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Family Planning Clinics Hard HIT by Budget Cuts

*Houston Chronicle*, (09.27.2012) Jennifer Radcliffe

Researchers from the University of Texas at Austin’s Population Research Center concluded that as a result of budget cuts last fiscal year, about 15 percent of Houston-area clinics that received state funds for family planning have closed and about 30 percent have shortened their hours. State family planning funds were cut in 2011 from $111.5 million to $37.9 million for a period of two years. This resulted in a cut in services to approximately 180,000 women in Texas. The number of clinics funded by the Texas Department of State Health Services dropped from 300 to 136 since funding was cut. The researchers commented that the purpose of the law was to defund Planned Parenthood in an attempt to limit access to abortion, although federal and state funding could not be used for abortion. The results of the funding cuts are limits that are now placed on women’s access to preventive reproductive health services and screenings.

Of 53 clinics that closed in Texas, seven were in the Houston area, and 13 clinics in Houston reduced their hours. None of the clinics operated by Planned Parenthood Gulf Coast closed, but they have been requiring more patients to pay for services. Rochelle Tafolla, spokesperson for Planned Parenthood Gulf Coast, noted that the number of medical visits has declined and anxiety among patients has increased. She said that the cuts have had a devastating impact on low-income, uninsured women who need the preventative health care. Clinics have started charging higher fees or restricting access to some highly effective methods of birth control because of the funding cuts. Women are steered toward contraceptive pills and receive fewer packs of pills per visit.

Planned Parenthood clinics were not the only ones to lose funding. The University of Texas Medical Branch in Galveston had its family planning funds reduced from $4.4 million in 2011 to $1.6 million in 2012. This means that almost 10,000 fewer women will receive cancer and STD screening, physical exams, counseling, and contraceptives. Peggy Smith, head of the Baylor College of Medicine Teen Health

**Family Planning Clinics Hard HIT by Budget Cuts**
Clinic, said that the state budget cuts took 25 percent of her clinic’s budget. The shortfall was covered by fundraising.

Rachel Bohannon, spokesperson for Texas Right to Life, stated that state money is being redirected to clinics that do not promote or refer to abortion services. She commented that women are better served in the long run. To illustrate, Bohannon used the example of a clinic that opened in partnership with a church and will offer the same services as Planned Parenthood minus abortions.

The study considers the consequences of the funding cuts if they result in higher costs to the state for births and unintended pregnancies. According to Kristine Hopkins, a University of Texas researcher and assistant professor of sociology who helped with the interviews for the research, “low-income women are not able to actualize their desires for their family size, and I believe that’s a basic human right.”


**Reducing STD Rates Among Black Young People May Hinge on Improved Communication Between Teens and Adults**

*Youth Today*, (09.28.2012) James Swift

Researchers at the University of Oregon suggest that the way to reduce sexually transmitted disease (STDs) in low-income, African American youth living in urban areas may be better communication between teens and adults. The study interviewed African American teens aged 15-17 years in San Francisco and Chicago. Results show that, while sexual education programs were almost universal, most teens had received very little accurate sexual health information from the majority of their information sources on sex and STDs. The teens made better sexual health choices when they had information from multiple sources about HIV and other STDs and infections. The researchers stated that abstinence education could be improved if more emphasis was placed on the impact of emotional interaction as an alternative to sexual activities. The study suggests that more collaboration between social institutions such as churches, schools, and health care providers could decrease the high rates of African Americans living with STDs. Also, sex education programs would be more effective for this audience if sex was discussed as a healthy aspect of life when age-appropriate and in the right circumstances. The study was published in the journal Research in Human Development.

**Washington Post Examines Haiti’s Efforts To Fight Lymphatic Filariasis**

The *Washington Post* reports on Haiti’s efforts to fight lymphatic filariasis, a parasitic mosquito-borne disease that can cause elephantiasis and is present in 80 percent of the country. Haiti’s health ministry is working to reach the country’s 10 million people with "mass drug administration" to prevent the disease, according to the newspaper, which notes IMA World Health, RTI International, and the University of Notre Dame are providing advice and a foundation associated with Abbott Laboratories is supplying salaries. "After years of mass drug administrations, nine countries—Burundi, Cape Verde, Costa Rica, Mauritius, Rwanda, Seychelles, the Solomon Islands, Suriname, and Trinidad and Tobago—were declared free of lymphatic filariasis in 2011 by the World Health Organization. Haiti hopes to join them," the Washington Post writes. In a separate article, the newspaper examines how beliefs in voodoo sometimes hamper care for people with elephantiasis, and it provides a fact sheet on the infection and other neglected tropical diseases, as well as a photographic slideshow (Brown, 9/30).

**News Outlets Examine Challenges To Fighting Polio In Pakistan, Nigeria**

In Pakistan, one of only three nations worldwide where polio remains endemic, "rumors and conspiracy theories about the vaccine ... have helped the country maintain its unenviable status," recording 91 cases of the disease in 2011, *Agence France-Presse* reports. Most cases of the disease this year have been recorded in the Pashtun tribal areas in the northwest of the country, "where education is limited and deeply conservative values hold sway," the news service writes, adding, "People in the area were already deeply distrustful of foreign intervention, and suspicions soared even further last year after the CIA used a hepatitis inoculation program as cover to try to find Osama bin Laden." According to AFP, "[f]ighting between government troops and tribal militias in the northwest, as well the Taliban banning inoculations in protest at U.S. drone strikes, have also hampered efforts to fight the disease." Health care workers are educating the public to build trust, and UNICEF is recruiting religious leaders to advocate for polio vaccination, the news service notes (Abdul, 9/29).
In Nigeria, another endemic country, health care workers have seen an increase in the number of polio cases in the north, "where authorities are already dealing with the unrest caused by the militant group Boko Haram," VOA News reports. Frank Mahoney, chief health officer for polio response at the Centers for Disease Control and Prevention, "said the rise in polio in northern Nigeria is particularly worrying because nomadic life-styles and cross-border trade are common there, and the disease could spread to other countries," according to the news service. In addition, the safety of health care workers is threatened, and they "struggle with access to remote, transitory communities, he says," VOA states. Nigerian President Goodluck Jonathan was in New York last week to attend U.N. meetings on polio eradication, the news service notes (Murdock, 9/28).

New SARS-Like Virus Not Spread Easily, WHO Reports
"A new strain of a potentially deadly virus related to SARS, which has killed one man in Saudi Arabia and left a Qatari man critically ill in London, does not appear to spread easily from person to person, the World Health Organization says," according to the New York Times (Santora, 9/29). "To ensure an appropriate and effective identification and investigation of patients who may be infected with the virus, without overburdening health care systems with unnecessary testing, WHO issued a revised interim case definition Saturday on its website," Xinhua reports (9/30). "On Saturday, the health organization, which was rushing to develop a diagnostic test, said that doctors should test for the virus only if the patient is severely ill," the New York Times states (9/29). "But [the agency] added anyone who has been in direct contact with a confirmed case and who has any fever or respiratory symptoms should also be tested," Reuters notes (Kelland, 9/29).

Sugar-free approach to treating Kaposi sarcoma
A sugar-loving protein drives the growth of Kaposi sarcoma (KS) tumors, according to a study published on October 1st in The Journal of Experimental Medicine Interfering with these sugary interactions inhibited growth of Kaposi sarcomas in mice, hinting at the potential for new treatment strategies in humans. KS is a cancer that is associated with infection with a herpes virus called HHV-8 and is prevalent in HIV patients. Effective antiretroviral drugs have decreased the incidence of KS, but the cancer eventually progresses in many patients and treatment options are limited.

A carbohydrate-binding protein called galectin-1 is released by a variety of tumors and promotes their growth and metastasis. A group of researchers at the University of Buenos Aires in Argentina now finds that blocking galectin-1 in mice bearing established Kaposi sarcomas slowed tumor growth in part by suppressing the formation of blood vessels that feed the tumor.

If the same holds true in humans, drugs targeting galectin-1 could provide new treatment options for patients with KS. These drugs might also hold promise for other diseases characterized by aberrant blood vessel growth, including macular degeneration and cardiovascular diseases.

Zinc Deficiency Mechanism Linked to Aging, Multiple Diseases
ScienceDaily (Oct. 1, 2012) — A new study has outlined for the first time a biological mechanism by which zinc deficiency can develop with age, leading to a decline of the immune system and increased inflammation associated with many health problems, including cancer, heart disease, autoimmune disease and diabetes.

The research was done by scientists in the Linus Pauling Institute at Oregon State University and the OSU College of Public Health and Human Sciences. It suggests that it's especially important for elderly people to get adequate dietary intake of zinc, since they may need more of it at this life stage when their ability to absorb it is declining.

About 40 percent of elderly Americans and as many as two billion people around the world have diets that are deficient in this important, but often underappreciated micronutrient, experts say.

The study was published in the Journal of Nutritional Biochemistry, based on findings with laboratory animals. It found that zinc transporters were significantly dysregulated in old animals. They showed signs of zinc deficiency and had an enhanced inflammatory response even though their diet supposedly contained adequate amounts of zinc.

When the animals were given about 10 times their dietary requirement for zinc, the biomarkers of inflammation were restored to those of young animals.
“The elderly are the fastest growing population in the U.S. and are highly vulnerable to zinc deficiency,” said Emily Ho, an LPI principal investigator. “They don’t consume enough of this nutrient and don’t absorb it very well.”

“We’ve previously shown in both animal and human studies that zinc deficiency can cause DNA damage, and this new work shows how it can help lead to systemic inflammation,” Ho said. “Some inflammation is normal, a part of immune defense, wound healing and other functions,” she said. “But in excess, it’s been associated with almost every degenerative disease you can think of, including cancer and heart disease. It appears to be a significant factor in the diseases that most people die from.”

As a result of this and what is now known about zinc absorption in the elderly, Ho said that she would recommend all senior citizens take a dietary supplement that includes the full RDA for zinc, which is 11 milligrams a day for men and 8 milligrams for women. Zinc can be obtained in the diet from seafood and meats, but it’s more difficult to absorb from grains and vegetables—a particular concern for vegetarians.

“We found that the mechanisms to transport zinc are disrupted by age-related epigenetic changes,” said Carmen Wong, an OSU research associate and co-author of this study. “This can cause an increase in DNA methylation and histone modifications that are related to disease processes, especially cancer. Immune system cells are also particularly vulnerable to zinc deficiency.”

Research at OSU and elsewhere has shown that zinc is essential to protect against oxidative stress and help repair DNA damage. In zinc deficiency, the risk of which has been shown to increase with age, the body’s ability to repair genetic damage may be decreasing even as the amount of damage is going up.

Medical tests to determine zinc deficiency are rarely done, scientists say, and are not particularly accurate even if they are done. The best approach is to assure adequate intake of the nutrient through diet or supplements, they said, especially in the elderly.

Even though elderly people have less success in absorbing zinc, the official RDA for them is the same as in younger adults. That issue should be examined more closely, Ho said.

Levels of zinc intake above 40 milligrams per day should be avoided, researchers said, because at very high levels they can interfere with absorption of other necessary nutrients, including iron and copper.

These studies were supported by the National Institutes of Health and other agencies.

Journal Reference:

Surprise HIV test at Brooklyn clinic outrages woman, so she sues doctor over bad news

Harlem woman claims doctor violated law by giving her test against her wishes and gave her result without mandated counseling. She seeks damages for 'terror, confusion, embarrassment and emotional distress.'

A BROOKLYN doctor saved a woman’s life, but is now being sued by his patient for finding she is HIV positive even though she never agreed to get tested.

The 31-year-old woman, identified as Jane Doe in court papers, was receiving treatments for vitamin B12 deficiency when she got the shock of her life — learning she carries the virus that causes AIDS.

Adding insult to injury, the suit alleged, Dr. Pavel Yutsis informed her of the devastating results without the counseling or support she needed — and the law requires.

“When he told me I was positive and threw the papers at me, I just went numb,” the woman recalled. “I was no good.”

The plaintiff, who hails from Harlem, was treated at Lifex Medical Care in Sheepshead Bay following gastric-bypass surgery she had at another facility.

A test showed her white blood cell count was low, so Yutsis suggested she get checked for HIV.

“(She) clearly stated that she did not want an HIV test,” according to the suit filed in Brooklyn Supreme Court last month.

But the doctor did the test anyway during a visit with his patient in September 2011, said the complaint.

New York law requires that HIV tests can only be performed after patients receive an explanation and give their consent. Those who test positive must be referred to counseling.

“It’s not about not wanting the results, it’s about her being able to make the decision of where and when she wanted the results,” said Daniel Pepitone, the woman’s lawyer.
That particular clinic, which provided only dietary treatments, was not where she wanted to learn such life-altering information, he added.

“I would have wanted to hear it in a better environment, from someone that I trusted,” said the woman. “I never felt comfortable in that place.”

The lawsuit also alleged that other staff members knew about the results — despite the law’s requirement of confidentiality — and one of them even told her she should get retested.

A receptionist at Lifex said Yutsis could not comment because he is sick and in the hospital.

Jane Doe is asking for unspecified damages for “terror, confusion, embarrassment and emotional distress.”

“He lied and he knew what he was doing,” she said of the doctor. “When his name is mentioned...it makes me sick to my stomach.”

Neither she nor her lawyer would comment on her current health condition.

**Bermudians May Have Been Exposed to Hepatitis C Virus at Johns Hopkins**

*The Royal Gazette (Bermuda)*, (10.03.2012) Ceola Wilson

Some Bermudians may have been infected with Hepatitis C while patients at the Johns Hopkins Hospital, thus, the US facility has asked the Bermuda Hospitals Board (BHB) to assist in collecting blood to forward to them for testing. The Baltimore, Md., facility is investigating whether any hospital patients were exposed to hepatitis C while a cardiac catheterization technician, who has since been implicated in an outbreak of the viral infection in a New Hampshire hospital, was working there.

The technician worked at Johns Hopkins for two 13-week periods from July 10, 2009 to January 9, 2010. He was not an employee of the Baltimore hospital but worked for an agency that placed him there. The issue centers around contaminated syringes that hospital personnel later used on patients at the hospital.

Of 1,567 Johns Hopkins patients have been sent letters notifying them of the situation and offering them free testing. Kim Hoppe, associate director of Communications and Public Affairs for John Hopkins Children’s Center, could not say how many of the letters were sent to Bermudians, but at least one Bermudian received a letter and went for testing.

Any individual who had a cardiac catheterization at the Johns Hopkins Hospital between July 10, 2009 and January 9, 2010, should call the toll-free number 1-855-546-3785. Patients are being told the results of their tests and counseling is being arranged for any with the hepatitis C infection. Johns Hopkins is one of several hospitals possibly affected and is offering free testing.

**Starting Antiretroviral Therapy Improves HIV-Infected Africans’ Nutrition**

*UCSF News Center*, (10.02.2012) Jeff Sheehy

Researchers from University of California San Francisco (UCSF) and Massachusetts General Hospital have found in a study focused on sub-Saharan Africa that starting HIV-infected patients on antiretroviral therapy (ART) reduces food insecurity and improves physical health, thus contributing to the disruption of a lethal syndemic. The study was recently published in the Journal of Acquired Immune Deficiency Syndromes. Sub-Saharan Africa is experiencing co-epidemics of food insecurity and HIV/AIDS, with almost 240 million people lacking access to adequate amounts of food and more than 20 million people infected with HIV/AIDS. Researchers noted that these co-epidemics intensify the vulnerability to and increase the severity of each other, creating a deadly vicious cycle.

Food insecurity augments the risk of HIV transmission by fostering practices that increase mother-to-child transmission of HIV, drive risky sexual behaviors, and contribute to poor nutrition and micronutrient deficiencies that diminish mucosal integrity and weaken the body’s overall ability to resist infection. For HIV-infected persons, food insecurity is associated with higher rates of opportunistic infections, poorer immune responses, declining mental and physical health, and higher risk of death. In turn, HIV infection worsens food insecurity due to death and illness of productive family members and increased burdens for caregivers. Additionally, the illness and stigma related to HIV/AIDS can make finding and performing work more difficult and lessen social network support for finding food in times of scarcity.

