria, "Shots" notes, adding, "Second, the delay has pushed the cholera vaccination campaign up against a long-planned national campaign to vaccinate children against measles, rubella, polio, rotavirus, Hemophilus influenzae and pneumonia." Because the cholera and polio vaccines should not be delivered simultaneously in young children, the organizers will have to "defer cholera vaccination in 9-and-under children until after they've received polio vaccine, and then to track them down and give them the cholera vaccine," the blog writes (4/12).

NTD Experts Push Forward On Plan To Eradicate Yaws
Yaws, a skin and bone disease caused by a treponematoses bacterium that can cause long-term deformities, "has recently been put on WHO's list of 17 so-called neglected tropical diseases (NTDs)" and, along with Guinea worm, is "slated for eradication," the Lancet reports. A "massive push to free the world from yaws failed in the 1950s and 1960s," and the WHO in 1995 estimated "there were 2.5 million cases of endemic treponematoses (mostly yaws)," according to the Lancet. A study published in the Lancet in January showed a single dose of the antibiotic azithromycin was effective at curing the disease among children, a finding that "jump-started the NTD community into action," the article states.

Experts met in March outside of Geneva to develop an eradication plan "that calls for a single dose of azithromycin to be given to entire populations in areas known to harbor yaws," with a deadline of 2020, the Lancet notes. Support for the plan was unanimous, but the experts raised several concerns over the plan, including whether political will and funding could be sustained and the possibility of the development of antibiotic resistance, according to the article (Maurice, 4/14).

Male circumcision for HIV prevention: What does the scientific evidence say?
By Joseph KB Matovu, Rhoda K. Wanyenze & David Serwadda (email the author)
Posted Thursday, April 12 2012 at 00:00

In Summary
Medics from Makerere University School of Public Health answer in detail the recent concerns over the male circumcision drive aimed at reducing the spread of HIV/Aids

Of recent, the media has published a number of articles related to male circumcision, including two articles in the Daily Monitor. The first article entitled 'Circumcision does not reduce HIV spread' (Daily Monitor, March 6, 2012) was written by Flavia Lanyero. Flavia's article is based on a paper published by
Gregory J Boyle and George Hill in the Journal of Law and Medicine in 2011. This paper is one among many articles authored by self-proclaimed anti-circumcision crusaders. Indeed, George describes himself as the Vice President for Bioethics and Medical Science under a programme known as 'Doctors Opposing Circumcision’ based in Seattle, Washington, D.C. As B.J. Morris and his colleagues have concluded, these anti-male circumcision crusaders “misrepresent good scientific studies, selectively cite references, some containing fallacious information; and draw erroneous conclusions” in order to reframe the male circumcision debate in their favor. The second article entitled, “Circumcision and HIV: are we being fed on half-truths?” (Daily Monitor, March 22, 2012) was written by Agnes Namaganda. Agnes questions the truth in the statement, “male circumcision reduces the risk of contracting HIV”, and presents contrasting views about male circumcision without necessarily helping the reader to reach a definite conclusion about the effect of male circumcision in HIV prevention. While she did not explicitly state which side of the debate she falls, we believe that the taste of her article hinged more on the side of those who are opposed to male circumcision, considering the nature of evidence cited. In writing this article, we intended to not only respond to these issues but also provide a more elaborate view of male circumcision and its role in HIV prevention based on scientific evidence at hand.

**How the male circumcision debate begun**

Male circumcision has been practiced for generations. It is one of the oldest surgical procedures known to mankind. Over time, the scientific community observed that the risk of acquiring sexually transmitted infections (STIs), including HIV, was lower in men who were circumcised than in those who were not. While nobody could clearly explain the science behind these observations, there was a general perception that male circumcision could be the reason for the observed differences. However, since there was evidence of high HIV prevalence in some circumcising communities, it was not possible to come to a conclusion about the protective effect of male circumcision, before subjecting it to rigorous scientific scrutiny. Whereas proponents argue for increased scale-up of male circumcision programs, opponents have initiated campaigns to discredit male circumcision. But what does science tell us about male circumcision?

Some studies indicated lower HIV prevalence in circumcised men vis-à-vis uncircumcised men, but these studies had methodical challenges. For example, in many parts of Africa where circumcision was shown to be associated with low HIV prevalence in men, these areas also happened to have a high number of Muslim men. It was, therefore, not clear whether it was circumcision per se that was protective or whether it was because of other attributes already known to be associated with Muslim men (e.g. Muslim men do not drink alcohol) that reduced their risk for HIV infection. On the other hand, there are studies that have shown that circumcised men have high HIV prevalence, which, on close examination, found that most of these men were circumcised as result of having STIs. All these observations made it difficult to conclude whether male circumcision per se reduced chances of acquiring HIV among adult men.

To respond to this question, scientists designed further research studies known as randomized clinical trials. These types of studies are taken as the “gold standard” of research evidence. In these studies men who were not circumcised and who were free from HIV infection were divided into two groups with one group circumcised immediately while the other group was asked to wait for some time to receive circumcision and thus acted as the comparison group. Scientists followed both groups for a defined period of time, and tested them for HIV at regular intervals. They also provided free counseling services to all men as well as free condoms to those who were interested in using them. These trials, conducted in three countries (South Africa, Kenya and Uganda) between 2000 and 2006, involving a total of 5,411 men in the circumcised arm and 5,497 in the comparison group indicated that circumcised men were less likely to acquire HIV than those who were not circumcised. The level of protection of male circumcision from the risk of HIV infection ranged between 50 per cent to 60 per cent across the three countries. These findings, from studies conducted in different countries and communities, were so convincing that in 2007 the World Health Organisation (WHO) together with the Joint UN Programme on HIV/AIDS (Unaids) recommended male circumcision as part of a comprehensive HIV prevention strategy (alongside condom use, being faithful to one’s HIV-free sexual partner, treatment of sexually transmitted infections, among others) in ‘countries with heterosexual epidemics, high HIV and low male circumcision prevalence’, such as those found in sub-Saharan Africa.

It is important to note that the WHO guidelines refer to ‘medical’ or ‘safe’ male circumcision as opposed to the culturally performed circumcision which may be associated with other risks such as serial use of unsterilized instruments that could potentially transmit HIV. This and other cultural practices around circumcision may partly explain the high HIV prevalence among communities that perform circumcision for cultural reasons, as has been cited in some communities in Botswana and elsewhere.
Recent evidence on the impact of male circumcision at the community level

Studies done after the end of the clinical trials in Kenya and Uganda have found that male circumcision’s protective effect against HIV is sustained and may even become stronger over time. The risk of HIV infection among circumcised men was reduced by 67 per cent after 4.5 years in Kenya and by 73 per cent after 4.8 years in Uganda.

Equally exciting are recent results confirming that this level of protection can be achieved outside the relatively controlled setting of a clinical trial.

Last year, a community-based study indicated that providing male circumcision in a South African township reduced the rate of new HIV infections among circumcised men by 76 per cent in three years. In a recent paper entitled Population-level impact of male circumcision on HIV incidence: Rakai, Uganda, Ronald H. Gray and colleagues found that the number of new HIV infections among non-Muslim men decreased with greater uptake of male circumcision. Dr. Gray and his colleagues conducted an observational study among 14,000 individuals in 50 communities in Rakai District between 2000 and 2009.

Male circumcision among non-Muslim men in Rakai increased from 5.6 per cent in 2000 to 25.3 per cent in 2009. The number of new HIV infections decreased by 37 per cent during the same period among non-Muslim men. No effect on new HIV infections was seen among females in this study. This study focused on non-Muslim men because it is the practice in the Muslim community to circumcise young boys.

There are concerns expressed that male circumcision will lead to an increase in risky sexual behaviors, such as less frequent use of condoms or increased numbers of sexual partners. However, recent evidence suggests that male circumcision does not lead to increased risky behaviors.

For instance, a study done among 2,500 circumcised men who were followed up for up to five years in Rakai did not find increased risk behaviour among these men compared to uncircumcised men with respect to number of sexual partners or condom use. Other studies in Kenya and South Africa have found out that male circumcision does not result in increased risky sexual behaviors such as having sex with multiple sexual partners or abandonment of condom use.

On the contrary, circumcised men report increased safer sexual practices following risk-reduction counselling, suggesting that male circumcision programmes should incorporate risk-reduction messages into the promotional campaigns. It is interesting to note that such concerns were also voiced with the introduction of antiretroviral drugs (ARVs), but this did not stop rolling out ARVs.

Does male circumcision protect uninfected women against acquiring HIV?
Although male circumcision reduces the risk of HIV acquisition in HIV-negative men, evidence of protection for HIV-negative female partners of HIV-positive men is not conclusive. Studies carried out earlier in Uganda, particularly among HIV discordant couples (with one partner HIV-negative and the other positive), had indicated that if the HIV positive partner was circumcised, there was a reduced risk of transmission of HIV to the HIV-negative women; these studies were conducted among men who were circumcised at birth.

However, no studies had demonstrated whether the same protective effect could be seen among men circumcised as adults. A randomised clinical trial by Maria J. Wawer and her colleagues shows that female partners of HIV-positive men, circumcised as adults, may be at an increased risk of acquiring HIV if the couple resumes sex before the wound of the HIV-positive partner has healed.

It is important to note that the trend towards increased risk was seen only among women in couples who resumed sex too soon after circumcision, i.e. before proper wound healing. Gregory and George’s article, and indeed other articles from anti-male circumcision crusaders don’t mention this fact. It is crucial for couples to follow the recommendation to abstain from sex for six weeks post-circumcision (after wound heals). One can argue that logically, when fewer men are infected, transmission to women at population level would also reduce over time. Indeed, there are several studies that indicate some protective effect for women, but until such evidence is available consistently across different studies, male circumcision will continue to be promoted as a strategy for the prevention of ‘heterosexually acquired HIV infection in men’, as per the WHO recommendations. Other benefits of male circumcision beyond HIV prevention

There is overwhelming evidence to prove that male circumcision provides other benefits beyond HIV prevention. Male circumcision improves male hygiene, reduces risk of genital ulcer disease and cancer of the penis, and lowers the risk of cervical cancer among women with circumcised male partners by reducing the prevalence of the virus that is associated with this cancer (Human Papilloma Virus).
The role of male circumcision in relation to other HIV prevention approaches

We should point out that a circumcised man can still acquire or transmit HIV (if HIV-positive), except that male circumcision reduces the risk of HIV infection among initially HIV-negative, circumcised men. We should also point out that the risk of acquiring as well as transmitting HIV among circumcised men increases when sexual intercourse is resumed too early (before complete healing) or when circumcised men increase their risky behaviors due to the belief that they are protected.

This is the reason why the campaigns for male circumcision still encourage other risk reduction interventions such as abstinence, faithfulness and condom use, and advise men not to resume sex until six weeks post-circumcision (when proper wound healing has occurred). The interventions around male circumcision also include HIV testing with associated risk reduction counseling as part of the package. This is important because whereas the protective effect of acquisition of HIV by a negative man has been proven, a HIV infected man who is circumcised can still transmit infection to their uninfected partner.

Opponents of male circumcision argue that if other interventions are required in addition to circumcision then it is not beneficial. To argue that any intervention that is not 100 per cent effective is not useful would invalidate many interventions in health (including for example several vaccines and car seat belts) and probably interventions in many other fields outside health. The realisation that no single intervention is 100 per cent effective in HIV prevention has led to the current efforts towards what is now called ‘combination prevention’ an approach that encourages the use of a comprehensive package of scientifically proven medical interventions as well as social and cultural factors that predispose women and men to HIV infection.

Policy implications

The Uganda Male Circumcision Policy (2010) recommends that “counselors should stress that male circumcision provides only partial protection against HIV, and that maintenance of other risk reduction strategies is necessary.” In addition, the National HIV Prevention Strategy indicates that “there is no single HIV prevention intervention or “magic bullet”. Thus, male circumcision is currently promoted as part of a comprehensive HIV prevention package rather than as a single magic bullet, as anti-male circumcision crusaders would like to make us believe.

The writers are lecturers at Makerere University School of Public Health, Kampala, Uganda

The Birth of Polio Eradication: The Salk Vaccine Turns 57

David Oshinsky
April 12, 2012

On April 12, 1955, scientists and reporters gathered in Ann Arbor, Michigan, for a momentous event. Millions of Americans huddled around radios and televisions that day to learn whether the world’s first polio vaccine, developed by Dr. Jonas Salk at the University of Pittsburgh, could prevent a devastating disease that killed and paralyzed thousands upon thousands of people, mainly children.

It’s hard to overstate the terror of polio back then. It would arrive each summer, like clockwork, leaving behind vivid reminders for all to see: wheelchairs, crutches, leg braces, iron lungs, deformed limbs. When Dr. Salk’s injectable vaccine was declared “safe, effective, and potent” that remarkable day in Ann Arbor, a nation celebrated. In churches, department stores, and coffee shops people wept openly with relief. President Eisenhower invited Dr. Salk to the White House where, in a trembling voice, he thanked the young researcher for saving children everywhere.

Asked whether he would patent his vaccine, Salk said no; it belonged to the world. “Could you patent the sun?” he replied.

A few years later, Dr. Albert Sabin of the University of Cincinnati developed the oral polio vaccine, or OPV. Its low cost and ease of use—both critical innovations—allowed us to envision a world where all children, rich and poor, were protected against polio. Since the World Health Organization launched its global initiative to eradicate the disease in 1988, OPV has reached billions of children worldwide, driving down polio cases by 99%.

This January, India—once thought to be the most difficult place to eradicate polio—celebrated an entire year without a case of wild poliovirus. To reach this milestone, volunteers and frontline health workers toiled relentlessly to deliver OPV to millions of children, even in the most remote areas.

The Shot Felt 'Round The World is a documentary using first-hand interviews with world-renowned experts to tell the remarkable story of Dr. Jonas Salk and his research team, and of a nation that quite literally rolled up its collective sleeves to conquer the most-feared disease of the 20th century.
Now, with an eye on the endgame, scientists and researchers are developing even better vaccines. A new, more potent oral version targeting two strains of the virus helped turn the tide in India and is making inroads in Pakistan, Nigeria and Afghanistan. Scientists are also advancing a lower-cost and easier-to-use version of Dr. Salk's vaccine for deployment in developing countries.

The fight to end polio will not be easy, but it surely can be done. We now face what the World Health Organization has called “the best—and perhaps last—chance to stop polio forever.” We must seize this historic opportunity, fulfilling the promise we made to our children—to all children—fifty-seven years ago today.

Research teams discover cellular system for detecting and responding to poisons and pathogens
Disruption of key cellular functions produces physiologic and behavioral responses
Two Massachusetts General Hospital (MGH)-based research teams, along with a group from the University of California at San Diego, have discovered that animals have a previously unknown system for detecting and responding to pathogens and toxins. In three papers published in the journals Cell and Cell Host & Microbe, the investigators describe finding evidence that disruptions to the core functions of animal cells trigger immune and detoxification responses, along with behavioral changes.

"Viewing many diseases through the prism of this newly discovered system will eventually allow a reinterpretation of disorders from several branches of medicine as aberrant responses to toxins and bacteria," says Gary Ruvkun, PhD, of the MGH Department of Molecular Biology, senior author of a paper in the April 13 issue of Cell. "While these initial studies are in the C. elegans roundworm, many of the regulatory factors that we have identified are also present in humans."

The Cell paper from the Ruvkun lab describes experiments by research fellow Justine Melo, PhD, revealing that inactivation by RNA interference of cellular components involved in core cellular functions – including translation of messenger RNAs into proteins on ribosomes or energy production in mitochondria – not only halted growth and reproduction in C. elegans but also induced the animals to move away from the E. coli bacteria they usually prefer to consume. Several of these deactivated components are known to be targets of chemical or protein toxins produced by bacteria and fungi, and Melo and Ruvkun showed that C. elegans exhibited the same aversive behavior when exposed to benign E. coli supplemented with any of several natural chemical toxins.

Additional experiments by Melo and Ruvkun revealed that inactivation of these core cellular components induced expression of genes known to be involved in the innate immune system's response against specific toxins and pathogens even when no toxins or pathogens were actually present. The researchers theorize that the observed behavioral response of C. elegans is similar to the way other animals avoid eating when they feel ill, whether or not food is the source of illness. They note that a fundamental cellular surveillance system that responds broadly to toxin-produced disruption of essential activities rather than to the presence of the toxin itself could protect against pathogens not previously encountered, and that directly monitoring these core components would allow early detection of and response to unknown toxins.

One of the reports appearing in Cell Host & Microbe from a team led by Frederick Ausubel, PhD, of MGH Molecular Biology reported similar results. That study found that consumption by C. elegans of E. coli induced to express a protein-synthesis-inhibiting toxin produced by the bacterial pathogen P. aeruginosa activated innate immune gene pathways that are also induced by protein-synthesis-inhibiting antibiotics produced by different pathogens. These pathways were not activated by an inactive version of the P. aeruginosa toxin that did not affect protein synthesis, indicating that it was the disruption of that core cellular activity and not the presence of the toxin itself that produced the immune response. The accompanying Cell Host & Microbe study from the UC San Diego team led by Emily Troemel, PhD, found that this same P. aeruginosa toxin also activates synthesis of a key immune regulator, directly stimulating the response against the toxin.

"It has been predicted for quite a while that animal immune systems would respond to the effects of bacterial toxins, but there has not been a lot of experimental support for this hypothesis," says Ausubel. "The experiments described in our Cell Host & Microbe paper, however, show very clearly that C. elegans can detect a disruption of protein synthesis that leads to a strong immune response, irrespective of whether they have been challenged with a pathogen. We are now testing whether the mammalian immune system responds the same way."
Ruvkun notes that these genetic pathways for responding to pathogens and their toxins will probably be important in many human diseases. Individual variations in responses to pathogen-produced toxins could explain the runaway inflammation and organ failure of sepsis and toxic shock, and drugs developed to target this pathway could help combat those potentially life-threatening responses. Activation of these pathways also may underlie nausea – which may be the human version of C. elegans aversion to toxin-laced food – a major problem plaguing both drug development and the use of current therapies such as chemotherapy drugs, making suppression of these responses a significant goal.

"This genetic analysis of how toxins are detected and the signals that are generated may identify new endocrine pathways in the worm and corresponding versions in humans," says Ruvkun, a professor of Genetics at Harvard Medical School (HMS). "Further study may reveal how these endocrine signals relate to human drug response and whether the endocrine state of these aversively stimulated animals corresponds to that of humans who have been ‘poisoned’ with pathogen-produced toxins. Identifying the genetic components of this aversive behavior could lead us to discover the endocrinology behind feeling ill and new ways to relieve that universal response."

**Blood type A may predispose to some rotavirus infections**

HOUSTON – (April 15, 2012) – Whether you become infected by some strains of rotavirus may depend on your blood type. Some strains of rotavirus find their way into the cells of the gastrointestinal tract by recognizing antigens associated with the type A blood group, a finding that represents a new paradigm in understanding how this gut pathogen infects humans, said Baylor College of Medicine researchers in an online report in the journal Nature.

Rotavirus is a major intestinal pathogen that is the leading cause of severe dehydration and diarrhea in infants around the world. An estimated 500,000 people worldwide die from the infection annually.

The structure of a key part of a strain of the virus known as P[14] provides a clue to how the virus infects human cells, said Dr. B. V. Venkataram Prasad, professor of biochemistry and molecular biology at BCM and the report’s corresponding author. In strains of rotavirus that infect animals, the top of a spike on the virus attaches to the cell via a glycan (one of many sugars linked together to form complex branched-chain structures) with a terminal molecule of sialic acid. The same did not appear to be true of virus strains that infect humans, and scientists believed the human rotavirus strains were bound to glycans with an internal sialic acid molecule, but they did not know how this occurs.

"We wondered how this genotype of rotavirus recognized a cellular glycan," said Prasad. "With colleagues at Emory (University School of Medicine), we did a glycan array analysis to see which glycans interacted with the top of the virus spike (called VP8*)."

The only type of glycan that interacted with VP8* was type A histo-blood group antigen, he said.

"That was surprising," he said. "We thought it had to be a glycan with sialic acid."

The histo-blood group antigen A does not have sialic acid.

However, when Dr. Liya Hu, a post-doctoral researcher in Prasad’s laboratory, determined the structure of the VP8* domain, she found that the type A glycan bound to the rotavirus spike protein at the same place as the sialic acid would have in an animal rotavirus. Histo-blood group antigens are known to promote binding of norovirus and Helicobacter pylori cells to intestinal cells, but this had never been demonstrated in rotavirus.

Hu’s structural study, using crystallography, showed subtle changes in the structure of the VP8* domain of the virus that allowed it to use the histo-blood group antigen A as a receptor.

In collaboration with the laboratory of Dr. Mary Estes, professor of molecular virology and microbiology at BCM, Prasad and his colleagues found that laboratory cells modified to express the histo-blood group antigen A were easily infected by this rotavirus strain. Cells that lacked this antigen were not easily infected.

An antibody to the histo-blood group antigen A blocked infection by the virus into human intestinal cells in culture.

"No one expected this," said Prasad. "Is there an emerging theme here with these intestinal pathogens? Do other viruses use these blood group antigens as a door to enter the cell?"

Further studies identified a second rotavirus strain P[9] that uses the histo-blood group antigen as a receptor, he said.

"The question now is do different strains use other histo-blood group antigens in this way?" he said.
Estes said, "These studies are significant because they provide a novel mechanism of transmission for a rotavirus strain that jumps from ungulates (such as horses, zebras, pigs, sheep) into humans."

The authors found humans infected with the P[14] strain had type A blood, but more studies are needed to confirm the connection.

Larger populations of infected individuals need to be studied to determine if there is a clear association of these virus strains using histo-blood group antigens as a receptor," they said.

This finding raises questions about why humans developed different blood groups, Prasad said. It may be an evolutionary change that occurred after the pathogen first invaded human cells.

**Chromosomes Organize Into 'Yarns': May Explain Why DNA Mutations Can Affect Genes Located Thousands of Base Pairs Away**

ScienceDaily (Apr. 11, 2012) — Chromosomes, the molecular basis of genetic heredity, remain enigmatic 130 years after their discovery in 1882 by Walther Flemming. New research published online in *Nature* by the team of Edith Heard, PhD, from the Curie Institute and Job Dekker, PhD, from the University of Massachusetts Medical School (UMMS), reveals a new layer in the complex organization of chromosomes. The scientists have shown that chromosomes fold in a series of contiguous "yarns" that harbor groups of genes and regulatory elements, bringing them in contact with each other and allowing them to work in a coordinated manner during development.

Chromosomes are relatively large molecules that, when spread out, can measure up to the length of an entire human arm. Despite their size, however, they are actually confined within the small space of the cell nucleus which is just a few micrometers in size. Furthermore, within each cell nucleus are multiple chromosomes. In humans, for example, there are 23 pairs of chromosomes. In order to fit all this material into this small area, chromosomes are folded, compacted and mingled in the three-dimensional space of the nucleus.

"Not quite," said Elphege Nora, PhD, a post-doctoral fellow on the team of Dr. Heard, head of the Genetics and Developmental Biology Lab at the Curie Institute. "Chromosome folding follows a pattern, and this actually turns out to be important for ensuring their proper function."

**A chromosome looks like a series of tiny yarns**

"We have known for decades that the DNA of individual genes is wrapped around nucleosomes to form the classical 'beads-on-a-string' structure," said Dekker, co-director of the Program in Systems Biology at UMMS. "Our new study now shows that these beads-on-a-string subsequently fold up to form 'yarns-on-a-string,' where each yarn is a group of genes. This domainal organization of chromosomes represents a previously unknown higher order level of folding that we believe is a fundamental organizing principle of genomes."

These globule-like yarns span anything from a few hundred thousand to a million base pairs, explained Heard. Base pairs (abbreviated as A, C, G and Ts) are the genome's unit of measurement, and a person's DNA consists of over 3 billion pairs. "The real surprise, however, lies in how this spatial folding of chromosomes links up to their functional organization," said Heard. "This chromosome folding pattern brings together, into the same 'yarn,' several genes, up to 10 of them, or even more."

However, there are not just genes in these yarns. So called "regulatory genomic elements," that can control the activity of neighboring genes like switches are also found clustered together with the genes in these chromosomal yarns. A group of genes belonging to the same yarn will therefore be likely to contact a similar set of regulatory elements, and this can result in the coordinated activity of these genes during development.

These new observations shed some light on several long-standing mysteries of genetics, such as the reason why some DNA mutations can end up affecting genes that are located thousands or even a million base pairs away.
"The cell nucleus is packed with genes, and the cell is faced with the challenge to turn on or off each one of them correctly," said Dekker. "By organizing groups of genes in isolated domains, or yarns that do not mingle or mix with other genes, the cell has solved the problem of how to regulate groups of genes coordinately and without interference from other genes."

However, damaging one of these "chromosome yarns" can lead to the misbehavior of all the genes it contains. "The three-dimensional organization of chromosomes allows distal genomic elements to be brought together and to functionally interact with each other. At certain points during development it is thus possible to precisely orchestrate the activity of genes that are far away from each other on the linear chromosome thread, but that are actually in contact physically, within a chromosome yarn," said Nora. "The down side of this type of organization is that a single mutation altering the organization of such a 'chromosome yarn' can affect a whole group of genes."

**Three-dimensional folding provides shortcuts through the chromosome**

"Together with Job Dekker, who has pioneered chromosome conformation capture technologies, we have discovered these principles by studying a critical region of the X chromosome, the X-inactivation center," said Heard. "Thanks to a parallel study conducted by the team of Bing Ren, PhD, at the University of San Diego (and published in Nature alongside the Heard and Dekker study), we now know that the principles of chromosome folding we have seen on the X chromosome actually apply to the whole mouse and human genomes."

Beyond advancing our fundamental understanding of chromosome biology, these studies also open up new avenues for studying certain diseases, such as genetic disorders that are due to mutations in the DNA sequence which disrupt the proper activity of certain genes. Sometimes the mutation causing these defects is not directly in the gene, but affects one of its regulatory elements somewhere in its extended chromosomal neighborhood. Finding such mutations along the chromosome has been a bit like looking for a needle in a haystack because scientists did not know which genes were partnered with which regulatory elements. The hunt for such mutations can now be directed first to the chromosomal region most likely to harbor the regulatory elements of the misbehaving gene—inside the chromosome "yarn" to which that gene belongs.

**Journal Reference:**


**Study Resolves Debate On Human Cell Shut-Down Process**

ScienceDaily (Apr. 12, 2012) — University of Liverpool researchers have resolved the debate over the mechanisms involved in the shut-down process during cell division in the body.

Research findings, published in the journal *PNAS*, may contribute to future studies on how scientists could manipulate this shut-down process to ensure that viruses and other pathogens do not enter the cells of the body and cause harm.

Previous research has shown that when cells divide, they cannot perform any other task apart from this one. They cannot, for example, take in food and fluids at the same time as managing the important process of dividing into 'daughter cells' to replicate the body's genetic information. Cells, instead, shut-down the intake of food and fluid during cell division and for many years it was thought that they did this by preventing a vehicle—called a receptor—from transporting nutrients through the cell membrane.

In recent years scientists have shown evidence to suggest that this theory may be wrong. Scientists have argued that the cell does not shut down the mechanisms that allow food and fluid to enter the cell as previously thought, but rather the receptors that transport this fuel are absent altogether during cell division, allowing the cell to focus on the one task of dividing.

Studies at Liverpool, however, have now shown that the original theory, first documented in 1965, is accurate. The receptors are present and able to transport food and fluid during cell division, but the mechanism that allows them through the membrane of the cell shuts-down until cell division is complete.

Dr Stephen Royle, from the University’s Institute of Translational Medicine, explains: "We know that cells in the body do not have the ability to multi-task during cell division. It can only focus on the job of dividing and not on other important tasks such as uptake of nutrients. If we think of the cell membrane like a dock at a port and the receptors as a boat delivering cargo, we have shown that the boat, or receptor, is present but the dock, or membrane, does not allow it to unload or go any further.

"Viruses and pathogens use the same route into cells as nutrients, so the next stage of this work is to identify the trigger for this shut-down process, so that we understand whether this on/off switch can be
manipulated to prevent harmful infections passing through the cell membrane. This is a long way in the future, but this work puts us closer to understanding how the cells in the body work."

Journal Reference:

Feral Pigs Can Carry Nasty Bacteria That Can Be Transmitted to People
ScienceDaily (Apr. 11, 2012) — A North Carolina State University study shows that, for the first time since testing began several years ago, feral pigs in North Carolina have tested positive for Brucella suis, an important and harmful bacteria that can be transmitted to people.

The bacteria are transmitted to humans by unsafe butchering and consumption of undercooked meat. Clinical signs of brucellosis, the disease caused by the bacteria, in people are fairly non-specific and include persistent flu-like symptoms. The bacteria can also spread in pig populations, causing abortions in affected swine.

In a study conducted to test N.C. feral pig populations for several types of bacteria and viruses, about 9 percent of feral pigs studied in Johnston County and less than 1 percent of feral pigs surveyed randomly at 13 other sites across the state showed exposure to B. suis.

Dr. Chris DePerno, associate professor of forestry and environmental resources at NC State and the corresponding author of a paper describing the research, says the results are troubling for people who hunt feral pigs for sport or food.

"Now that exposure to Brucella suis has been found in North Carolina's feral pig populations, people need to take care when hunting, butchering and cooking feral pigs," DePerno says. "That means wearing gloves when field dressing feral pigs and cooking the meat to the proper temperature."

Dr. Suzanne Kennedy-Stoskopf, an NC State research professor of wildlife infectious diseases and a co-author of the paper, says that testing positive for antibodies to B. suis means the feral pigs have been exposed to and mounted an immune response against the bacteria. Antibodies do not eliminate B. suis from pigs, so the animals are considered infected and capable of transmitting the bacteria to other pigs and people. She adds that control and eradication programs introduced in the late 1990s eliminated swine brucellosis from all commercial pig populations in the United States.

Kennedy-Stoskopf says that B. suis can be transmitted among pig populations when pigs ingest infected tissue or fluids. Direct contact with infected pigs or ingestion of contaminated food and water could cause currently uninfected pig populations to become infected.

"Spillover from infected feral pigs to commercial pigs is an economic and a public-health concern," Kennedy-Stoskopf says. "The biggest public-health risk is to pork processors and hunters who field dress feral pigs. Although cases of brucellosis are rare in the United States, people need to understand the clinical signs—like intermittent fevers and persistent headaches—and go to the doctor for diagnosis and treatment if they have these flu-like symptoms." Because clinical signs are so non-specific, it is important to tell your physician if you have had any exposure to feral swine carcasses and meat.

Feral pig populations are exploding across the country, DePerno says. Besides the rabbit-like reproductive proclivity of feral pigs, people are partially responsible for the population boom. There is strong evidence that humans have transported feral pigs into new areas for hunting.

"Control of feral pig populations is difficult at best," DePerno says. "Research indicates that about 70 percent of the population will need to be removed each year to keep a wild population stable. Regarding feral pigs, hunting usually removes from 8 to 50 percent of a given wild population."

Feral pigs can be destructive to the environment and can out-compete native animals. They dig, root and tear up crop lands; eat just about anything; and can spread disease to animals and people.

DePerno hopes that more research on how far feral pigs travel—and increased scrutiny of hunters who move feral pigs from place to place—will help keep feral populations from spreading.

NC State graduate student Mark Sandfoss and postdoctoral researcher Dr. Maria Palamar conducted research and co-authored the paper, which is published in the Journal of Wildlife Diseases. Researchers from the U.S. Department of Agriculture and Rollins Animal Disease Diagnostic Laboratory contributed to the research.

Journal Reference:
Does CMV underlie the increased risk of cardiovascular disease in patients with HIV?

Michael Carter
Published: 16 April 2012

Cytomegalovirus (CMV) antibody levels are associated with some important markers of vascular disease in HIV-positive women, US researchers show in a study published in the online edition of the *Journal of Infectious Diseases*. "Our findings suggest that CMV IgG [antibody level] is associated with increased carotid artery stiffness and carotid artery lesions in HIV-infected women," write the investigators.

An association was also found between antibody levels and an increased risk of lesions in the carotid artery, but only for women taking HIV therapy and with an undetectable viral load.

The authors of an accompanying editorial believe the study takes us "one step closer to understanding the relationship between CMV and development of coronary heart disease."

Infection with CMV was linked to faster HIV disease progression and poorer outcomes in HIV-positive people in the era before highly active antiretroviral therapy (HAART) was available. Research conducted in the general, HIV-negative population has established a relationship between the infection and the development of cardiovascular disease.

It is well established that people with HIV have an increased risk of diseases such as heart attack and stroke. Investigators from the Women's Interagency Health Study (WIHS) speculated that this could, in part, be because CMV infection causes subclinical vascular disease. They tested this hypothesis in a prospective study involving 601 HIV-positive women and 90 HIV-negative women.

All the study participants underwent a carotid artery ultrasound. The key measures of vascular disease assessed were arterial intima-media thickness (cIMT), distensibility (ability to be distended or stretched under pressure) and elasticity.

To see if CMV antibody level was associated with these key measures of arterial stiffness, the investigators performed a series of analyses which controlled for established risk factors of vascular disease.

Most of the women (64%) were African American and their mean age was 40 years. There was a high prevalence of risk factors for cardiovascular disease. Half the women were smokers, 20% were diabetic and the mean body mass index (BMI) was within the overweight/obese range.

Analysis of vascular health found little difference between the HIV-positive and HIV-negative women. Nor were there any significant differences between the HIV-positive women according to their use of antiretroviral therapy and viral load.

However, the investigators found that CMV antibody levels were significantly higher among the HIV-positive women compared to their HIV-negative peers (p < 0.01).

In the HIV-positive women, there was no significant relationship between CMV antibody levels and either CD4 cell count or viral load.

Nevertheless, the investigators identified a highly significant relationship between CMV antibody levels and carotid artery distensibility and elasticity (both p < 0.01) in HIV-positive women, but not in the HIV-negative control group.

"No associations between CMV IgG levels and subclinical cardiovascular disease parameters were observed in an HIV-uninfected control group that was studied using similar methods," comment the researchers.

The magnitude of this association in the HIV-positive patients was similar to that associated with each additional two to three years of ageing.

Among the HIV-positive women, there was no overall association between CMV antibody levels and either cIMT or the presence of arterial lesions.

However, the presence of arterial lesions differed significantly according to the use of antiretroviral therapy and viral load.

For women taking virologically suppressive HIV therapy, each 10 iu/ml increase in CMV antibody titers was associated with a significant increase in the prevalence of lesions (prevalence ratio = 1.58; 95% CI, 1.09-2.30). This association was not observed in women with a detectable viral load.

"CMV-specific T-cell responses may expand among HIV-infected patients once they are placed on effective antiretroviral therapy, as compared with patients in the early or untreated phases of HIV infection or in HIV-uninfected controls," suggest the authors. However, they believe that future research is needed to clarify this apparent association. This research should also "test the hypothesis that therapies
directed against CMV infection may reduce HIV disease progression and associated vascular complications.”

The authors of the accompanying editorial hypothesise that the lesions observed in the women taking suppressive HIV therapy were due to immune reconstitution inflammatory syndrome (IRIS). They also believe that CMV may contribute towards the “aging” of the immune system, thereby increasing the risk of cardiovascular disease.

They conclude, “with a growing literature supporting the role of CMV in immune aging, inflammation and cardiovascular disease...further research on the immunology and epidemiology of CMV in HIV infected and non-infected populations is crucial.”

Reference

Genetic testing for drug intolerance
Testing could prove an effective remedy to a widespread problem. But there may be hidden hazards to our privacy

Angela Saini

Three years ago, Theo Dingermann, a professor of pharmaceutical biology at Goethe University in Frankfurt, sent a glob of spit to the United States. For $200 a company there sequenced part of his genome using DNA from his cheek cells. The test revealed that if he were to take the cholesterol-lowering drugs statins, they would have little effect. In fact, they might harm him.

"I'm healthy at the moment, but if I took statins, there's a risk I would get muscle pain," he says. Statins work through the blood, coursing through the body until they reach the liver. Here, they pass through a door, known as a carrier, which takes them from the blood into the liver, where they lower cholesterol production. Dingermann's genetic test showed that he has fewer carriers than usual, which means that statins could stay in his bloodstream and start harmfully reducing the cholesterol in his muscles instead.

Realising that he might have to live without these artificial cholesterol-busters, he decided to get healthy. "I lost some kilos and started running. Last year, I jogged 1,400km."

Intolerance to a drug is something most people learn about themselves only after it's prescribed.
"There are some tumour drugs, for certain cancers, that 70% of the population won't respond to. For some asthma drugs, it's 40%," says Dingermann, who has been collecting research on the topic for the past four years. His source is a 2001 article published in the journal Trends in Molecular Medicine, which also stated that antidepressants were ineffective for 38% of people, diabetes drugs for 43%, arthritis drugs for 50% and Alzheimer's drugs for as many as 70%.

Ann Daly, a professor of pharmacogenetics at Newcastle University Medical School, says these rates are difficult to verify. Some people, for instance, don't take the medicines they are prescribed. But for a very small minority, the consequences of taking their medications are dire. A paper in the Journal of the American Medical Association in 1998 estimated that adverse drug reactions ranked between the fourth and sixth biggest killers in the United States. "Medical practice hasn't changed all that much since this paper appeared. Adverse drug reactions remain a big killer in Europe, as well as in the US," Daly says. Part of the problem lies in how medicines are developed. Clinical trials deliberately ignore a patient's background and genetics so they can avoid bias. But this in turn means that, so long as a drug works well for most people, doctors will prescribe it to everyone with that condition. "Such a study doesn't tell you how a particular patient responds to a drug. Some people have a personal biochemistry which means it doesn't work at all," says Dingermann.

The tiny risk of side-effects is something we accept almost every time we swallow a pill, but Dingermann argues it's one we need no longer live with. If everyone had their genomes analysed the way he did and if medical trials included patients' genetic backgrounds, they could steer clear of the drugs that don't suit them, he says. He has been urging governments and health insurance companies to adopt widespread genetic testing. This kind of personalised medicine could save millions in unnecessary medical bills.

Scientists are beginning to back the idea with greater force. A report in January 2012 by the Human Genomics Strategy Group, which advises the UK government, laid out a vision for the NHS in 2020 that includes using patients' genetic profiles to avoid drugs that could harm them. The group's chair, Sir John
Bell, a former president of the Academy of Medical Sciences, said that a national DNA database might be needed in the future.

One successful example of genetic testing is the HIV and AIDS drug, Abacavir. "Around 1–2% of people develop a severe, allergic-type reaction to it, and for them, it can be life threatening," says Daly. Studies have shown that this reaction is linked to a specific set of genes, so since around 2008, doctors have been advised to screen patients before prescribing Abacavir.

Scientists are developing similar tests for the blood thinner Warfarin, which is already carefully dosed but can cause severe bleeding in up to 5% of patients. There are also "more and more genetic tests on tumours," adds Geoff Tucker, emeritus professor of clinical pharmacology at the University of Sheffield. "In cancer therapy, the application of genetic testing has been very successful."

But he is sceptical that genetic screening will be rolled out across the entire population any time soon. "The reasons that people don’t respond to drugs are more than genetic," he says. Tucker suggests a possible alternative might be to pump a variety of indicators, including age, weight, diet and environmental factors, along with genetics, into software that could determine how much a patient's dose of a drug should be.

Research linking genes to drug intolerance "is only halfway there", agrees Daly. "Not to mention, if you wanted to screen everybody, that would be expensive and require a big infrastructure." Keeping this kind of personal information also raises privacy issues. Where they exist, DNA banks are kept under strict controls, but with widespread databases and weaker security, genetic data could be used to discriminate against people based on their genetic traits. Insurers, for instance, might raise premiums for patients with a higher susceptibility to heart disease.

But Daly admits that, as the cost of genetic testing plummets, it may become a bigger issue. Like Theo Dingermann, more people could simply start paying to have their spit checked.

Utah Schools Rank Last for Lessons on Condoms
Salt Lake Tribune, (04.11.2012) Lisa Schencker
In 2010, only 11.3 percent of Utah's public secondary schools taught teens about the efficacy of condoms, how to obtain them, and the importance consistent and proper use—the lowest percentage out of 45 states surveyed by CDC.

Utah law permits schools to teach about contraception, but bars advocating its use. Schools districts may choose abstinence-only or abstinence-based curriculum, and students must have their parents' consent to participate. Gov. Gary Herbert recently vetoed a bill that would have let school districts drop sex education completely, banning contraceptive instruction for those that retained it.

Karrie Galloway, CEO of the Planned Parenthood Association of Utah, noted that “teens are making their own decisions” on the issues while adults continue fighting. A Youth Risk Behavior Surveillance System report found that, in 2009, 46 percent of US teens reported having had sex. Utah, however, does not survey teens on sexual activity.

Galloway referred to the condom education statistics as “abysmal.” “Take the morality out of it,” she continued. “Focus on it as a public health issue and say, ‘Do we want our kids this ignorant?’” The Utah Department of Health reported the highest rates of chlamydia in 2010 were among girls ages 15 to 19.

Dalane England, vice president for issues with the Utah Eagle Forum, disagrees. “When you talk about abstinence-only ... you get more abstinence.”

Brigham Young University Assistant Professor Cougar Hall, who trains health teachers, was most surprised that 12.4 percent of surveyed schools reported teaching teens how to access condoms. To avoid violating state law, he said he would advise teachers not to tell students where to get condoms, even though he personally feels schools should advocate for correct and consistent condom use.

Doctors Without Borders Alarmed over Plans to Cut US AIDS Program
Voice of America, (04.10.2012) Gabe Joselow
The Obama administration’s proposed cut to the President’s Emergency Plan for AIDS Relief (PEPFAR) program is “problematic” and could have a “chilling effect” worldwide, said Jennifer Cohn, Doctors Without Borders’ (DWB) policy advisor for East Africa.

Obama’s budget for fiscal year 2013 cuts more than a half-billion dollars from PEPFAR—about 13 percent of its current funding. In an official blog post in February, Global AIDS Coordinator Eric Goosby said the administration is “freeing up resources by reducing programs in countries with a lower HIV
prevalence,” like Ethiopia and Kenya. According to analyses by DWB, that translates to a 50 percent cut to Kenya and 82 percent for Ethiopia.

PEPFAR senior advisor Tom Walsh said all budget discussions are preliminary, though some country allocations are certain to change. Furthermore, the program is benefitting from a “dramatic gain in efficiency,” and the 2013 amount proposed is realistic, he said. “Over the years, we’ve gotten the cost of treating an individual person per year with antiretroviral therapy down from about $1,100 in 2004 to $335 in 2011,” he added.

However, Cohn said DWB is concerned not only about the proposed cut, but also with the way PEPFAR counts the number of people it assists. “What we’re finding is actually that whereas PEPFAR is not necessarily directly supporting people on treatment in certain countries, they’re actually counting those people toward the 6 million people they promise to put on treatment by 2013, so we find that concerning and somewhat disingenuous,” she said, citing a recent program report from Malawi.

“In every country there’s a different combination of resources that it takes to deliver treatment,” said Walsh.

When They Break Up and Get Back Together: Length of Adolescent Romantic Relationships and Partner Concurrency


Given the important role sex partner concurrency plays as an STD risk factor, the authors introduced the current study by noting that gaining an understanding of how teenagers “conceptualize the length of their relationships when they break up and get back together is essential to the assessment of concurrency.”

From two clinics in Baltimore, a prospective cohort of 392 people ages 14-19 at baseline were recruited. In semiannual interviews conducted during a three-year period, the youths were asked to report on all their sex partners in the previous six months, the length of the relationship, and whether they thought their partner had other sex partners. For relationships that had involved breaking up and getting back together, reports of the relationship’s length were compared before and after the breakup. The association between length of relationship and both breakup and partner concurrency was examined using random effects logistic regression.

In relationships where the partners had broken up and gotten back together, participants indicated that they considered the length of the relationship to be inclusive of the period when they were broken up. Longer relationships had increased odds of both having broken up and gotten back together (odds ratio=1.04, 95 percent confidence interval: 1.02, 1.05) and of partner concurrency (OR=1.03, 95 percent CI 1.02, 1.04). The odds of concurrency were higher in relationships where the partners had broken up and reunited (OR=1.07, 95 percent CI: 1.02, 1.11).

“Findings from this study emphasize the need for an improved understanding of the association between the temporal dynamics of late adolescent and emerging adult romantic relationships and concurrency,” the authors concluded.

Should Low-Risk Gay Men Be Allowed to Donate Blood?


The United States’ current lifetime ban on blood donations by sexually active gay men will be the subject of an online discussion with medical writer Laura Unger of the Louisville Courier-Journal on April 18 at noon. The nation’s ongoing shortage of blood donors is leading many people to rethink the ban, which some activists have called discriminatory given advances in blood-screening technology. For more information, visit http://live.washingtonpost.com/gay-men-blood-donation.html.

Use Of Sewage-Contaminated Water To Irrigate Crops Poses Disease Risk In Zimbabwe, IRIN Reports

IRIN examines how local Zimbabwean farmers’ usage of water containing raw sewage to irrigate their crops poses a risk of disease transmission to people who consume the vegetables. In the capital Harare, less than half of the raw sewage produced is treated before being sent back into tributaries, according to IRIN, which notes, "In a recent report, Harare mayor Muchadeyi Masunda said 60 percent of the capital’s residents did not have access to clean water, and 10 percent relied on boreholes and unprotected wells." Since a cholera outbreak in 2008, UNICEF and other international donors have been helping
Zimbabwean municipalities treat their water, but the UNICEF program is winding down, leaving some unsure whether local authorities "can go it alone," IRIN writes (4/16).

**Genetically Modified Mosquitoes Offer Hope Of Malaria Eradication Amid Growing Drug Resistance**

"In recent weeks, the emergence on the Thai-Myanmar border of malaria strains resistant to artemisinin, a plant-derived drug, have led to pessimistic headlines and reminders of the setback caused by resistance to the drug chloroquine, which began in the 1950s," columnist and author Matt Ridley writes in the Wall Street Journal’s "Mind & Matter," noting, "April 25 is World Malaria Day, designed to draw attention to the planet’s biggest infectious killer." He continues, "For this reason, prevention generally works better than cure in eradicating infectious diseases: Vaccination beat smallpox, clean water beats cholera, less crowded living beats tuberculosis and protection from mosquitoes beats malaria."

Ridley examines "a new control technique developed by a former Oxford University scientist named Luke Alphey," which involves releasing mosquitoes that have been genetically modified so that they would not produce viable offspring, and writes, "Predictably, perhaps, the genetic modifications have led to objections from some Western pressure groups, showing their now customary tendency to elevate theoretical principles above the battle against human suffering." He continues, "Yet the great advantage of Dr. Alphey’s approach, in contrast to the fogging of dengue-affected areas with insecticide, is that it is pest-specific" and "[n]o other insect is hurt." Ridley concludes, "With such a technique, the eventual eradication of human malaria from the planet is far from being an impossible dream" (4/13).
Method Developed to Detect Stealthy, 'Hypervirulent' Salmonella Strains

ScienceDaily (Apr. 12, 2012) — A recent discovery of "hypervirulent" Salmonella bacteria has given UC Santa Barbara researchers Michael Mahan and Douglas Heithoff a means to potentially prevent food poisoning outbreaks from these particularly powerful strains.

Their findings have been published in the journal PLoS Pathogens.

Salmonella is the most common cause of infection, hospitalization, and death due to foodborne illness in the U.S. This burden may continue to worsen due to the emergence of new strains that would tax current health-control efforts. To address this problem, researchers sought out—and found—hypervirulent strains that present a potential risk to food safety and the livestock industry.

An international team of scientists—which also included Robert Sinsheimer and William Shimp from UCSB; Yi Xie and Bart Weimer from UC Davis; and John House from University of Sydney, Australia—conducted a global search for hypervirulent Salmonella strains. They were found among isolates derived from livestock, and rendered current vaccines obsolete.

Bacteria behave like a Trojan Horse, exposing their weapons only after initiating infection. "These strains exhibit this behavior in the extreme—essentially having a '5th gear' they can switch to during infection," said Heithoff, lead author of the paper.

Previous efforts to find hypervirulent strains were unsuccessful since bacteria behave much like their less-virulent cousins after environmental exposure. "The trick was to assess their virulence during infection—before they switch back to a less-virulent state in the lab," said Professor Mahan.
Now that researchers know what to look for, they are developing methods to rapidly detect and discriminate the more harmful strains from their less-virulent cousins. The strategy is aided by a special medium utilized by the researchers that forces the bacteria to reveal their weapons in the laboratory—the first step in the design of therapeutics to combat them.

Humans usually get Salmonella food poisoning from eating contaminated beef, chicken, or eggs. However, animal waste can contaminate fields where fruits, nuts, and vegetables are grown, thus posing a particular health concern for vegetarians. The threat is exacerbated when these foods are not cooked. Salmonella control efforts are expensive—recent estimates place this cost up to $14.6 billion annually in the U.S.

As hypervirulent strains pose a potential risk to human and animal health, mitigation efforts warrant researchers' careful attention. "Now that we have identified the problem—and potential solutions—we just need to get to work," Heithoff said.

**Journal Reference:**

**From Herd Immunity and Complacency to Group Panic: How Vaccine Scares Unfold**

ScienceDaily (Apr. 5, 2012) — Worries over vaccine risks can allow preventable contagious diseases, such as measles and whooping cough, to make a comeback. A new study, published in *PLoS Computational Biology*, shows how to predict ways in which population vaccinating behavior might unfold during a vaccine scare.

"These findings might help in evaluating and developing global immunization programs and public health policy," said Professor Chris Bauch of the University of Guelph’s Department of Mathematics and Statistics.

Prof. Bauch and Samit Bhattacharyya of the University of Utah developed a mathematical, "Behavior-incidence" model based on game theory and social learning. They tested the model with real data from two infamous vaccine scares in England and Wales: the 1970s pertussis outbreak and the measles-mumps-rubella vaccine scare in the 1990s. In both cases, the publication of alleged vaccine risks was followed by a media firestorm in national newspapers, television, and radio. In light of this, the fact that it took 4-5 years for vaccine uptake to bottom out was puzzling. They found that the model could explain the patterns of the vaccine scares very well, and could also be applied predictively to the data sets.

The model captured the interplay between disease dynamics and vaccination behaviour during those episodes. One of the theoretical dynamics for the model was the phenomenon known as "herd immunity"; an entire population—including unvaccinated individuals—can be protected from infection by vaccinating only a certain percentage of the population. This suggests that immunization programs can be victims of their own success as past vaccinations drive disease incidence to such low levels that unvaccinated individuals feel no incentive to get vaccinated, creating ideal conditions for vaccine scares and thus future outbreaks.

Due to these conditions, as Prof. Bauch says, "Vaccine scares could become more common as eradication goals are approached for more vaccine-preventable diseases. Such models could help us predict how vaccine scares might unfold and assist in mitigation efforts."

**Journal Reference:**
**Promoting Death**  
Editor's choice in biochemistry  
By Edyta Zielinska | March 1, 2012

TAGGING FATE: Like the Moirai, the three fates in Greek mythology, the promoter sequence can decide the lifespan of some messenger RNAs (shown here) as they are first transcribed in the nucleus. shunyufan/istockphoto.com

**The paper**

**The finding**
Researchers have long thought mRNA degradation by cytoplasmic nucleases occurred randomly. But when Robert Singer and colleagues at Albert Einstein College of Medicine in New York City traced the lives of two mRNA species from birth in the nucleus to death in the cytoplasm, they found that the fate of some mRNAs was decided by the promoter sequence that instigates gene transcription.

**The vanishing act**
To track how mRNA degrades, first author Tatjana Trcek chose two genes, *SWI5* and *CLB2*, whose transcription is regulated by the cell cycle. Looking at individual yeast cells using tools the lab had developed to count mRNA transcripts, the researchers were surprised to find that during mitosis, the mRNAs disappeared in 2 minutes or less. “They went from completely stable to bam, just gone,” says Singer.

**The culprit**
The researchers figured that there must be something in the genetic code that marked those mRNAs for rapid degradation, but when Trcek inserted pieces of code for longer-lasting mRNA into the *SWI5* and *CLB2* genes, nothing changed. However, when the promoter from the long-lasting mRNA was inserted at the front of the *SWI5* and *CLB2* genes, the normally short-lived mRNAs remained in cytoplasm into the beginning of the next cell cycle.