Conducted in Uganda, the study followed 228 untreated HIV-infected patients for up to three years. More than 80 percent had some level of food insecurity, and more than 40 percent were severely food insecure at baseline. Once patients began ART, food insecurity declined and nutritional status and physical status increased in conjunction with time on therapy. Along with a study published in 2011
showing a potent prevention benefit from treatment—HIV-infected participants on therapy reduced their risk of transmitting HIV to their uninfected partners by 96 percent in the earlier study—the findings from this study establish additional evidence supporting initiating treatment with antiretrovirals as soon as possible after diagnosis. “In addition to improving health and decreasing HIV transmission, our study adds to the growing evidence that treating with ART is cost-effective by improving health and productivity over the long term,” said the study’s senior author, David R. Bangsberg, MD, MPH, Director of the Center for Global Health at Massachusetts General Hospital.

Sheri Weiser, MD, the study’s principal investigator and assistant professor of medicine in the UCSF HIV/AIDS Division at the San Francisco General Hospital and Trauma Center, stated that “We have also shown in other work that food insecurity leads to worse outcomes for HIV-infected patients.” Weiser and Bangsberg concluded that to best address these overlapping epidemics, programs targeting food insecurity should be integrated into HIV treatment programs.

Editor’s Note: This research was published in the Journal of Acquired Immune Deficiency Syndromes (JAIDS): 61 (2):179–186, October 1, 2012. doi: 10.1097/QAI.0b013e318261f064

BPA’s real threat may be after it has metabolized
Chemical found in many plastics linked to multiple health threats
Bisphenol A or BPA is a synthetic chemical widely used in the making of plastic products ranging from bottles and food can linings to toys and water supply lines. When these plastics degrade, BPA is released into the environment and routinely ingested.

New research, however, from the University of California, San Diego School of Medicine suggests it is the metabolic changes that take place once BPA is broken down inside the body that pose the greater health threat.

More than 90 percent of all Americans are believed to carry varying levels of BPA exposure.

In recent years, numerous studies have reported alarming associations between BPA exposure and myriad adverse health and development effects, from cancer and neurological disorders to physiological defects and, perhaps, a cause of childhood obesity.

Of particular concern is that BPA exposure is correlated with disruption of estrogen signaling. The chemical’s molecular structure is similar to that of estradiol, one of the human body’s three main estrogens, suggesting that BPA binds to estrogen receptors. The estrogen receptor is designed to grab and hold estradiol and related estrogens. Disparate chemicals, however, can share some structures found in estrogens, enabling them to bind to the estrogen receptor. When that happens, problems can occur.

In binding to the estrogen receptor, BPA can disrupt the body’s endocrine or hormone system, with consequences especially worrisome for fetuses, infants and young children. Earlier this year, the U.S. Food and Drug Administration banned BPA in baby bottles and sippy cups. Its use is more broadly banned elsewhere in the world.

In new research published in the October 4 online issue of the journal PLOS ONE, two scientists at UC San Diego School of Medicine say three-dimensional modeling suggests a metabolite of BPA – a molecule produced when BPA is metabolized or broken down by the body – actually binds to the estrogen receptor much more strongly than BPA itself. The finding could point the way to development of a new class of drugs designed to specifically inhibit excessive estrogen activity linked to disease.

According to Michael E. Baker, PhD, UCSD professor of medicine, and Charlie Chandsawangbhuwana, a graduate student in the UCSD Department of Bioengineering, several research labs have reported that BPA binds weakly to the estrogen receptor, suggesting that something else is interacting with this receptor.

In 2004, Shin’ichi Yoshihara, PhD, and colleagues at Hiroshima International University, discovered that another compound, dubbed MBP, was produced when BPA was metabolized. **MBP has a 100-fold to 1,000-fold stronger bond to the estrogen receptor than BPA.** However, the structural basis for MBP’s high affinity for the estrogen receptor was not investigated further.
In their *PLOS ONE* study, Baker and Chandsawangbhuwana revived Yoshihara's research by creating three-dimensional, molecular models of MBP and BPA in the estrogen receptor and matching it against the crystal structure of estradiol in the estrogen receptor. They found that MBP’s longer structure allows both ends of the chemical to interact with the estrogen receptor in a way similar to estradiol. The shorter BPA molecule contacts the receptor at just one end, resulting in a weaker connection, providing an explanation for BPA's lower affinity for the estrogen receptor.

"In other words, MBP is basically grabbing onto the estrogen receptor with two hands compared to just one hand for BPA," said Baker. "Two contact points makes a much stronger connection."

Baker said the 3D modeling supports the idea that BPA is not the endocrine disruptor culprit. Instead, MBP is one (of perhaps several BPA metabolites) that causes disruption of estrogen signaling in humans and other animals.

He said the research points to the need to measure MBP levels in urine and blood of patients suspected of BPA-mediated health effects, and may fuel development of a new therapeutic treatment for conditions linked to excessive estrogen levels and activity, such as some forms of breast and prostate cancers.

"One could use MBP, which has a novel structure, as a template to develop a new class of chemicals that could bind to the estrogen receptor with high affinity," Baker said. "The goal would be to have these chemicals inhibit the action of estradiol instead of activating the estrogen response. These chemicals could control unwanted growth of estrogen-dependent tumors."

**No evidence for 30-nm chromatin fibres in the mouse genome**

HEIDELBERG, 4 October 2012 — Scientists in Canada and the United States have used three-dimensional imaging techniques to settle a long-standing debate about how DNA and structural proteins are packaged into chromatin fibres. The researchers, whose findings are published in *EMBO reports*, reveal that the mouse genome consists of 10-nm chromatin fibres but did not find evidence for the wider 30-nm fibres that were previously thought to be important components of the DNA architecture.

"DNA is an exceptionally long molecule that can reach several metres in length. This means it needs to be packaged into a highly compact state to fit within the limited space of the cell nucleus," said David Bazett-Jones, Senior Scientist at the Hospital for Sick Children, Toronto, and Professor at the University of Toronto, Canada. "For the past few decades, scientists have favoured structural models for chromatin organization where DNA is first wrapped around proteins in nucleosomes. In one possible model, the strand of repeating nucleosomes is wrapped further into a higher-order thick 30-nm fibre. In a second model, the 30-nm fibre is not required to compact the DNA. Differences between these models have implications for the way the cell regulates the transcription of genes."

Chromatin is the complex of DNA and proteins that is the fundamental constituent of chromosomes in the nucleus of the cell. The researchers used a combination of state-of-the-art imaging techniques, in this case energy spectroscopic imaging and electron tomography, to generate high-resolution three-dimensional images of chromatin in mouse cells. This approach allows for visual analysis of chromatin fibres without the need to add chemical agents to improve the contrast of images.

“Our results revealed that the 30-nm chromatin fibre model is not consistent with the structure we found in our three-dimensional spectroscopic images,” said Bazett-Jones. “It was previously thought that the transition between thinner and thicker fibres represented a change from an active to repressed state of chromatin. However, our inability to detect 30-nm fibres in the mouse genome leads us to conclude that the transcriptional machinery has widespread access to the DNA packaged into chromatin fibres."

The results are consistent with recent studies of the human genome which suggest that approximately 80% of the genome contains elements that are linked to biological function. Access to enhancers, promoters and other regulatory sequences on such a wide region of the genome means that all of these sites must be accessible. The 10-nm model of chromatin fibres provides sufficient access to DNA to allow potential target sites to be reached. The 30-nm model would not accommodate such widespread access.

The researchers offer several reasons for the observation of wider fibres in earlier studies. In some cases, the conditions outside of the cell, including those used in earlier studies where chromatin was extracted from the cell, may have given rise to structural artifacts. For some of the earlier spectroscopic studies, it may even be a question of poor resolution of existing 10-nm fibres.

**Open and closed domains in the mouse genome are configured as 10-nm chromatin fibres**

Eden Fussner, Mike Strauss, Ugljesa Djuric, Ren Li, Kashif Ahmed, Michael Hart, James Ellis, and David P. Bazett-Jones
Could Sangamo’s ‘functional cure’ for HIV disrupt the drug market?
October 4, 2012, 4:28 PM

According to Sangamo Biosciences SGMO -3.78% CEO Ed Lanphier, the biotech group’s gene-therapy technology could end up disrupting the broader pharmaceutical market by providing ‘cures’ for diseases caused by certain genetic malfunctions, thereby freeing patients of cumbersome and often expensive drug regimens.

The company’s lead product, a cellular therapy called SB-728, has already shown considerable promise in treating HIV/AIDS. Sangamo is currently running Phase II trials to see if it can help rebuild the immune systems of HIV and AIDS patients, which would conceivably allow them to go off their anti-viral drug regimens. The company plans to unveil preliminary Phase II data during the first half of 2013.

“Our goal is not just to treat but to create a ‘functional cure’ for HIV,” said Lanphier, during a recent interview with MarketWatch.

Excitement over the experimental HIV treatment has helped pushed shares of Sangamo up 11% in the last 30 days and 116% since the beginning of the year. The shares also got a huge boost in February when Sangamo announced a partnership with Shire PLC SHPG +0.08% to develop treatments for hemophilia, Huntington’s, and other genetic diseases.

Sangamo shares hit a 52-week high of $6.80 on Sept. 21, a few days after it presented positive Phase I data for its HIV therapy at a medical conference.

“I think the excitement is around the increasing perception that our technology can drive genetic cures,” said Lanphier. He noted that many patients suffering from genetic diseases are often dependent on highly expensive and complicated drug regimens to survive.

“Our treatment could definitely be disruptive to some very established pharmaceutical markets,” he added.

Sangamo’s next potentially newsworthy event will be in November, when it presents preclinical data at a meeting of the Society for Neuroscience on its experimental therapy for Huntington’s disease.

“People will see why we and Shire are so enthusiastic,” said Lanphier.

According to a survey of analysts by FactSet, the average rating for Sangamo is a buy, with a price target of $7.

Increased Risk of Stomach and Esophageal Cancer in People With AIDS

_Gastroenterology Vol. 143; No. 4: P. 943-950.e2_, (10.2012) E. Christina Persson; Meredith S. Shiels; Sanford M. Dawsey; Kishor Bhatia; Lesley A. Anderson; Eric A. Engels

A study by E. Christina Persson of the National Cancer Institute, Rockville, MD, and colleagues indicated that there is an increased risk of cancers of the stomach and esophagus in people with AIDS.

The researchers analyzed data from 596,955 people from the HIV/AIDS Cancer Match Study, which links data from 1980 to 2007 for 16 US population-based HIV and AIDS cancer registries. They compared stomach and esophageal malignancies in people with AIDS with those of the general public and evaluated the risks of different histological and anatomic subtypes of carcinomas and non-Hodgkin lymphomas of the stomach and esophagus in people with AIDS.

Results show that people with AIDS have 69 percent and 44 percent increased risks of esophageal and stomach carcinomas respectively, compared with the general population. The incidence of carcinomas remained fairly constant over time, but rates of non-Hodgkin lymphoma decreased from 1980–2007. The incidence of both esophageal and stomach carcinomas increased with age, and the risk of these cancers among people with AIDS did not decline across calendar years even with the introduction of highly active antiretroviral therapy in 1996.

Compared with non-Hispanic White subjects, Hispanic subjects had a lower risk of esophageal carcinoma, and non-Hispanic Black and Hispanic subjects had a higher risk of stomach carcinoma. No associations were observed between sex and risk of esophageal or stomach cancer. Compared with men who have sex with men, heterosexuals with HIV had a higher risk of esophageal carcinoma. Compared with the general population, the risks of carcinomas of the esophagus or stomach were not elevated in people with HIV only; compared with people with HIV only, individuals with AIDS had a higher risk of carcinomas of the esophagus and the stomach. The CD4 count at the onset of AIDS was not associated with risk of esophageal or stomach carcinoma.

The researchers provide possible explanations for these results, including an increased prevalence of H. pylori infection in people with AIDS.
**Combination Pill To Treat Malaria Pre-Approved By WHO**

"A malaria drug made by India's Cipla has been pre-qualified by the World Health Organization (WHO), an important step towards its roll-out across Asia, where millions of people are infected with the mosquito-borne disease every year," Reuters reports. "The drug, which has already been used to treat 18,000 adults in India, is intended as the first-line treatment in a number of South East Asian countries, Cipla and the Drugs for Neglected Diseases Initiative said in a joint statement on Wednesday," the news service writes (10/3). "The pre-qualified status means the drug meets WHO standards of quality, safety and efficacy, making it eligible for bulk procurement under programs that receive funding from international agencies like the United Nations Children's Fund and the Global Fund to Fight AIDS, Tuberculosis and Malaria," Fox Business notes (Ahmed, 10/3). The pill is the first to offer a combination of drugs in one tablet, and it requires a single daily dose of one or two tablets over three days, according to a video report from Al Jazeera (10/3).

**Uganda Declares End Of Ebola Outbreak**

"Uganda is now free from Ebola, the Health Ministry said, two months after an outbreak of the deadly virus killed at least 16 people," Reuters reports. "The Ministry of Health has ... officially declared an end of the Ebola outbreak that broke out in Kibaale district in July. This follows completion of the 42 days of the post-Ebola surveillance countdown period which is a prerequisite of the World Health Organization,' it said in a statement late on Thursday," the news service writes. "Uganda has suffered several Ebola outbreaks before, the biggest in 2000, when 425 people were infected by the virus and more than half of them died," Reuters notes (Biryabarema, 10/5).

**Experts Challenge Super Food Claims: Healthy-Giving Properties of Broccoli, Blueberries, May Not Make It Past the Gut**

ScienceDaily (Oct. 5, 2012) — They have been the mainstay of the health industry for the best part of a decade, but now researchers at London's Kingston University are using an approach that allows them to delve deeper into the effectiveness of health-promoting 'super foods' and their elixir-giving ilk. While there's no doubt foods such as broccoli, blueberries and whole grains contain polyphenols—compounds that have antioxidant and anti-inflammatory properties—the academic experts contend that little of these health-giving properties actually make it past the gut.

"Polyphenols may well work when cells are exposed to them directly, such as under laboratory conditions, but what needs to be established is how effective they are when consumed as part of a food. If they don't actually get through the gut membrane and into the rest of the body, then they're not a super food," Dr Lucy Jones, Deputy Dean of the University's Faculty of Science, Engineering and Computing, said.

Dr Jones and her colleague Dr Elizabeth Opara have taken a model developed in the early 1980s by US cancer research institute Sloane Kettering and adapted it to see if and how medicinal Chinese herbs, known to limit the growth of cancer cells, are absorbed in the body. Known as the Caco-2, the model mimics the action of the small intestine, the principal place where nutrients are taken up. The Kingston researchers have used it to assess what does and doesn't make it through the gut.

"The Caco-2 is a single layer of cells grown in a laboratory environment that develops the characteristics and functions of the micro-villi, the tiny hair-like projections that aid efficient absorption found mainly in the small intestine," Dr Opara said. "This method allows us to look at what nutrients pass through into the body and could be used to test food supplements, drugs and foodstuffs. We found that while some compounds may have a local effect in the gut itself, in terms of the rest of the body the impact could be negligible."

Products so far tested by the Kingston University research team include herbs such as parsley, rosemary, sage and thyme. "We are also looking into the possibility of using the model to test a dietary nitrate supplement which is currently being investigated for its impact on performance by Kingston University's sport and exercise scientists," Dr Opara said.

Beyond its use for debunking exaggerated health claims and benefits, the Caco-2 model could form a key part of a screening process to determine the effectiveness of a range of dietary compounds. "It can also be used to study compounds in combination," Dr Jones said. "For example, a cancer patient may want to take Chinese medicines in addition to their prescribed medication. The Caco-2 model would allow researchers to look at the pros and cons of this and provide an insight into the various interactions."
CNS symptoms common in people taking raltegravir

Michael Carter
Published: 10 October 2012

Approximately 10% of patients taking the antiretroviral drug raltegravir (Isentress) develop central nervous system (CNS) side-effects, research published in the online edition of AIDS shows. The development of CNS side-effects was associated with the co-administration of tenofovir (Viread, also in Truvada, Atripla and Eviplera) and of proton pump inhibitors (drugs used to reduce gastric acid). The investigators believe these drugs interact with raltegravir, increasing its plasma concentrations.

Raltegravir is the only integrase inhibitor so far approved for the treatment of HIV. Clinical trials conducted during the development of raltegravir showed that the drug had a good safety profile. However, some people developed CNS symptoms and there have been case reports of worsening depression and the development of insomnia in people initiating raltegravir therapy.