**The myth-buster**
Evidence is mounting that the promoter plays a much bigger role in RNA processing than previously suspected, says Roy Parker of the University of Arizona. It’s “the Greek tragedy model. The fate of the hero is determined at birth,” says Singer, who is now interested in learning just how the promoter conveys instructions to the mRNA.
Identifying Diet-Treatable Diseases
Scientists test which mutations underlie metabolic diseases that may benefit from changes in diet.
By Sabrina Richards | April 10, 2012
Scientists have classified which alleles of a mutated enzyme can benefit from changes in diet, in a new yeast study published last week (April 1) in Genetics. Mutations in the cystathionine-β-synthase (CBS) enzyme can lead to a variety of diseases, such as mental retardation and homocystinuria. Some patients benefit from supplementing their diet with vitamin B₆, a cofactor that aids CBS’s enzymatic activity, but it depends on which mutation they carry.

To identify the CBS mutations whose resulting diseases could be aided by diet, scientists from the University of California, Berkeley, expressed different alleles of the human CBS gene in yeast that were missing the CBS ortholog Cys4p. They then measured yeast growth and enzyme activity with and without vitamin B₆ or heme, another CBS cofactor.

The researchers were able to successfully sort alleles based on response to cofactor supplementation, which will help doctors identify which patients will respond well to early dietary interventions.

“This study moves us a step closer toward better understanding the genetic variability among people,” Mark Johnston, editor-in-chief of the journal Genetics, said in a press release. “More immediately, knowledge of these gene mutations will help physicians prescribe treatment based on genotype rather than outward symptoms or trial and error.”

Opinion: The Risk of Forgoing Vaccines
Herd immunity, or the protection of individuals who are not vaccinated due to generally high vaccination rates within a population, does not currently exist in many pockets of the US.
By Juliette K. Tinker | April 3, 2012
In his book The Selfish Gene, Richard Dawkins devises a population of birds to explain reciprocal altruism. In this population, there is a deadly disease that is spread by ticks. The birds can groom themselves to remove ticks, and thus protect themselves from disease, in all but one spot—the top of the head. On that spot, they must rely on other birds to remove their ticks. Thus, for the birds in this population to survive, they must work together. If they don’t, and some birds decide to “cheat” by having their ticks removed by “suckers,” but not reciprocating, the population will suffer. As fewer and fewer birds help their peers remove ticks, the population will become overrun with disease.

Given the direct benefit to the individual of immunity against disease, vaccination, is not completely altruistic. However, immunization provides a significant benefit to society. One can liken a human newborn, or a person who cannot get vaccinated, to a vulnerable bird with ticks on the top of its head. As individuals, we cannot fully protect these people from infectious disease, and instead we rely on herd immunity. If society is made up mostly of “suckers” that have expended the energy and cost to get vaccinated, then the vulnerable will be protected due to the absence or reduction of disease transmission. But if a significant percentage of individuals decides against vaccination, for one reason or another, we may lose herd immunity, and infectious disease will spread.

Unfortunately, we are beginning to see signs of this phenomenon, due in part to parents refusing to vaccinate their children because of the fear that it could cause autism—the now completely debunked message delivered by Andrew Wakefield in 1998.

In 2010, Idaho was ranked last in the country for routine childhood vaccination rates. Low rates have been a trend in this state for the last several years, and are likely due to limited access to vaccines as well as vaccine refusal. According to the National Immunization Survey, Idaho has only a 63.7 percent vaccination rate for the early childhood vaccination schedule (aged 19-35 months). These rates of vaccination are nowhere near the 85-95 percent levels required for herd immunity protection against most diseases. Unfortunately this means many children in Idaho are running the risk of diseases like pertussis, measles, and meningitis. And Idaho is not alone; other states, such as Montana, New Jersey, and Utah, also report low rates for early routine vaccinations. These rates are lower than some developing countries, and while overall childhood vaccination in the United States remains reassuringly high (levels at 90 percent or higher on average), these pockets of vulnerability are very concerning to public health officials.

Indeed, we are already seeing evidence of disease reemergence. In 2000, there was no endemic transmission of measles in United States, and this disease was declared eliminated. However, measles is
one of the most transmissible diseases on earth, requiring vaccination rates of higher than 95 percent to achieve herd immunity. And in 2011, the country had more than 200 cases, many of which were imported from Europe, which is currently experiencing large measles outbreaks, with over 26,000 cases in 36 countries, as reported by the World Health Organization. Whooping cough is also on the rise. From January to October 2010, there were 455 infants hospitalized in California and 10 deaths due to *Bordetella pertussis*, the highest number of cases in over 60 years, according to the Centers for Disease Control and Prevention.

Parental refusal has contributed to this increase in disease transmission. It is clear that Andrew Wakefield’s work, though it has been thoroughly debunked and removed from the literature, is far from forgotten.

As a scientist I recognize that we are not always the best communicators. When it comes to vaccines, this is particularly relevant. It is not enough to make safe vaccines that protect people from disease; we must convince the public that they are safe and effective. This may be a tall order given the current cultural climate, but one that is imperative for immunization programs to be effective. Showing data and statistics that refute claims by detractors does not do much to stop the spread of fear about vaccine safety. However, there are real lives that are saved by vaccines, and information about vaccine-preventable diseases may be the best way to inform. Among the many differences between us and the tick-pickers is that we are capable of seeing the future and the need to protect the population. Even if this means we have to go against individualism and act a little bit like a sucker.

**Juliette K. Tinker** is an assistant professor in the Department of Biological Sciences at Boise State University.

### Bird Flu Mutations Revealed

**One of the researchers who created a highly transmissible form of the bird flu virus has broken his silence and shared which mutations made it possible.**

**By Bob Grant | April 5, 2012**

Speaking at a meeting of the Royal Society in London on Tuesday (April 3), one of the scientists whose research resulted in an H5N1 virus that could spread easily between ferrets has revealed the details of how he did it. University of Wisconsin, Madison, virologist Yoshihiro Kawaoka told about 150 attendees of the 2-day meeting that 4 mutations and genes from the H1N1 virus appeared to make the bird flu virus strain readily transmissible between ferrets in his lab.

Kawaoka’s revelations, which came on the heels of last Friday’s National Science Advisory Board for Biosecurity recommendation that his paper be published in full, detailed his methodology. First, he introduced two mutations—N224K and Q226L—into the haemagglutinin (HA) protein of H5N1 that made the virus capable of sticking to receptors on human tracheal cells. Then he created a chimeric virus by combining the mutated HA protein with genes from the H1N1 virus, which sparked a pandemic in 2009. Kawaoka identified another HA mutation, called N158D, that allowed the virus to spread between ferrets that were not in direct physical contact. A fourth mutation, T318I, also showed up in the H5N1 strain, but its role in making the virus more transmissible among mammals is less clear.

Though Kawaoka broke his silence, Ron Fouchier of Erasmus Medical Center in Rotterdam, the Netherlands, the lead author of the parallel study that resulted in a highly transmissible H5N1 strain, was unable to do so. The Dutch government is preventing Fouchier from publishing his results until they determine if doing so violates export rules. “I wish Ron could report everything,” Kawaoka told *ScienceInsider*. “We found striking similarities.”

Neither Kawaoka’s nor Fouchier’s versions of the virus were lethal to the animals in their experiments, and they were both vulnerable to current drug treatments.

According to *Nature*, the journal to which Kawaoka’s group submitted their results, the paper will be published in full “as soon as possible.”
Antibiotics in the Animals We Eat
By Bonnie M. Marshall and Stuart B. Levy | April 1, 2012
For as many decades as antibiotic resistance has thwarted the cure of bacterial infections, scientists have pondered the origins of resistance genes and how they became such a problem. Fingers were pointed squarely at the overprescription of antibiotics in human medicine—and rightly so, as early on, these drugs were liberally utilized for every imaginable malady without concern for the possible consequences. Not long after their discovery, however, these miracle drugs were applied not only to sick humans and animals, but to healthy ones as well.

Nowhere is this practice more prevalent and controversial than in animal husbandry, where animal feeds laced with small amounts of antibiotic are provided over extended periods of rearing. Labeled as “growth promotion” and employed primarily in large, concentrated feedlots for poultry, swine, and cattle, this nontherapeutic application appeared to fatten the animals faster, prevent rampant herd disease, and help bring healthy animals to market more quickly.

While US farmers and other stakeholders have argued tenaciously for the continuation of subtherapeutic dosing, Europeans adopted the “precautionary principle,” instituting sequential bans on the practice beginning in the mid-1990s. Arguments on both sides of this issue continue to the present day, but evidence of the negative consequences of low-dose antibiotic feeding has been mounting. Since 1976, several persuasive scientific studies have illustrated how animals fed low-dose antibiotics not only propagate resistant bacteria, but spread these resistant strains to farmers, their families, community residents, and ultimately, hospitalized patients. Particularly worrisome is the continued use in animals of antibiotics that are close structural relatives of those that are used in human medicine. It is feared that, in time, these drugs will lose potency as bacteria express “cross-resistance” to the related drugs.

Some researchers have countered that the resistant bacterial strains found in serious hospital infections bear little or no resemblance to the strains found in farm animals. They argue that eliminating antibiotics on the farm would harm animal health, result in economic loss, and have little or no impact on reducing human morbidity and mortality. However, these rebuttals overlook the inherently promiscuous nature of bacteria—in particular, the transferable genetic elements they often carry (e.g., bacterial plasmids, transposons, phages) that can readily share DNA segments bearing resistance genes. They pass among strains, species, and even diverse bacterial genera, rearranging and accumulating even more resistance genes. Tracking the evolution of such complex bacterial exchanges from food animals to people poses a daunting challenge, making definitive proof elusive. But we argue that the preponderance of evidence, coupled with a diminishing pipeline of new antibiotics and the appearance of multidrug-resistant “superbugs,” warrants closer scrutiny of how and where we are using these antimicrobials—and the adoption of stricter measures of control.

While still declining to issue an all-out ban on subtherapeutic feeding, the US Food and Drug Administration has taken measured steps in the right direction. First, in 2005, the agency prohibited the use of fluoroquinolones in poultry, and just this January, it prohibited certain off-label uses of cephalosporins in livestock generally. It is a matter of concern, however, that the FDA does not address the ongoing use of penicillins and tetracyclines as growth promoters. Thus, we are still a long way from the steps needed to safeguard precious classes of drugs for effective treatment of human disease.

Judicious surveillance in Europe in the decades following the bans on antibiotic use in animals has shown that the emergence and spread of resistant bacteria can be controlled and even reversed. Alternatives to antibiotics in animal husbandry in these countries, including improving hygiene practices and reducing overcrowding, need to be more fully explored for implementation in the United States.

Bushmeat Roulette
Pathogens lurk in illegal wildlife products confiscated at US airports.
By Megan Scudellari | April 1, 2012
In October 2008, US Customs and Border Protection agents at John F. Kennedy International Airport in Queens, New York, seized a suspicious postmarked container shipped from Nigeria. Moments later, at the airport’s Centers for Disease Control New York Quarantine Station, personnel in full protective gear gingerly opened the package and pulled out dark, misshapen objects—hunks of meat. They photographed
and cut off a sample from each, placing them into a container of liquid nitrogen. The remaining meat was incinerated.

In the following 2 years, US Customs confiscated an additional seven postal shipments at JFK and seized 20 more packages straight out of the arms of passengers at four other US airports. Some of the meat was dried, some smoked, some still raw and dripping blood.

This bizarre sting operation was part of a pilot program run by the CDC, the Wildlife Conservation Society, the EcoHealth Alliance, and other institutions to assess the risk of dangerous pathogens entering the country via the illegal wildlife trade (PLoS One, 7:e29505, 2012). Nearly 75 percent of emerging infections—SARS, HIV, Ebola, and more—originate in nonhuman animals, mostly wildlife, says Kristine Smith, the EcoHealth Alliance veterinarian who led the study. And the United States is the number-one importer of live wildlife and wildlife products. Approximately 1.5 billion live wild animals were legally imported into the country between 2000 and 2006, but no one knows the scope of illegal game imports.

The frozen samples collected between 2008 and 2010 were identified and analyzed by researchers at the CDC National Center for HIV/AIDS and Columbia University’s Center for Infection and Immunity. Since investigators couldn’t determine the species of many of the specimens by sight, the team used DNA barcoding—a popular way to identify a species using only a tiny snippet of one mitochondrial gene—to ID 9 primates and 35 rodents, including some threatened and endangered species. But the scientists were less concerned with the species of the tissue samples and more worried about potentially lethal hitchhikers lurking in their cells.

The team screened the meat for multiple pathogens and got unsettling results: the rodents were free of viruses, but half of the primate samples were riddled with simian foamy virus (SFV), cytomegaloviruses, and lymphocryptoviruses, all of which can pose a threat to humans. Scientists have already documented that SFV, which is related to HIV, can cross over into human populations, though those infected with the virus have not become ill. The finding implies that other, more virulent simian viruses could also reside in imported bushmeat, says William Switzer, a retro-virologist at the CDC who screened the meat for SFV. “This is a way for viruses to bypass human carriers and go directly into a biomaterial to expose people in distant locations,” he says. “I believe if we had tested a larger number of confiscations, we would have found more of these known pathogens,” Smith says.

That viruses are present in the imported meat is not surprising, says Mark Woolhouse, a professor of infectious disease epidemiology at the University of Edinburgh in Scotland, who was not involved in the study. “But this is the first time it’s been properly demonstrated in a systematic way,” he says.

The researchers did not assess how efficiently the viruses could infect human cells, but the spread of infections to humans via the animal trade is well documented. In June 2003, 93 cases of monkeypox in the United States were traced to contact with prairie dogs that got the virus from an imported Gambian giant rat. In 2007, an outbreak of bird flu at farms in the United Kingdom was traced to imported Hungarian poultry. “This is not just a theoretical possibility,” says Woolhouse. “This is a cause for concern.”

The pilot project has since expanded to 12 US airports, but the scope of the problem—just how much illegal meat is imported and what types of viral stowaways are onboard—remains unknown. “We just don’t know how often this is happening,” says Switzer. “We may be seeing just the tip of the iceberg.” As sequencing technologies become cheaper, the possibility of wider surveillance of both the legal and illegal animal trade will be more feasible, says Woolhouse. But random screening alone isn’t going to solve the problem. Instead, the animal trade needs regulation to ensure that only healthy, disease-free animals pass from country to country. “There really hasn’t been a big push for this in the international arena,” says Woolhouse. “This is a wake-up call that it needs to happen.”

**Fungus Thwarts Dengue**

A mosquito-killing fungus shows promise as an effective dengue-control agent.

*By Harvey Black | April 16, 2012*

The fungus *Beauveria bassiana* effectively kills *Aedes aegypti*, the mosquito responsible for carrying dengue, and sharply reduces the rate at which mosquitoes seek human targets, according to a study published earlier this month in *The American Journal of Tropical Medicine and Hygiene*. The results offer a potential alternative to pesticides to control the mosquito-borne viral disease.

“I think it’s encouraging. The experiments they did are consistent with the fact that [the fungus] could affect *aegypti* in ways that could prevent dengue transmission,” said Tom Scott of the University of California, Davis, who did not participate in the study.
Dengue is a viral disease transmitted by mosquitoes that infects between 50 and 100 million people annually, according to the World Health Organization. Current control mechanisms rely heavily on insecticides, but recent reports of mosquitoes acquiring insecticide-resistance in Mexico have raised concerns about the effective management of the disease.

So scientists have been turning to the fungus *B. bassiana* in hopes of identifying a new way to control dengue spread. The fungus, which grows naturally in soil and is an insect parasite, is currently used to control a number of agricultural pests, and recent studies have shown it may also kill dengue-carrying mosquitoes. But so far, there has only been one field study of the fungus on dengue-carrying mosquitoes, so questions remain about its effectiveness in the wild where temperature and humidity variations may affect mosquito survival.

In the new study, Jonathan Darbro of the Queensland Institute of Medical Research in Brisbane, Australia, and his colleagues tested the fungus under laboratory and “semi-field” conditions in which the mosquitoes were housed in large cages in an area in Australia where dengue is endemic. In the lab trials, fungal-infected mosquitoes were 30 percent less likely to bite humans than controls and laid fewer eggs over their lifetime, similar to previous lab findings with other disease-carrying mosquitoes and other fungi. And in both the lab and semi-field trials, the fungus increased the mortality rate of infected mosquitoes—by 88 percent in the lab and between 59 and 95 percent in the field.

“This has been an important step towards confirming what we see in the laboratory, we also see in the field,” said Darbro, noting that the fungus killed mosquitoes “equally well” in both lab and semi-field conditions, albeit more variably in the latter.

“I think the fact that they have used this semi-field condition is important,” agreed Adriana Costero of the National Institute of Allergy and Infectious Diseases, who was not involved in the study. “This paper adds another bit of knowledge that we need to know before we can determine if this is a feasible approach for large scale control.”

If it works, the fungal technique has the advantage of using inherent resistance management, said Darbro, meaning that mosquitoes are unlikely to evolve a defense against it. “The fungus kills the pathogen before the pathogen can become infective, but slow enough so the mosquito can reproduce,” he explained. This allows both fungus-susceptible and fungus-resistant mosquitoes to pass on offspring to the next generation. “That means that natural selection is not pushing as hard for the mosquitoes to resist the fungus as they would for a chemical insecticide,” Darbro said.

He acknowledges that when it comes to *Aedes aegypti* and dengue fever, this idea is hypothetical. The fungus is found in nature, said Darbro, and is used to control agricultural pests. But to control dengue, it would be used in areas near where people live. Thus, Costero cautioned, it’s important to make sure that humans aren’t harmed by the fungus.

But Darbro isn’t worried. While a small number of people, often with weakened immune systems, has been infected by the fungus, he said, they’ve always been successfully treated.

Another hurdle to be overcome is developing a way successfully to infect the mosquitoes with the fungus. “That’s the million dollar question,” said Darbro. “The challenge is finding a place to put the fungus where the mosquitoes will land on it and get infected.”

**J.M. Darbro et al., “Effects of Beauveria bassiana on survival, blood-feeding success, and fecundity of Aedes aegypti in laboratory and semi-field conditions,” The American Journal of Tropical Medicine and Hygiene, 86:656-64, 2012.**

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**Monday, April 16, 2012**

**Rectal microbicides become a high priority in the fight against HIV in Africa**

IRMA launches African-inspired, African-led initiative that says 'yes' to rectal microbicides

SYDNEY – Today IRMA (International Rectal Microbicide Advocates) will officially release "On the Map: Ensuring Africa’s Place in Rectal Microbicide Research and Advocacy" at a special evening reception at the international Microbicides 2012 conference at the Sydney Convention and Exhibition Center.

The report can be found [here](#).

A cornerstone of IRMA’s Project ARM (Africa for Rectal Microbicides) initiative, the strategy document developed by African advocates, researchers, and global allies outlines priority actions to ensure Africa fully engages in rectal microbicide research and advocacy activities, including the integration of safe anal-sex messaging into HIV prevention programs.

"For far too long the operating principle concerning the HIV epidemic in Africa has been that it is solely heterosexual, and that sexual transmission is entirely driven by unprotected vaginal intercourse between men and women," said Jim Pickett, IRMA chair. "But an increasing body of evidence tells us..."
quite clearly that unprotected anal intercourse is happening all across the continent – amongst heterosexuals as well as gay men, other men who have sex with men (MSM), and transgender individuals. Unprotected anal intercourse is not uncommon in Africa," he continued, "and compared to unprotected vaginal intercourse, it is 10 to 20 times more likely to result in HIV infection. We absolutely need to be concerned about this."

"We still face significant hurdles regarding human rights for gay men, MSM, and transgender individuals in Africa, but the collective, long-term efforts of advocates and scientists are indeed lifting the denial around anal sex in the African context," said Morenike Ukpong, New HIV Vaccines and Microbicides Advocacy Society in Nigeria, IRMA member, and one of the chief architects of the Project ARM strategy. "Great efforts have long been underway to develop safe and effective vaginal microbicides for African women. We need the same level of commitment and resources for the development of safe, effective, acceptable and accessible rectal microbicides for Africans regardless of gender identity or sexual orientation."

"Our diverse sexualities in Africa shouldn't be defined only by the prevention tools we have available. HIV prevention tools must be adapted to our sexualities." – Alliance Nikuze, Rwanda, IRMA member, as quoted in the report.

"On the Map: Ensuring Africa's Place in Rectal Microbicide Research and Advocacy" is the result of an intensive two-day consultation conducted with over 40 Africans and allies that took place in Addis Ababa, Ethiopia in early December 2011. It calls for a set of activities related to research and community mobilization designed to fully engage Africans, including a Knowledge, Attitudes and Behaviours study on anal sex, advocacy for increased condom-compatible lubricant access, and communication and education activities.

Even as this report is being released, Africa has already made great strides in rectal microbicide research and advocacy. A global Phase II rectal microbicide trial looking at tenofovir gel in gay men and transgender women, planned by the Microbicide Trials Network (MTN), includes the Desmond Tutu HIV Foundation in Cape Town, South Africa as one of its clinical trial sites.

As IRMA member and Desmond Tutu research assistant Brian Kanyemba says in the report, "I am incredibly proud to say we will be the very first African trial site for a rectal microbicide study. I hope the field will conduct rectal microbicide research in other African countries as well as South Africa!"

"Africans need rectal microbicides and they need to be part of the advocacy, research and development processes that are essential to creating products that are not only safe and effective but acceptable and accessible too. I pledge our full support for the efforts of Project ARM." – Dr. Ian McGowan, United States, MTN co-principal investigator and IRMA Scientific Vice Chair, as quoted in the report.

**For how long will anal health and hygiene be neglected?**

"It is high time that anal health [and hygiene] comes out of the closet" said Dr Ross Cranston, Assistant Professor, University of Pittsburgh, USA. Dr Cranston was referring to the multitude of anal health complications people practicing receptive anal intercourse are likely to be dealing with in their lives and very little quality care and products that exist to relieve them. Dr Cranston was speaking at the International Microbicides Conference (M2012) in Sydney, Australia. According to the UNAIDS, United Nations joint programme on HIV/AIDS, men-who-have-sex-with-men (MSM) are at a high risk of HIV around the world.

Many countries such as those in Africa who had earlier reported no significant HIV rates in people with same sex behaviour, have reported alarming HIV rates in recent past.

Although ‘anal’ and ‘rectal’ words are used as synonyms, but they aren’t same – and rather refer to different parts biologically. Anal canal is distinct from rectal canal with a unique set of diagnosis. Rectal canal is made up of columnar epithelial cells and anal canal is made up of stratified epithelial cells. Anal canal is also a high pressure environment with about 77 mmHg pressure when sphincters are resting and 180 mmHg pressure when sphincters constrict. In contrast, pressure in human vagina is 0 mmHg in resting phase.

Anal canal is very sensitive to hot, cold, wet, dry, light touch, pin prick, distension, pleasure or pain, however rectal canal is only sensitive to distension, pleasure or pain.

The **incidence of adverse events in rectal microbicides studies is quite high** with 11% symptoms and signs of anal adverse events in anal canal and 13% in rectal canal. These adverse events include prolapsing haemorrhoids (piles), anal fissure, anal fistula, anal abscess, anal warts, anal or rectal
canal cancers, fungal infections, herpes simplex virus (HSV) infection, or sexually transmitted infections (STIs).

The need for right awareness in healthcare providers and their appropriate training is acute as often anal adverse events are misdiagnosed or ill-treated.

The awareness level in people (men and women) who reported to practice receptive anal intercourse was abysmally low. Zero per cent of such respondents had knowledge related to their anal cancer risk, and just half of them knew about HSV. Awareness certainly needs to be upped in people practicing receptive anal sex.

One of the desired products for anal health and hygiene is the one which can protect people who have receptive anal sex from contracting STIs including HIV, such as rectal microbicides.

Rectal microbicides are products that could take the form of gels or lubricants – being developed to reduce a person’s risk of HIV or other sexually transmitted infections (STIs) through anal receptive sex.

Currently under development, rectal microbicides research sadly began much later than that of vaginal microbicides. However now, not only vaginal microbicides are being tested for rectal safety and efficacy but some researchers are even exploring potent candidates for rectal microbicides research.

Jim Pickett, who co-founded the International Rectal Microbicides Advocacy (IRMA) and is the Director of Advocacy, AIDS Foundation of Chicago, agrees: "We have to recognize that these are human needs of people and they must be able to connect to these products [anal health and hygiene products, including rectal microbicides when available after research]." Jim strongly articulated that these anal health and hygiene products must not be medically projected instead should be marketed and made available in a manner so as to be able to connect to the people for whom they are made.

Dr Cranston made a strong case to raise awareness about anal health and hygiene among people practicing receptive anal sex, and develop safe and effective products that can serve the need too. He cited the example of products that line the shelves in shopping malls on vaginal health and hygiene, and similarly it should become acceptable one day in near future to have anal health and hygiene products, said Dr Cranston.

Dr. Orin Levine reports on the Nigerian Vaccine Summit, where Nigeria’s leaders will meet this week to discuss children’s health in the country. "With the world’s second largest number of child deaths each year, many of which are due to diseases that could be prevented with vaccines, yet with immunization coverage rates that are lower than many other countries in the region, Nigeria has a major opportunity to save lives by raising immunization coverage and introducing new vaccines against pneumonia and diarrhea, the leading killers of children worldwide," he writes. Levine recounts progress made in recent years to address immunization and child mortality, but notes that "more remains to be done."

Levine provides an overview of the findings of a study (.pdf) released by IVAC this week "that identifies the six main barriers keeping vaccines from reaching Nigerian children and recommends packages of solutions tailored to overcoming them." He notes, "As our Landscape Analysis of Routine Immunization in Nigeria (LARI) shows, these barriers can be overcome with dedicated funding, coordinated effort and importantly, political will." Levine concludes, "On Monday and Tuesday, Vice President Namadi Sambo will host leaders from all over the country to put forth an action plan to address these barriers and get vaccines to children across Nigeria, with the goal of scaling up access to reach all kids by 2015. ... The challenge will then be to turn that well-intentioned political will into a well-executed plan with measurable impacts on Nigeria’s children and communities" (4/13).

Scientists Discover Tool That Uncrosses Chromosomes

ScienceDaily (Apr. 12, 2012) — Researchers at the University of California, Davis, have discovered a key tool that helps sperm and eggs develop exactly 23 chromosomes each. The work, which could lead to insights into fertility, spontaneous miscarriages, cancer and developmental disorders, is published April 13 in the journal Cell.

Healthy humans have 46 chromosomes, 23 from the sperm and 23 from the egg. An embryo with the wrong number of chromosomes is usually miscarried, or develops disorders such as Down syndrome, which is caused by an extra copy of chromosome 21.
During meiosis, the cell division process that creates sperm and eggs, matching chromosomes pair up and become connected by “crossing over” with each other, said Neil Hunter, a professor of microbiology at UC Davis and senior author of the new study.