Italian investigators therefore looked at the prevalence of and risk factors for CNS side-effects in people taking raltegravir in routine HIV care.

Their study sample included 453 raltegravir-treated participants. They were monitored at six-monthly intervals, when they were asked if they had developed CNS symptoms such as headache, dizziness, anxiety, depression and sleep disturbances.

Two-thirds of the participants were men and their median age was 46 years. The mean CD4 cell count was 378 cells/mm³ and mean viral load was 1250 copies/ml. The participants were followed for a median of 23 months.

During this time, 47 individuals (10%) developed at least one drug-related CNS side-effect.

Four people stopped taking their therapy because of CNS symptoms.

There was evidence that the risk of CNS symptoms was increased by certain drug interactions.

Symptoms developed in 14% of participants who were taking the anti-HIV drug tenofovir, compared to 7% of those who were taking an alternative antiretroviral (p = 0.03). CNS symptoms were observed in 26% of people taking a proton pump inhibitor, compared to 9% of individuals who were not taking this type of therapy (p = 0.006).

After controlling for potential confounders, the investigators found that concomitant treatment with tenofovir almost doubled the risk of CNS symptoms (OR = 1.9; 95% CI, 1.0-3.5, p =0.04), whereas treatment with a proton pump inhibitor was associated with a more than three-fold increase in the risk of these symptoms (OR = 3.4; 95% CI, 1.3-8.8, p = 0.01).

The authors draw attention to the results of pharmacokinetic studies that showed that tenofovir can increase plasma levels of raltegravir by up to 64%, and that proton pump inhibitors can increase raltegravir levels by up to 415%.

“Our data suggest a possible correlation between high raltegravir plasma concentrations and CNS symptoms,” write the authors.

They recommend “a careful evaluation of patients with psychiatric disease prior to starting raltegravir and a continuous monitoring of CNS symptoms in clinical practice in those starting the drug”. The authors also stress the need to check for drug interactions than could lead to an increase in raltegravir levels. Therapeutic drug level monitoring could be useful, they suggest, for people experiencing CNS symptoms.

“Further prospective studies are needed to better clarify risk factors, the role of drug-interactions and the clinical significance of CNS symptoms in patients receiving raltegravir,” conclude the researchers.

Reference

HIV-tainted blood donations continue to increase

BY AMANDA LAGO, GMA NEWS October 10, 2012 12:11am

The number of units of donated blood contaminated with the Human Immunodeficiency Virus (HIV) rose by 18 percent this year, according to data from the latest Philippine HIV/AIDS Registry.

The registry’s data, which was posted on the Philippine National Aids Council website, showed that there were 167 units of HIV-positive donated blood as recorded by the Research Institute for Tropical Medicine (RITM) from January to August this year.

About 142 HIV-positive units were found in the same time period last year.
Of the increase in HIV-tainted blood donations, LPG Marketers Association partylist Rep. Arnel Ty said “the rising figures clearly suggest that we have many HIV cases which remain undiagnosed and unreported.”

Ty is one of the authors of the proposed Comprehensive HIV/AIDS Prevention, Treatment, Care and Support Policy Act. The bill enjoins specific agencies to support Filipinos living with HIV, as well as raise awareness about the disease.

Data from the registry also showed that HIV cases in general are also on the rise, following a trend that has been going on for the last decade.

From Jan. to Aug. this year, there was a total of 2,150 recorded HIV cases, with 272 cases reported in August alone. In the same period last year, there were 1,416 recorded HIV cases.

According to the registry, the highest number of infections is reported to have come from sexual contact. Less than one percent of the total number o

Oct 9, 2012

Invisible RNAs as Anti-HIV Drug Targets

Scientists say they have visualized, for the first time, fleeting changes in RNA structure that direct biological function through altered cell signalling, and may represent a completely new class of targets for the development of drugs, including those against viral and bacterial pathogens. A team at the University of Michigan’s Department of Chemistry and Biophysics combined an NMR technique with mutagenesis and secondary structural prediction to effectively capture RNA molecules in ‘invisible’ excited states (Es) that last for just milliseconds, but involve changes in localized base-pairing that modify the RNA architecture and cell signalling.

Advances in NMR technology have allowed scientists to characterize rare and transient ‘excited’ protein structures and demonstrate their importance in catalysis, protein folding, signalling, and recognition, but to date, it hasn’t been possible to verify evidence that RNA can also exist in transient excited states. Hashim M. Al-Hashimi, Ph.D., and colleagues now report on the NMR visualization of these RNA ESs on the hexanucleotide apical loop of HIV’s transactivation response element (TAR), HIV-1’s stem loop 1 (SL1, which the studies showed can exist in two different excited states), and the bacterial ribosomal A-site. The results suggest that targeting these ES structures may represent a completely new approach to developing anti-HIV and antibacterial drugs.

More specifically, the team’s findings showed that the TAR ES sequesters four of the apical loop bases into base pairs, essentially preventing them from carrying out binding activities that lead to active transcription of the HIV-1 genome. In essence, they suggest, finding a way to stabilize this transcription-inhibitory excited state may represent a means of targeting TAR in the development of anti-HIV drugs. The two ESs of the HIV-1 SL1, meanwhile, involved base pairs in, above, and below the SL1 internal loop, which appears to impact on the ability SL1 has to form kissing dimmers. And the ES structure of the ribosomal A-site sequesters two adenines into base pairs that makes them unavailable to decode mRNA, and may represent a new way of targeting the A-site for the development of antibiotics.

“These excited states correspond to rare alternative forms that have biological functions,” Dr. Al-Hashimi explains. “These alternative forms have unique architectural and chemical features that could make them great molecules for drugs to latch onto. In some sense they provide a whole new layer of drug targets.”

The University of Michigan team describe their technology and findings in Nature. “Compared to secondary structural transitions observed in many regulatory RNA switches, transitions between the ground and excited states uncovered here involve much more localized changes in RNA structure, occur at rates that are two-to-four orders of magnitude faster, and do not require assistance from external factors,” they write. “Thus, they can meet unique demands in biological circuits and macromolecular machines. The ESs also present new drug targets and offer new opportunities in the engineering of RNA-based devices. Line broadening indicative of ESs is routinely observed in NMR spectra of RNA, and we therefore predict that RNA ESs exist in great abundance throughout the transcriptome.”

Dr. Al-Hashimi and colleagues report their findings in a paper titled “Visualizing transient low-populated structures of RNA.”

Learning from Past Flu Epidemics to Model Outbreaks as They Happen

ScienceDaily (Oct. 9, 2012) — A new model of influenza transmission, published in BioMed Central’s open access journal BMC Medicine, using more detailed information about patterns and severity of infection than previous models, finds that cases and transmission rates of H1N1 during the 2009-2010 flu
pandemic have been underestimated. This model can provide a more robust and accurate real-time estimate of infection during a pandemic, which will help health services prepare and respond to future outbreaks.

During an epidemic one of the most important pieces of information health services need in order to respond efficiently is how ‘transmissible’ a disease is. In other words how many people are going to be infected and how easily the infection spreads. Although people exposed to flu can experience a range of symptoms from no infection through to serious illness, most models of disease transmission simplify this to infectious or not. Such a simplification makes the data easier to handle but also potentially disguises important aspects of how an epidemic develops.

A new model, developed by a team led by Dr Thomas House from the University of Warwick, includes within household transmission, as well as size of household, disease severity, and other key factors during the first seven weeks of the 2009 H1N1 epidemic in Birmingham. This information was collected by the BADGER flu clinic and Health Protection Agency centred on laboratory confirmed cases and their household contacts.

By combining transmission possibilities from people with a positive test for flu, people tested for flu and people who had flu symptoms but were not tested, this model gave a much more accurate picture of how the pandemic progressed.

Dr House explained, "By using stratified data we are able to estimate within house infection rates directly. We found that infection rates were higher than previously thought from models relying solely on laboratory confirmed cases and that a large number of people who were likely to have been real cases even if they did not have a positive swab (for example if they had recovered before the swab was taken). We also found that transmission probabilities between two people decrease with increasing household size."

This model will be able to provide real-time information about how an epidemic or pandemic is evolving. It also shows how excluding people without confirmed diagnosis can skew the results and make outbreak seem much less serious than it really is, leaving health services ill-prepared.

Journal Reference:

“Bug chasing” HIV positive man used his “toxicity” to try to kill sex partners: Crown

By Andrew Seymour, Ottawa Citizen October 11, 2012

OTTAWA — An HIV positive man accused of trying to kill his sex partners by deliberately infecting them with the disease boasted online about having unprotected sex with teenage virgins and tried to convince potential partners that condoms caused cancer, his attempted murder trial heard Thursday.

Steven Paul Boone also wrote in an online chat that he had “lost count” of how many HIV negative men he had sex with without telling them he had human immunodeficiency virus.

The online conversations were among approximately 3,000 pages of highly sexualized and graphic chats with 600 different people seized by police following Boone’s arrest in May 2010. Portions of the chats were entered into evidence on the first day of Boone’s trial on charges of attempted murder, aggravated assault and administering a noxious substance, namely, HIV.

In an opening address to a jury, prosecutor Louise Tansey-Miller said the chats were evidence Boone “was aroused by and deeply committed to achieving his goal of spreading HIV to his sexual partners.”

Boone, she alleged, was a member of a “disturbing” subculture called “bug chasing” where HIV-positive men seek out HIV-negative men to try to infect them with the disease.

Boone, 30, is accused of attempted murder and administering a noxious substance on three men. He is also accused of aggravated sexual assault on two of the same men along with three others.

He has pleaded not guilty to the charges.

In her opening address, Tansey-Miller alleged that Boone used sex, his own “toxicity” and deceit to try to infect as many people as possible with the potentially deadly disease.

Tansey-Miller said the Crown believes they can prove he infected one man, although a second man he is accused of sexually assaulting also contracted the disease.

A third alleged victim was already HIV positive before he met Boone, but allowed Boone to have unprotected sex with him as part of a fantasy, Tansey-Miller alleged.

All of the men willingly engaged in sex acts with Boone, Tansey-Miller alleged, although five of the six wouldn’t have agreed had they known Boone was HIV-positive.
“Mr. Boone intentionally acted in a way that he knew could result in the deaths of his sexual partners,” alleged Tansey-Miller. “He exposed all of his sexual partners to a realistic possibility of infection with a fatal disease. He tried and succeeded in endangering the lives of his sexual partners.

“This case is not about pointing the finger at someone because of their sexual orientation or because they have a terrible or terminal disease,” Tansey-Miller added. “Mr. Boone’s status as HIV-positive is important because this case is about Mr. Boone’s intention to surreptitiously infect as many sexual partners as he could with that fatal disease.”

The first day of the trial focused heavily on Boone’s MSN chats with men he met on gay websites. In some of the conversations, Boone—who went by the name RoCkSt(*)r PrinCe—claims he is “clean.” In others, he reveals he is HIV-positive and expressed a desire to infect others with his “strain” — whether they know it or not.

Sex with a condom was “too scary,” Boone told one man, because condoms caused cancer. Boone also claimed that condoms were going to be banned, something he said he knew because he was the Health Canada researcher who recommended it. He was actually unemployed.

Another conversation involved a man asking Boone to have sex with his boyfriend. The boyfriend wanted him to use a condom.

“I’ll let him think I’m using one and then take it off when he’s not looking,” replied Boone. “I’ve done it before.”

Another conversation focused on Boone’s desire to become HIV-positive.

All of the chats occurred after Boone found out he was HIV-positive on Oct. 30, 2009. Earlier in the day, Boone’s former roommate, Matthew Baillie, testified his “mind was blown” when he learned in April 2010 that Boone wasn’t using protection.

Baillie said Boone had earlier messaged him that he had sex with a 17-year-old “over and over” without telling him about his status.

But Boone’s lawyer, Ian Carter, suggested that Boone was prone to exaggeration and making things up.

“I guess. Sometimes,” said Baillie.

The trial is expected to take four weeks.

HIV Diagnoses Among U.S. Hispanics Vary by Region: CDC

A new study by the Centers for Disease Control and Prevention finds that Hispanic Americans are diagnosed with HIV infection nearly three times as much as whites, but the rates and causes differ by region. Analyzing 2010 data from 46 states and Puerto Rico, researchers found that at 55 per 100,000 individuals, the rate of HIV diagnosis for Hispanics in the Northeast was more than twice that of any other region in the United States. They also found that the largest percentage of HIV diagnoses—35.4 percent—among Hispanics occurred in the South.

The report, published in the October 12 issue of CDC’s Morbidity and Mortality Weekly Report, noted that male-to-male sex was the primary method of HIV transmission among Hispanics overall, but for those living in the Northeast it was more likely that they became infected through injection drug use. Hispanics in the Northeast were also more likely to be of Puerto Rican descent, while those in other areas of the country were more likely to be of Mexican or Central American descent. According to researcher Qian An of the Division of HIV/AIDS Prevention (DHAP) at CDC’s National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention, these regional differences point to the need for HIV testing, prevention, and treatment efforts to be tailored to the unique needs of each area of the country.

Girls Become the Voice of Sex Education in Haiti

Sexual and reproductive health education is not part of formal education for girls in Haiti, but with the establishment of nurse-led sex education and life skills clubs, girls in rural regions are taking control of their futures. These clubs help young girls avoid early pregnancies, sexually transmitted diseases, and HIV as well as helping them to understand how their bodies work. The girls also go on to become advocates of safe sex practices among their peers. According to a UNICEF survey, only 29 percent of females between 15 and 24 who had sex with a partner with whom they were not married or cohabiting during the year
before the survey say that their partner used a condom, and 15 percent of that same age group gave birth before the age of 18.

Nurse Carmensize Guerrier says that the sex education and life skills clubs became more popular after the 2010 earthquake, when young women lived in camps, with a heightened risk for sexual abuse. Several international organizations are involved in the efforts to create the clubs, including CARE, the Haiti Red Cross Society and Catholic Relief Services, as well as local organizations such as Fondation pour la Santé Reproductrice et l’Éducation Familiale.

Indian Bureaucracy Slows Treatment of Tuberculosis

*Wall Street Journal*, (10.11.2012)  
Geeta Anand, Shreya Shah

A tuberculosis (TB) patient in India was one of 16 patients identified by Mumbai doctors to be resistant to all traditional TB treatments. Now the patient is perilously close to running out of life-saving medicines. The patient returned home to Uttar Pradesh, a thousand miles from the Mumbai treatment center, expecting to die, only to find that the experimental treatment prescribed by a Mumbai TB expert has held the disease in check—but the patient must continue the treatments for 18 more months for a chance of being cured. The latest twist in the patient’s story exposes the bureaucratic tangle that can hinder treatment for India’s TB patients. India now has 42 labs that can make the diagnosis, but the patient’s home state of Uttar Pradesh—India’s most populous state—does not have a lab yet. India’s incomplete national network for treating the most virulent forms of TB has complicated this patient’s treatment.

National health officials have pledged free treatment to the patient; however, on October 8, Dr. Mini Khetrapal, Mumbai’s top TB official, said that the city would stop providing the medicines because the patient no longer resides in Mumbai. Dr. Khetrapal further stated that if the patient wants more medicines, the patient must return to Mumbai so that Mumbai doctors can monitor the side effects of the medicines administered.

The patient is too poor to return to Mumbai, and does not wish to be homeless and living on the streets in such a weak condition. The patient’s family already sold all their land and spent their life savings to pay for treatment during the past six years. On October 10, Dr. Ashok Kumar, head of India’s national TB program, reiterated that the government would keep providing the patient’s medication and would courier the medicines to the patient’s home state until Uttar Pradesh is able to take over the treatment. However in the past, medicines from Mumbai have arrived several weeks late.

TB affects approximately 2.3 million Indians per year. Although in 1977, India began to build a national program to diagnose and treat TB, India was slow to diagnose and treat patients with multidrug-resistant TB. Thus, there are now signs of an epidemic in some parts of the country, especially in Mumbai.

Indonesia Licenses Patents for Seven HIV & Hepatitis B Medicines

*InfoJustice*, (10.11.2012)  
Peter Maybarduk

On September 3, Indonesia’s President Dr. H. Susilo Bambang Yudhoyono signed a decree authorizing the government’s use of patents for seven HIV/AIDS and hepatitis medicines. By doing so, the Indonesian government expanded access to medicines that will help save and improve the lives of people with HIV/AIDS and hepatitis B. If fully implemented, the measure will introduce widespread generic competition and generate major cost savings in the world’s fourth most populous country. The decree licenses patents for several HIV medicines, and represents one of the most robust uses of pharmaceutical patent licensing power by a country since the World Trade Organization’s 1995 Agreement on Trade-Related Aspects of Intellectual Property Rights.

The presidential decree greatly expands Indonesia’s access to newer and more appropriate antiviral and antiretroviral treatments, including efavirenz, abacavir, didanosin, lopinavir + ritonavir, tenofovir, tenofovir + emtricitabine, and tenofovir + emtricitabine + efavirenz. For more information, including a copy of the decree (in Indonesian and an unofficial English translation), analysis, a table of the licensed medicines, and Indonesia’s response to HIV and hepatitis B, visit www.citizen.org/actions-indonesia.

HIV-Positive Men Head to Clinic for the 'Other Meningitis' Vaccine

*WNYC News Blog*, (10.10.2012)  
Fred Mogul

An outbreak of contagious bacterial meningitis unrelated to the larger fungal version spreading across the United States is causing some New York City men to go clinics for vaccines. This smaller outbreak of the bacterial version of the disease has only struck local men who are HIV-positive—12 this year, including
five in the last month. One man has died, and another was in critical condition, but appears to be recovering.

Health authorities advise HIV-positive men to get vaccinated against bacterial meningitis, if they have had intimate contact with new acquaintances that they have met through the Internet, at bars or parties, or through digital apps in recent weeks. The New York City Health Department estimates approximately 10,000 men fit these criteria.

Dr. Gal Mayer, the medical director at the Callen-Lorde Community Health Center in the Chelsea neighborhood, said the clinic has received about 20 calls a day from people about meningitis. Many of them are confused between the two outbreaks, and some of them have reported symptoms. Mayer stated that “There’s a lot of clarification that we have to do.” Those with symptoms have been directed to hospital emergency rooms, but none of their cases have been confirmed as meningitis. Meningitis can be deadly if not detected and treated early with intravenous antibiotics. The steroid-related meningitis has no vaccine and is not contagious.

**Tuberculosis Outbreak To Be Investigated**

*The Australian*, (10.11.2012) Rebecca Le May

An outbreak of tuberculosis (TB) at Osborne Park Hospital in Perth will be investigated amid union claims of mismanagement by the North Metropolitan Health Service (NMHS). 110 staff have been informed by letter that they may have been exposed to the disease “within days” of discovering that a former patient had been diagnosed with TB, and the letters encouraged staff to be tested. Of the 100 who did so, 9 tested positive. According to a spokesperson, it was a latent variety of the disease, so most would not become ill. The spokesperson rejected the Australian Nurses Federation’s claims of mismanagement concerning the outbreak and said that NMHS had followed up with patients and visitors who may have been exposed to the infected man, and the agency would also follow up with the 10 staff who were not tested.

**GlaxoSmithKline To Make Clinical Trial Data Available To Other Researchers**

GlaxoSmithKline (GSK) CEO Andrew Witty “said on Thursday detailed data from its clinical trials would be made available to other researchers,” *Reuters* reports, adding, “That would include anonymized patient-level results that sit behind clinical trials of approved and failed drugs” (Hirschler, 10/11). In a speech to the Wellcome Trust in London on Thursday, Witty said that “openness to the public and active collaboration with scientists and firms outside GSK are essential to finding new drugs to treat the diseases plaguing the world, from novel antibiotics to cures for malaria and tuberculosis,” the *Guardian* writes (Boseley, 10/10). “The initiative will enable researchers to examine the data more closely or combine data from different studies to carry out further research and learn more about how medicines work, the company said,” according to the *Wall Street Journal* (Falconi, 10/11).

"Researchers contacted about the plan on Wednesday expressed a mix of enthusiasm and skepticism, citing the recent $3 billion settlement by GlaxoSmithKline with the federal government over charges that the company had misrepresented trial data for popular drugs like Avandia and Paxil," the *New York Times* writes. "Still, the company is taking a step in the right direction, the researchers said, and might set a precedent in an industry that could use more transparency," the newspaper notes, adding, “Whether more disclosure might lead to safer, more effective drugs remains to be seen” (Thomas, 10/11). "Witty also pledged to seek publication of the results of all clinical trials that evaluate Glaxo’s medicines—regardless of what they say—to peer-reviewed scientific journals," the Wall Street Journal notes (10/11).

**Mexican Government, NGOs Working To Expand Access To Clean Syringes To Prevent HIV Among IDUs**

*Inter Press Service* examines how Mexico’s government and non-governmental organizations are working to stem the spread of HIV among people who use injection drugs. "According to a project financed by the Global Fund to Fight AIDS, Tuberculosis and Malaria since 2011, the prevalence of HIV/AIDS in Mexico is 5.77 percent among intravenous drug users ... compared to 0.24 to 0.3 percent in the general population aged 15 to 49,” IPS writes, noting HIV prevalence among drug users is highest in "northern Mexico, one of the areas in the country hit hardest by drug trafficking." The news service adds "[t]here are 28 syringe exchange programs in this country of 112 million people, insufficient to serve the entire population of intravenous drug users." IPS discusses funding shortfalls for syringe exchange programs, legal hurdles to obtaining clean injection equipment, and how the government aims to continue receiving Global Fund money through 2013 (Godoy, 10/11).
Blog Examines Contraceptive Coverage In Sub-Saharan Africa

"Between 1970 and 2010, most emerging countries achieved impressive gains in contraceptive coverage," but, "[b]y contrast, many sub-Saharan African (SSA) countries ... have started their contraceptive revolution very late and progress to date has been minimal," John May, a visiting fellow at the Center for Global Development (CGD), and Jean-Pierre Guengant, researcher emeritus at the Research Institute for Development (IRD) in Marseille, France, write in CGD’s "Global Health Policy" blog. "The widespread belief in SSA that ‘development was the best contraceptive’ has been the major reason why countries did not launch organized family planning programs," they write, adding, "By and large, the lack of progress in contraceptive coverage has precluded significant decreases in fertility in the region" (10/11).

Scientists discover that shape matters in DNA nanoparticle therapy

Particles could become a safer, more effective delivery vehicle for gene therapy

Researchers from Johns Hopkins and Northwestern universities have discovered how to control the shape of nanoparticles that move DNA through the body and have shown that the shapes of these carriers may make a big difference in how well they work in treating cancer and other diseases.

This study, to be published in the Oct. 12 online edition of the journal Advanced Materials, is also noteworthy because this gene therapy technique does not use a virus to carry DNA into cells. Some gene therapy efforts that rely on viruses have posed health risks.

"These nanoparticles could become a safer and more effective delivery vehicle for gene therapy, targeting genetic diseases, cancer and other illnesses that can be treated with gene medicine," said Hai-Quan Mao, an associate professor of materials science and engineering in Johns Hopkins’ Whiting School of Engineering.

Mao, co-corresponding author of the Advanced Materials article, has been developing nonviral nanoparticles for gene therapy for a decade. His approach involves compressing healthy snippets of DNA within protective polymer coatings. The particles are designed to deliver their genetic payload only after they have moved through the bloodstream and entered the target cells. Within the cells, the polymer degrades and releases DNA. Using this DNA as a template, the cells can produce functional proteins that combat disease.

A major advance in this work is that Mao and his colleagues reported that they were able to "tune" these particles in three shapes, resembling rods, worms and spheres, which mimic the shapes and sizes of viral particles. "We could observe these shapes in the lab, but we did not fully understand why they assumed these shapes and how to control the process well," Mao said. These questions were important because the DNA delivery system he envisions may require specific, uniform shapes.

To solve this problem, Mao sought help about three years ago from colleagues at Northwestern. While Mao works in a traditional wet lab, the Northwestern researchers are experts in conducting similar experiments with powerful computer models.
Erik Luijten, associate professor of materials science and engineering and of applied mathematics at Northwestern's McCormick School of Engineering and Applied Science and co-corresponding author of the paper, led the computational analysis of the findings to determine why the nanoparticles formed into different shapes.

"Our computer simulations and theoretical model have provided a mechanistic understanding, identifying what is responsible for this shape change," Luijten said. "We now can predict precisely how to choose the nanoparticle components if one wants to obtain a certain shape."

The use of computer models allowed Luijten's team to mimic traditional lab experiments at a far faster pace. These molecular dynamic simulations were performed on Quest, Northwestern's high-performance computing system. The computations were so complex that some of them required 96 computer processors working simultaneously for one month.

In their paper, the researchers also wanted to show the importance of particle shapes in delivering gene therapy. Team members conducted animal tests, all using the same particle materials and the same DNA. The only difference was in the shape of the particles: rods, worms and spheres.

"The worm-shaped particles resulted in 1,600 times more gene expression in the liver cells than the other shapes," Mao said. "This means that producing nanoparticles in this particular shape could be the more efficient way to deliver gene therapy to these cells."

The particle shapes used in this research are formed by packaging the DNA with polymers and exposing them to various dilutions of an organic solvent. DNA's aversion to the solvent, with the help of the team's designed polymer, causes the nanoparticles to contract into a certain shape with a "shield" around the genetic material to protect it from being cleared by immune cells.

Development of 2 tests for rapid diagnosis of resistance to antibiotics

With their excellent sensitivity and specificity, the use of these extremely efficient tests on a world-wide scale would allow us to adapt antibiotic treatments to the individual's needs and to be more successful in controlling antibiotic resistance, particularly in hospitals. These works were published in September in two international reviews: *Emerging Infectious diseases* and *The Journal of Clinical Microbiology*.

These diagnostic tests will allow rapid identification of certain bacteria that are resistant to antibiotics and hence:

- Allow us to better adapt the treatment to the infected patients
- Avoid the inappropriate use of certain antibiotics, thus avoiding the over-use of certain wide-spectrum antibiotics
- Isolate patients infected with these resistant bacteria and thus avoid the development of epidemics in hospitals

There is an ever-increasing number of emerging bacteria that cause cross-border epidemics. Researchers all agree on the fact that it is not the number of bacteria that is the problem, but their increasing resistance to antibiotics. The situation is particularly dramatic for certain species of bacteria, Gram-negative bacilli such as enterobacteriacae.

A worrying situation both for banal infections and for major treatments.

Whereas certain antibiotics such as wide-spectrum cephalosporins used to be reserved for the most serious cases, now there are cases where they are totally inactive against certain bacterial germs and consequently there is no effective antibiotic treatment for these. And so we are now faced with situations where the treatment of banal infection such as urinary or intra-abdominal infections has no effect. And this puts the life of the patients at risk. Every year, an estimated 25,000 deaths in Europe are due to multi-resistance to antibiotics.

Furthermore, the development of resistance to antibiotics affects an entire aspect of modern medicine that needs efficient antibiotics (grafts, transplants, major surgery, reanimation, etc.).

Undetected importation of multiresistant strains from foreign countries can also considerably accelerate the diffusion of this multiresistance phenomenon.

**Two ultra-rapid tests: from Red to Yellow**

In an attempt to slow down these increasing resistances, the Inserm researchers have developed a system that can rapidly detect the two enzymes responsible for causing resistance to the bacteria of two classes of common antibiotics: wide-spectrum cephalosprins and carapenemases. In these tests, the presence of an enzyme indicates the presence of a resistant bacteria.

These tests (Corba NP test and ESBL NDP test) are based on the acidification properties generated by the activity of the enzymes (ß-lactamases and carapenemases) when they are in the presence of an
antibiotic. If any one of these enzymes is present, the medium becomes acid and the acidity indicator (pH) turns from red to yellow (Figure, Corba NP test).

At present, these tests can be performed using bacteria isolated from urine samples taken during a detected infection, or from bacteria present in stools. The result is obtained in less than 2 hours (compared to 24 to 72 hours using current techniques). These tests are highly sensitive and highly reliable (100%). They are totally inoffensive since they are carried out on bacteria isolated from patients or on biological products such as urine, etc.

Patrice Nordmann, Inserm Research Director and main author of this work, points out that "These tests are currently being assessed in order to ascertain their sensitivity directly from infected sites such as blood or urine".

The invention of these tests is an important breakthrough in the fight against the resistance to antibiotics. These tests will provide a simple, inexpensive (less than 4 to 5 euros) means of very rapidly detecting the most serious cases of resistance to antibiotics in human medicine and will contribute to limiting international diffusion.

As Patrice Normann states "We can hope, in particular in many Western countries where the situation has not yet reached endemic proportions multi-resistances (France, in particular), to be able to preserve to a certain extent the efficiency of wide-spectrum cephalosporins and carbapenems, antibiotics used as a "last resource". Used straight at the patient's bedside, these tests will help us to optimise the use of antibiotic treatment, in particular in the developing countries where the levels of resistance are extremely high.

Two international patent applications have been filed with Insert Transfert. Their commercialisation is in the course of development and they should be available in about 12-16 months, however the techniques are available for any specialised laboratories who wish to develop them.

The body's own recycling system

Researchers discover "molecular emergency brake" in charge of regulating self-digestion

12.10.2012

Ralf Höcker/HZI

Using a microscope, the researchers are able to zoom in on the cells: If autophagy proceeds undisturbed, they are able to observe little digestive bubbles, shown in red, inside of which material is being degraded (left). If the final step is blocked, autophagosomes accumulate inside the cell, shown here in green (right). The dark circular area at the center is the nucleus.

Times of distress literally eat away at the core of starving cells: They start to digest their own parts and recycle them for metabolic purposes. This process – called autophagy – also plays a role in immune defense. In that context, however, the digestive machinery is switched on for an entirely different purpose: the elimination of pathogens that have invaded the body. Now, Prof. Ingo Schmitz at the Helmholtz Centre for Infection Research (HZI) in Braunschweig, Germany, together with a team of researchers, has discovered that a "molecular brake" is in charge of regulating autophagy to keep it from getting out of control. They published their findings in the scientific journal, Cell Death & Differentiation.

Almost everything that happens inside a cell, including autophagy, is tightly regulated on a biochemical level. Like that, the cell makes sure that processes only take place when they are needed and that they are shut off when the need has expired. "Inside the cell, there exists a network of molecules. Between them, information is constantly being exchanged," says Schmitz, head of the research group “Systems-oriented Immunology and Inflammation Research” at HZI, who also holds a chair at the Otto von Guericke University in Magdeburg. "In a way, it looks like a big city subway map.” However, only the starting point and the destination of a given "cellular subway line" are relatively easy to study. To explore the different stops along the way, is more difficult. But because other lines intersect and interact with each other at these points, it is very exciting for researchers to decode all molecules involved in these signal transduction processes. It also helps them better understand diseases caused by defects in these information highways.
What exactly happens on a molecular level during the later stages of autophagy was largely unknown — until now. Schmitz and his team, along with researchers from the Otto von Guericke University Magdeburg, the Heinrich Heine University Düsseldorf, the Tübingen University, and the Temple University School of Medicine in Philadelphia, USA, have decoded one part of the molecular subway map. Under the microscope, researchers can observe how larger-sized cellular components destined for degradation and recycling are enclosed within a small bubble, the so-called autophagosome. This structure then fuses with yet another little bubble, which digests the autophagosome’s contents. "Autophagy is a survival mechanism to ensure that the cell is able to obtain the necessary nutrients during times of starvation," explains Schmitz.

For their studies, the scientists stained certain molecules and autophagosomes inside cells. This allowed them to observe microscopically which molecules are in charge of regulating the formation of the little digestive bubbles. To prompt self-digestion, they either starved the cells or simulated an infection. In the process, they discovered that the cells simultaneously also turned on autophagy-inhibiting molecules — "like some kind of emergency brake that ensures autophagy doesn’t get out of control." Such negative feedback loops are not unusual for cells, they frequently help prevent overshoooting reactions.

The researchers managed to identify the components of this feedback loop and found a protein called p38 to play a key role in the process. The scientists were especially surprised to observe p38 proteins on the surface of the autophagosomes. Normally, this protein is localized inside the nucleus where it gets switched on whenever the cell is under stress. On the surfaces of autophagosomes, p38 performs a very different job: It alters another molecule, called Atg5, to get it to block the final step of autophagy, involving formation of the little digestive bubble. Autophagy is inhibited, and, essentially, the cell pulls the "molecular emergency brake."