These connections are essential for precise chromosome sorting and the formation of sperm and eggs with exactly the right numbers of chromosomes. Crossovers also play a fundamental role in evolution by allowing the chromosomes to swap chunks of DNA, introducing some variety into the next generation.

Each pair of chromosomes must contain at least one crossover. But there shouldn’t be more than about two crossovers per pair, or the genome could be destabilized.

In their paper, Hunter and his colleagues describe a "missing tool" that explains how crossovers are regulated.

"There must be enzymes that ensure at least one crossover, but not too many," said Hunter, who is also a member of the UC Davis Comprehensive Cancer Center research program.

Hunter, graduate students Kseniya Zakharyevich and Shangming Tang, and research associate Yunmei Ma looked for enzymes that could cut DNA to form crossovers in yeast, which form sexual gametes, or spores, in much the same way that humans and other mammals form sperm and eggs.

"There were several good candidates, but none turned out to play a major role," Hunter said.

Then they discovered the missing tool for crossing over: three yeast enzymes, Mlh1, Mlh3 and Sgs1, which work together to cut DNA and make crossovers.

It turns out that the human equivalents of these enzymes are well known for their role in suppressing tumors. Human MLH1 and MLH3 are mutated in an inherited form of colon cancer. BLM, the human equivalent of Sgs1, is mutated in a cancer-prone disease called Bloom’s syndrome.

"Sgs1 was the biggest surprise," Hunter said. "We previously knew it as an enzyme that unwinds DNA to prevent crossovers. Its role in making crossovers had been hidden by other enzymes that can step in when it is absent."

"While other enzymes cut DNA randomly, Mlh1-Mlh3-Sgs1 only makes crossovers. This unique activity is essential for meiosis and its discovery is a huge step forward," he said.

Journal Reference:

Douching does not seem to increase STI risk
Gus Cairns
Published: 18 April 2012

Neither rectal douching nor vaginal washing appears to be as significantly associated with sexually transmitted infections or other microbial conditions that increase the risk of HIV, as had been feared, the International Microbicides Conference heard yesterday.

In the case of women, vaginal washing and other vaginal health practices have been associated with bacterial vaginosis (BV), an imbalance in the types of bacteria that colonise the mucous surfaces of the vagina. BV can cause pelvic inflammatory disease and premature delivery in pregnant women and is associated with a higher risk of both acquiring and transmitting HIV.

The HPTN 035 trial of the candidate microbicide PRO2000 therefore included a survey of vaginal health practices, counselling against ones associated with a raised risk of BV, and assessing any link between these practices and BV. It found none, though a smaller study of women in Los Angeles did find an association not with douching, but with the use of petroleum jelly as a lubricant and BV.

In the case of rectal douching in women and gay men, there is very little we currently know about the practice. However, findings over the last couple of years that the use of lubricants for anal sex, particularly water-based ones, is associated with higher rates of sexually transmitted infections have raised concerns that other practices that impact on the fragile rectal mucosa may also raise the risk of sexually transmitted infections (STIs) and HIV. International Rectal Microbicide Advocates (IRMA) has therefore conducted a survey of rectal douching practice. Interim results were presented yesterday, although the survey is still ongoing.

Vaginal and rectal practices in women in HPTN 035 and in Los Angeles
In HPTN 035, vaginal hygiene practices were assessed at quarterly visits and the 3087 participants were counselled to try not to use the practices. They were divided into women who did not practice vaginal washing, ones who only used water, and those who used other products such as soap and water or commercial douches (Kasaro).
The proportion of women not practise any vaginal hygiene fell from 60% at baseline to 36.5% at last visit, and this was a steady fall over time, not just occurring immediately after the baseline visit.

Bacterial vaginosis was common at baseline and the proportion of women with it did not change over time – at any visit 36 to 38% of women had it. There was no association between vaginal hygiene practices and BV.

Another study of women in Los Angeles (Brown) assessed vaginal hygiene lubricant practices in an observational cohort of 141 women. The cohort was structured to reflect a mix of ethnicity and HIV serostatus: 26% had HIV and 40% were black, 34% white and 26% Latina. Their median age was 33 (range 18 to 65). Rates of anal sex were quite high: 71% had ever had it and 18% had had it over the last month.

Forty-five per cent reported vaginal douching and 4% rectal douching over the past month: the most common method was diluted vinegar in water, used by 71% of women who douchted. As for sexual lubricants and similar products, 21% reported using commercial lubricants and other products such as petroleum jelly or oil over the last month vaginally, and 11% rectally.

Black women were more likely to report vaginal douching (55% reported it) and rectal lubricants (16%). They tended to favour petroleum jelly as the most often-used product whereas white and Latina women used commercial lubes more. Most women were consistent in their practices across all visits. There was no association between women’s HIV status and their use of douching or lubes.

There was a strong association between use of petroleum jelly and bacterial vaginosi: averaged over all visits, women who used this were 2.6 times more likely to have BV. But there was no association between any kind of douching or with other kinds of lubricants.

**Rectal douching: the IRMA survey**

Shauna Stahlman of the University of California, Los Angeles, presented findings from the first three months of the IRMA rectal douching survey. During that time, 926 people answered the survey; most were gay men but 16% were women and 2% transgender. Two-thirds came from North America and 19% from Europe (7% from the UK), and their mean age was 38, with a quartier under 30. Over three-quarters of respondents (726) reported anal sex in the last three months and only they were included in this analysis.

Over 90% of people who had anal sex reported using lubes during the last three months and 63% reported rectal douching. Only 32% reported that their partner had always used a condom when they had been the receptive partner in anal sex.

Of the 440 people who reported rectal douching over the last three months, the vast majority (94%) were gay men – there were only 26 women reporting this. Three-quarters douchted before having anal sex; about a third did it afterwards and one-fifth before and after. Three-quarters used a ’homemade product’ while 35% used commercial products. ’Homemade product’ usually meant wine but people reported douching with things ranging from wine to urine.

Douching was associated with lube use and drug use and douchers had more sexual partners, an average of five over the last three months rather than two. It was strongly associated with having HIV: 44% of douchers had HIV compared with 18% of non-douchers. It was also associated with having an STI diagnosis: 21% of douchers reported that they had had an STI recently but only 11% of non-douchers. There was no association, however, with condom use: douchers were neither more nor less likely to use them.

In multivariate analysis, being HIV positive and recreational drug use remained strongly associated with douching, as did – to a lesser extent – age (older people were more likely to douche). But STI diagnosis was no longer significant as an independent risk factor as even though it was 43% more likely in douchers; this could be explained by the fact that they tended to have more sexual partners.

Although this is a self-selected sample and may not represent all the likely users of rectal microbicides, the survey suggests that rectal hygiene practices are already common amongst those likely to benefit from rectal microbicides and that formulation as an enema as well as a lube would probably be acceptable and not in itself likely to raise STI risk.

Future analyses will look at trends by region, gender and partners type: the survey is still open and can be participated in at [www.keysurvey.com/votingmodule/s180/survey/382277/d7a7/](http://www.keysurvey.com/votingmodule/s180/survey/382277/d7a7/).

**References**


Recapitulation of the entire hepatitis C virus life in engineered mouse cell lines

A US study presented today at The International Liver CongressTM 2012 demonstrates that the entire HCV lifecycle can be recapitulated in murine cells, implying that HCV permissive mouse models could soon be developed.(1)

The data suggests that HCV replication in the murine environment is limited by innate immune responses. Inactivating these pathways and the expression of the appropriate entry factors and miR-122 creates murine fibroblasts that can be infected and support replication.

The study also corroborates previous data that the expression of apoE promotes production of infectious virus.

Although mouse orthologs of MAVS and TRIF could be cleaved by the HCV NS3/4A protease, this was not enough to establish robust HCV replication.

In contrast, impairment of type I and type III IFN signaling enhanced the permissiveness of murine fibroblasts for persistent HCV replication.

The in-depth study of hepatitis C pathogenesis and immune responses is currently hampered by the lack of suitable small animal models. This study is a positive step to addressing this issue.

References
Vogt A. Recapitulation of the entire Hepatitis C virus life in engineered mouse cell lines. Abstract presented at the International Liver CongressTM 2012

N.Y. Advocates Want Condoms Out of Prostitute Cases


A Manhattan-based group that advocates for sex workers wants New York to be the first state to ban police officers from confiscating condoms as evidence in prostitution cases. The Sex Workers Project at the Urban Justice Center said Tuesday that fear of police harassment and arrest has led some prostitutes to carry fewer or no condoms and have unprotected sex.

State Sen. Velmanette Montgomery (D-Brooklyn) has sponsored a bill to ban condoms as evidence. “We are not endorsing prostitution,” she said. “It is simply related to the fact that over 100,000 people right now are infected with HIV and AIDS in New York City.”

Although New York City health officials have given out 192 million free condoms since 2007, health department spokesperson Alexandra Waldhorn said the city opposes the pending legislation.

Kate Hogan, a prosecutor, said giving up supporting evidence would be giving pimps and sex traffickers “a lot of leeway we don’t want to give them.”

Surveys of sex workers were done in 2010 and 2011 by the city and the PROS Network, a coalition of workers and advocates. The network survey included 35 sex trade workers; of those, 15 said police had taken or destroyed their condoms with only five arrests. Six said they had sex later, and only half of them used a condom. Of 63 people in the city survey, 36 said their condoms were taken and 26 said they were arrested.

Human Rights Watch researchers Kathleen Todrys and Megan McLemore said preliminary results from their study of sex workers in New York City and other cities raise similar concerns. McLemore said that after San Francisco supervisors directed police to stop confiscating condoms in 1996, officers instead began photographing the condoms to use as evidence.

Engineers Enter Fight Against AIDS in Africa

Associated Press, (04.10.2012) Donna Bryson

Communications engineers in Africa are installing cell phone technology in printers to wirelessly and immediately relay babies’ HIV test results to health clinics. The project has been successful in Mozambique for a year and will be rolled out elsewhere in Africa.

HIV-positive babies who get treatment quickly are much more likely to survive, according to health workers. But Mary Pat Kieffer, with the Elizabeth Glaser Pediatric AIDS Foundation, said babies in remote villages were dying before doctors could get test results and start treatment.

To help avoid delays, health workers have created networks to pick up blood samples stored on filter paper and deliver them to labs.

The advanced technology needed to check for HIV in newborns is available at four laboratories in Mozambique, said Dr. Ilesh Jani, director of Mozambique’s National Institute of Health. But because labs
lack the staff to call clinics or send results by cell phone message, results stacked up until they could be sent in batches by courier.

Two technology companies are involved in the improved diagnostic system: Britain's Sequoia Technology Group and Telit Wireless. Tim Clayton of Sequoia said engineers removed the working parts from standard printers and replaced them with cell phone technology. Lab computers then can relay results from multiple tests simultaneously to clinics using GPRS technology, which he said is reliable and cheaper than text messaging.

The Mozambique program cost about $400,000. Jani said a cell company donated all the airtime the project needs and noted that involving the private sector is crucial in impoverished countries.

Setting up the Britain-based system linking lab computers to clinic printers was tricky, according to Clayton. Now that it is running, it can be easily replicated elsewhere, he said. Plans are in place to use the printers in Botswana, Kenya, Tanzania, Uganda, and Zimbabwe.

**Evaluation of inSPOTLA.org: An Internet Partner Notification Service**

*Sexually Transmitted Diseases Vol. 39; No. 5: P. 341-345, (05..2012) Aaron Plant; Harlan Rotblatt; Jorge A. Montoya; Ellen T. Rudy; Peter R. Kerndt*

The website inSPOTLA.org, a Los Angeles STD partner notification service chiefly targeting men who have sex with men (MSM), is the subject of the current study. Launched in 2005, the site has had more than 400,000 visitors, and more than 50,000 e-mail postcards have been sent from it. But only limited quantitative data have been collected concerning the use of the site “for actual partner notification,” observed the authors, who undertook this study to investigate MSM’s awareness and use of the service, as well as the effect of an advertising campaign.

The researchers accessed data from two cross-sectional surveys using time-location samples; the baseline survey was conducted in 2007, with follow-up in 2009. The ad campaign took place between the two surveys, in 2008.

No statistically different awareness of inSPOTLA was noted between baseline (15.8 percent) and follow-up (14.4 percent). Also, no significant difference was seen in reported use of the site for partner notification (less than 2 percent in both surveys).

In addition to the two surveys, a high-volume sexual health clinic serving Los Angeles MSM collected information on patients’ reasons for visiting, including being referred through inSPOTLA, from all clients from 2007 through 2009. In these three years, two patients indicated their visit was prompted by an inSPOTLA e-mail postcard.

"While website user statistics seemed to indicate an impressive level of use, our evaluation of inSPOTLA found very limited evidence of program effectiveness for the purpose of actual partner notification among MSM in Los Angeles County," the team concluded.

**U.N. SG Ban Warns Of 'Cascading Crisis' Of Drought, Conflict In African Sahel**

U.N. Secretary-General Ban Ki-moon this week "called on the global community to act quickly to address what he described as a 'cascading crisis' sweeping the Sahel region of West Africa, where 15 million people have been affected by the drought and conflict-related crisis in the area," the U.N. News Centre reports. Speaking to the Luxembourg Parliament on Tuesday, Ban said, "I call upon the world to respond. Simply put, we must do more—and do it quickly" (4/17). On Wednesday, UNICEF Executive Director Anthony Lake appeared on *BBC World News* to discuss the drought and malnutrition among children. "Lake tells the BBC's Jane O'Brien that his organization is trying to fight ‘donor fatigue,’ after years of crises in the region by” portraying the success stories of children in the region and through a social media campaign to raise awareness and funds, the news service notes (4/18).

**Experts Discuss Interconnectedness Of Gender Issues, Family Planning, Access To Safe Water**

"In the last of its series called ‘7 Billion: Conversations That Matter,’ Aspen Institute's Global Health and Development [on Wednesday] hosted a panel of experts based in Africa and the United States on the interconnectedness of gender issues, family planning, population, and access to safe water," GlobalPost's "Global Pulse" blog reports. According to the blog, "The point of the series was to ask questions about why it mattered that the world was passing the seven billion mark, and the questions [addressed] in Washington were appropriately big: Will water wars replace oil wars? What are the solutions to expand water and sanitation to the 2.5 billion people who don’t have it? And just how many people can the world
support in an equitable fashion?” The blog recaps the discussion, providing quotes from several of the panelists, and writes, "The panelists kept coming back to the connections among access to water, family planning, and finding ways to use resources more efficiently” (Donnelly, 4/18).

**Access To Family Planning Services Important For Adolescent Women**

In a Huffington Post "Global Motherhood" opinion piece, UNFPA Executive Director Babatunde Osotimehin writes, "[I]t warms my heart to see that safe motherhood and women's reproductive health are finally being recognized as important development issues," but "millions of women in developing countries still lack even the most basic care during pregnancy," leading to maternal death and injury and hundreds of millions of women lack access to family planning services, including modern contraceptives. "It is inexcusable that in the 21st century motherhood remains so dangerous for so many. It is not only morally wrong but also hampers economic development and the survival and well-being of families, communities and nations,” he writes.

Noting "maternal death [is] the most common cause of death for girls between 15 and 19 years old," Osotimehin continues, "Both in my current job and when I was Minister of Health in Nigeria, I have seen the tremendous effect of investing in the education and health of adolescent girls. When a girl gets an education, has the power to delay her first pregnancy, and is healthy and equipped with the right skills and opportunities, she holds the key to unlocking many of the world's most pressing problems: reducing maternal and child death, halting the spread of HIV, breaking the cycle of poverty, advancing gender equality and propelling countries' social and economic development." He concludes, "It is my sincere hope that all young people, including adolescent girls, will get the needed opportunities to realize their potential and to live fulfilling, healthy lives” (4/18).

**Gut microbiota regulates bile acid metabolism**

A new study presented today at the International Liver Congress™ 2012 demonstrates that the gut microbiota has a profound systemic effect on bile acid metabolism.(1)

Bile acids are synthesised from cholesterol in the liver and further metabolised by the gut microbiota into secondary bile acids. The main function of bile acid is to promote processing of dietary fat. In addition, hepatic synthesis of bile acids is a major mechanism of cholesterol breakdown in the body. Farnesoid-x-receptor (FXR) is known to play a key role in the regulation of bile acid synthesis and homeostasis.

The authors propose that the gut microbiota modulates bile acid synthesis by changing the bile acid pool composition and, hence, reducing FXR inhibition in the small intestine.

The study found that germ-free mice (without any gut microbiota) had elevated muricholic bile acid levels, in particular TβMCA (tauroconjugated β-muricholic acid), while conventionally housed mice (with gut microbiota) had reduced levels of muricholic acids. TβMCA blocks the activation of FXR.

The results demonstrate the gut microbiota’s suppression of biosynthetic genes in the liver cholesterol-7α-hydroxylase (CYP7A1) was consistent with increased FXR-dependent activation of FGF15 (ileal fibroblast growth factor-15) in the small intestine, due to reduced TβMCA mediated inhibition of FXR.

The gut microbiota performs unique digestive functions that cannot be performed by a germ-free intestinal tract. The cells constituting the microbial organ form metabolic and signalling networks with each other and their host.

**References**

Islam S et al., Gut microbiota regulates bile acid metabolism by reducing the levels of tauro-beta-muricholic acid, a naturally occurring FXR antagonist. Abstract presented at The International Liver Congress™ 2012.

**Study finds cancer-fighting goodness in cholesterol**

A Simon Fraser University researcher is among four scientists who argue that cholesterol may slow or stop cancer cell growth. They describe how cholesterol-binding proteins called ORPs may control cell growth in A Detour for Yeast Oxyysterol Binding Proteins, a paper published in the latest issue of the Journal of Biological Chemistry.

The scientists came to their conclusion while trying to understand how cholesterol moves around inside cells in the fat's journey to cell surfaces where it reinforces their outer membrane.

"The assumption was that ORPs bind and transport cholesterol inside cells in a similar fashion to how lipoproteins bind and move around the fat outside cells through the blood stream,” explains Chris Beh. The SFU associate professor of molecular biology and biochemistry co-authored this paper.
Beh and his colleagues noted that genetic changes engineered by them block the ability of ORPs to bind cholesterol but don’t stop ORPs from functioning. In fact, these altered ORPs work better and activate other regulator proteins, which in turn trigger a variety of cellular processes that stimulate cell growth.

The scientists believe this happened because cholesterol-binding normally interferes with ORPs’ ability to bind to another lipid or fat called PI4P, which is important for cell growth.

"That told us that ORPs probably have nothing to do with moving around cholesterol within cells," says Beh. "Rather cholesterol-binding puts the brakes on ORP’s ability to bind to PI4P which, if left unchecked, could accelerate cell growth like crazy," says Beh. "Given that uncontrolled cell growth is a key feature of cancer, this means gaining a better understanding of the true purpose of cholesterol-binding within cells could be important in cancer treatment."

Beh and his colleagues draw on two important facts to support their conclusion.

"First, cancer cells require ORPs to survive," explains Beh. "Second, other scientists have previously shown that a new class of natural compounds that look like steroids or cholesterol can kill a broad spectrum of different cancer cells."

Beh says he and his research partners will now find out exactly which proteins respond to ORP activation and under what circumstances does cholesterol turn off ORP’s activation of them.

19th Century Therapy for Parkinson's Disease May Help Patients Today

ScienceDaily (Apr. 19, 2012) — In the 19th century, Jean-Martin Charcot, the celebrated neurologist, developed a "vibration chair," to relieve symptoms of Parkinson's disease. Charcot reported improvements in his patients, but he died shortly thereafter and a more complete evaluation of the therapy was never conducted. Now, a group of neurological researchers at Rush University Medical Center have replicated his work in a study to see if Charcot's observation holds true against modern scientific testing.

Results from the study indicate that while vibration therapy does significantly improve some symptoms of Parkinson's disease, the effect is due to placebo or other nonspecific factors, and not the vibration. The findings are published in the April issue of Journal of Parkinson's Disease.

"We attempted to mimic Charcot's protocol with modern equipment in order to confirm or refute an historical observation," explains lead investigator Christopher G. Goetz, MD, director of the Parkinson's disease and Movement Disorders Center at Rush. "Both the treated group and the control group improved similarly, suggesting other factors had an effect on Parkinson's disease motor function."

Charcot's patients told him that during long carriage rides or train journeys, uncomfortable or painful symptoms of Parkinson's disease seemed to disappear, and the relief lasted quite some time after the journey. He developed a chair that mimicked the continuous jerking of a carriage or train.

Goetz and his colleagues randomly assigned 23 patients to either a vibrating chair or the same chair without vibration. During the treatment sessions, both groups of study participants listened to a relaxation CD of nature sounds. Study participants underwent daily treatment for a month.

The patients in the vibration treatment group showed significant improvement in motor function after daily 30-minute treatments for four weeks. Although not as high, motor function scores for the no vibration group also improved significantly. Both groups showed similar and significant improvement in depression, anxiety, fatigue, and nighttime sleep and both groups reported similar high satisfaction with their treatment.

"Our results confirm Charcot's observation of improvement in Parkinson's disease symptomology with chronic vibration treatment, but we did not find the effect specific to vibration," said Goetz. "Instead,
our data suggest that auditory sensory stimulation with relaxation in a lounge chair or simply the participation in a research protocol has equivalent benefit as vibration on motor function."

"While we can agree that our results may not change scientific thinking on treatment mechanisms, our results will allow clinicians to guide patients to at least one apparatus that is safe and associated with objective changes in parkinsonian impairment scores," said Goetz. "Charcot's advice to colleagues resonates as one places vibration therapy in the context of potential options for patients. 'It is no small gain to be able to relieve the sufferers of paralysis agitans.'"

Journal Reference:

Joint Failures Potentially Linked to Oral Bacteria
ScienceDaily (Apr. 18, 2012) — The culprit behind a failed hip or knee replacements might be found in the mouth. DNA testing of bacteria from the fluid that lubricates hip and knee joints had bacteria with the same DNA as the plaque from patients with gum disease and in need of a joint replacement.

This study is one of many coming from the Case Western Reserve University School of Dental Medicine that have linked oral bacteria to health problems when they escape from the mouth and enter the blood.

Working with University Hospitals Case Medical Center researchers, the dental, orthopedic and arthritis researchers suggest it might be the reason why aseptic loosening or prosthetic wear of the artificial joints fail within 10 years when no infection appears to be present. The pilot study's findings were reported in the April issue of the Journal of Clinical Rheumatology.

Dr. Nabil Bissada, chair of the Department of Periodontics at the dental school, said the objective of the study, "Identification of Oral Bacterial DNA in Synovial Fluid of Patients with Arthritis with Native and Failed Prosthetic Joints," was to see if bacteria like Fusobacterium nucleatum and Serratia proteamaculans found in patients with gum disease were present in the fluid.

"For a long time, we've suspected that these bacteria were causing problems in arthritis patients, but never had the scientific evidence to support it," Bissada says.

The researchers recruited and studied 36 patients seeking care at the University Hospitals Case Medical Center for osteoarthritis (the wearing of the joints) and rheumatoid arthritis (an autoimmune disease).

These study participants had both natural and artificial joints. Researcher extracted samples of their synovial fluid, which is much like oil that keeps a door from squeaking. These patients also had signs of periodontitis or gum disease and undergone exams where dental plaque was obtained for the study.

Plaque build-up from the bacteria, associated with gum disease, breaks down the walls of the pockets around the teeth. The inflammation process from the bacteria acts like a gate that gives bacteria access to the blood stream. Once in the blood, the oral bacteria have induced inflammation in remote sites where the bacteria has been linked to heart, kidney and cancer diseases and premature births and fetal deaths.

Because these bacteria cannot be found with routine lab tests, detection of bacteria in the plaque and fluid was done through a process called polymerase chain reactions and DNA sequence analysis of specific genes (16S-23S rRNA). This is a sophisticated DNA tracking procedure.

Five of the 36 patients (14%) showed direct DNA links between the bacteria in the fluid and plaque from the mouth. The breakdown in patients was: one from a rheumatoid arthritis (RA) patient with a failed natural joint and one RA patient with a failed replacement joint; two osteoarthritis (OA) patients with failed artificial joints and one OA patient with a failed natural joint.

Bissada said researchers will continue exploring the oral health link in a larger study. "We have a link now and want to see just how much of a trend this is. We also will be able to see if treating the periodontal disease, can reduce the number of future costly joint replacements."

Journal Reference:
Témoin, Stéphanie; Chakaki, Alia; Askari, Ali; El-Halaby, Ahmed; Fitzgerald, Steven; Marcus, Randall E.; Han, Yiping W.; Bissada, Nabil F. Identification of Oral Bacterial DNA in Synovial Fluid of Patients With Arthritis With Native and Failed Prosthetic Joints. Journal of Clinical Rheumatology, 18(3):117-121, April 2012 DOI: 10.1097/RHU.0b013e3182500c95

Next Generation: Painless Vaccine Patch
Vaccination via tiny microneedles elicits a powerful immune response in the skin.
By Megan Scudellari | April 2, 2012
An array of microneedles can be coated with medicine and act as a painless drug delivery system for vaccines. Emory University
THE DEVICE: In the near future, your annual flu shot may not be a sharp jab in the arm but a sticky, spiny band-aid applied gently to your skin. Over the past five years, researchers at Emory University and the Georgia Institute of Technology have developed a dime-sized vaccine patch sprinkled with a hundred microscopic needles and coated with a vaccine solution. The patch, which could someday be self-administered, comes in two versions: metal or dissolvable polymer. It has successfully protected mice from influenza, and now researchers know exactly how the tiny microneedles elicit an immune response in the skin.

WHAT'S NEW: In 2011, the Emory-Georgia team demonstrated vaccine delivery via microneedle patches is often more protective than inoculation under the skin or into muscle, but they weren't sure why. “We wanted to know what happens initially, within that acute first response, that explains why we have a better immune response later on,” said Maria del Pilar Martin, who helped develop the patch at Emory and now works for Sanofi Pasteur, the vaccine division of Sanofi, in New York.

It turns out, microneedle immunization results in an immediate and dramatic local increase in cytokines under the skin, according to a paper published by del Pilar Martin and colleagues in the January/February issue of mBio. Cytokines are proteins that recruit important immune cells, including neutrophils, monocytes, and dendritic cells, to the site of immunization. The skin immunization also resulted in a prolonged presence of antigens—viral targets of the immune cells. “That creates a constant recruitment of [immune] cells into the skin,” said del Pilar Martin.