If it didn’t, diseases could potentially result. As such, defective molecules of the Atg family have been implicated in the etiology of the inflammatory bowel disease, Morbus Crohn. "Looking at Atg5-deficient mice, which die of nutrient-deficiency shortly after they are born, we see just how important it is to tightly regulate autophagy," emphasizes Ralf Höcker, one of the study’s first authors. As so often, it is important to find the right balance, in this case, between too much and too little self-digestion.

**Original publication:**

**Rare cells regulate immune responses; May offer novel treatment for autoimmune diseases**
DURHAM, NC—Reproducing a rare type of B cell in the laboratory and infusing it back into the body may provide an effective treatment for severe autoimmune diseases such as multiple sclerosis or rheumatoid arthritis, according to researchers at Duke University Medical Center.

The findings, which were demonstrated in mice, highlight the unique properties of a subset of B cells that normally controls immune responses and limits autoimmunity, in which an organism mistakenly attacks its own healthy tissue. The work appears Oct. 14, 2012, in the journal *Nature*.

B cells are the component of the immune system that creates antibodies, which fight pathogens like bacteria and viruses. However, a small subset of B cells, called regulatory B cells, works to suppress immune responses. These B cells are characterized by a cell-signaling protein called interleukin-10 (IL-10), giving these regulatory B cells the name B10 cells.

While B10 cells are small in number, they are important for controlling inflammation and autoimmunity. B10 cells can also limit normal immune responses during infections, reducing inadvertent damage to healthy body tissue.

"Regulatory B cells are a fairly new finding that we’re just beginning to understand," said Thomas F. Tedder, PhD, professor of immunology at Duke and study author. "B10 cells are important because they make sure an immune response doesn’t get carried away, resulting in autoimmunity or pathology. This study shows for the first time that there is a highly controlled process that determines when and where these cells produce IL-10."

Tedder and his colleagues studied the process of IL-10 production in the B10 cells of mice. Creating IL-10 requires physical interactions between B10 cells and T cells, which play a role in turning on the immune system.
The researchers found that B10 cells only respond to very specific antigens. Recognizing these antigens drives the function of B10 cells, causing them to turn off certain T cells when they bind the same antigen to prevent them from harming healthy tissue.

With this understanding of B10 cells, researchers set out to learn whether B10 cells could be harnessed as a cellular therapy, given their ability to regulate immune responses and autoimmunity.

"Since B10 cells are extremely rare, it was important that we find a feasible solution to reproduce these cells outside the body to make them available," Tedder said.

The researchers learned that the B10 cells could be isolated from the body and would maintain their ability to regulate immune responses. Moreover, they could be reproduced in large numbers.

"Normal B cells usually die quickly when cultured, but we have learned how to expand their numbers by about 25,000-fold. However, the rare B10 cells in the cultures expand their numbers by four-million-fold, which is remarkable. Now, we can take the B10 cells from one mouse and increase them in culture over nine days to where we can effectively treat 8,000 mice with autoimmune disease," said Tedder.

When a small amount of B10 cells were introduced into mice with multiple sclerosis-like autoimmune disease, their symptoms were significantly reduced, essentially turning off the disease.

"B10 cells will only shut off what they are programmed to shut off. If you have rheumatoid arthritis, you would want cells that would only go after your rheumatoid arthritis," continued Tedder. "This research shows that we may have the potential to unhover regulatory cells, make millions of copies, and introduce them back into someone with autoimmune disease to shut down the disease. This may also treat transplanted organ rejection."

Additional research is needed to learn how to expand human B10 cells and determine how B10 cells behave in humans, building on the study's insights into the mechanisms behind their function and autoimmunity.

"Autoimmune diseases are very complicated, so creating a single therapy that allows us to go after multiple disease targets without causing immunosuppression has proven to be difficult." Tedder said. "Here, we're hoping to take what Mother Nature has already created, improve on it by expanding the cells outside of the body, and then put them back in to let Mother Nature go back to work."
**Molecular Basis of Infection of Tick-Transmitted Disease Uncovered**

The image depicts two *Anaplasma phagocytophilum* bacteria (arrows) that are bound to the surfaces of host cells. The bacterium on the right (thick arrow) is invading its host cell by triggering its own uptake. A team of VCU researchers led by Jason Carlyon, Ph.D., has identified a key mechanism by which this pathogen invades host cells. Their findings provide a direction for developing a vaccine for protecting against *A. phagocytophilum* and related bacterial pathogens. (Credit: Image courtesy of Jason Carlyon, Ph.D. and Matthew J. Troese, Ph.D./VCU)

ScienceDaily (Oct. 12, 2012) — Virginia Commonwealth University School of Medicine researchers have identified the "keys" and "doors" of a bacterium responsible for a series of tick-transmitted diseases. These findings may point researchers toward the development of a single vaccine that protects against members of an entire family of bacteria that cause disease in humans, domestic animals and livestock.

Survival for many bacteria is dependent on their ability to invade human or animal cells. And it needs to be done in a very precise fashion. Bacteria use a specific set of "keys" on their surfaces to unlock specific "doors," or entryways into their host cells.

By understanding how these bacteria invade cells, researchers are able to identify potential targets to block the spread of infection, and from there, develop safe and effective vaccines.

In the study, now published online and appearing in the November (Volume 80, Issue 11) issue of the journal *Infection and Immunity*, a journal of the American Society for Microbiology, researchers reported that a protein called OmpA on the surface of *Anaplasma phagocytophilum* is important for invading host cells. *Anaplasma phagocytophilum* is an *Anaplasmataceae* bacterium that infects humans to cause granulocytic anaplasmosis. It is the second most common tick-transmitted disease after Lyme disease in the United States, and it also is found in Europe and Asia.

The team also identified the particular sugar residue on the surfaces of host cells to which OmpA binds.

"In other words, we identified both a key and door that together promote *Anaplasma phagocytophilum* infection," said lead investigator Jason A. Carlyon, Ph.D., associate professor and a
George and Lavinia Blick Scholar in the Department of Microbiology and Immunology in the VCU School of Medicine.

"These findings are important because our data also establish a direction for development of a single vaccine that protects against members of an entire family of bacteria that cause disease in humans, domestic animals and livestock," he said. According to Carlyon, the region of OmpA that mediates infection is shared among other Anaplasmataceae bacteria.

Experts have seen a steady rise in the incidence of human infections caused by tick-transmitted bacterial pathogens in the past several years. Many tick-transmitted bacterial pathogens are considered "emerging pathogens" because it was only recently discovered that they infect humans. Moreover, evidence suggests that many of these infections go unrecognized, signifying that the prevalence of human diseases caused by Anaplasmataceae pathogens is even higher, said Carlyon. Livestock infections carry a significant economic burden, costing the U.S. cattle industry $100 million per year, he added.

Researchers in Carlyon's lab are presently refining their understanding of how OmpA promotes infection and testing its efficacy in protecting against infection by A. phagocytophilum and other Anaplasmataceae members.

Journal Reference:

Diverse Intestinal Viruses May Play a Role in AIDS Progression
ScienceDaily (Oct. 11, 2012) — In monkeys and humans with AIDS, damage to the gastrointestinal tract is common, contributing to activation of the immune system, progressive immune deficiency, and ultimately advanced AIDS. How this gastric damage occurs has remained a mystery, but now researchers reporting in the Cell Press journal Cell provide new clues, implicating the presence of potentially pathogenic virus species other than the main virus that causes AIDS. The findings could provide an opportunity to explain and eventually intervene in the processes that lead to AIDS progression.

To investigate what causes gastrointestinal damage in monkeys and humans with AIDS, researchers used a sequencing method that allows them to obtain genetic sequences of all of the bacterial, viral, and other organisms residing in the gastrointestinal tract. Using this technique, they examined the feces of monkeys with SIV-induced AIDS, monkeys without SIV infection, and monkeys infected with SIV strains that do not cause AIDS. (SIV is the monkey counterpart to HIV.)

"We found that the gastrointestinal tract of the animals with AIDS contained a large number of previously undescribed viruses—including potential pathogens, but we did not see any obvious changes in the bacteria. This means that previously unrecognized viruses may contribute to AIDS disease progression in monkeys," explains co-author Dr. Dan Barouch, of Harvard Medical School and the Beth Israel Deaconess Medical Center, in Boston. It’s not clear why monkeys with AIDS have more intestinal viruses, but it may be related to their compromised immune system.

The researchers also noted that some of the viruses in the feces of monkeys with AIDS were also found circulating in the animals’ blood. In addition, many were RNA viruses, meaning that their genetic material is made up of RNA rather than DNA. "This is the first time anyone has looked at both DNA- and RNA-based organisms in the fecal matter in association with AIDS. The striking finding of so many RNA viruses to go along with DNA viruses opens up the broader issue of whether we need to rethink how we study the genomes of microorganisms that may affect disease," says senior author Dr. Herbert Virgin, of the Washington University School of Medicine, in Saint Louis.

In addition to providing new information on how AIDS advances, and therefore how to potentially intervene to slow it down, the results indicate that the viruses found in AIDS patients’ intestines could indicate how progressive their disease will be.

Journal Reference:
High-dose multivitamins have no benefit for patients starting HIV treatment but cause serious liver disturbances

Michael Carter
Published: 17 October 2012

Taking high-dose multivitamins has no health benefits for patients starting antiretroviral therapy, but causes serious disturbances in liver function, according to the results of a large randomised trial published in the Journal of the American Medical Association.

The study was stopped early after interim results showed that high-dose multivitamins were associated with a more than five-fold increase in ALT levels, a key marker of liver function. The interim results also showed that multivitamins did not reduce the risk of HIV disease progression or improve CD4 cell count or viral load.

The double-blind study involved over 3418 patients starting HIV therapy in Tanzania. The patients were randomised to take either high-dose multivitamins or standard dose multivitamins.

“We found that high-dose multivitamin supplementation provided no benefit to patients with HIV initiating HAART [highly active antiretroviral therapy] compared with standard-dose multivitamin supplementation,” comment the authors. “The study was stopped early due to an increase in the risk of ALT elevations with high-dose multivitamin supplementation.”

Results of previous studies had shown that treatment with high-dose multivitamins reduced the risk of HIV disease progression and death in patients who were not taking antiretroviral therapy.

Since then, access to antiretrovirals has increased in resource-limited settings, but the risks and benefits of high-dose multivitamins for individuals taking HIV therapy are far from clear.

Investigators therefore designed a study involving patients who were initiating HIV treatment in Tanzania. Recruitment took place between late 2006 and late 2008. The study was intended to last 24 months.

Patients were randomised to receive either a high-dose multivitamin or a standard dose vitamin supplementation. The high-dose supplement contained between two and 21 times the recommended daily intake of B vitamins, twice the recommended dose of vitamin E and six times the daily allowance of vitamin C.

The investigators compared rates of HIV disease progression and death between the two study arms; changes in CD4 cell count and viral load; the risk of blood disorders such as anaemia and neutropenia; and changes in liver function.

Patients had been followed for a median of 15 months when the study was stopped early in March 2009. At this point there had been 2374 HIV progression events and 453 deaths.

Rates of disease progression and death were identical between the patients taking the high-dose supplements and those taking standard dose multivitamins (72% vs. 72%).

There was no difference between the two treatment groups in terms of all-cause mortality (13% vs. 13%) or AIDS-related mortality (4% vs. 4%).

In a subsidiary analysis the investigators looked at the impact of multivitamin dose on the outcomes of the most severely malnourished patients (body mass index below 16). They found that high-dose multivitamins were associated with a modest increase in the risk of death compared with standard dose supplements (38% vs. 28%).

Changes in CD4 cell count and viral load were similar between the high-dose and standard treatment, and therapy with high-dose supplements had no impact on the risk of anaemia.

The only benefit associated with high-dose multivitamin therapy was a 19% reduction in the risk of neutropenia (IRR = 0.81; 95% CI, 0.70-0.94).

However, high-dose therapy was associated with serious safety issues.

An increase in ALT levels of five or more times the upper limit of normal was observed in 38% of patients receiving high-dose supplements compared to just 2% of patients taking standard dose treatment. This finding, coupled with the lack of any benefit from high-dose treatment, led to the study being stopped early.

Although the provision of high-dose vitamin supplements has been safe among patients infected with HIV not receiving HAART, safety cannot be presumed in the context of potent combination therapies due to the potential negative interactions among nutrients and antiretrovirals,” comment the authors. “In the absence of clear evidence of the benefit of high-dose micronutrient supplementation on morbidity and mortality in adults receiving HAART, it is prudent to follow current recommendations to promote and support dietary intake of micronutrients at recommended daily levels.”
Cidofovir cream an effective and safe treatment for high-grade pre-cancerous HPV lesions

Michael Carter
Published: 17 October 2012
Topical cidofovir cream had a 50% efficacy for the treatment of high-grade pre-cancerous anal and vulvar lesions in HIV-positive people, US investigators report in the online edition of AIDS. The small study involved 33 patients who received up to six two-week courses of treatment.

Human papillomavirus (HPV)-associated cancers of the anus and vulva are more common in HIV-positive people than the general population.

High-grade pre-cancerous lesions are the precursors to invasive anal and cervical cancer. They are difficult to treat and have a high rate of recurrence.

Cidofovir is currently licenced for the treatment of cytomegalovirus (CMV). It also has activity against HPV. A number of small studies involving HIV-positive people have shown that cidofovir is an effective therapy for genital warts and has a generally mild side-effect profile. But little is known about the safety and efficacy of cidofovir cream for the treatment of high-grade pre-cancerous lesions of the anus and vulva in HIV-positive people.

US investigators therefore designed a prospective, open-label study involving 24 men and nine women (eight who also had lesions of the vulva). The participants had biopsy-proven high-grade lesions measuring at least 3 cm².

The participants were instructed to apply the study cream sparingly in a thin layer over the affected area with a gloved finger once daily and to wash the cream off six to eight hours later. Individuals received up to six two-week cycles of treatment. Treatment response was evaluated after each treatment cycle.

Response was defined as:
- Complete response – absence of any high-grade lesions.
- Partial response – no new lesions and a 50% or greater decrease in lesion area.
- Stable disease.
- Disease progression – a 25% or greater increase in lesion size or the development of anal or cervical cancer.

The participants were enrolled between February 2008 and August 2009. Their median age was 44 and 97% were taking antiretroviral therapy. The median CD4 cell count was 412 cells/mm³ and median viral load was below 75 copies/ml. Average lesion size on enrolment was 6.6 cm².

A total of 26 people completed the study. Four were lost to follow-up, two withdrew because of mild side-effects, and one person was excluded as biopsy results showed that he did not have high-grade lesions.

In the intention-to-treat analysis (comprising those who had completed the study as per protocol), 15% had a complete response and 36% had a partial response. Disease remained stable in 21% of individuals and 6% experienced disease progression with one participant developing anal cancer.

“The diagnosis of cancer in one of our participants is concerning, and may represent an occult lesion that was present prior to treatment and not sampled by biopsy,” comment the investigators. “It could also be the failure of the study agent to prevent progression of the precancerous lesion.”

All but one participant (97%) reported side-effects. These were generally mild and consisted of irritation, burning or ulceration at the site of treatment.

The authors were encouraged by their results and conclude: “Phase 3 trials should be conducted with more prolonged treatment courses and longer follow-up to assess the durability of response.”

Reference

Chelsea Clinton in Nigeria to Promote Program Distributing Zinc, Oral Rehydration Solutions

"Chelsea Clinton is taking on the discomforting issue of diarrhea, throwing her family's philanthropic heft behind a sweeping effort in Nigeria to prevent the deaths of one million mothers and children each year from preventable causes, including 100,000 deaths from diarrhea," Reuters reports. "The 32-year-old..."
daughter of President Bill Clinton and Secretary of State Hillary Rodham Clinton joined Nigerian officials, the prime minister of Norway and other leaders on Tuesday in promoting expanded access to zinc and oral rehydration solutions or ORS, a treatment that could prevent more than 90 percent of diarrhea-related deaths in the country," the news agency writes (Steenhuysen, 10/17).

The program is coordinated by the Clinton Health Access Initiative (CHAI), which "estimates making [ORS] tablets available to children could help prevent as many as 220,000 child deaths a year in Nigeria," the Associated Press notes (10/16). "A range of companies and organizations have signed on to the effort," Agence France-Presse adds (10/16). "It is unconscionable that in the 21st century, children still die of diarrhea," Clinton, who serves on the board of CHAI, said in an exclusive interview with Reuters, the news agency reports (10/17).

**Trial Results Of First New TB Vaccine Candidate In 90 Years Expected Next Year**

"Researchers will find out early next year whether the first new vaccine against tuberculosis [TB] for 90 years protects against a disease that was once neglected but is now resurgent worldwide," Financial Times reports. Helen McShane, professor of vaccinology at Oxford University, said on Monday that clinical trial results of the MVA85A vaccine—developed in her laboratory over 10 years at a cost of £30 million [$48 million]—would be known in the first quarter of 2013," the newspaper writes (Cookson, 10/15). "Today, most babies in the world are immunized with the old Bacille Calmette-Guerin (BCG) vaccine, first used in 1921," PlusNews/IRIN writes. "Oxford's vaccine, known as MVA85A, is designed to boost the effects of BCG," the news service adds (10/16).

"MVA85A is the most advanced of a dozen TB vaccines being developed around the world, as governments and charities increase investment in the fight against a disease estimated to have killed 1.45 million people in 2010," according to the Financial Times (10/16). "After decades of neglect, the world is seeing a flurry of activity around the development of new TB vaccines, reflecting increased interest and funding from donors such as the Bill & Melinda Gates Foundation and the British and Dutch governments," PlusNews notes (10/16). "Increasingly concerned over the rise of drug resistant tuberculosis, [experts] in the field have long insisted that success in tackling the resurgence of the illness will depend on access to a better vaccine," BMJ writes (Watts, 10/16).

**NPR Examines Efforts To Eradicate Polio In Nigeria**

NPR's "Shots" blog reports on efforts to eradicate polio in Nigeria. "[N]orthern Nigeria is the only place in the world where polio cases are increasing," the blog writes, noting, "As of Sept. 1, it had recorded 90 polio cases in 2012—or nearly three times as many as in the same period last year." The blog highlights the city of Kano in northern Nigeria, which "has been called the 'epicenter' of the current polio outbreak," and where "remnants of the paralyzing disease are visible even on its streets." "Vaccination campaigns are regular fixtures here," the blog writes, adding, "In the past few years, religious leaders in this region have gone from opposing vaccination to requiring it."

"This new-found zeal from Muslim leaders has helped overcome resistance to the vaccine, but there's still a major problem of kids falling through the cracks during immunization drives," the blog continues, noting, "The local ministry of health is attempting to address this by restructuring the campaigns" so that volunteers are paid a small stipend each month to "mak[e] sure every child under the age of five in their particular neighborhood, village or slum gets the vaccine." The blog discusses other challenges—such as security, poor sanitation, and a lack of organization—and states that "the main strategy for fighting polio in northern Nigeria is to do more of everything: more surveillance, more staff and more vaccinations; and launch an all-out offensive until the virus has nowhere left to hide." A link to an audio version of the story from NPR's "Morning Edition" also is available (Beaubien, 10/16).
Hard evidence grows for including meditation in government-sponsored health programs

More people still die from cardiovascular disease than any other illness. Dubbed the number one killer and the silent killer, modern medicine has been researching and incorporating complementary and alternative approaches to help treat and in some cases reverse and hopefully prevent this health problem at an earlier stage of the disease. One of those modalities is meditation.

A new research review paper on the effects of the stress-reducing Transcendental Meditation (TM) technique on the prevention and treatment of heart disease among youth and adults provides the hard evidence needed to include such evidence-based alternative approaches into private- and government-sponsored wellness programs aimed at preventing and treating cardiovascular disease. The paper, "Prevention and Treatment of Cardiovascular Disease in Adolescents and Adults through the Transcendental Meditation® Program: A Research Review Update" is published in Current Hypertension Reviews, 2012, Vol. 8, No. 3.

- In teens, the TM technique has been found to reduce blood pressure, improve heart structure and improve school behavior. According to the paper, the technique has been shown to be a safe alternative. The NIH-sponsored clinical trials conducted with TM mentioned in this review did not observe any adverse effects from TM practice.

- In adults the technique reduced stress hormones and other physiological measures of stress and produced more rapid recovery from stress, decreased blood pressure and use of blood pressure medication, decreased heart pain in angina patients, cleared the arteries, reducing the risk of stroke, improved distance walked in patients with congestive heart failure, and decreased alcohol and tobacco use, anxiety, depression, and medical care usage and expenditures. The technique also decreased risk of death from heart disease, cancer, and all causes.

"These findings have important implications for inclusion of the Transcendental Meditation program in medical efforts to prevent and treat cardiovascular disease," says Dr. Vernon Barnes, lead author and research scientist at Georgia Health Sciences University, in Augusta, Georgia.

"This review is potentially more important than individual research papers because it shows that TM has an integrated, holistic effect on all levels of cardiovascular disease," says co-author, Dr. David Orme-Johnson.

Orme-Johnson says that no other meditation technique has been shown to produce this constellation of changes, especially when it comes to hard measures of cardiovascular disease.
Dr. Barnes said it was important to start preventing heart disease with adolescents before the disease sets. "Adding Transcendental Meditation at a young age could prevent future cardiovascular disease and save many lives, not to mention reduce the national medical bill by billions of dollars."

**Uniqueness of the Transcendental Meditation technique**

The uniqueness of the outcomes of the TM technique may have something to do with the mechanics of the practice of the technique itself says Dr. Barnes. "Meditation practices are different from each other and therefore produce different results. And this is a very important consideration when evaluating the application of meditation as an alternative and complementary medical approach."

A paper in *Consciousness and Cognition* discusses three categories to organize and better understand meditation. See *Are all meditation techniques the same?*

The two common categories are focused attention, concentrating on an object or an emotion, like compassion; and open monitoring, being mindful of one's breath or thoughts, either contemplating the meaning of them, or just observing them.

**Transcendental Meditation** uses a different approach and comes under the third category of automatic self-transcending, meditations that transcend their own activity.

The TM technique does not employ any active form of concentration or contemplation, but allows the mind to effortlessly experience the thought process at more refined levels until thinking comes to a quiet settled state without any mental activity. The mind is awake inside and the body is resting deeply, a level of rest much deeper than deep sleep. It is this state of restful alertness that allows the body to make the necessary repairs to rebalance its normal functioning. This cumulative process resets the physiology and shows up as reduced symptoms of cardiovascular disease and improved health.

**New malaria drug requires just one dose and appears twice as effective as existing regimen**

Scientists are reporting development of a new malaria drug that, in laboratory tests, has been twice as effective as the best current medicine against this global scourge and may fight off the disease with one dose, instead of the multiple doses that people often fail to take. A report on the drug appears in ACS' *Journal of Medicinal Chemistry*.

Gary Posner and colleagues explain that malaria continues to kill almost 1 million people annually. The best existing treatment is so-called artemisinin combination therapy (ACT). It requires patients to take pills every day for several days, and many patients fail to complete the regimen. As a result, these patients don't get better, and it opens the door for malaria parasites to develop resistance to ACT. To stop that from happening, the researchers developed a new type of ACT that could stop malaria in a single dose.

They describe a series of new compounds they developed that, given once, are more effective than traditional artemisinin-derived substances. One of the new compounds, when combined with mefloquine, killed off all of the parasites in some mice with just a single oral dose and allowed those mice to live almost twice as long as those treated with conventional ACT.

**Epigenetic Difference in Twins Explains Different Risk of Breast Cancer**

*ScienceDaily* (Oct. 17, 2012) — It can be detected an epigenetic alteration associated with an increased risk of breast cancer in the sick twin a few years before the clinical diagnosis.

Monozygotic twins have the same genome, that is, the same DNA molecule in both siblings. Despite being genetically identical, both twins may have different diseases at different times. This phenomenon is called "twin discordance." But how can people who have the same genetic sequence present different pathologies and at different ages? The explanation partly lies in the fact that the chemical signals added in the DNA to "switch off" or "switch on" genes can be different. These signals are known as epigenetic marks.

The research team led by Manel Esteller, director of the Cancer Epigenetics and Biology Program at the Bellvitge Biomedical Research Institute (IDIBELL), Professor of Genetics at the University of Barcelona and ICREA researcher, has identified an epigenetic change in the twin who will develop breast cancer but not in the healthy one. The finding has been advanced this week in the journal *Carcinogenesis*.

The research group led by Dr. Esteller studied the levels of DNA methylation (the best known epigenetic mark) in the blood of 36 pairs of twins diagnosed with breast cancer or healthy. Researchers analyzed half a million pieces of the genome in each twin and compared them with each other, and they found that women who have developed breast tumours showed a pathological gain of methylation in the
DOK7 gene. "an epigenetic alteration associated with an increased risk of breast cancer can be detected in the sick twin a few years before the clinical diagnosis," said Dr. Esteller about the research results.

The next step for the researchers will be knowing the exact function of the DOK7 gene. "We believe it is a regulator of tyrosine kinases, an antitumor drug target already used for the treatment of breast cancer. If DOK7 performs this function, new studies to test drugs with tumour chemopreventive effects in breast cancer could be planned in the future," concludes the research coordinator.

Journal Reference:

**Study Questions Feasibility of Entire Genome Sequencing in Minutes**
ScienceDaily (Oct. 17, 2012) — The claim that nanopore technology is on the verge of making DNA analysis so fast and cheap that a person’s entire genome could be sequenced in just minutes and at a fraction of the cost of available commercial methods, has resulted in overwhelming academic, industrial, and global interest. But a review by Northeastern University physicist Meni Wanunu, published in a special issue on nanopore sequencing in *Physics of Life Reviews,* questions whether the remaining technical hurdles can be overcome to create a workable, easily produced commercial device.

Earlier this year Oxford Nanopore Technologies, one of the pioneering companies of sequencing discoveries, announced that they expect nanopore strand sequencing to achieve a 15-minute genome by 2014 at a cost of $1,500. This is a far cry from the $10 million it cost to sequence an entire genome just 5 years ago.

Since the idea of nanopore sequencing was first proposed in the mid 1990s, huge advances have been made. The basic idea is exceedingly simple: a single thread of DNA is passed through a tiny molecule-sized hole—or nanopore—and the various DNA bases are identified in sequence as they move through the pore.

But according to Wanunu, the reality of manipulating technology based on pores so tiny that 25,000 of them can fit side by side on a human hair has proved a daunting task. The main challenge has been to slow the process down and control the movement of the DNA strand through the pore at a rate slow enough to make individual DNA bases readable and usable. A new approach using enzyme-controlled movement, developed to overcome this problem, has its own drawbacks including poor enzyme activity resulting in limited processivity and uncontrolled forward-reverse motion.

Another major dilemma has been whether protein or solid-state pores provide the most promising technique. At first, naturally occurring porous proteins were investigated. But in the early 2000s, heralded as offering better capability and flexibility, various solid-state nanopores made of silicon or graphene were tested. "Since both lipid-embedded protein channels and solid-state nanopores have drawbacks, it will be interesting to see which device, or what combination of devices, will be available in years to come, if any," Wanunu says.

At this time there are still many hurdles to overcome, he adds, including the inability of nanopores to provide any spectroscopic information about the identity of a molecule, uncertainties about whether translocation occurs at a constant speed, and the complications of pore clogging.

Writing in a comment published in the same issue, John Kasianowicz from the National Institute of Standards and Technology in the US, a pioneer in the field, agrees that plenty of challenges remain: "There are indeed still many problems to address in order to enable practical electronic nanopore-based sensing devices. However, by better understanding the road already developed in this nascent field, the journey will hopefully appear a little less daunting."

In a final comment on Wanunu’s review, the founder and Director of Oxford Nanopore, Hagan Bayley, looks ahead to the future: "In the longer term, by using solid-state pores... it may be possible to read DNA sequences at microseconds rather than milliseconds per base. This could be done by using tunnelling currents or other characteristics of the DNA bases for which graphene—with its unusual electronic properties—might after additional development provide a superior substrate and in so doing deliver another massive leap forward on top of a decade of unprecedented progress."

Journal References:
Examining How Issue Of Abortion Portrayed In Kenyan Constitution

In an opinion piece in the Huffington Post’s "Global Motherhood" blog, David Olson, a global health communications consultant who worked as a communications adviser to the Reproductive Health and Rights Alliance in Kenya earlier this year, describes how "abortion rights [in the country] have been liberalized in certain cases in a Constitution approved in a public referendum two years ago." He continues, "The new constitution says clearly that 'the life of a person begins at conception' and 'abortion is not permitted unless...‘" Olson writes, "And that innocuous 'unless' is what keeps the abortion issue alive in Kenya, almost two years after the constitutional referendum: '...unless, in the opinion of a trained health professional, there is need for emergency treatment, or the life or health of the mother is in danger, or if permitted by any other written law.'"

Olson says "[a]bortion opponents say that those loopholes are tantamount to making abortion available 'on demand,'" while "[a]bortion-rights advocates say it's not abortion on demand at all, and that these reasonable exemptions will save the lives of thousands of Kenyan girls and women who would otherwise be exposed to dangerous, back street abortions." He notes Kenya’s high maternal mortality rate, saying "unsafe abortions account for anywhere from 30 percent to 50 percent of those deaths," and he adds that "60 percent of costs incurred by public hospitals go to treating probable unsafe abortions." With presidential elections scheduled for early 2013, "no one really knows how the outcome of that will affect the abortion issue," he writes, adding, "Parliament is expected to enact legislation to implement the intent of the Constitution." Olson concludes, "One thing is clear: The 2010 Constitution is here to stay and unlikely to be changed. So the Kenyan people—including those who support and oppose abortion—are going to have to find a way to live with it" (10/17).

Rethinking toxic proteins on the cellular level

Lipid droplets play an unexpected role in embryo development

Histones are proteins needed to assemble DNA molecules into chromosomes. They have long represented a classic balancing act in biology; too few histone molecules result in DNA damage, while too many histones are toxic to the cell. New research at the University of Rochester is causing a fundamental shift in the concept of histone balance and the mechanism behind it.

Previous studies of Drosophila embryos showed massive amounts of histones located on lipid droplets, the structures associated with fat storage. While it had been speculated that the lipid droplets provide a place for safe, temporary storage of the histones, scientists had no clear proof for this storage idea nor did they understand how the histones attached to the surface of the droplets.

"What we discovered is that the lipid droplets serve as a holding space, making the histones available for the formation of chromosomes at the precise time they're needed," said Associate Professor of Biology Michael Welte. "We also found that when there are no lipid droplet-bound histones in the embryo, there are problems with the structure of chromosomes that can lead to death."

Welte and his research team were able to come to these conclusions by identifying the protein called "Jabba" as the specific molecule that anchors histones onto the surface of the lipid droplets.

"Jabba" is the specific molecule that anchors histones onto the surface of the lipid droplets. The other scientists on the research team were Zhihuan Li in Rochester, and Katharina Thiel, Peter Thul, Mathias Beller and Ronald Kühnlein in Germany. Their work will be published next month in the journal Current Biology.

Histones not bound to DNA have long been considered toxic, prompting them to be destroyed by the cells. Welte’s work demonstrates that binding to lipid droplets protects the histones, while storing them for later use in chromosome assembly.

Since there is evidence that histones and other proteins are associated with lipid droplets in a variety of organisms, including humans, Welte believes there may be medical relevance in the future.

"We've shown that lipid droplets have a function beyond fat metabolism, and it raises the possibility that, in some cases, fat storage may be beneficial," said Welte. "Additional lipid droplets may allow more toxic proteins to be sequestered, thus protecting the organism."

The next step for Welte and his lab is to determine how Jabba attaches the histones to the lipid droplets and how the binding is regulated. Welte also wants to know if proteins other than histones are being sequestered on the droplets for future use by the Drosophila embryo.
Researchers Elucidate Transport Pathway of Immune System Substances

To transport substances from the site of their production to their destination, the body needs a sophisticated transport and sorting system. Various receptors in and on the cells recognize certain molecules, pack them and ensure that they are transported to the right place. One of these receptors is Sortilin. It is present in the cells of the nervous system, the liver, and the immune system. Studies by Stefanie Herda and Dr. Armin Rehm (Max Delbrück Center for Molecular Medicine, MDC, Berlin-Buch and Charité–Universitätsmedizin Berlin) and the immunologist Dr. Uta Höpken (MDC) have now shown that the receptor Sortilin plays an important role in the function of the immune system (*Immunity*, doi: 10.1016/j.immuni.2012.07.012)*.