Dissolving microneedle patch

IMPOR TANCE: “It is the first real mechanistic look at how microneedle delivery of antigen through skin works,” said Thomas Kupper, chief of dermatology at Brigham and Women’s Hospital in Boston, who was not involved in the study. Kupper and colleagues recently demonstrated that a population of immune cells in the skin mediate a stronger immune response than T cells in the blood stream, which also supports the idea that skin vaccine delivery may be more effective than intramuscular inoculation. As scientists understand more about the early immune responses in the skin, they can expand use of the patch by testing other antigens, in addition to influenza, and observing the immune response.

Microneedle patch immunization could simplify vaccination programs in schools and assisted living facilities because it eliminates the need for trained personnel to give the injection, the authors noted. It could also cut risks associated with the re-use of hypodermic needles, which occurs in developing countries.

NEEDS IMPROVEMENT: If the team can develop a patch that does not need to be kept at cold temperatures, as most vaccines currently are, the method will be especially valuable for developing countries. “Hopefully, that’s the future for this type of delivery method,” said del Pilar Martin. But before the patches can be made commercially available, clinical trials must verify their safety and effectiveness in humans.

The Emory/Georgia Tech team hopes to begin a phase I trial with their patch in the next year or so, but they aren’t the only group pursuing vaccine patches: TremRx, founded by Kupper and colleagues, and Intercell vaccines, based in Vienna, Austria, are also pursuing techniques to deliver vaccines to the skin. Intercell has an ongoing phase I/II trial for an H5N1 vaccine enhancement patch and a phase II trial for a traveler’s diarrhea patch.

Study Suggests HIV Infection Induces Age-Related Changes to Monocytes and Innate Immune Activation That Persist in Young Men Despite Combination Antiretroviral Therapy

"[The objectives of this study are to] compare the impact of HIV infection and healthy ageing on monocyte phenotype and function and determine whether age-related changes induced by HIV are reversed in antiretroviral treated individuals.

"A cross sectional study of monocyte ageing markers in viremic and virologically suppressed HIV-positive males aged 45 years or less and age-matched and elderly (≥65 years) HIV-uninfected individuals.

"Monocytes from young viremic HIV-positive males resemble those from elderly controls, and show increased expression of CD11b (P<0.0001 on CD14 and CD16 subsets) and decreased expression of CD62L and CD115 (P=0.04 and 0.001, respectively, on CD14 monocytes) when compared with young uninfected controls. These changes were also present in young virologically suppressed HIV-positive males. Innate immune activation markers neopterin, soluble CD163 and CXCL10 were elevated in both young viremic (P<0.0001 for all) and virologically suppressed (P=0.0005, 0.003 and 0.002, respectively) HIV-positive males with levels in suppressed individuals resembling those observed in elderly controls. Like the elderly, CD14 monocytes from young HIV-positive males exhibited impaired phagocytic function (P<0.007) and telomere-shortening (P=0.03) as compared with young uninfected controls.

"HIV infection induces changes to monocyte phenotype and function in young HIV-positive males that mimic those observed in elderly uninfected individuals, suggesting HIV may accelerate age-related changes to monocytes. Importantly, these defects persist in virologically suppressed HIV-positive individuals."

WHO Issues New HIV Guidelines for Couples

The World Health Organization now recommends providing antiretroviral (ARV) treatment to HIV-positive partners in serodiscordant couples, even if their immune system is still strong, given research showing that such treatment can prevent transmission.

The new guidelines were lauded by Dr. Bernhard Schwartlander, the director of the evidence, strategy, and results department at UNAIDS. He said the recommendations “respond to the scientific evidence that has been accumulated over the past year” showing that when an infected partner is treated with ARVs, “then the chance that the person would pass on the virus to a partner is dramatically reduced.”

“About half of all people living with HIV who live in a regular partnership have a partner who’s not of the same status—a partner who is HIV-negative, both for men and for women,” said Schwartlander.

Doctors Without Borders also praised WHO’s announcement, calling the guidelines a major advance in halting the global epidemic.

Kala-Azar Disease 'Still Raging' In Remote Areas Of South Sudan, VOA Reports
"In newly independent South Sudan, deadly kala-azar disease is still raging in some of the most remote areas lacking basic health services," VOA News reports. "An infectious disease carried by a parasite and transmitted by the bite of a sand fly, kala-azar causes a fever that does not subside," the news service writes, noting that American physician Jill Seaman, who came to South Sudan in 1989, "said around 95 percent of kala-azar patients simply waste away or die after catching other infectious diseases" if the initial infection is left untreated.

According to VOA, attacks from rebel groups in the area are displacing thousands, who already have poor living conditions and nutrition, and making them more susceptible to infection. Abdi Nasir, a communicable disease specialist for the WHO, "said kala-azar usually comes in cycles about every 10 years," the news service writes, adding, "Nasir said an outbreak that began in 2009 has now affected 25,000 people and still is raging. It is the worst in 30 years," VOA notes (McNeish, 4/19).

Scientists find Achilles' heel in life-threatening malaria parasites
Scientists have identified a link between different strains of malaria parasites that cause severe disease, which could help develop vaccines or drugs against life-threatening cases of the infection.

Researchers have identified a key protein that is common to many potentially fatal forms of the condition, and found that antibodies that targeted this protein were effective against these severe malaria strains.
The protein has sticky properties that enable it to bind to red blood cells and form dangerous clumps that can block blood vessels. These clumps, or rosettes, can cause severe illness, including coma and brain damage. Presently, between 10 and 20 per cent of people with severe malaria die from it, and the disease—which is spread by blood-sucking mosquitoes—claims about one million lives per year.

Malaria parasites, once in the bloodstream, are able to alter the protein molecules on their surfaces to evade attack by the immune system. These surface proteins are usually poor targets for treatments or vaccines because they are highly variable between different malaria parasite strains. Now, researchers have found that the surface proteins of rosette-forming parasites share similarities that may allow them to act as a target for treatments to block progress of the disease.

Scientists from the University of Edinburgh worked with collaborators from Cameroon, Mali, Kenya and The Gambia to test their antibodies against parasites collected from patients. The study, published in *PLoS Pathogens*, was supported by the Wellcome Trust.

Professor Alexandra Rowe of the University of Edinburgh’s School of Biological Sciences, who led the study, said: "We knew that clusters, or rosettes, of blood cells were found in many cases of severe or life-threatening malaria, so we looked at rosette-forming parasites and found a common factor that we could target with antibodies. We hope this discovery will inform new treatments or vaccines to block the formation of rosettes and so prevent many life-threatening cases of malaria."

**Gut Microbiota Transplantation May Prevent Development of Diabetes and Fatty Liver Disease**

ScienceDaily (Apr. 19, 2012) — Exciting new data presented April 18 at the International Liver Congress™ 2012 shows the gut microbiota’s causal role in the development of diabetes and non-alcoholic fatty liver disease (NAFLD), independent of obesity. Though an early stage animal model, the French study highlights the possibility of preventing diabetes and NAFLD with gut microbiota transplantation—the engrafting of new microbiota, usually through administering fecal material from a healthy donor into the colon of a diseased recipient.²

In the 16 week study, two groups of germ free mice received gut microbiota transplants; one set from donor mice displaying symptoms of insulin resistance and liver steatosis (responders), the other from normal mice (non responders). The donor mice were selected due to their response to being fed a high fat diet.

The germ free group that received microbiota from symptomatic mice (responder receivers—RR) showed higher levels of fat concentration in the liver as well as being insulin resistant. The germ free group that received microbiota from healthy mice (non-responder-receivers—NRR) maintained normal glucose levels and sensitivity to insulin.

EASL Scientific Committee Member Dr Frank Lammert said: "The factors leading to Non-Alcoholic Fatty Liver Disease (NAFLD) are poorly understood, but it is known that NAFLD and Type 2 diabetes are characterized, respectively, by liver inflammation and metabolic disorders like insulin resistance."

"This study shows that different microbiota cause different metabolic responses in animals. By implanting microbiota from healthy mice, the study authors prevented the development of liver inflammation and insulin resistance, both indications of liver disease and diabetes. Thus, gut microbiota transplants could have a therapeutic role in the development of these diseases."

The RR mice also showed lower levels of microorganisms than usually found in the healthy gut. *Lachnospiraceae* was identified as the species most important in developing fatty liver and insulin resistance.

At present, the intestinal microbiota is considered to constitute a "microbial organ": one that has pivotal roles in the body’s metabolism as well as immune function. Therefore transplantation aims to restore gut functionality and re-establish a certain state of intestinal flora.

**Notes:**


**'Mystery’ skin disease kills 19 in Vietnam: WHO**

The World Health Organisation said Monday it was “concerned” about an outbreak of a mysterious skin disease in central Vietnam which has killed 19 people, mostly children. More than 170 people have fallen ill with the unidentified illness, which causes stiffness in the limbs and ulcers on victims’ hands and feet that look like severe burns.
“We are concerned about this. WHO is very aware of this case,” said Wu Guogao, the organisation’s chief officer in Hanoi, adding Vietnam had not asked for help with an investigation into the outbreak. The WHO has not been given access to any official reports on the issue.

“It is difficult to say the exact cause at this stage,” he told AFP.

The disease appears to have been concentrated mainly in Ba To district in central Quang Ngai province and the WHO said it had not heard of similar outbreaks elsewhere in the country. Local doctors said they were waiting for the results of a recent Ministry of Health probe.

“The results of the investigation (are) not yet available. Therefore, we don’t know anything more concerning the disease,” said doctor Dang Thi Phuong, director of Ba To district healthcare centre.

“As far as I know, the Ministry intends to invite foreign experts to the area to help us know more,” she told AFP, adding that many of the victims were under 10 years old.

Media reports said about one in 10 of those infected had developed serious liver disorders, but said the infection does not appear to be highly contagious.

**Synthetic Genetic Evolution**

*Scientists show that manmade nucleic acids can replicate and evolve, ushering in a new era in synthetic biology.*

*By Ruth Williams | April 19, 2012*

Synthetic genetic polymers, broadly referred to as XNAs, can replicate and evolve just like their naturally occurring counterparts, DNA and RNA, according to a new study published today (April 19) in *Science*. The results of the research have implications not only for the fields of biotechnology and drug design, but also for research into the origins of life—which, on this planet and beyond.

“It’s a breakthrough,” said Gerald Joyce of The Scripps Research Institute in La Jolla, California, who was not involved in the study—“a beautiful paper in the realm of synthetic biology.”

“It shows that you don’t have to stick with the ribose and deoxyribose backbones of RNA and DNA in order to have transmittable, heritable, and evolvable information,” added Eric Kool of Stanford University, California, who also did not participate in the research.

Over the years, scientists have created a range of XNAs, in which the ribose or deoxyribose portions of RNA and DNA are replaced with alternative molecules. For example, threose is used to make TNA, and anhydrohexitol is used to make HNA. These polymers, which do not exist naturally, are generally studied with various biotechnological and therapeutic aims in mind. But some researchers, like Philipp Holliger of the MRC Laboratory of Molecular Biology in Cambridge, UK, think XNAs might also provide insights into the origins of life. They might help to answer questions such as, “why is life based on DNA and RNA, and, if we ever find life beyond earth, is it likely to be based on the same molecule or could there be other possibilities?” Holliger said.

To get at some of these questions, Holliger and his colleagues had to first create enzymes that could replicate XNAs, a necessary first step to evolution. They did this both by randomly mutating and screening existing DNA polymerases for their ability to read XNA, and by an iterative process of selecting polymerase variants with capacities for XNA synthesis. In the end, they had several polymerases that could synthesize six different types of XNA.

To see whether XNAs could evolve, they generated random HNA sequences, then selected for those that could bind to two target molecules. After selection, the HNAs were amplified by the newly designed polymerases and again selected for their ability to bind the targets. Eight rounds of selection later, the HNA sequences were no longer random, as those with a particular target-binding motif became more abundant. Through selection and replication, the HNAs had evolved.

The finding in itself is not surprising, said Kool. “Chemists have been working for 20 years to find new backbones for DNA and the feeling always was that it would be interesting and quite possible that some of them might be replicated one day.” It was, nevertheless, impressive, he added. “The hard part was finding the enzymes that could do it. So the big leap ahead for this paper was finding those enzymes.”

The new polymerases synthesized XNA through rounds of DNA-to-XNA and XNA-to-DNA synthesis. Generating polymerases that can make XNA direct from XNA will be the next step, Holliger said, but it will be a lot harder “because both strands would be foreign to the polymerase.”

Holliger also explained that there was actually a benefit to having a DNA intermediate. “It allowed us to access the whole gamut of technologies that are available for analyzing DNA sequences.” Working with XNAs uniquely, he said, “is like being thrown back to the way molecular biology was in the early 1970s, in that we have to develop all our tools afresh.”
Holliger’s polymerases maybe the first addition to the XNA toolbox but, as more tools are created the potential for XNA biology will grow, said Jack Szostak of Harvard Medical School, who was not involved in the study. “In the longer run, it may be possible to design and build new forms of life that are based on one or more of these non-natural genetic polymers,” he said. That said, “I think it’s too early to say whether such novel life-forms would have any practical applications,” he added.

Regardless of what the future holds, the new polymerases could have applications right away. “We hope to be able to evolve XNA aptamers”—molecules that bind specific targets—“against medically interesting targets,” Holliger said. Scientists are already creating DNA and RNA aptamers, but their use in the body is severely hampered by their susceptibility to naturally occurring nucleases that degrade DNA and RNA. “XNAs are not natural and so are not susceptible to nucleases,” explained Joyce. “These things are bullet-proof.”

Beyond the medical applications of the work, Holliger is finally getting some answers about the basis of life. “The exciting finding of our work is that there really seems to be many possibilities,” he said. “There isn’t anything Goldilocks about DNA or RNA.” Does this mean that life elsewhere in the cosmos is more likely than previously thought? “I would say a cautious yes,” said Holliger.


RNA-DNA Virus Hybrid Found
Researchers discovered a virus produced from recombination between RNA and DNA viruses, suggesting a possible new mechanism of virus evolution.

By Sabrina Richards | April 20, 2012

“It’s a mythological beast of a virus, but it actually exists,” virologist Ken Stedman told Nature of the virus hybrid his team discovered in a volcanic hot spring. Stedman’s team from Portland State University sequenced the DNA genome of the virus, and found that contained sequences encoding proteins from an RNA virus, according to their report published yesterday (April 19) in Biology Direct.

Boiling Springs Lake RNA–DNA hybrid virus (BSL RDHV, for short) is a single-stranded DNA virus with a circular genome, identified in acidic lake samples in Boiling Springs Lake in Lassen Volcanic National Park in California. The scientists realized they had something unusual when their characterization of viral sequences turned up the sequence for a protein from an RNA virus—encoded in its DNA. It’s not clear how two unrelated viruses that carry different forms of genetic material combined to form the resulting single-stranded DNA hybrid, as the original RNA virus does not have the reverse transcriptase necessary to translate RNA to DNA.

Stedman proposed two possible scenarios. He hypothesized that if three different viruses—the RNA virus, the DNA virus, and a retrovirus—co-infected a cell, the retrovirus’s reverse transcriptase could have converted the RNA virus’s genes to DNA and allowed recombination with the DNA virus. Or, a viral ligase could have attached the RNA and DNA genomes into one, which was then replicated as a single DNA genome.

Regardless of how it happened, the discovery of a hybrid virus opens the possibility of a much broader pool of recombination partners for the world’s viruses, with even distantly related viruses having the capability to combine their genetic material. How wide-spread such chimerism is among viruses remains to be determined, although database surveys by Stedman’s team suggest other possible RNA-derived proteins lurking in DNA genomes. Eugene Koonin, an evolutionary geneticist at the National Institutes of Health in Bethesda, Maryland, told Nature, “Stedman’s findings show that such recombination between diverse viruses indeed takes place and could be an important route of virus evolution.”

Bacterial Insecticide Resistance
By cultivating detoxifying bacteria in its gut, a pest called the bean bug can become instantly resistant to a common insecticide.

By Ed Yong | April 23, 2012
Japanese scientists have found that the bean bug, a major pest of soybean crops, swallows bacteria that breakdown an insecticide chemical. The bacteria allow the bug to continue munching on treated crops with no ill effects, according to a study published today (April 23) in the *Proceedings of the National Academy of Sciences*.

Insecticide resistance typically takes many generations to evolve, usually because tweaks to the insects’ own genomes. But the bean bug’s strategy allows it to acquire such resistance with unprecedented speed by exploiting the genes of bacterial partners.

“It makes perfect sense,” said Nancy Moran, an evolutionary biologist at Yale University, who was not involved in this study. “Bacteria have a much greater diversity of enzymatic functions than do animals.”

While the phenomenon may fascinate many biologists, it is bad news for soybean farmers. “This study should cause pest managers to think more broadly about the evolution of resistance in pests,” said Molly Hunter, an entomologist from the University of Arizona. “The source of resistance can be sitting in the field in the bacterial population, just waiting for the arrival of the insect.”

As nymphs, bean bugs swallow *Burkholderia* bacteria from the surrounding soil. Though the details of the relationship between the species are unclear, one bug can harbour up to 100 billion of these microbes inside a special organ in its gut. Infected bugs grow bigger than their uninfected peers.

Some *Burkholderia* strains can break down the insecticide fenitrothion for their own nourishment. In doing so, they render the chemical harmless to insects. These strains are normally so rare as to be undetectable, but Yoshitomo Kikuchi from the National Institute of Advanced Industrial Science and Technology in Japan found that they can increase rapidly in soils that are treated with fenitrothion, comprising some 80 percent of *Burkholderia* populations after just 1 month.

If bean bugs swallow these fenitrothion-degrading strains, they gain immediate resistance to the pesticide. In the lab, more than 70 percent of the bugs that ate fenitrothion-degrading *Burkholderia* survived a meal of seeds laced with the pesticide. Only 10 to 20 percent of bugs that ate normal *Burkholderia* strains could tolerate such exposures. “Now we are investigating how the symbionts confer insecticide resistance,” said Kikuchi.

Unlike many bacterial partners, which are passed down from mother to offspring, every bean bug must pick up its own microbes anew. This might seem inefficient, but “there can be benefits to an open-source symbiosis, in which the insect gains the bacterium from the environment in each generation,” said Hunter. Namely, it prevents the bacteria from becoming so dependent on their hosts for survival that they lose important genes. Free-living bacteria thus have wider sets of metabolic abilities, and may be more likely to carry genes that allow them to detoxify chemicals like insecticides.

Pesticide resistance from bacterial symbionts may also occur with other insects and other insecticides. Kikuchi found that *Burkholderia* strains can break down fenitrothion can also degrade three other insecticides for example. These bacteria also form alliances with many species of stinkbugs, a family that includes many important crop pests, including the sugarcane-eating oriental chinch bug. On the remote island of Minami-Daito, where fenitrothion is heavily used, the team found that 8 per cent of chinch bugs were resistant to the pesticide because of *Burkholderia* in their guts.

However, farmers on the Japanese mainland spray very low levels of fenitrothion. After surveying 13 different locations, the team could not find any bean bugs that harbour the resistant bacteria. “The jury is still out on whether this is really going to be an important issue in determining efficacy of different insecticides,” said Moran, “but it certainly seems worth knowing more.”


Incidence of hepatitis C re-infection and clearance may be underestimated
Hepatitis C and HIV
Michael Carter
Published: 26 April 2012

The incidence of hepatitis C re-infection among high-risk individuals who have spontaneously cleared the infection may be higher than previously assumed, a modelling study published in the May 1st edition of the *Journal of Infectious Diseases* suggests.

The study has implications for the design of a hepatitis C vaccine and more immediately for prevention campaigns. It also has implications for assumptions about rates of sustained virological response after completion of hepatitis C therapy, Prof. Jason Grebeley of the Kirby Institute, University of New South Wales, one of the authors of the study, told delegates at the *International Liver Congress* in Barcelona.

“Are we detecting re-infection or failure of treatment? It depends on the [viral] sequence being examined,” he told a symposium on hepatitis C virus (HCV) prevention and treatment in injecting drug users, organised by the European Liver Patients Association (ELPA). He noted that sequencing needed to distinguish between reactivation of low-level quasispecies of HCV that had not been fully suppressed by treatment, and infection with a new variant of HCV.

People receiving HCV treatment need to be counselled about the risk of re-infection, both during treatment and after treatment, he added.

Recent research in HIV-positive gay men who have undergone treatment and been cured of hepatitis C infection has shown substantial rates of re-infection due to ongoing risk behaviour.

There have been important recent advances in hepatitis C therapy. Nevertheless, incidence of new infections remains high. Many of these are in injecting drug users, but there is also an epidemic of sexually transmitted hepatitis C in HIV-positive gay men.

Spontaneous clearance of the virus occurs in approximately a quarter of patients with primary hepatitis C infection. This does not provide immunity against subsequent re-infection, but there is some evidence that it is associated with better subsequent control of the virus and a more attenuated course of disease. Some investigators are hopeful that learning more about spontaneous clearance and its correlates will assist in the development of a therapeutic vaccine against the infection.

Moreover, understanding the risk of re-infection has important implications for the design of hepatitis C prevention campaigns for at-risk populations.

Seven studies have looked at the incidence of re-infection and spontaneous clearance following re-infection. Estimates of the incidence of re-infection range from a low of 1.8 per 100 person years to a high of 47 per 100 person years. There is also wide variability in estimated probability of spontaneous clearance of re-infection (29 to 100%).

The interval between testing in these studies ranged between one and sixteen months.

An international team of investigators hypothesised that this variability in testing intervals could explain the lack of concordance between the findings of these studies. The investigators were especially concerned that testing intervals of over three months would miss many cases of re-infection and spontaneous clearance.

They therefore designed a model which simulated the dynamics of re-infection and clearance in a simulated cohort of 50 injecting drug users who were followed for 48 months.

Their initial calculations were based on the earlier study with the shortest testing interval (one month) which found a re-infection incidence of 32 per 100 years and that the probability of subsequent spontaneous clearance was 75%.

Results of their analysis confirmed that if the testing interval is greater than the time taken for spontaneous clearance, then the incidence of re-infection is likely to be considerably underestimated.

For example, if the testing interval was three months and the re-infection clearance duration was two months, then the estimated incidence of re-infection would be reduced to 23 per 100 person years, some 28% lower than the real re-infection incidence of 32 per 100 person years.

“Studies using long HCV RNA testing intervals underestimate the incidence of HCV re-infection and the probability of spontaneous HCV clearance following re-infection,” comment the authors. “The results of these studies have important implications for HCV vaccine design because they suggest that, although absolute protection against primary re-infection (sterilizing immunity) is probably overestimated, the rate of spontaneous clearance of re-infection (partial protective immunity against persistent HCV re-infection) is also underestimated.”
The findings are also likely to be relevant to those working to control the hepatitis C epidemic. A high and rising incidence of sexually transmitted hepatitis C has been seen in HIV-positive gay men. UK care guidelines recommend annual testing for this group and more frequent screening for those at greatest risk. However, the average interval between HIV care appointments in the UK is three to four months. The results of this study suggest a substantial number of infections may be occurring but are spontaneously cleared between follow-up appointments.

Reference
Vickerman P et al. The more you look, the more you find: effects of hepatitis C testing interval on reinfection incidence and clearance and implications for future vaccine study design. J Infect Dis, 201: 205-50, 2012 (click here for the free abstract).

April 25, 2012

Report Outlines HIV Cure Research, Important Gaps
by Tim Horn

Three HIV/AIDS activist groups convened a meeting in March with researchers and representatives of the U.S. Food and Drug Administration (FDA) to describe the current state of cure research and identify barriers to moving such research forward swiftly and smoothly. The proceedings of this meeting, which took place immediately before the 19th Conference on Retroviruses and Opportunistic Infections (CROI) that began on March 5 in Seattle, are now available in a report online.

“A cure for HIV will be essential to ending the AIDS pandemic, but science that is focused directly on a cure is still in early stages and will likely require the support of multiple stakeholders to proceed at the fastest pace,” reads the executive summary of the report, authored by David Evans, Kevin Fisher, Jeff Taylor and Siegfried Schwarz.

In the past four years, the report notes, there have been signs of increasing scientific momentum and funding directed toward curing HIV infection.

The remarkable case of “Berlin Patient” Timothy Brown—a man who all signs suggest has been cured of HIV—has catalyzed and expanded what was once a small and somewhat fragmented effort to understand how HIV persists despite effective antiretroviral (ARV) therapy and to explore mechanisms to eliminate the hidden pool of virus in people on ARV treatment (a sterilizing cure) or to enable the immune system to control HIV without the need for ARVs (a functional cure).

This momentum, the activists write, has been greatly enhanced by the NIH-funded Martin Delaney Collaboratory projects, partnerships between academia and industry focused on the possibility of discovering and developing a safe, effective, feasible and scalable HIV cure.

Among recent signs of progress, researchers have contributed new insights into where and why HIV persists despite potent ARV therapy. In addition, the first controlled clinical trials of drugs to activate cells harboring archived HIV, such as histone deacetylase (HDAC) inhibitors, are yielding promising signals, and other types of treatments designed to teach the immune system to either clear or control the virus on its own have been initiated.

But central questions remain, the report stresses.

For example, it is still not clear what types of cells and anatomical compartments harbor HIV, nor is it understood which methods work best for measuring the latent virus in these reservoirs. Knowledge regarding how HIV is able to replenish these reservoirs, even when ARVs with “maximally suppressive” effects on viral load are being used consistently and correctly, is also needed. Actually, it’s not entirely clear if modern ARV therapy is, in fact, fully suppressing HIV replication. And does the immune system play a role in HIV persistence? In addition, what are the forms of immunologic HIV control that can potentially be enhanced without major safety issues?

Finally, the report asks, what are “reasonable” risks for the people living with HIV who will be participating in early—and potentially dangerous—studies, and how can these individuals be best protected?

To address these questions, members of the AIDS Treatment Activists Coalition (ATAC), the Treatment Action Group (TAG) and Project Inform sat down with several industry and academic researchers on March 4 in Seattle, who described their current projects, outlined the obstacles and facilitators to cure research and offered suggestions for the kinds of activities that community advocates might undertake to overcome current obstacles.

Highlights include: an overview of AIDS Clinical Trials Group (ACTG) clinical trial development by Dan Kuritzkes, MD; laboratory testing for new compounds, including work being conducted by Romas Geleziunas, PhD, at Gilead Sciences; the prospects of gene therapy, notably ongoing zinc finger nuclease work at Sangamo Biosciences, discussed by Dale Ando, MD; stem cell research after the Berlin Patient,
highlighted by John Zaia, MD, who underscored the importance of not overselling this approach; and work focusing on the enhancement of immune responses, reviewed by Pablo Tebas, MD.

The post-meeting report, issued in April, provides a brief synopsis of each presentation, followed by an outline of areas identified by the workshop speakers and participants for further exploration, development and incorporation into a cure advocacy agenda.

“The prevailing view of all the speakers was that we must not raise premature and unrealistic hopes of a cure for HIV either in people who volunteer their bodies for cure research, or in the wider community of people with HIV and their allies,” the authors write. “Critical early steps have been identified, but we need many more successes in analytics, basic science and translational research—in both animals and people—before the cure will be within our grasp.”

April 25, 2012

**First Religious Leader With HIV Speaks Out in Zimbabwe**

For several years, the Reverend Maxwell Kapachawo has been the only religious leader in Zimbabwe to openly speak about his HIV status, All Africa reports. If others would disclose their status, he said, “things would start to change.” After testing positive in 2004, Kapachawo was dismissed from his Anglican ministry and spent two years fighting opportunistic infections. After recovering and joining a network of religious leaders living with or affected by HIV, he started a network in Zimbabwe and returned to Christian ministry work. Kapachawo is now speaking out and hoping that other religious leaders will join him and help fight stigma and discrimination.

**Chained AIDS protesters arrested in Wall St. area**

By VERENA DOBNIK, Associated Press — 21 hours ago

NEW YORK (AP) — Longtime AIDS activists who have chanted in the streets for a quarter century joined supporters of the much newer Occupy Wall Street movement Wednesday in a march through lower Manhattan to demand better health services.

The protest marked 25 years since ACT UP — the AIDS Coalition to Unleash Power — was formed in the same Wall Street neighborhood.

Now, the group is asking government to impose a small tax on each Wall Street trade — a so-called "Robin Hood tax" to finance treatment and services for people with HIV.

"We just want one tiny portion of each penny," said Sharonann Lynch, an HIV policy adviser to Doctors Without Borders, an international medical humanitarian organization.

New York Stock Exchange workers jeered from the sidewalk as protesters wearing Robin Hood costumes were dragged across the pavement to clear Broadway for the stalled morning rush-hour traffic.

The nine who had stood across Broadway, chained to each other, were then handcuffed and loaded into police vans.

Police used metal cutters to remove the chains.

About an hour later, more than 200 activists gathered near City Hall for the march on Wall Street. They were flanked by police in riot gear and on scooters.

ACT UP was founded in March 1987 with hundreds of activists staging a protest in the same area against the high cost and low availability of HIV medications.

Eric Sawyer, a founding member of the group that now includes chapters worldwide, said he and others returned for good reason.

When it comes to AIDS treatment and other services, he said, "big business is not funding anything, but they got the bailout."

Another longtime ACT UP member, Julie Davids, said it made sense for the organization to march with Occupy supporters.

"ACT UP has always looked at the AIDS crisis through an economic justice lens and has always recognized that obstacles were rooted in greed and the profit motive," she said.

At another point in the march, protesters dragged couches and chairs into the middle of Broadway, chanting "Housing saves lives!" to draw attention to what they said was the lack of adequate housing assistance available to people with HIV. One protesting woman faced police while sitting on a toilet that was part of the makeshift "home" and its furnishings.

New York City Council member Ydanis Rodriguez, whose district includes upper Manhattan's largely minority Washington Heights, said HIV patients have been hurt by a reduction of services because of budget cuts.
"We're asking the mayor and other politicians to be more creative with finances — for instance, by supporting this Wall Street tax," he said.

Sawyer said supporters of the transaction tax would like to see it implemented both in the United States and abroad — especially on the two biggest stock exchanges, in London and New York — potentially raising billions of dollars over time.

The money could be used for medical and social services for people with HIV and AIDS, as well as help implement universal health care, said Sawyer, who works for UNAIDS, the Joint United Nations Programme on HIV and AIDS, the world body’s main advocate for global action on the epidemic.

Giving Away, and Then Seizing, Condoms

By JIM DWYER
NYTimes, Published: April 24, 2012

Last year, New York City health workers gave out 37.2 million condoms. That works out to an average of 70 condoms every minute of the year. The city got into mass-scale condom distribution to help prevent the spread of debilitating and deadly diseases.

On the other hand, the condoms are also used to mark people for arrest on prostitution charges.

Here, for example, are affidavits filed in criminal court by two police officers in Brooklyn. They are part of the routine paperwork assembled in prostitution arrests. The first officer wrote that he “recovered from the defendant’s person currency in the following denominations: $1.25. Sexual paraphernalia, namely: One condom.”

The other wrote that he had found “condoms in the quantity of seventeen.”

One arm of the government is giving people condoms. Another arm is confiscating them from the very people who are most vulnerable to catching bugs and passing them along. How, precisely, does this make sense?

Beginning at least three years ago, the city’s Department of Health and Mental Hygiene tried to figure that out. Working with the Sex Workers Project of the Urban Justice Center, the city began collecting information on the confiscation of condoms from people in the commercial sex trade, and on whether the practice discouraged their use.

Audacia Ray, a former sex worker, said police officers often seized condoms, not for arrests, but to roust street prostitutes. “They need to make up their mind, whether the health department wants condoms to be used to protect people, or the Police Department wants to use it to arrest,” Ms. Ray said on Tuesday. “I know that prostitution is illegal and the district attorney does not want to make it any easier for people to do it, but it’s really problematic for public health. At times the condoms are being destroyed in front of people.”

Ms. Ray, who founded the Red Umbrella Project to support people in commercial sex work, said that she regularly stocked up on condoms at a clinic in the Chelsea section of Manhattan.

A year ago, the health department supported state legislation to ban the use of condoms as evidence of prostitution, and to “reduce all legislative barriers to condom use.” It planned to do mini-training sessions at police roll calls on the impo

DESPITE the clear language of its own report, the city's health department reversed its position on changing the law.
“After the commissioner reviewed the study, which found that the current law has not resulted in sex workers consistently failing to carry condoms because of fear of arrest, he decided not to support the legislation,” Ms. Caraway said. “We have seen no evidence that the current law undermines the public health aims of condom distribution.”

About 2,000 people a year are arrested on prostitution charges in New York, and the vast majority quickly plead guilty. On one of the rare occasions when a case went to trial, a judge scoffed at the presentation of a condom as evidence.

“I find no probative value at all in finding a condom,” said the judge, Richard M. Weinberg of Manhattan Criminal Court. “In the age of AIDS and H.I.V., if people are sexually active at a certain age, and they are not walking around with condoms, they are fools. I don’t need anything else on condoms.”

**Case Western Reserve University Researcher Seeks Trigger for HIV Latency**

*Plain Dealer (Cleveland, OH), (04.17.2012) Angela Townsend*

The American Foundation for AIDS Research (amfAR) has announced its first research grants for 2012. The four $250,000 two-year awards are the latest grants among the more than $340 million the group has given since 1985 for HIV/AIDS education, prevention and treatment programs.

The recipient researchers are:

- A California Institute of Technology team that is studying whether HIV continues to replicate when a patient has an undetectable viral load and, if so, how.
- A Massachusetts General Hospital team that is focused on a newly discovered cell type that is resistant to antiretroviral therapy.
- A team at Ghent University Hospital in Belgium that is developing a new test that can show a patient’s viral load beyond levels currently deemed undetectable.
- A Case Western Reserve University (CWRU) team that will seek to identify features of cells that are necessary to maintain HIV latency.

Leading the CWRU work is Jonathan Karn, a professor and chair of molecular biology and microbiology in the School of Medicine. Karn and his 10-person team are using specialized viruses to inactivate genes in these cells to identify targets for drugs that can treat and eradicate HIV, while not affecting anything else.

“The challenge in developing strategies for HIV is that the virus becomes silent. You have no way of touching it,” Karn said. “The immune system can’t see it. Drugs can’t reach it. You have a reservoir sitting around in patients, even if they’ve been on intensive therapy for decades.” During the next five years, Karn’s team hopes to figure out how to reverse latency or prevent it from happening.

**HPV-Related Information Sharing and Factors Associated with US Men’s Disclosure of an HPV Test Result to Their Female Sexual Partners**

*Sexually Transmitted Infections Vol. 88; No. 3: P. 171-176, (04..2012) Stephanie L. Marhefka; and others*

While prevalence of human papillomavirus is high in men and women alike, the authors noted that men “have seldom been involved” in HPV education and prevention efforts, and men’s “disclosure of known HPV infection has rarely been studied.” In the current research, the team set out to identify factors associated with HPV test result disclosure by men, as well as men’s sharing of HPV-related information with their partners.

The subjects of the study were 251 men who reported having a main female partner and were enrolled in a psychosocial study of responses to testing between 2007 and 2010. The men completed surveys that included questions about HPV test results, disclosing HPV tests results to partner(s), relationship characteristics, and stigma (for men who reported HPV-positive test results) approximately three weeks after receiving the result of their HPV test. Factors associated with disclosure of HPV test result in cross-sectional analysis were determined using logistic regression.

Eighty-two percent of the men disclosed their test result to a main partner. In multivariate analysis, factors significantly associated with increased disclosure were self-reported negative HPV test result, a high-school education, and a greater commitment to a sexual partner. Compared with men who did not disclose, those who did so were significantly more likely to provide their sexual partners with HPV-related information. Nearly half the men who disclosed to a main partner said the partner asked them questions about HPV.
“Results from this study highlight the critical role that men who are symptomatic for, who are tested for or who are vaccinated against HPV can play in educating their sexual partners, independent of whether they actually disclose their test results,” the authors concluded.

Royal Society Report Calls For Renewed Global Action To Slow Population Growth, Reduce Consumption
"Over-consumption in rich countries and rapid population growth in the poorest both need to be tackled to put society on a sustainable path," according to a report by an expert group convened by the Royal Society, BBC News reports (Black, 4/25). The report "concludes that tackling global inequality is central to solving the problem of too many people exploiting dwindling natural resources," the Independent writes (Connor, 4/26). "Population and consumption should no longer be regarded as separate issues," said Sir John Sulston, chair of the international working group that prepared the study," according to the Financial Times (Cookson, 4/26). "Firm recommendations include giving all women access to family planning, moving beyond [gross domestic product (GDP)] as the yardstick of economic health and reducing food waste," BBC notes.

"The report, published on Thursday, is a sign of how population control is moving back up the international political agenda after last year's announcement by the U.N. that the number of people on Earth had exceeded seven billion and would reach as many as 11 billion in 2050," according to the Financial Times (4/26). "Professor Sarah Harper of Oxford University, another of the authors, said the issue of population had fallen off the development agenda in the last 10-15 years but it should be reinstated and coupled closely with environmental challenges, starting at the Rio+20 United Nations Conference on Sustainable Development to be held in Rio in June," Reuters writes (Wickham, 4/25).

World Must Extend Access To Life-Saving Vaccines To All Children
"For too long, there has been an unwritten rule that it can take 15 years or more before children in the poorest nations benefit from new life-saving vaccines in use in rich countries," Seth Berkley, CEO of the GAVI Alliance, writes in this post in the Independent's "Notebook" blog. "But national celebrations in Ghana this week show how this shameful gap is rapidly being closed," he continues, noting, "This week the rotavirus vaccine to protect against severe diarrhea and the pneumococcal vaccine which targets the primary cause of pneumonia—the two biggest killers of children—are being introduced" in the country, making it the first in Africa to roll these vaccines out simultaneously.

"The power of vaccines is vital in every society, rich or poor. But their impact is even greater in developing countries because of the quality of basic health services," Berkley continues. He notes, "Developing countries have made vaccination a major health priority, putting in place the systems to deliver immunization programs and helping fund the cost of vaccines through their own resources," and as a result, "some 325 million additional children have been vaccinated against a wide variety of diseases since 2000, helping prevent five million early deaths." He concludes, "This week's celebrations in Ghana show just what can be achieved. But we can't rest while 1.7 million children—one every 20 seconds—are still dying every year from diseases which we can prevent" (4/26).

Florida Senator Marco Rubio Addresses Future Of U.S. Foreign Policy
"On April 25, Foreign Policy at Brookings hosted Senator Marco Rubio (R-Fla.) for a major address on the future of U.S. foreign policy," according to an event summary on the organization's website. "Senator Rubio, a member of the Senate Foreign Relations Committee and the Senate Select Committee on Intelligence, examined whether U.S. global leadership is sustainable and even necessary in the 21st century" and "explored what Americans need to do at this juncture, abroad and at home, to adapt and prepare for the changing international environment in the years ahead," the summary states (4/26).
"Millions of human beings are alive today because the United States, and others in the global community, are paying for their antiviral medication. ... We need to continue this kind of foreign aid investment, not just in PEPFAR, but in malaria control and vaccine programs and in agriculture initiatives so that we can make similar strides in preventing hunger and establishing a healthy global community," he said, according to a speech transcript (.pdf) (4/25).
Scientists have demonstrated a new technique that will transform epigenetics research

Scientists at the University of Cambridge and the Babraham Institute have demonstrated a new technique that will transform epigenetics research

Collaboration between scientists at Cambridge University and the Babraham Institute have demonstrated a new technique that will significantly improve scientists' ability to perform epigenetics research and help unlock the door to understanding how cells develop and function. Epigenetics is a branch of genetics that studies modifications to the DNA which affect gene activity. The research, published today (26 April) in the journal Science, has important implications for stem cell research and the development of regenerative medicines.

All the cells in the body have the same DNA sequence (genome), but it is how this DNA sequence is interpreted that results in the formation of different cell types. Epigenetic changes control how a DNA sequence is interpreted, specifically how different genes are switched on and off in different cell types, tissues and organs.

One of the most studied epigenetic marks is the addition of a very small chemical modification called a methyl group to DNA, which turns associated genes off. Methyl groups are always added to the DNA base cytosine and so this chemical modification is called 5-methylcytosine (5mC). Babraham Institute scientists are involved in researching the role of another DNA chemical modification in mammals called 5-hydroxymethyl-cytosine (5hmC), which is believed to be important for stem cell function, helping to define how the body develops. 5hmC may be a separate epigenetic mark or possibly be part of the process which removes methyl groups from DNA, allowing genes to be switched on again. Decoding the 'epigenome' will provide greater understanding of how cells are regulated and has major implications for regenerative medicine and how cells such as stem cells can be controlled.

Professor Shankar Balasubramanian FRS, of the University of Cambridge Chemistry Department and Cancer Research UK Cambridge Research Institute, and his PhD student Michael Booth invented new chemistry to allow the recently discovered base 5hmC to be sequenced in DNA at single base resolution. This was not possible using existing methods. In a fruitful collaboration between the Cambridge group (led by Balasubramanian) and the Babraham Institute (led by Professor Wolf Reik FRS), this method was applied to sequence 5hmC and 5mC in embryonic stem cell genomic DNA.

Balasubramanian, whose group previously co-invented Solexa sequencing, explained, "Sequencing DNA is becoming an increasingly important part of science and medicine and we are pleased to have met the challenge of finding a way to sequence this important new base modification." Michael Booth, co-inventor of the technique, said, "We developed a chemistry that was specific for this new modified DNA base, 5hmC. This allowed us to accurately distinguish between 5mC and 5hmC at single base resolution in the genome."

Dr Miguel Branco from the Babraham Institute who is joint lead author commented, "There was a real need in the field for a technique that would map both 5hmC and 5mC in the genome quantitatively and at high resolution. We applied this new technology to embryonic stem cells and immediately recognised its power in furthering our understanding of the biological functions of these DNA modifications."

Professor Wolf Reik who led the study at the Babraham Institute, which receives strategic funding from the Biological Sciences Research Council (BBSRC) said, "It has recently become apparent that in addition to DNA methylation, there are other modifications of DNA, such as for example hydroxymethylation. This suggests that DNA modifications are more dynamic than we previously thought. With the new method we are now in a position to map these modifications at great precision, and to relate them to stem cell function, ageing, and perhaps more generally to how the environment interacts with the genome."

The Babraham Institute undertakes world-leading life sciences research to generate new knowledge of biological mechanisms underpinning ageing, development and the maintenance of health. Professor Michael Wakelam, Director of the Babraham Institute, said, "This is an excellent example of collaboration between research institute and University research scientists. The work will improve our knowledge of how cells develop, with potential long-term benefits to society." In addition to the BBSRC, this research was supported by the MRC, the Wellcome Trust and the EU.

Professor Daan Frenkel ForMemRS, Head of the Department of Chemistry at the University of Cambridge, commented, "This new technique, which reflects the continued innovative work of Professor Balasubramanian and his team, will dramatically change how epigenetic research is conducted. By
collaborating with experts at Babraham, they have also demonstrated how the technique will have significant implications for regenerative medicine."

**Bacteria subverts immune response to aid infection**

*Listeria*, one of the most deadly causes of bacterial food poisoning, subverts a normally protective immune response to spread its infection more effectively, according to new research at National Jewish Health. Immunologists Laurel Lenz, PhD, Peter Henson, PhD, and their colleagues report online April 26, 2012, in the journal *Immunity* that production of nitric oxide (NO) by activated macrophages, which is normally thought of as an infection-fighting response, actually helps *Listeria monocytogenes* to more efficiently disseminate between infected and neighboring uninfected cells.

"In the course of evolution, pathogens and their hosts engage in an ongoing arms race, responding to and countering each other's tactics to gain the upper hand," said Dr. Lenz. "In this case, *Listeria* has learned to evade a response that is normally protective and to do so in a way that substantially increases the spread of infection. Several other pathogens, including Rickettsia, Burkholderia, Vaccinia and HIV, spread throughout the host in a similar manner and may use similar strategies."

When *Listeria* or other pathogens first enter the body, receptors on white blood cells recognize general features of the pathogen and sound an early alarm that activates the innate immune response. When activated, macrophages and other innate immune cells can more readily prevent free-floating pathogens from surviving upon entering cells. However, these activated cells also release of nitric oxide (NO), an important signaling molecule that triggers several defense mechanisms.

Dr. Lenz and his colleagues found that production of NO by activated cells helped to increase *Listeria* spread directly from cell to cell and replicate in its host. When *Listeria* spreads directly from cell to cell, it produces small buds on the surface of an infected cell. Neighboring cells that touch the infected cell absorb the buds containing the *Listeria*. Thus, the bacteria are transferred without ever entering the extracellular environment. The absorbed *Listeria* are initially contained within small bubbles, known as vacuoles or phagosomes. Normally when a white blood cell absorbs a particle or organism, these phagosomes are targeted by a sort of cellular Death Star that fuses with them and destroys its contents. NO, however, delays the attack of these Death Stars, or lysosomes. This delay gives *Listeria* more time to escape the phagosome into the cell interior before it can be destroyed by the lysosomes.

"Delaying lysosome fusion with phagosomes tips the scale in favor of *Listeria*, allowing this pathogen to more effectively infect cells through cell-to-cell spread and thus to multiply in its host," said Dr. Lenz.

**How stem cell therapy can keep the immune system under control**

Ostrow School of Dentistry of USC study in Cell Stem Cell outlines the mechanism behind stem cells' beneficial effects on immune disorders

A new study, appearing in *Cell Stem Cell* and led by researchers at the University of Southern California, outlines the specifics of how autoimmune disorders can be controlled by infusions of mesenchymal stem cells.

Mesenchymal stem cells (MSC) are highly versatile stem cells that originate from the mesoderm, or middle layer of tissue, in a developing embryo. MSC can be isolated from many different kinds of human tissue, including bone marrow and the umbilical cord.

Principal investigator Songtao Shi, professor at the Ostrow School of Dentistry of USC Center for Craniofacial Molecular Biology, said that recent studies have shown the benefits of administering MSC to patients with immune-related disorders such as graft versus host disease, systemic lupus erythematosus, rheumatoid arthritis, and more.

These studies showed that infusions of MSC appeared to quell the production and function of overactive immune cells, including T- and B-lymphocytes. However, the specific mechanism behind how MSC get the immune cells under control hasn’t been fully understood.

"Mesenchymal-Stem-Cell-Induced Immunoregulation Involves FAS-Ligand-/FAS-Mediated T Cell Apoptosis" shines light on how infused MSCs target and defeat overactive immune cells. Examining the effects of MSC infusion in mice with systemic sclerosis (SS)-like immune disorders, Shi and his colleagues discovered that a specific cellular mechanism known as the FAS/FAS-ligand pathway was the key to the remarkable immune system benefits.

Specifically, in mice with SS-like disorders, infusions of MSC caused T-lymphocyte death with FASL/FAS signaling and lessened symptoms of the immune disorder. However, MSC deficient in FAS-ligand failed to treat immune disorders in SS-afflicted mice.
With the hopeful results of the animal model study in mind, Shi's colleagues in China performed a pilot study with patients suffering from systemic sclerosis. Infusions of MSCs provided similar clinical benefits to patients, and experimental analysis revealed that the FASL/FAS pathway was also at work in humans with SS.

The identification of the cellular workings responsible for the stem cell treatments’ success may eventually help doctors find optimal cell-based treatment for some immune diseases, Shi said.

**How probiotic bacteria protect against inflammatory bowel diseases**

Some lactic acid bacteria can alleviate inflammation and therefore prevent intestinal disorders. Scientists have now decoded the biochemical mechanism that lies behind the protective effect of the bacteria. In experiments with mice, the researchers succeeded in demonstrating that lactocepin – an enzyme produced by certain lactic acid bacteria – selectively degrades inflammatory mediators in diseased tissue. This new evidence might lead to new approaches for the treatment of inflammatory bowel diseases.

Yoghurt has been valued for centuries for its health-promoting effects. These effects are thought to be mediated by the lactic acid bacteria typically contained in yoghurt. Evidence from recent scientific studies show that some bacterial strains actually have a probiotic effect and can thus prevent disease. A team of biologists and nutrition scientists working with Prof. Dirk Haller from the Technische Universitaet Muenchen (TUM) has now discovered the mechanisms at work behind this protective effect (Cell Host & Microbe).

In experiments with mice, the scientists observed that lactocepin – an enzyme produced from the lactic acid bacterium Lactobacillus paracasei – can selectively interrupt inflammatory processes. As the scientists observed, lactocepin degrades messengers from the immune system, known as chemokines, in the diseased tissue. As a part of the “normal” immune response, chemokines are needed to guide defense cells to the source of the infection. In chronic intestinal disorders like Crohn’s disease and ulcerative colitis, the otherwise highly effective defense mechanism against infectious agents is malfunctioning. Chemokines such as “IP-10” then contribute to the tissue damage due to chronic inflammatory processes, preventing the tissue from healing.

“Lactocepin is a familiar element in food technology research,” says Prof. Dirk Haller, who holds the Chair for Biofunctionality of Food at the TUM. “What is surprising, however, is its biomedical effect, namely the force with which the enzyme attacks and degrades very specific inflammatory mediators.” Haller is certain that, based on this mechanism, it will be possible to develop new approaches to the targeted prevention and treatment of chronic bowel diseases as well as skin disorders: “The anti-inflammatory effect of lactocepin is limited to specific areas and up to now it has no known side effects.”

The scientist therefore plans to carry out clinical studies in order to test the possible pharmaceutical application of the enzyme. Questions also remain to be answered in relation to the “production” of lactocepin by lactic acid bacteria. Some bacterial strains, such as Lactobacillus paracasei, produce highly potent lactocepins; however, the effectiveness of other microorganisms has not yet been proven. Dirk Haller therefore warns against false promises: “Not every product labeled as ‘probiotic’ actually earns this name.”


**Breastfeeding isn't free: Study reveals 'hidden cost' associated with the practice**

WASHINGTON, DC, April 26, 2012 — Pediatricians and other breastfeeding advocates often encourage new mothers to breastfeed their babies for at least the first six months of their infants' lives based on the purported health benefits to both mothers and children. Many breastfeeding proponents also argue that breastfeeding has financial advantages over formula-feeding—breastfeeding is free, they say. But, according to a new study, the notion that there’s no cost associated with breastfeeding for the recommended amount of time is patently untrue.

"Breastfeeding for six months or longer is only free if a mother’s time is worth absolutely nothing," said Mary C. Noonan, an Associate Professor of Sociology at the University of Iowa, and coauthor of the study, "Is Breastfeeding Truly Cost Free? Income Consequences of Breastfeeding for Women," which appears in the April issue of the *American Sociological Review*. 
The study relies on a nationally representative sample of 1,313 first-time mothers in the United States, who were in their 20s or 30s when they gave birth between 1980 and 1993 and who were employed in the year before their first children were born. Noonan and Phyllis L. F. Rippeyoung, an Assistant Professor of Sociology at Canada's Acadia University, found that formula-feeders (i.e., mothers who never breastfed), short-duration breastfeeders (i.e., mothers who breastfed for fewer than six months), and long-duration breastfeeders (i.e., mothers who breastfed for six months or longer) all experienced earnings losses after giving birth. However, on average, long-duration breastfeeders experienced much steeper and more prolonged earnings losses than did mothers who breastfed for shorter durations or not at all.

"When people say breastfeeding is free, I think their perspective is that one doesn't have to buy anything to breastfeed whereas one needs to purchase formula and bottles to formula-feed," Rippeyoung said. "But, this simplistic view doesn't take into consideration the hidden cost: the substantial income women often lose when they breastfeed for a long duration. To me, I see it as being highly related to how women's unpaid work has always been undervalued."

According to the study, long-duration breastfeeders sacrificed considerable income after giving birth compared to short-duration breastfeeders and formula-feeders, largely because long-duration breastfeeders were more likely to switch to part-time work or to leave the workforce entirely.

"We see that the ability to intensively mother via long-duration breastfeeding is class-biased," Noonan said. "Women who breastfeed tend to be white, college educated, and married. Additionally, on average, women who breastfeed are more likely to be married to college-educated men, men who can financially facilitate women taking time out of the labor force."

The authors noted that there are extremely few datasets that consider both breastfeeding and women's work behaviors. "There are some longitudinal datasets that look at breastfeeding and parenting, but we needed longitudinal data that included information on both breastfeeding and women's work behaviors," Rippeyoung said. "Very recent data with that type of information proved difficult to come by. We hope this study will encourage people to collect newer data looking at breastfeeding and work behaviors, so that we can determine whether the trends we see from mothers who gave birth in the 1980s and early 90s still hold true today. However, there is little to make us believe the trends would be very different."