In the search for diseases, the T cells of the immune system go on patrol throughout the body. If they encounter a cell infected by viruses, they bind to it and secrete substances that ensure that the target cell dies. One of these substances is granzyme A, which penetrates the infected cell and induces programmed cell death. In addition, the immune cells secrete interferon-gamma, which induces the surrounding cells to have a stronger immune response.

**Interferon-gamma** is produced by cytotoxic T cells (formerly: T killer cells), T helper cells and natural killer cells. It enhances the activity of immune cells and induces other cells of the body to increasingly present fragments of the pathogen on their surface so that the T cells can find the affected cells more easily. **To facilitate the transport of interferon-gamma from the interior of the T cell where it is produced to the cell membrane where it can be released, the cell uses its interior processing and transport system, to which the Golgi apparatus belongs.**

If one were to imagine the Golgi apparatus as a post office, **Sortilin’s task is to wrap the interferon-gamma cargo into these packages and navigate them to their destination.** Without Sortilin, however, the packages cannot be delivered and remain in the post office, that is in the Golgi apparatus. Correspondingly, in the serum, i.e. outside of the cell, too little interferon-gamma is present. Thus, lack of interferon-gamma is not caused by diminished production, but rather by reduced or abrogated transport activity, eventually preventing the interferon-gamma from reaching its destination. This in turn leads to a weakened immune defense system since the interferon can only exert its immune-stimulating effect when it is released from the immune cells.

While the transport of interferon-gamma is disturbed in the absence of Sortilin, the transport of granzyme A, which destroys diseased cells directly, is more effective. Granzyme A uses another transport pathway, which is dependent on a multi-part receptor complex. This complex includes the molecule VAMP7. Together with its binding partners, this molecule ensures that transport packages containing granzyme A as part of its cargo reach their correct address in the cell. The work of the researchers led by Dr. Rehm suggests that Sortilin has an indirect influence on VAMP7 by promoting transport routes that lead to the degradation of VAMP7. In cells lacking Sortilin the researchers were able to detect increased VAMP7. This condition allowed for a more efficient transport and therefore an increased release of granzyme A.

Accordingly, Sortilin influences two different transport pathways for key immunological effector molecules in an opposite manner. Without Sortilin, less interferon-gamma is available, instead there is an increased level of granzyme A. But the increased concentration of granzyme A cannot compensate for the interferon gamma deficiency. In the experiment, the immune system of mice in which the researchers had deactivated Sortilin was significantly weaker and the fight against viruses and bacteria was less effective. The advantage for these animals, however, was that autoimmune diseases – that is, diseases in which one’s own immune system reacts against the body – were much less pronounced.

*The sorting receptor Sortilin exhibits a dual function in exocytic trafficking of interferon-γ and granzyme A in T cells.*

Researchers Unveil 3-D Structure of 'Molecular Machine' That Initiates DNA Transcription

ScienceDaily (Oct. 18, 2012) — A team of Rutgers University scientists led by Richard H. Ebright and Eddy Arnold has determined the three-dimensional structure of the transcription initiation complex, the key intermediate in the process by which cells read out genetic information in DNA.
In a paper to be published in Science and released online in Science Express, the Rutgers scientists show how the “molecular machine” responsible for transcription initiation—a protein complex that consists of the enzyme RNA polymerase and the initiation factor sigma—recognizes a specific site on DNA preceding a gene, binds to DNA, unwinds the DNA helix, and pre-organizes the unwound DNA to enable subsequent reactions.

"Determining the structure of a functional, specific transcription initiation complex has been a goal of researchers for three decades," said Ebright, a professor in the Department of Chemistry and Chemical Biology at Rutgers, a laboratory director at the Waksman Institute of Microbiology at Rutgers, and an investigator of the Howard Hughes Medical Institute.

The structure determined by the Rutgers researchers is the structure of a transcription initiation complex from a bacterium. The structure provides a foundation for understanding bacterial transcription initiation and transcriptional regulation and provides a starting point for developing new antibacterial agents that function by inhibiting bacterial transcription. Because the transcription machineries in bacteria and higher organisms are structurally and mechanistically related, the structure also provides a framework for understanding transcription and transcriptional regulation in higher organisms, including humans.

The structure defines the interactions that RNA polymerase and sigma make with the DNA site for transcription initiation, known as the "promoter." In particular, the structure defines interactions with a segment of the promoter that RNA polymerase and sigma unwind to form single-stranded DNA (the "transcription bubble") and specific DNA sequences that RNA polymerase and sigma recognize and bind to within this segment of the promoter (the "-10 element," the "discriminator element," and a new DNA sequence identified in this work, the "core recognition element").

The structure shows that a first part of sigma recognizes the -10 element through contacts with single-stranded DNA that entail the unstacking and insertion of DNA bases of the -10 element into pockets. A second part of sigma recognizes the discriminator element through contacts with single-stranded DNA that entail the unstacking and insertion of a DNA base of the discriminator element into a pocket. A third part of sigma contacts the other strand of DNA and pre-organizes it to serve as the template for RNA synthesis. Finally, RNA polymerase recognizes the core recognition element through contacts with single-stranded DNA, unstacking and inserting a DNA base into a pocket.

"This study represents a very significant contribution to our understanding of the workings of this central macromolecular machine of gene expression," said Peter von Hippel, professor of biophysical chemistry and molecular biology at the University of Oregon, who was not part of the study. "A particular significance of this work is the very systematic way the researchers built nucleic acid scaffolds bound to various nucleic acid and protein complexes involved in the various steps of initiation and were able to show in detail how the sigma initiation factor interacts with the various individual nucleotide residues involved in the recognition of the important elements of the promoter."

The research was funded by the National Institute of General Medical Sciences and the National Institutes for Allergy and Infectious Diseases, both part of the National Institutes of Health.

**Journal Reference:**
Yu Zhang, Yu Feng, Sujoy Chatterjee, Steve Tuske, Mary X. Ho, Eddy Arnold, and Richard H. Ebright. Structural Basis of Transcription Initiation. Science, 2012; DOI: [10.1126/science.1227786](http://dx.doi.org/10.1126/science.1227786)

**What We Know and Don't Know About Fungal Meningitis Outbreak ***

ScienceDaily (Oct. 18, 2012) — In a new perspective piece being published Online First tonight in Annals of Internal Medicine, a physician recalls lessons learned from treating patients affected by the 2002 outbreak of Exophiala (Wangiella) dermatitidis meningitis or arthritis related to contaminated, injectable corticosteroids prepared from a compounding pharmacy.

According to the author, the lessons he learned in 2002 are applicable to the current outbreak. He warns that compounding of preservative-free corticosteroids requires meticulous sterility to ensure lack of fungal contamination. Without this sterility, fungus grows aggressively.

As seen with the current cases, once injected, the fungus can travel through the body's tissues rapidly, leading to invasive mycosis. However, the incubation period from exposure to disease could be up to six months, so exposed patients will need to be followed for a long time. While there were many people exposed to the fungus in 2002, all but one fatal case were successfully treated with voriconazole.

Treatment decisions should be made on a case-by-case basis, but the author writes that evidence from the previous outbreak suggests voriconazole as the logical antifungal drug for initial treatment. Due to the aggressive and deadly nature of the disease, it is important for physicians to act decisively and early.
The author warns that these outbreaks will happen again if pharmacy societies, the FDA, and the pharmaceutical industry do not work together to regulate pharmacy compounding.

**Journal Reference:**
John R. Perfect. *Iatrogenic Fungal Meningitis: Tragedy Repeated*. Annals of Internal Medicine, 2012; [link]

**Non-infected Babies Born To HIV Mothers Have Decreased Resistance For Measles**

**Editor's Choice**

**Article Date: 19 Oct 2012 – 0:00 PDT**

Newborns without the HIV virus who have infected mothers need to be vaccinated immediately against measles, a new study says, in order to prevent the obtained and transmission of the virus.

This study, published in Acta Paediatrica, has found that despite being born without HIV, babies born to infected mothers still have weakened protection against measles due to their mother's positive HIV status.

Dr Lars Smedman from the Department of Pediatrics at Karolinska University Hospital, Stockholm, Sweden, says:

"The eradication of measles is high on the agendas of the World Health Organization and other international agencies and it is important to define and target any new group of susceptible infants."

Measles is one of the leading causes of death among young children, according to the World Health Organization. Problems associated with this extremely contagious disease include:

- blindness
- bacterial pneumonia
- ear infections
- severe diarrhea
- dehydration

In 2010, 139,300 deaths were reported globally, which is roughly 380 per day, or 15 an hour. Before universal immunization, an estimated 2.6 million deaths per year were recorded in 1980.

Since 2000, immunizations have risen by 72 percent, and in 2010, by their first birthday, 85 percent of children around the world had at least one dose of a measles vaccine.

Dr. Smedman and his team compared blood serum samples from 10 babies, ranging in age from one to four months, who were born to HIV mothers, but had not contracted the infection, to 10 healthy babies with non infected mothers.

The mothers, who spanned from 25 to 35 years old, were all immigrants from Kenya, Thailand, Ethiopia, Uganda, and Ivory Coast. Their CD4 cell counts ranged from 237 to 754, and their viral loads ranged from under 20 up to 8,870.

Of these mothers, nine gave birth by planned or emergency caesarean, with just one vaginal birth. The gestational age of the babies spanned from 32 to 41 weeks.

Dr. Smedman explains: "We used a new cell ELISA technique to demonstrate how the serum samples drawn from the infants would inactivate the measles virus. This found statistically significant differences between the maternal antibodies received by the two sets of babies and showed that the non-infected babies born to HIV positive mothers had weaker protection. This was because the antibodies normally produced by the mother to help protect her baby from measles had lost their sharp edge due to her HIV positive status."

The conclusions suggest that babies born to HIV mothers would not have the capability to neutralize the measles virus as successfully, resulting in loss of protection at a higher rate than babies born to healthy mothers.

This puts this population of babies at a significantly higher risk of contracting and passing the measles virus, making their immunizations essential.

**Zimbabwe: HIV Prevalence in Donated Blood Down**

*allAfrica*, (10.17.2012)

In Zimbabwe, the prevalence of HIV in donated blood has decreased over the past years from a high of 2 percent of the collected blood to a low of 0.7 percent, according to Zamile Musekiwa, a finance and administration manager with the National Blood Services Zimbabwe. Speaking at a function held at NBSZ in Harare recently, Musekiwa said the prevalence of HIV in donated blood has been decreasing over the years. According to 2011 statistics, only 0.7 percent of the collected blood was HIV positive. He stated that blood collections have fluctuated over the same years. "Zimbabwe had about 75,000 units in 1995, but dropped to about 42,000 in 2009. Collections have picked up again between 2010 and 2011 to over 80,000 units," reports Musekiwa. Screening is done on all donated blood for STDs, including HIV and AIDS, but consumption of blood at hospitals is lower than before because of the inadequate infrastructure and low budgets for purchasing blood products at the hospitals.
An estimated 40 percent of blood products are provided to women following complications of birth; 35 percent are used in surgery and trauma; and 25 percent are used in other medical care and pediatrics. Musekiwa stated that fees charged by the organization for a pint of blood were below production costs. He added that it costs about US $128 to produce a pint of blood, but it is sold for US $50 to government institutions. Some subsidies are provided from the government and other donors, but they do not adequately cover the recurrent and capital expenditures, stated Musekiwa. Government institutions pay US $50 for a pint of blood, mission hospitals US $65, while private institutions pay US $105. "With this financial crisis, our capacity to introduce new technology so as to improve blood products and safety is limited. Debtors are also unable to pay and a ‘stop supply service’ is not the first choice," Musekiwa said.

**Studies target high rates of HIV medication errors among hospitalized patients**

Findings among the research featured at first IDWeek conference

San Diego, CA (October 19, 2012) – Research presented at IDWeek 2012™ concludes that despite advances in electronic medical records, mistakes are still commonly made in the prescription of antiretroviral medications for hospitalized HIV-positive patients. At the same time, a trio of studies suggests however, that electronic records in combination with increased clinical education can help to greatly decrease medical errors.

The three studies are among the significant research being discussed at the inaugural IDWeek meeting, taking place through Sunday October 21 in San Diego. With the theme Advancing Science, Improving Care, IDWeek will feature the latest science and bench-to-bedside approaches in prevention, diagnosis, treatment, and epidemiology of infectious diseases, including HIV, across the lifespan. More than 1,500 abstracts from national and international scientists will be highlighted over five days.

"Treatment of HIV infection is complex, involving the administration of multiple drugs that often have the potential for major interactions," noted Joel E. Gallant, MD, IDWeek chair for the HIV Medicine Association. "Hospitalized patients are at risk for serious medication errors, especially when drugs are added or changed by physicians without HIV expertise. These studies emphasize the critical importance of electronic medical records and early expert consultation in hospitalized HIV-infected patients to prevent dangerous and costly medication errors."

Antiretroviral therapy, or HAART, combines three to four powerful drugs to prevent HIV resistance. These drugs can cause toxicity and serious side effects and improper administration can also lead to decreased efficacy.

Two studies featured at IDWeek describe the challenges that hospitals face in ensuring that patients infected with HIV are not put at risk of treatment failure or drug toxicity through dosage, timing and/or other errors with these medications.

In one study, researchers at the Cleveland Clinic looked retrospectively at the charts for 162 admissions of HIV patients over a 10-month period in 2011. The rate of prescription errors in their HAART regimens was 50 percent, and two-thirds of those mistakes were not identified and resolved before the patients were discharged.

Lead researcher Elizabeth Neuner, PharmD, an infectious disease clinical pharmacist at the clinic, points to the changing nature of HIV care as one explanation. Many hospital physicians are less familiar with HAART regimens because so much HIV care is now administered in outpatient settings, she said. "The number and complexity of medications used to treat HIV and an unfamiliarity with seeing patients with these medications can lead to errors," Neuner said.

Since the study, the Cleveland Clinic has implemented numerous quality improvement measures, including increased education about potential drug interactions with antiretroviral medications and greater coordination of care between inpatient and outpatient settings. The clinic also added dosing and frequency alerts to its electronic medical records system.

Similar error rates were seen over an 18-month period by the University of Chicago Medical Center. Researchers in this second study reviewed 155 HAART regimens, which had been evaluated within 24 hours of the patients’ admission. Nearly half of the initial hospital-prescribed HAART regimens required intervention, most typically so that dosages could be modified.

Lead researcher Natasha Pettit, PharmD, a clinical pharmacy specialist with University of Chicago Medicine, suggests that teaching hospitals could have high error rates in part because their medical and pharmacy residents do not have much experience with HIV drugs early in their training. "A first-year resident may not know the nuances related to administering these medications appropriately," she said.
"Data indicate that hospitals need to provide additional educational trainings and create innovative ways to catch and prevent these errors," Pettit added. The University of Chicago Medical Center responded to the findings by developing dosing cards with cautions on drug interactions, timing recommendations and other safety points. They are planning a more detailed evaluation as a step toward modifying HAART medication order entry in their electronic records system.

A third study in Michigan looked at the impact on medication mistakes when an HIV outpatient clinic worked to actively maintain patients' antiretroviral prescriptions in a major hospital's electronic records system. The result: The error rate plunged—by 93 percent—among clinic patients who were later admitted to the hospital.

The approach required extensive preparation by Special Immunology Services, the HIV clinic at Saint Mary's Health Care. Although the two are affiliated, their electronic medical records systems don't communicate, and the drug records of nearly 900 clinic patients had to be individually uploaded and then continually updated in the hospital system. Through much of 2010, meetings followed with emergency room physicians. Educational notices went out through various hospital communications to other physicians, nurses, and other departments.

"It resulted in better care for our patients when they were hospitalized," said lead researcher Jean Lee, PharmD, a clinical pharmacist for HIV medicine at Special Immunology Services. In addition, based on a sample of 20 HIV-positive patients, the researchers found that the direct cost of medication errors fell by 85 percent. "We demonstrated that we can improve patient safety and show a financial benefit," said Lee.

**Using human stool to treat C. diff is safe, effective**

DETROIT – A novel therapy that uses donated human stool to treat the deadly and contagious *C. diff* infection is safe and highly effective, according to a Henry Ford Hospital study. Researchers found that 43 of 49 patients recovered swiftly after treatment and had no adverse complications from *C. diff* three months later. Treatment is performed either through a nasogastric tube or colonoscopy on an outpatient or inpatient basis.