As for the study's policy implications, Rippeyoung and Noonan said their research highlights the need to consider federal legislation that would more broadly protect the rights of all mothers to breastfeed at the workplace and compensate them for the unpaid labor associated with this type of infant feeding, especially if the government is going to continue to push for women to breastfeed. Until 2010, the authors said, no federal legislation existed in this arena, which meant that employers were not bound by federal law to accommodate or not discriminate against breastfeeding mothers. The Patient Protection and Affordable Care Act of 2010 includes limited protections for breastfeeding that simply ensure women get breaks to express their breast milk during the work day and have non-bathroom space where this activity can take place.

"Currently, breastfeeding promotion focuses almost exclusively on encouraging women to breastfeed—without providing adequate economic and social supports to facilitate the practice—a reality that helps reproduce gender, class, and racial inequality," Rippeyoung said. "Legislation more supportive of breastfeeding would include paid parental leave and onsite daycares. Unless these or other policies are put in place, formula-feeding will continue to be the only realistic option for many women in the United States."
Rare Protozoan from Sludge in Norwegian Lake Does Not Fit On Main Branches of Tree of Life

ScienceDaily (Apr. 26, 2012) — Humankind's remotest relative is a very rare micro-organism from south-Norway. The discovery may provide an insight into what life looked like on earth almost one thousand million years ago.

Biologists all over the world have been eagerly awaiting the results of the genetic analysis of one of the world's smallest known species, hereafter called the protozoan, from a little lake 30 kilometer south of Oslo in Norway.

When researchers from the University of Oslo, Norway compared its genes with all other known species in the world, they saw that the protozoan did not fit on any of the main branches of the tree of life. The protozoan is not a fungus, alga, parasite, plant or animal.

"We have found an unknown branch of the tree of life that lives in this lake. It is unique! So far we know of no other group of organisms that descend from closer to the roots of the tree of life than this species. It can be used as a telescope into the primordial micro-cosmos," says an enthusiastic associate professor, Kamran Shalchian-Tabrizi, head of the Microbial Evolution Research Group (MERG) at the University of Oslo.

His research group studies tiny organisms hoping to find answers to large, biological questions within ecology and evolutionary biology, and works across such different fields as biology, genetics, bioinformatics, molecular biology and statistics.

World's oldest creature

Life on Earth can be divided up into two main groups of species, prokaryotes and eukaryotes. The prokaryote species, such as bacteria, are the simplest form of living organisms on Earth. They have no membrane inside their cell and therefore no real cell nucleus. Eukaryote species, such as animals and humankind, plants, fungi and algae, on the other hand do.

The family tree of the protozoan from the lake near Ås starts at the root of the eukaryote species. "The micro-organism is among the oldest, currently living eukaryote organisms we know of. It evolved around one billion years ago, plus or minus a few hundred million years. It gives us a better understanding of what early life on Earth looked like.," Kamran says to the research magazine Apollon.

How they move

The tree of life can be divided into organisms with one or two flagella. Flagella are important when it comes to a cell's ability to move. Just like all other mammals, human sperm cells have only one flagellum. Therefore, humankind belongs to the same single flagellum group as fungi and amoebae.

On the other hand it is believed that our distant relatives from the family branches of plants, algae and excavates (single-celled parasites) originally had two flagella.

The protozoan from Ås has four flagella. The family it belongs to is somewhere between excavates, the oldest group with two flagella, and some amoebae, which is the oldest group with only one flagellum. "Were we to reconstruct the oldest, eukaryote cell in the world, we believe it would resemble our species. To calculate how much our species has changed since primordial times, we have to compare its genes with its nearest relatives, amoebae and excavates," says Shalchian-Tabrizi.

Caught with a tasty morsel

The protozoan is not easy to spot. It lives down in the sludge at the bottom of a lake.

It is 30 to 50 micrometres long and can only be seen with a microscope. When Professor Dag Klaveness of MERG wants to catch the protozoan he sticks a pipe down into the lakebed, removes a column of sludge and pours a bile green algae mixture over it.

The algae are such tempting morsels for the small protozoa that they swim up.

"We can then pick them out, one by one, with a pipette," says Klaveness.

There are not many of them. And the University of Oslo biologists have not found them anywhere else other than in this lake.

"We are surprised. Enormous quantities of environmental samples are taken all over the world. We have searched for the species in every existing DNA database, but have only found a partial match with a
gene sequence in Tibet. So it is conceivable that only a few other species exist in this family branch of the tree of life, which has survived all the many hundreds of millions of years since the eukaryote species appeared on Earth for the first time."

**Not very sociable**
The protozoan lives off algae, but the researchers still do not know what eats the protozoan. Nor do they know anything about its life cycle. But one thing is certain:

"They are not sociable creatures. They flourish best alone. Once they have eaten the food, cannibalism is the order of the day," notes Klaveness.

The protozoan has a special cell indentation. It looks like a groove.

"The species has the same intracellular structure as excavates. And it uses the same protuberances as amoebae to catch its food. This means that the species combines two characteristics from each family branch of the main eukaryote groups. This further supports the hypothesis that the species from this lake belongs to a primordial group. Perhaps it descended from the antecedents of both the excavates and amoeba?" asks Shalchian-Tabrizi.

The protozoan was discovered as early as 1865, but it is only now that, thanks to very advanced genetic analyses, researchers understand how important the species is to the history of life on Earth.

**Breeding enormous quantities of the protozoan**
Dag Klaveness has, together with research fellow Jon Bråte, managed to breed large quantities of the species. No one has done this before. Klaveness has spent the last 40 years specialising in breeding organisms that are difficult to breed or that are difficult to isolate from other species.

Breeding is important if we want to analyse the creature's genes. More than just a few are needed for a genetic test. Researchers have needed to breed large quantities. The work is demanding and has taken many months.

The protozoan's favourite food is green algae, but since both the protozoan and the green algae are eukaryote species, i.e. species with real cell nuclei, it is easy to confuse the genes of the protozoan with those of its food in the gene sequencing. Therefore, Klaveness has chosen to feed the protozoan with blue green bacteria, which are genetically very different to the protozoan. Blue green bacteria are not exactly its favourite dish, but the protozoan can only choose between eating or dying.

Blue green bacteria are prokaryotes, i.e. species without membranes or real cell nuclei. This allows the researchers to differentiate between the genes of the protozoan and its food in the gene sequencing.

Klaveness has a number of vats of the protozoan in the laboratory. The algae mixture sinks to the bottom. The protozoan dives down when it wants to eat.

In optimum conditions they divide every second day. However, with blue green bacteria on the menu, which is just as boring as if you only got carrots for several months and nothing else, the protozoan grows much more slowly.

When the protozoa have reproduced enough, they are centrifuged out and gene sequenced. The genes are then compared with equivalent gene sequences from other species. "We have gene sequenced 300,000 parts of the genome (the total genetic material), but we still do not know how large the genome is. We are currently only looking for the most important parts," explains Kamran Shalchian-Tabrizi.

**Traces from primordial times**
The problem is that DNA sequences change a lot over time. Parts of the DNA may have been wiped away during the passing of the years. Since the protozoan is a very old species, an extra large amount of gene information is required.

"It is often the case with such ancient organisms that features they share in common with other known species have been wiped away from the DNA sequence because of long-term mutations. You can compare it with tarmacing. If you tarmac a road enough times, you will no longer see the cobblestones. Therefore, you have to collect large gene sequences to find common traces from prehistoric times."

Research fellow Sen Zhao was responsible for the extensive, statistical calculations. In order to calculate the family link they have used information from the research group's own Bioportal in cooperation with the high performance computing group at the University of Oslo.

**Resolving evolutionary mysteries**
Kamran Shalchian-Tabrizi explains that the tree of life can provide fundamental answers to great evolutionary mysteries.

"In order to understand what a species is today, we have to understand how they have changed genetically. The tree of life allows us to explain cellular change processes by connecting the genome and morphology (appearance) with its way of life."
Among other things, Shalchian-Tabrizi wants to use the protozoan to investigate when photosynthesis arose among eukaryote organisms. Photosynthesis takes place in chloroplast. Chloroplasts were originally free-living, blue green bacteria. If the researchers find genetic residues of these bacteria in the protozoan from Ås, this may indicate that photosynthesis arose earlier than supposed.

"There are many likely scenarios, but we still do not know the answer," acknowledges Shalchian-Tabrizi.

The researchers also want to question when other characteristics arose, e.g. mitochondria, which are the energy motors of our cells.

**Purifying drinking water in Japan**

In recent years researchers have found some apparently matching examples of the protozoan from Ås in Japan and South East Asia. A researcher from Japan arrived in Oslo with a glass of the species solely so that Klaveness could breed them.

"We are now going to gene sequence these organisms, because it is not certain that the genes are the same, even if the morphology is similar," says Klaveness.

The Japanese hope that the protozoan can be used to purify drinking water by removing toxic, blue green bacteria.

**Can Organic Food Feed the World? New Study Sheds Light On Debate Over Organic Vs. Conventional Agriculture**

ScienceDaily (Apr. 25, 2012) — Can organic agriculture feed the world? Although organic techniques may not be able to do the job alone, they do have an important role to play in feeding a growing global population while minimizing environmental damage, according to researchers at McGill University and the University of Minnesota.

A new study published in *Nature* concludes that crop yields from organic farming are generally lower than from conventional agriculture. That is particularly true for cereals, which are staples of the human diet—yet the yield gap is much less significant for certain crops, and under certain growing conditions, according to the researchers.

The study, which represents a comprehensive analysis of the current scientific literature on organic-to-conventional yield comparisons, aims to shed light on the often heated debate over organic versus conventional farming. Some people point to conventional agriculture as a big environmental threat that undercuts biodiversity and water resources, while releasing greenhouse gases. Others argue that large-scale organic farming would take up more land and make food unaffordable for most of the world’s poor and hungry.

"To achieve sustainable food security we will likely need many different techniques—including organic, conventional, and possible 'hybrid' systems—to produce more food at affordable prices, ensure livelihoods to farmers, and reduce the environmental costs of agriculture," the researchers conclude.

Overall, organic yields are 25% lower than conventional, the study finds. The difference varies widely across crop types and species, however. Yields of legumes and perennials (such as soybeans and fruits), for example, are much closer to those of conventional crops, according to the study, conducted by doctoral student Verena Seufert and Geography professor Navin Ramankutty of McGill and Prof. Jonathan Foley of the University of Minnesota’s Institute on the Environment.

What’s more, when best management practices are used for organic crops, overall yields are just 13% lower than conventional levels. "These results suggest that today’s organic systems may nearly rival conventional yields in some cases—with particular crop types, growing conditions and management practices—but often they do not," the researchers write. Improvements in organic management techniques, or adoption of organic agriculture under environmental conditions where it performs best, may help close the yield gap, they indicate.

"Our study indicates that organically fertilized systems might require higher nitrogen inputs to achieve high yields as organic nitrogen is less readily available to crops. In some cases, organic farmers may therefore benefit by making limited use of chemical fertilizers instead of relying only on manure to supply nitrogen to their crops," Seufert says. "At the same time, conventional agriculture can learn from successful organic systems and implement practices that have shown environmental benefits, such as increased crop diversity and use of crop residues."

Yields are only part of a set of economic, social and environmental factors that should be considered when gauging the benefits of different farming systems, the researchers note. "Maybe people are asking..."
the wrong question," Prof Ramankutty says. "Instead of asking if food is organically grown, maybe we should be asking if it’s sustainably grown."

The results point to a need to get beyond the black-and-white, ideological debates that often pit advocates of organic and local foods against proponents of conventional agriculture, Prof. Foley adds. "By combining organic and conventional practices in a way that maximizes food production and social good while minimizing adverse environmental impact, we can create a truly sustainable food system."

**Journal Reference:**
*Nature*, 2012; DOI: [10.1038/nature11069](http://dx.doi.org/10.1038/nature11069)

**Wind Pushes Plastics Deeper Into Oceans, Driving Trash Estimates Up**

ScienceDaily (Apr. 25, 2012) — While working on a research sailboat gliding over glassy seas in the Pacific Ocean, oceanographer Giora Proskurowski noticed something new: The water was littered with confetti-size pieces of plastic debris, until the moment the wind picked up and most of the particles disappeared.

After taking samples of water at a depth of 16 feet (5 meters), Proskurowski, a researcher at the University of Washington, discovered that wind was pushing the lightweight plastic particles below the surface. That meant that decades of research into how much plastic litters the ocean, conducted by skimming only the surface, may in some cases vastly underestimate the true amount of plastic debris in the oceans, Proskurowski said.

Reporting in the journal *Geophysical Research Letters* this month, Proskurowski and co-lead author Tobias Kukulka, University of Delaware, said that data collected from just the surface of the water commonly underestimates the total amount of plastic in the water by an average factor of 2.5. In high winds the volume of plastic could be underestimated by a factor of 27.

"That really puts a lot of error into the compilation of the data set," Proskurowski said. The paper also detailed a new model that researchers and environmental groups can use to collect more accurate data in the future.

Plastic waste in the oceans is a concern because of the impact it might have on the environment. For instance, when fish ingest the plastics, it may degrade their liver functions. In addition, the particles make nice homes for bacteria and algae, which are then transported along with the particles into different regions of the ocean where they may be invasive and cause problems.

Proskurowski gathered data on a 2010 North Atlantic expedition where he and his team collected samples at the surface, plus an additional three or four depths down as far as 100 feet.

"Almost every tow we did contained plastic regardless of the depth," he said.

By combining the data with wind measurements, Proskurowski and his co-authors developed a simplified mathematical model that could potentially be used to match historical weather data, collected by satellite, with previous surface sampling to more accurately estimate the amount of plastic in the oceans.

In addition, armed with the new model, organizations and researchers in the future might monitor wind data and combine it with surface collections in order to better estimate how much plastic waste is in our oceans.

"By factoring in the wind, which is fundamentally important to the physical behavior, you're increasing the rigor of the science and doing something that has a major impact on the data," Proskurowski said.

The team plans to publish a "recipe" that simplifies the model so that a wide range of groups investigating ocean plastics, including those that aren't oceanographers, can easily use the model. Following the recipe, which is available now by request, might encourage some consistency among the studies, he said.

"On this topic, what science needs to be geared toward is building confidence that scientists have solid numbers and that policy makers aren't making judgments based on CNN reports," he said. Descriptions of the so-called great Pacific garbage patch in widespread news reports may have led many people to imagine a giant, dense island of garbage while in fact the patch is made up of widely dispersed, millimeter-size pieces of debris, he said.

In the future, Proskurowski hopes to examine additional factors, including the drag of the plastics in water, complex ocean turbulence and wave height, that might improve the accuracy of the model. He also may have the chance to examine the relationship between wind speed and depth of plastic particles. The 2010 expedition had near-uniform wind conditions so the researchers were unable to test that relationship.
"This is a first pass," he said.

**Journal Reference:**

**Strong Support for Once-Marginalized Theory On Parkinson’s Disease**

ScienceDaily (Apr. 25, 2012) — University of California, San Diego scientists have used powerful computational tools and laboratory tests to discover new support for a once-marginalized theory about the underlying cause of Parkinson’s disease.

The new results conflict with an older theory that insoluble intracellular fibrils called amyloids cause Parkinson’s disease and other neurodegenerative diseases. Instead, the new findings provide a step-by-step explanation of how a “protein-run-amok” aggregates within the membranes of neurons and punctures holes in them to cause the symptoms of Parkinson’s disease.

The discovery, published in the March 2012 issue of the *FEBS Journal*, describes how α-synuclein (α-syn), can turn against us, particularly as we age. Modeling results explain how α-syn monomers penetrate cell membranes, become coiled and aggregate in a matter of nanoseconds into dangerous ring structures that spell trouble for neurons.

"The main point is that we think we can create drugs to give us an anti-Parkinson's effect by slowing the formation and growth of these ring structures," said Igor Tsigelny, lead author of the study and a research scientist at the San Diego Supercomputer Center and Department of Neurosciences, both at UC San Diego.

Familial Parkinson’s disease is caused in many cases by a limited number of protein mutations. One of the most toxic is A53T. Tsigelny’s team showed that the mutant form of α-syn not only penetrates neuronal membranes faster than normal α-syn, but the mutant protein also accelerates ring formation.

"The most dangerous assault on the neurons of Parkinson’s patients appears to be the relatively small α-syn ring structures themselves," said Tsigelny. "It was once heretical to suggest that these ring structures, rather than long fibrils found in neurons of people having Parkinson’s disease, were responsible for the symptoms of the disease; however, the ring theory is becoming more and more accepted for this neurodegenerative disease and others such as Alzheimer’s disease. Our results support this shift in thinking."

The modeling results also are consistent with the electron microscopy images of neurons in Parkinson’s disease patients; the damaged neurons are riddled with ring structures.

Wasting no time, the modeling discoveries have spawned an intense hunt at UC San Diego for drug candidates that block ring formation in neuron membranes. The sophisticated modeling required involves a complex realm of science at the intersection of chemistry, physics, and statistical probabilities. A kaleidoscope of interacting forces in this realm makes α-syn proteins bump and tremble like they’re in an earthquake, coil and uncoil, and join together in pairs or larger groups of inventive ballroom dancers.

The modeling is creating a much better understanding of the mysterious α-syn protein itself, according to Tsigelny. A few years ago it was shown to accumulate in the central nervous system of patients with Parkinson’s disease and a related disorder called dementia with Lewy bodies.

The new modeling study has revealed precisely how two α-syn proteins insert their molecular toes into the membrane of a neuron, wiggle into it in only a few nanoseconds and immediately join together as a pair. The pair isn’t itself toxic; however, when more α-syn proteins join the dance, a key threshold is
eventually crossed; polymerization accelerates into a ring structure that perforates the membrane, damaging the cell.

Tsigelny said many ring structures may be required to actually kill neurons, which are known for their durability. The nerve cells may be able to repair dozens of ring-induced perforations, keeping pace with α-syn assault. But at some point, the rate of perforations surpasses the ability of neurons to repair them. As a result, symptoms of Parkinson’s disease gradually appear and worsen.

"We think we can create a drug that stops the α-syn polymerization at the point of non-propagating dimers," Tsigelny said. "By interrupting the polymerization at this crucial step, we may be able to slow the disease significantly."

Tsigelny’s research team included Yuriy Sharikov, with SDSC and UC San Diego’s Department of Neurosciences; Wolfgang Wrasidlo, with the university’s Moores Cancer Center; and Tania Gonzalez, Paula A. Desplats, Leslie Crews, and Brian Spencer, all with UC San Diego’s Department of Neurosciences. The experimental validation studies were performed by Eliezer Masliah, a professor in the UC San Diego departments of Neurosciences and Pathology, and his associates. They relied on 3-D models of proteins, plus molecular dynamics simulations of the proteins, other modeling techniques and cell-culture experiments.

Given their deeper understanding of α-syn polymerization in neurons, they are now focused on understanding how monomers of α-syn stick to one another. Their search for drug candidates will include molecules that induce different conformations of α-syn proteins that are less inclined to stick together. Tsigelny said this effect, even if small, could reduce symptoms.

This computationally intensive approach includes an examination of the many possible three-dimensional arrangements of α-syn dimers, trimmers and tetramers. Pharmaceutical companies have used versions of the approach to develop drug candidates designed to bind to ‘anchor residues’ or ‘hot spots’ within target proteins. Algorithms assess in virtual experiments the theoretical ability of thousands of candidate drugs to bind to human proteins in the ever-expanding database of known 3-D structures of those proteins.

However, attempts to find drugs this way have generated promising candidates that fail in clinical trials with expensive regularity.

"Out of these failures we’ve come to appreciate that proteins change their shapes so often that what would appear to be a primary drug target may be present one nanosecond, gone the next, or it wasn’t relevant in the first place," said Tsigelny, a physicist-turned-drug-designer.

Tsigelny’s approach takes advantage of classical drug-discovery algorithms, but adds additional analytical techniques to expand the search to include how a target protein’s conformations change in response to the forces operating on the scale of molecules.

"Sometimes, the drug-discovery models, despite being 'nice looking,' can be completely wrong," Tsigelny said. "Scientists involved in drug discovery need to know when and to what extent to trust them. Even a slight shift in a cell's environment can profoundly change the interactions of proteins with neighboring molecules. We think it’s realistically possible to design a drug to treat neurodegenerative diseases such as Parkinson’s disease and other diseases like diabetes with a more fundamental understanding of the proteins involved in those diseases."

Journal Reference:

How Ancient Viruses Became Genomic 'Superspreaders'
ScienceDaily (Apr. 23, 2012) — Scientists have uncovered clues as to how our genomes became riddled with viruses. The study, supported by the Wellcome Trust, reveals important information about the so-called ‘dark matter’ of our genome.

For years scientists have been struggling with the enigma that more than 90 percent of every mammal's genome has no known function. A part of this ‘dark matter’ of genetic material is known to harbour pieces of DNA from ancient viruses that infected our ancestors going back as far as the age of the dinosaurs.

Researchers at Oxford University, the Aaron Diamond AIDS Research Center in New York and the Rega Institute in Belgium wanted to know how these ancient viruses got into their hosts' genomes in such abundance.
The team searched the genomes of 38 mammals covering a large range of species: from mouse, rat and bat to human, elephant and dolphin. Genetic material from all of the residing viruses was collected and then compared using mathematical models.

The findings revealed that one particular group of viruses had lost the ability to infect new cells. Their genetic material is still able to amplify itself but the whole lifecycle of the virus is passed within a single cell. This change, they found, was followed by a dramatic proliferation of the virus’ genetic material within the genomes.

A comparison with all of the other viruses in the genomes revealed this to be a universal phenomenon, and that loss of cell infectivity is associated with a roughly 30-fold increase in the abundance of the virus.

The pattern resembles that which we see during epidemic outbreaks, whereby a small proportion of infected people are often responsible for most of the spread of an infectious agent to the rest of the population. They are described as 'superspreaders'.

According to the lead author, Dr Gikas Magiorkinis from Oxford University's Zoology Department: "We know that much of the 'dark matter' in our genome plays by its own rules, in the same way as an epidemic in an infectious disease, but operating over millions of years."

Robert Belshaw from the same department, who led the study, goes on to explain: "We suspect that these viruses are forced to make a choice: either to keep their 'viral' essence and spread between animals and species, or to commit to one genome and then spread massively within it. This is the story of the epidemic within every animal's genome, a story which has been going on for 100 million years and which continues today."

**Journal Reference:**

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**New Concept for Fast, Low-Cost DNA Sequencing Device**

ScienceDaily (Apr. 24, 2012) — Researchers at Oak Ridge National Laboratory and Yale University have developed a new concept for use in a high-speed genomic sequencing device that may have the potential to substantially drive down costs.

"The low cost—if it can be achieved—would enable genomic sequencing to be used in everyday clinical practice for medical treatments and preventions," said Predrag Krstic, project director and former ORNL physicist now at the University of Tennessee-ORNL Joint Institute for Computational Sciences.

The research is part of a nearly decade-long drive by the National Human Genome Research Institute of the National Institutes of Health to support the science needed to bring the cost of sequencing a human genome down to $1,000.

ORNL and Yale University researchers have created nanopores, or extremely narrow channels of water, with a radio-frequency electric field capable of trapping segments of DNA and other biomolecules.

In a paper published in the scientific journal *Small*, ORNL and Yale University researchers used theory and computation, validated by experiments, to prove that a charged micro or nano particle, such as a DNA segment, can be confined in an "aqueous virtual pore." The water provides a stable environment for DNA integrity while the virtual "walls" allow DNA to move through the nanopore without interacting with physical walls.

As an added advantage, scientists can control the size and stability of a virtual nanopore by external electric fields, something they cannot do with a physical nanopore.

"As a single DNA polymer is translocated through a synthetic nanopore, we use the physical detection of single molecules to read electric signals that identify DNA bases," Krstic said.

To help control and localize DNA, ORNL and Yale scientists created the aqueous nanopore embedded in water based on a linear Paul trap—a device that traps particles in an oscillating electric field—and experimentally proved its trapping functionality.

There were some doubts that a charged micro or nano particle could be confined by the quadrupole oscillating electric field of the Paul trap when filled by aqueous solvent, but ORNL computation and Yale
experiments prove that water actually helps stabilize trapping mechanisms, making sequencing methods more feasible.

**Journal Reference:**
Jae Hyun Park, Weihua Guan, Mark A. Reed, Predrag S. Krstić. **Tunable Aqueous Virtual Micropore.** *Small*, 2012; 8 (6): 907
DOI: 10.1002/smll.201101739

**Vermont Debates Letting Parents Say No to Vaccines**
*Associated Press*, (04.22.2012) Dave Gram

Vermont lawmakers are deliberating whether to terminate the “philosophical exemption” that allows parents to enroll children in school or child care without being immunized.

The state Health Department and CDC call for about 20 shots before a child begins kindergarten. Both agencies also note Vermont has one of the highest state exemption rates for childhood vaccinations.

A March state Senate vote (26-4) eliminated the philosophical exemption, but a subsequent April House vote (93-36) retained it. Left unresolved, the legislation will die, leaving Vermont one of 20 states allowing philosophical exemptions from required immunizations.

All states allow medical exemptions, and nearly all offer religious exemptions from immunization. An Associated Press analysis of state health department data for 2010-11 found that Alaska exempted 9 percent of kindergarteners; Colorado exempted 7 percent; and Vermont and Washington each exempted 6 percent.

State Health Department Immunization Manager Christine Finley said Vermont’s percentage of fully immunized kindergarteners fell from 93 percent in 2005 to 83 percent in 2010. While exemption proponents decry a perceived profit-driven pharmaceutical industry, exemption critics assert the decline in state immunizations must be halted to preserve “herd immunity.”

Some theorize that Vermont’s recent outbreak of pertussis (whooping cough), a vaccine target, is related to exemption. “Do you want to wait until you’ve got a measles outbreak?” asked Finley, who added that Vermont had 102 whooping cough cases between January and the beginning of April, more than in all of 2011. Washington had 640 cases from January through March; 94 cases were reported for the same time in 2011.

Gov. Peter Shumlin has endorsed the House’s call for more education on immunization over the Senate’s move to drop the philosophical exemption.

**Britain Has Third-Highest Proportion of Sexually Active Teens**

Britain ranks third-highest for early teenage sexual activity, according to new studies published in The Lancet. This research and a just-released UNICEF report both make the case for more attention to the needs of youths.

Data from 40 comparably affluent countries ranked England fourth-highest for adolescents who had been drunk by age 13; Wales ranked fifth, and Scotland eighth. Wales also ranked third for weekly drinking by 15-year-olds. England ranked fourth, with Scotland at eighth.

The United States’ violent death rate for adolescents is 10 to 20 times greater than that of other developed countries; Britain ranked in the middle for this indicator. US binge-drinking rates were high, and its cannabis use rate topped all high-income countries supplying data.

Professor Susan Sawyer of Murdoch Children’s Research Institute and Professor George Patton of the University of Melbourne in Australia maintain that earlier puberty and later marrying have delayed societal transition to adulthood, expanding years of experimentation, substance and alcohol abuse, and early and unsafe sex. Inadequate education and employment prospects also play a role.

The professors assert that “marketing of unhealthy products and lifestyles” targets young people, and that habits begun young result in 70 percent of premature adult deaths. The empowering benefits of social media were noted as coming with inherent potential harms like cyberbullying, pornography, sexually explicit texting, copycat suicides, self-harm, and sleep deprivation.

Upwards of 2.6 million 10- to 24-year-olds died in 2004. Most deaths were due to injuries (including traffic accidents and suicides); pregnancy and childbirth; communicable, nutritional, and perinatal diseases (like tuberculosis and HIV/AIDS); and non-communicable diseases (like diabetes and cancer). Most of these deaths were preventable.
Incarceration, High-Risk Sexual Partnerships and Sexually Transmitted Infections in an Urban Population

Sexually Transmitted Infections Vol. 88; No. 1: P. 63-68, (02..2012) Susan M. Rogers; Maria R. Khan; Sylvia Tan; Charles F. Turner; William C. Miller; Emily Erbelding

Examining the associations between personal and partner incarceration, high-risk sexual partnerships, and biologically confirmed STI in an urban population were the goals of the current study.

The researchers analyzed data from a probability survey of people ages 15-35 in Baltimore to examine the prevalence of personal and partner incarceration and its association with measures of high-risk sexual partnerships, including current STI, multiple partners, and partner concurrency.

In the study population, a history of incarceration was common: 24.1 percent among the men, and 11.3 percent among the women. For the 15.3 percent of women with an incarcerated partner in the past year, the risk of current STI was significantly increased (adjusted prevalence ratio=2.3, 95 percent confidence interval 1.5 to 3.5). Among men and women who had been incarcerated or who had sex partners who had recently been incarcerated, reports of five or more partners in the past year and partner concurrency were disproportionately high. The authors noted that these associations remained robust independent of illicit drug use and personal sociodemographic factors.

"Incarceration may contribute to STI risk by influencing engagement in high-risk behaviors and by influencing contact with partners who engage in risky behaviors and who hence have elevated risk of infection," the researchers concluded.

Uganda: Nation to Test Anti-HIV Vaginal Ring

By Kakaire Ayub Kirunda, 24 April 2012

Uganda could start testing the effectiveness of a vaginal ring to protect women against HIV infection by the end of this year, The Observer has learnt. Dubbed ASPIRE (A Study to Prevent Infection with a Ring for Extended Use), the planned two-year study seeks to determine whether a woman's use of a vaginal ring containing the antiretroviral drug Dapivirine offers effective protection against the sexual transmission of HIV.

Dr Samuel Kabwigu, co-principal investigator of the planned study in Uganda, told this writer at the just-ended 2012 microbicides conference in Sydney, Australia, that approval from the Uganda National Council for Science and Technology (NCST) and the National Drug Authority (NDA) would determine the actual date when the research starts.

"We can only begin after the two have given us a go-ahead," said Dr Kabwigu of the Makerere University-Johns Hopkins University research collaboration centre at Mulago. The latter is the designated ASPIRE site for Uganda.

Lisa Rossi, communications director at the Microbicides Trials Network (MTN), a US-based organisation that owns the study and is planning similar ones at MTN affiliated sites in Malawi, South Africa, Zambia and Zimbabwe, said she was "very optimistic" the approvals would be granted soon.

"The Institutional Review Board of our site in Uganda has already approved the study. We have in the past met all the requirements of both the NCST and NDA, so I'm very positive that we've done all that's required of us."

ASPIRE is targeting up to 3,476 women in the five countries. However, she added, the International Partnership for Microbicides, which developed the Dapivirine ring, is planning a parallel study (IPM 027) on 1,650 women at multiple sites in Africa, using the same product.

Years of research into microbicides for HIV prevention have produced little success, with the best study showing only 39 percent effectiveness against infection.

If ASPIRE or even IPM 027 produces positive results in late 2014 or early 2015, scientists will turn to rings as an alternative to microbicide gels that are used daily or at the time of sex. On the other hand, vaginal rings are products designed to allow the slow delivery of a drug or multiple drugs to cells inside the vagina over a period of weeks or months. And in the case of the dapirivine ring, it has been designed to be used by women for four weeks at a time.

The scientific community is under great urgency to find female-controlled HIV prevention strategies. Over half of the global HIV burden is borne by women. Preliminary results of the 2011 Uganda HIV Indicator Survey released last month show overall prevalence at 6.7 percent in the 15-49 year age group. Of this, prevalence among women stands at a high 7.7 percent, compared to 5.6 percent among men.
Progress with HIV undercut by unmet needs
Erin Allday
Friday, April 27, 2012

Scientists have been hailing recent triumphs in the treatment and prevention of HIV, but a UCSF study released this week shows that for a large group of impoverished HIV patients, a simple lack of food and shelter is making them sicker than the infection itself.

Unmet subsistence needs—not having a place to sleep and not having access to regular meals, clean clothes or good hygiene—had the largest single effect on the physical and mental health of patients in the UCSF study of 288 homeless men. A study conducted on homeless women last year found similar results.

Lacking basic necessities had a larger negative health effect than drug abuse, the virus in their blood or lack of treatment. Even among patients who were getting drug therapy for their HIV, the effects of being homeless offset most of the positive effects of treatment. But for many very poor patients, being homeless keeps them from getting consistent drug treatment at all.

Basic human needs must be addressed in parallel with HIV treatment if patients are going to stay healthy, said Elise Riley, lead author of the study. And until these needs are addressed, and the poorest HIV-positive patients are able to manage their illness, the virus will continue to circulate in the United States, she added.

"We're willing to spend all this money on medication, but it's not going to be doing as much good if we don't have more opportunities for housing or other needs," said Riley, an associate professor in the UCSF HIV/AIDS division at San Francisco General Hospital.

Meds being ignored
Despite major advances in the treatment of HIV—most notably, the success of antiretroviral drugs that can keep patients alive and relatively healthy for decades—people are still dying from their illness, often because they aren't taking the medication regularly, doctors say.

Instead, those patients often are focused on "where they're sleeping that night or where their next meal is coming from," said Dr. Brad Hare, the medical director of San Francisco General Hospital's HIV clinic, known as Ward 86.

"We're always struggling with people who need to be on HIV treatment for their health but that's not the priority," Hare said. "This study validates what we've seen. It recognizes just how important the structural barriers are to HIV care."

The issue has become increasingly critical, Hare and other HIV experts said, as the recession sends more people below the poverty line while government programs that provide housing and other social services face threats to their funding.

Hare said he's already seeing more patients who were doing well on antiretroviral therapy, only to lose jobs—and, subsequently, health insurance—and end up sick because simply making ends meet takes priority over their health.

"I have a patient in the hospital like that right now, who went off his meds for six months," Hare said. "He's an IT consultant and he was between jobs and thought he'd be OK for a while. He wasn't."

The study
In the UCSF study, participants were given physical and mental health scores, on a scale of 0 to 100; the median physical health score was 43 and the median mental health score was 46. Researchers then determined the effects of various positive and negative influences on their health.

Unmet subsistence needs had the greatest effect, lowering the physical health score by 3.8 percent and the mental health score by 3.5 percent. Regular use of antiretroviral drugs improved their mental health score by 1.7 percent but had a negligible effect on their physical health score.

Dr. Edward Machtinger, director of the Women's HIV Program at UCSF who was not associated with the homeless study, said it was not surprising that a lack of basic needs has such a profound effect on people's health. In similar studies, he's found a connection between trauma and poor health outcomes in HIV-positive women.

"Our focus in medicine needs to be broader than simply seeing patients in clinic and prescribing medications for them," Machtinger said. "Doctors and public health officials need to ask the real questions about what are the unmet needs of their clients, and be willing to respond to those needs, even if they're outside of the typical realm of a doctor's office."

The kicker, Machtinger said, is that the services to help people find food and housing already exist—but connecting them more closely with health care needs to be a priority.

It worked for her
That worked for Connie Sprinkle, 58, who became infected with HIV in 1985 when she was homeless. She didn’t start regular antiretroviral treatment until three years ago, when she moved into Leland House, which provides housing for low-income adults with HIV and AIDS. Her health has improved dramatically.

"I’m doing real good now. But being homeless made me at risk for everything," Sprinkle said. "You have to eat to be able to take these pills. If you have no way of getting any food, these pills are going to make you sick. And I wasn’t eating regularly for so long. I didn’t know where my next meal was coming from."

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MHA red-flags HIV Bill: ‘can’t take infected in paramilitary’
Abantika Ghosh Posted online: Thu Apr 26 2012, 00:19 hrs

New Delhi: A clause in the HIV and AIDS (Prevention and Control) Bill 2012 that HIV testing cannot be a precondition for employment has raised some practical roadblocks in the recruitment process of the paramilitary forces and police, and become a bone of contention between the Ministry of Home Affairs and the department of AIDS control.

The MHA holds that it is not possible to recruit HIV-positive people in the paramilitary forces because of the high physical requirement standards and also because community living in such forces could spread the infection through “cuts and bruises” — ironically, a notion the government’s own AIDS awareness programmes try hard to dispel.

The long-pending Bill, which seeks to stop discrimination against people suffering from HIV/AIDS by making it a penal offence, is going to be taken up by the Cabinet soon. It provides for imprisonment of three months to two years and a fine of up to Rs 1 lakh or both for HIV-related discriminatory propaganda.

There are two major points of disagreement between MHA and the AIDS control department.

MHA has said that the confidentiality clause on HIV status cannot be honoured for men in the forces or personnel living a community life often in enclosed quarters with common barbers and paramedics because not making HIV status of a person known would make others sharing the place with him/her susceptible. They have also demanded that the clause banning mandatory testing for employment should not apply to the forces and police.

It has also raised concerns about the risk of infection to all those around an HIV-positive person and in case of injuries which are a common occurrence because of the nature of the job. It also raised concerns on paramedical and medical staff tending to the person, particularly in a remote area where it is not possible to undertake HIV testing.

The AIDS control department has tried to dispel MHA doubts with laborious explanations about how the spread of the disease through common cuts and bruises is “minimal” and countries like Canada, Belgium and Ukraine — and also the United Nations — have rejected discriminatory practices in their armed forces and instead focused on HIV prevention information among the forces.

MHA also holds that the clause that no person can be denied job on the basis of their HIV status is not acceptable because in the paramilitary forces and police, there is a very high physical standard set and even a squint or a flat foot could render a person ineligible. How would a person suffering from HIV/AIDS, who is already immuno deficient, then undergo such rigorous training and duties in difficult positions.

The department of AIDS control counters this, saying medical evidence shows persons living with HIV can remain physically fit for up to 15-20 years while on anti-retroviral therapy during which they are good enough for any work.

The final call on the debate will have to be taken by the Cabinet when it takes the Bill up for consideration.

EAST AFRICA: Regional HIV Bill passed without criminalization clause
Photo: Allan Gichigi/IRIN

The Bill seeks to harmonize HIV policy and legislation across the region (file photo)
NAIROBI, 27 April 2012 (PlusNews)—East Africa’s Legislative Assembly has passed a regional HIV/AIDS Bill that seeks to protect the rights of people living with HIV and harmonize regional legislation and policy on the prevention and treatment of HIV.

Activists have welcomed the passing of the Bill, which, unlike some of the laws in the region's individual member states, does not criminalize the deliberate transmission of HIV.
"Criminalization impedes rather than promotes the fight against HIV, because it violates the rights of people living with HIV on many fronts," Nelson Otuoma, the coordinator of the Network of People Living with HIV and AIDS in Kenya (NEPHAK), told IRIN/PlusNews.

Member countries whose HIV legislation has criminalization clauses will be pressed to amend the laws to reflect the spirit of the regional Bill. Three of the East Africa Community's five member states—Burundi, Kenya and Tanzania—have passed HIV laws with clauses that criminalize willful transmission, while Rwanda and Uganda have not yet passed legislation.

"This [regional] Bill has a human rights approach to HIV as a major component, and criminalization was never its intention. We expect countries to use this Bill as a template for their legislation and we will lobby towards that end," said Joyce Abalo, a programme officer at the East Africa National Networks of AIDS Service Organizations (EANNASO).

"This Bill is an important first step towards strengthening HIV response in the region, because HIV issues must also be at the core of regional cooperation, which countries are quickly embracing," Abalo said. The proposed legislation also outlaws discrimination, guarantees rights to privacy and ensures the provision of health care, regardless of HIV status.

NEPHAK's Otuoma said the Bill would improve access to HIV services in the regional bloc. "You can't move freely to another country if you are not sure you will get your [HIV] treatment there. Now, should this bill become law, one knows that even he is Kenyan, he can get his treatment in Uganda."

The East Africa Community HIV and AIDS Prevention and Management Bill (2012) was passed by the East Africa Legislative Assembly on 23 April at its fifth session, held in the Kenyan capital, Nairobi. The heads of state of the member countries are expected to assent to it before it becomes law.

**Health Care Debate: High Stakes for Those with HIV**


HIV/AIDS advocates and patients are closely monitoring the Supreme Court’s review of the Affordable Care Act. President Obama’s health care overhaul includes two key benefits for HIV-positive people: It expands Medicaid to more low-income adults, paving the way for earlier access to treatment, and it eliminates limits on pre-existing conditions that prevent many from obtaining private health insurance. But the act is in limbo as the high court considers its constitutionality, particularly the requirement that most Americans carry health insurance.

“The HIV treatment community sees the act as a critical step in our fight against the AIDS epidemic,” said Scott Schoettes of the gay-rights group Lambda Legal. “People have been counting on it, making plans based on its implementation, so for it to be pulled out from under their feet at this point would be a tremendous loss.”

Data from the US Department of Health and Human Services indicate just 13 percent of HIV-positive Americans have private insurance, and around 24 percent have no coverage at all. Many who are eligible rely on public programs like Medicaid and Medicare, while those who meet low-income criteria seek assistance through the federal Ryan White Care Act. Advocates say this patchwork of coverage makes it difficult to effectively address the US epidemic.

“Once on treatment, transmission of HIV is cut to almost zero, but where do these people get treatment?” asked Dr. Michael Saag, an HIV expert at the University of Alabama-Birmingham.

“HIV is a disease of poverty,” said Saag, past chair of the HIV Medicine Association, which represents more than 4,800 health care researchers and providers. “That’s why the health care law is critically important.”

**Most Utahns Support Governor’s Veto of Sex Education Bill**

*Salt Lake Tribune*, (04.22.2012) Lisa Schencker

In a new Salt Lake Tribune poll, 69 percent of Utah voters sided with Gov. Gary Herbert’s veto of a bill that would have scaled back sex education in public schools.

Support for vetoing the legislation—which would have allowed school districts to drop sex education and required those that kept it to offer abstinence-only instruction—was diverse, encompassing 64 percent of Republicans, 63 percent of Mormons, and 69 percent of both men and women.

“It was not a good policy for us,” Herbert said, adding that the measure “went too far in taking away parental choice.”

Murray school bus driver Paul Krueger collected tens of thousands of signatures through an online petition urging the gubernatorial veto. Noting the conservative nature of mandated sex education in the
schools already, Krueger said, “There was just no reason to try and change that.” “The government should not be telling you how to parent,” he said.

Current law requires that sex education stress the importance of abstinence; permits abstinence-only instruction; allows the discussion of contraception so long as its use is not advocated; and lets parents opt their kids out of the classes.

Bill sponsor Rep. Bill Wright (R-Holden) maintains Utahns did not support the bill because it was misrepresented as restricting choices, when it actually would have expanded choice by allowing school districts to drop sex education.

Wright is considering sponsoring a similar bill next session that may completely erase sex education. “The inherent problem is still there. It’s inappropriate we destroy the innocence of youth to teach contraception in public education,” he said.

Conversely, Salt Lake City poll respondent Grant Nelson hopes “a little education and schooling before the kids become sexually active” will help reverse state problems with unwanted pregnancies and STDs.

'Abrstinence Alone Does Not Work'

'The Guardian (London)', (04.25.2012) Mary O’Hara
Several influential charities have decried a government blueprint for a recovery-based drug treatment system as “dangerously and deeply flawed” and an “ideological attack” on established interventions.

The blueprint document, “Putting Full Recovery First,” was published in March and is supported by eight government agencies, including the Department of Health. It comforms to the official governmental drug strategy published in December 2010.

Opponents include top HIV/AIDS charities the Terrence Higgins Trust (THT) and the National AIDS Trust (NAT), and the drugs/human rights charity Release. The coalition wrote to Drugs Minister Lord Henley and Prime Minister David Cameron warning the plan would be “disastrous” for drug-dependent people.

The charities say the plan overreachs governmental strategies to prioritize abstinence and “full recovery” above “proven” drug treatments such as methadone for heroin addiction. Conservative Member of Parliament David Burrowes helped draft the plan and disagrees, adding that charities and service providers collaborated on the document.

The coalition labeled the full recovery concept as disingenuous considering the propensity for relapse and the potential for transmitting blood-borne viruses should “evidence-based interventions” like needle-exchange programs cease. The charities upheld evidence crediting NEPs for the low HIV prevalence among UK injecting drug users (IDUs), and they acknowledged substitute treatments for reducing overdose rates.

Advocates also fear the plan’s compensation of service providers per person becoming “chemical-free” trivializes “the complex nature of drug dependence.” The coalition noted that the absence of a comprehensive cost analysis could find service providers trying to ensure their compensation by excluding those less likely to recover fully. THT Policy Director Lisa Power admonished Britain against abandoning the harm-reduction models that have helped curb the spread of HIV among IDUs, which also helped protect the heterosexual population.

Confusion Regarding Cervical Cancer Screening and Chlamydia Screening Among Sexually Active Young Women

'Sexually Transmitted Infections Vol. 88; No. 1: P. 35-37', (02..2012) Oluwatobi Awele Ogbechie; Michele R. Hacker; Laura E. Dodge; Mitalee Milan Patil; Hope A. Ricciotti
Given that the American Congress of Obstetricians and Gynecologists (ACOG) recently called for cervical cancer screening starting at age 21 and occurring biennially for low-risk women under 30, and that previous studies indicate women’s limited understanding of the differences between cervical cancer and chlamydia screening, the study authors assessed younger women’s knowledge of chlamydia and cervical cancer screening tests and schedules.

Sixty women ages 18-25 at an OB/GYN clinic of an urban community health center completed a survey regarding chlamydia and cervical cancer screening knowledge. Most recalled having had a Pap smear (93.3 percent) or chlamydia test (75.0 percent). While many respondents understood that a Pap test checks for cervical cancer (88.3 percent) and human papillomavirus (68.3 percent), 71.7 percent erroneously believed that a Pap smear checks for chlamydia. No respondent correctly identified ACOG’s
revised cervical cancer screening recommendations, and 83.3 percent selected annual screening. Just 23.3 percent of respondents identified the annual chlamydia screening schedule, and 26.7 percent were unsure.

“Many younger women in an urban community health center believed that cervical cancer screening also screens for chlamydia and were confused about chlamydia screening schedules,” the authors concluded. “As there is limited knowledge of the revised ACOG cervical cancer screening guidelines, there is a risk that currently low chlamydia screening rates may decrease further after these new guidelines are better known. Obstetrician/gynecologists and primary care providers should educate younger women about the differences between chlamydia and cervical cancer screening and encourage sexually active younger women to have annual chlamydia screening.”

**Ghanaian Vaccination Campaign Hopes To Prevent Up To 14,000 Child Deaths**

In a [Huffington Post Blog opinion piece](https://www.huffpost.com), Orin Levine, executive director of the International Vaccine Access Center (IVAC), describes watching the suffering of an infant with severe pneumonia and his parents while in Ghana on Thursday, writing that the experience was "a personal reminder as to why our work to prevent disease is so perilous, and why disease control so promising in Africa." Noting that last year in Ghana, "approximately 50,000 young children—nearly seven out of every 100—died before their fifth birthday," Levine adds, "I also saw the promise of prevention in Ghana," with the launch of an immunization campaign to provide both pneumococcal and rotavirus vaccines. With support from the GAVI Alliance, Ghana is the first country in Africa to introduce two new vaccines against pneumonia and diarrhea at the same time," he notes.

"Together these deadly conditions claimed the lives of nearly 10,000 Ghanaian children last year, or about 20 percent of the child deaths overall," Levine writes, adding that IVAC has "projected that by scaling up these new vaccines, Ghana can prevent 14,000 child deaths and 1.4 million illnesses in the decade ahead, and avert more than $300 million in economic losses in the process." He concludes, "My work requires me to know these statistics chapter and verse. But today, seeing [the boy] and his father imploring him to stay alive, I’m reminded that the most important benefit for Ghanaian families from this day is simply this—the chance to celebrate more fifth birthday parties" (4/26).

**Doubling the information from the double helix**

**Novel regulatory molecules called mirror-microRNAs control multiple aspects of brain function**

Our genes control many aspects of who we are — from the colour of our hair to our vulnerability to certain diseases — but how are the genes, and consequently the proteins they make themselves controlled?

Researchers have discovered a new group of molecules which control some of the fundamental processes behind memory function and may hold the key to developing new therapies for treating neurodegenerative diseases.

The research, led by academics from the University of Bristol's Schools of Clinical Sciences, Biochemistry and Physiology and Pharmacology and published in the *Journal of Biological Chemistry*, has revealed a new group of molecules, called mirror-microRNAs.

MicroRNAs are non-coding genes that often reside within 'junk DNA' and regulate the levels and functions of multiple target proteins — responsible for controlling cellular processes in the brain. The study's findings have shown that two microRNA genes with different functions can be produced from the same piece (sequence) of DNA — one is produced from the top strand and another from the bottom complementary 'mirror' strand.

Specifically, the research has shown that a single piece of human DNA gives rise to two fully processed microRNA genes that are expressed in the brain and have different and previously unknown functions. One microRNA is expressed in the parts of nerve cells that are known to control memory function and the other microRNA controls the processes that move protein cargos around nerve cells.

James Uney, Professor of Molecular Neuroscience in the University's School of Clinical Sciences, said: "These findings are important as they show that very small changes in miRNA genes will have a dramatic effect on brain function and may influence our memory function or likelihood of developing neurodegenerative diseases. These findings also suggest that many more human mirror microRNAs will be found and that they could ultimately be used as treatments for human neurodegenerative diseases such as dementia."
MicroRNAs can be seen as a novel regulatory layer within the genome, relying on the interaction between different RNA molecules. Through binding to messenger RNA (mRNA), they adjust the levels of proteins. Due to their small size, they are able to regulate many different RNAs. MicroRNAs have already been found throughout the double helix, lying in between genes or in areas of the code for a single gene that would normally be discarded. Such areas that were once considered "junk DNA" are now revealing a more complex and important role. In addition microRNAs can be produced in conjunction with their genes, within which they lie, or be controlled and produced entirely independently.

Helen Scott and Joanna Howarth, the lead authors on the study, added: "We have now found that both sides of the double helix can each produce a microRNA. These two microRNAs are almost a perfect mirror of each other, but due to slight differences in their sequence, they regulate different sets of protein producing RNAs, which will in turn affect different biological functions. Such mirror-microRNAs are likely to represent a new group of microRNAs with complex roles in coordinating gene expression, doubling the capacity of regulation."

**DNA Fingerprinting Enters 21st Century**

ScienceDaily (Apr. 27, 2012) — As any crime show buff can tell you, DNA evidence identifies a victim's remains, fingers the guilty, and sets the innocent free. But in reality, the processing of forensic DNA evidence takes much longer than a 60-minute primetime slot.

To create a victim or perpetrator's DNA profile, the U.S. Federal Bureau of Investigation (FBI) scans a DNA sample for at least 13 short tandem repeats (STRs). STRs are collections of repeated two to six nucleotide-long sequences, such as CTGCTGCTG, which are scattered around the genome. Because the number of repeats in STRs can mutate quickly, each person's set of these genetic markers is different from every other person's, making STRs ideal for creating a unique DNA fingerprint.

The FBI first introduced their STR identification system in 1998, when STRs were the darling of the genetics community. However, other identifying genomic markers were soon discovered and gained in popularity. Around the same time, high throughput sequencing allowed researchers to process vast amounts of DNA, but using methods that were ineffectual in repeated DNA, including STRs. STRs were mostly forgotten by geneticists, and innovations to study them stalled.

Now Whitehead Institute researchers have pulled STR identification into the 21st Century by creating lobSTR, a three-step system that accurately and simultaneously profiles more than100,000 STRs from a human genome sequence in one day—a feat that previous systems could never complete. The lobSTR algorithm is described in the May issue of *Genome Research*.

"lobSTR found that in one human genome, 55% of the STRs are polymorphic, they showed some difference, which is very surprising," says Whitehead Fellow Yaniv Erlich. "Usually DNA's polymorphism rate is very low because most DNA is identical between two people. With this tool, we provide access to tens of thousands of quickly changing markers that you couldn't get before, and those can be used in medical genetics, population genetics, and forensics."

To create a DNA fingerprint, lobSTR first scans an entire genome to identify all STRs and what nucleotide pattern is repeated within those stretches of DNA. Then, lobSTR notes the non-repeating sequences flanking either end of the STRs. These sequences anchor each STR's location within the genome and determine the number of repeats at the STRs. Finally, lobSTR removes any "noise" to produce an accurate description of the STRs' configuration.

According to Melissa Gymrek, who is the first author of the *Genome Research* paper, lobSTR's ability to accurately and efficiently describe thousands of STRs in one genome has opened up many new research opportunities.

"The first and simple next step is to characterize the amount of STR variation in individuals and populations," says Gymrek, who was an undergraduate researcher in Erlich's lab when she worked on lobSTR. "This will provide knowledge of the normal range of STR alleles at each locus, which will be useful in medical genetics studies that would like to determine if a given allele is normal or likely to be pathogenic. Another direction we are looking at is to look at STRs in case/control studies to look for STRs associated with disease. The list goes on, but these are some of the first questions we're looking to tackle."

**Journal Reference:**