Mayur Ramesh, M.D., a Henry Ford Infectious Diseases physician and senior author of the study, says the treatment, while appearing unconventional, has striking results.

"More than 90 percent of the patients in our study were cured of their *C. diff* infection," says Dr. Ramesh. "This treatment is a viable option for patients who are not responding to conventional treatment and who want to avoid surgery."

The study is being presented Friday at the annual Infectious Diseases Society of America meeting in San Diego.

In their study, researchers evaluated 49 patients who contracted *Clostridium difficile*, or *C. diff*, a germ that causes diarrhea and other intestinal problems and is linked to 14,000 deaths annually. Symptoms include water diarrhea, fever, loss of appetite, nausea and abdominal pain and tenderness. *C. diff* occurs in patients taking antibiotics, and can spread from person-to-person contact or from touching contaminated equipment and objects like doorknobs.

Patients with a *C. diff* infection are typically treated with the antibiotics metronidazole or vancomycin. However, surgery could be required to remove the infected part of the intestines. In its study, Henry Ford treated patients between May 2010 and June 2012 with a therapy called intestinal microbiota transplantation (IMT), using donated stool from a healthy family member.

Dr. Ramesh says the healthy stool, when mixed with warm tap water and administered, helps to re-establish the normal intestinal flora in the patient's gastrointestinal tract. Intestinal flora is healthy bacteria that stimulates the immune system and aids the digestion and absorption of food.

"Patients who receive treatment through a nasogastric tube don't taste or smell the stool mixture as it's administered," Dr. Ramesh says. "Patients often resume their diet within a couple hours and are feeling better within 24 hours."

Of the 49 patients, 43 fully recovered, four died of causes unrelated to *C. diff*, one had intestinal surgery and one had no improvement.

**Cholera discovery could revolutionize antibiotic delivery ****

October 19, 2012

Three Simon Fraser University scientists are among six researchers who've made a discovery that could help revolutionize antibiotic treatment of deadly bacteria.
Lisa Craig, Christopher Ford and Subramaniapillai Kolappan, SFU researchers in molecular biology and biochemistry, have explained how Vibrio cholerae became a deadly pathogen thousands of years ago.

V. cholerae causes the diarrheal disease cholera, which is endemic in many developing countries and can emerge in regions devastated by war and natural disasters. An outbreak following the 2010 earthquake in Haiti has killed at least 7,500 people.

Two genes within V. cholerae’s genome make it toxic and deadly. The bacterium acquired these genes when a viral or bacteriophage called CTX-phi infected it.

The SFU researchers and their colleagues at the University of Oslo and Harvard Medical School propose that a Trojan horse-like mechanism within V. cholerae enabled CTX-phi to invade it.

The CTX-phi latches onto a long, hair-like pilus filament floating on the surface of V. cholerae. The filament then retracts, pulling the toxin-gene-carrying CTX-phi inside the bacterium where it binds to TolA, a protein in the bacterial wall.

The process transforms V. cholerae into a deadly human pathogen.

The Journal of Biological Chemistry has just published a paper written by the researchers describing the atomic structures of the CTX-phi protein pIII alone and bound to V. cholerae TolA.

The authors recommend that pilus filaments be explored further as a transport mechanism to deliver antibiotics into a bacterium.

“We’d be exploiting the pilus retraction mechanism to introduce antibiotics directly into a cell, bypassing its outer membrane barrier,” explains Craig. The SFU associate professor is an expert on the role that pili play in bacterial infections.

“We do have antibiotics for V. cholerae, but these antibiotics also kill beneficial bacteria in the gut. The idea of using pili as a Trojan horse for antibiotic delivery is new and allows us to specifically and effectively target a given bacterial pathogen.”

Craig says her team’s discovery of V. cholerae’s retractable pili is made all the more exciting by the simplicity of its workings. “We know that other deadly bacteria have retractable pili but it’ll be much easier to isolate how the mechanism can be used to uptake antibiotics in Vibrio cholerae.”

Craig says using pili as an antibiotic delivery mechanism to treat Pseudomonas aeruginosa, a deadly bacterial respiratory infection that hits mainly people with Cystic Fibrosis, could save many lives.

HIV Evolves Vulnerability ****

In mutating to evade immune detection, HIV becomes susceptible to detection by different antibodies, suggesting new strategies for vaccination.

By Sabrina Richards | October 22, 2012

In response to the initial flood of antibodies the immune system releases upon infection with HIV, the virus shifts the location of sugar groups on its envelope protein to evade detection. But in doing so, the virus creates new glycosylation patterns that can be recognized by different antibodies, which appear to target a much broader range of viruses.

The research, published Sunday (October 21) in Nature Medicine, suggests that focusing on eliciting antibodies with a wide range of different specificities, to both acute and chronic viruses, may be a promising strategy for vaccination.

special,” eliciting the most broadly neutralizing antibodies, but the new work challenges this assumption, explained Hanneke Schuitemaker, an immunologist at the University of Amsterdam who did not participate in the research.

HIV is an especially tricky virus for vaccine developers. Many important viral proteins that could be targeted by antibodies, regions known as epitopes, are often hidden—and thereby protected from immune detection—until HIV binds to CD4-expressing target cells, including T lymphocytes and macrophages. Furthermore, HIV’s rapidly mutating genome allows it to evade immune attack by changing its appearance, preventing recognition by initially effective antibodies.

But sometimes the immune system is successful in generating antibodies that block HIV binding and infection of CD4-expressing cells. Understanding what epitopes the immune system targets to generate
such broadly cross-neutralizing responses is a promising area of inquiry by researchers hoping to develop a vaccine against the virus. The most potent class of known broadly cross-neutralizing antibodies recognizes a particular glycan sugar, found at position 332 on the gp120 envelope glycoprotein that facilitates viral entry into cells by binding CD4.

To investigate the evolution of HIV and the antibody responses against it, Penny Moore and Lynn Morris at South Africa’s National Institute for Communicable Diseases of the National Health Laboratory Service tracked the antibody titers of HIV-1-C-infected women. The scientists noticed that as time passed, more patients began expressing broadly cross-neutralizing antibody responses.

Two women, who had high levels of viral replication, produced antibodies that neutralized viruses glycosylated at 332. But the viruses that had first infected the women had no sugar group at 332.

“We were astonished,” said Moore. The infecting viruses were not glycosylated at position 332, but the immune system began making antibodies to target that epitope. The answer, it turned out, had to do with viruses that arose later in infection, which did express this sugar group. About a year into infection, all viruses were glycosylated at 332, at which point the broadly neutralizing antibodies were found at high levels in the blood.

The timing of this switch suggests that viral escape from the first wave of antibodies, which target epitopes found on the initially infecting viruses, had led HIV to carry the glycan group that is susceptible to the broadly cross-neutralizing antibodies. To test this hypothesis, Moore and colleagues combined antibodies generated during acute infection with viruses expressing the 332 glycan epitope. Sure enough, the antibodies were unable to block cell entry, supporting the idea that evolving this epitope enables HIV to avoid the initial wave of antibodies generated in response to infection.

Widening her scope to almost 70 patients, Moore found the pattern—the appearance of glycosylation at 332 only later in infection—repeated in nearly a third of infections. Though rare in viruses establishing infections, glycosylation at this residue is common in viruses from chronically infected individuals, helping to explain how antibodies that target this epitope often neutralize viruses from many different patients.

“This is the first time we’ve really understood that viral evolution itself shapes the antibodies that come out,” said Moore. “Being able to work out the pattern of viral evolution will help us think about designing vaccines,” she added. One strategy that may prove successful could be to provide sequential immunizations with vaccines containing different epitopes, “mimicking what happens naturally” as the viruses evolve, she speculated.

It’s unclear, however, why viruses that initially establish infections tend to not to be glycosylated at this position, but vaccine developers may still have success using this epitope in combination with others, said David Montefiori, a viral immunologist at Duke University who did not participate in the study.

Another lingering question is how new epitopes generate different antibodies, said Schuitemaker—specifically, whether the broadly neutralizing antibodies are produced by the same B lymphocytes that responded to the initial infection, or by different B cells only called into action after the viruses have switched epitopes. “If they’re different B cells, maybe a vaccine could trigger them immediately,” rather than waiting for the virus to evolve, said Schuitemaker.

Of course, it won’t be easy to find the perfect vaccine strategy amongst the constantly shifting interplay between B cells and viruses for vaccine development. “It really blew my mind—how incredibly dynamic the whole system is,” said Moore.


A Parasite’s Parasites

French scientists identify a new giant virus, which carries the genome of a smaller virus and a new breed of mobile DNA.

By Ed Yong | October 15, 2012

In the contact lens fluid of a French woman with inflamed eyes, scientists have discovered several new parasites, nested inside one another like Russian dolls.

Bernard La Scola and Christelle Desnues from the CNRS in France found that the fluid was contaminated with an amoeba infected by a new giant virus, which they called Lentille virus. Inside that, they found a virophage—a virus that can only replicate in cells infected by another virus—which they called Sputnik 2. Deeper still, they found tiny chunks of parasitic DNA, which they called transpovirons, that can hop around Lentille virus genomes and stow away inside Sputnik 2. They published their results today (October 15) in the Proceedings of the National Academy of Sciences.
Lentille belongs to a group of giant viruses called Mimiviridae. First discovered in 2003, new members have been rapidly added to the family tree ever since. “This story again reveals another aspect of the remarkable complexity and diversity of giant viruses,” said Curtis Suttle, a virologist from the University of British Columbia who was not involved in the study.

Sputnik 2 is the fourth known virophage. La Scola and Desnues found the first—Sputnik—in 2008, under similar circumstances. It infected a giant virus called mamavirus, which infected an amoeba found in dirty water from a Parisian cooling tower. Mamavirus copies itself by creating large viral factories inside the amoeba, and Sputnik replicates by hijacking these factories at the giant virus’s expense.

Two more virophages were found in giant viruses last year—Mavirus, discovered by Suttle, and OLV, found in an Antarctic Lake by Ricardo Cavichioli from the University of New South Wales.

Of the virophages found so far, however, Sputnik 2 holds a important distinction: it can insert its DNA into its host’s genome, just as other viruses such as HIV and herpes, insert their DNA into the genomes of infected animals.

Jean-Michel Claverie, also at the CNRS but not involved in this study, says that this discovery could explain why different giant viruses often carry similar genes. By fusing with the genomes of their hosts and hopping out again, virophages could act as “vehicles for gene transfer between these giant viruses,” he said.

The team also looked “in the trash,” said team leader Didier Raoult, examining DNA fragments found inside the giant viruses did not seem to be a part of the Lentille virus or Sputnik 2 genomes. In doing so, they found an independent stretch of DNA inside Lentille virus that outnumbers the giant virus’s own DNA by as much as 14 times and can insert itself into the virus’s genome or stay outside of it. Mobile pieces of DNA have been found in giant viruses before, but Raoult saw this as a new type, one with similarities to the transposons that jump in and out of the genomes of living cells. The researchers dubbed the new mobile element a transpoviron.

The transpovirons seem to rely on the giant virus to replicate, and while the details are unclear, these sequences are very good at reproducing. When Lentille virus first infects the amoeba, the transpovirons are “produced like mad” according to Raoult, at an earlier stage and to a greater extent than the genes of either the virophage or virus. They can also stow away inside Sputnik 2, and Raoult thinks that they may ride from one giant virus to another aboard virophages.

The transpovirons seem to be a mish-mash of DNA from many sources. They contain between six to eight genes, including some that look to have come from giant viruses, others that are similar to virophage genes, and at least one that may have come from bacteria.

The same is true for virophages themselves. Sputnik’s tiny genome contains genes that look like they came from giant viruses, bacteria, or eukaryotic cells. Mavirus has genes that look like jumping genes called “Maverick transposons,” which are also found in eukaryotic cells, including those in humans. These eukaryotic Maverick sequences may evolved from virophages. Since virophages hamper the replication of giant viruses, Suttle suspects that early cells might have protected themselves from such viruses by incorporating virophages into their own genomes, effectively domesticating them.

Raoult suspects that many more virophages and transpovirons await discovery. “Very few people work on giant viruses, and [transpovirons] may have been neglected as they are unexpected,” he said. His team has already found more such elements in the genomes of three other giant viruses.

Suttle agrees. “The natural viral world encompasses the greatest genetic and biological diversity on Earth,” he said. “Its continued exploration will undoubtedly unlock many more secrets that fundamentally change our understanding of the evolution and diversity of life on our planet.”


Comment

Curculio, October 16, 2012
The term virophage will not stand the test of time. Phage is derived from the Greek -phagei- to eat, a concept easily seen in bacteriophages when they literally explode a cell. This aspect doesn’t work for these viruses as they have more in common with inquiline social parasites than they do with bacteriophages. Even then the analogy is rough so I would suggest a new class of parasitism for them. They hinder reproduction of their vector host, which limits their own ability to move. They do so by promoting their own growth at the expense of both the primary cell host and the vector host. I would call them Virovenivici, which is a virus that came and conquered. This term is alliterative and emphasizes both essential aspects of its life history with the mimivirus and its cell host: travelling (veni) and dominance over both cell and vector host (vici). Yes, this would be a Greek-Latin hybrid term but remember, we live in the age of multiculturism.

cyberдрев, October 17, 2012
This is an exciting discovery. It will lead to new models on the origin and evolution of life. It provides support to the idea the NCLD viruses evolved from archaea like cells that became parasites. Likewise the virophages evolved from earlier parasitic cells and their mobile genetic elements (transvirus) may represent the early forms of replicative genetic elements that arose before the
evolution of these cells. These developments will give us a better understanding of how cells evolved. My synthesis of some of these discoveries is discussed here http://www.telemedical.com/prokaryoticevolution.htm.

**SIV and the Expanding Viome**
Monkeys infected with simian immunodeficiency virus have a higher diversity of gut viruses, pointing to a possible role of the virome in SIV pathogenesis.

By Sabrina Richards  |  October 11, 2012

J.M.Garg. Pathogenic infection with simian immunodeficiency virus (SIV), a relative of HIV that infects non-human primates, is associated with increased diversity of gastrointestinal virus species in rhesus macaques, according to findings published today (October 11) in *Cell*. Though previous work has implicated intestinal bacteria in stimulating chronic inflammation, which is believed to promote progression from HIV or SIV infection to AIDS, the new findings suggest that gut viruses may also play a role.

“This elegant study takes [the role of the gut microbiome] to another level, suggesting the idea that these viruses could be opportunistic infections in the gut of these monkeys,” said microbiologist Donald Sodora, at the Seattle Biomedical Research Institute, who did not participate in the study. In turn, the immune response caused by these viral infections could then fuel the progression of SIV to AIDS.

Some monkey species can be infected with SIV without acquiring full-blown AIDS, while others routinely contract the disease. One difference between these primates appears to be their immune response, with those that develop AIDS showing signs of immune hyperactivation, such as higher levels of inflammatory chemokines and cytokines and activated T cells. This suggests that such excessive inflammation is an important factor in progression to AIDS, possibly because it increases the number of cells vulnerable to HIV and SIV infection. These viruses “love to infect activated CD4 T cells,” which are generated by this immune hyperactivation, explained Sodora. Opportunistic infections that arise as immunocompetence fades are thought to then perpetuate the cycle of immune activation that supports continued and worsening SIV or HIV infection.

Previous work has investigated the influence of gut bacteria in exacerbating inflammation and promoting AIDS, but the role of viruses have been relatively understudied, said immunologist Larissa Thackray of the Washington University School of Medicine. The gastrointestinal viromes of the species generally used as SIV models—rhesus macaques, sooty mangabees, and African green monkeys—are not well described in healthy animals, let alone immunocompromised individuals, she added.

In order to examine the virome of pathogenic and non-pathogenic SIV infections, Thackray and her colleagues turned to rhesus macaques, which succumb to AIDS as a result of SIV infection, and African green monkeys, which regularly resist the disease. Using next-generation RNA and DNA sequencing, the team searched for viral sequences in the guts of both infected and non-infected monkeys, and found that SIV-infected rhesus macaques, some of which succumbed to AIDS during the study, showed an expanded repertoire of gastrointestinal viruses. SIV-infected green monkeys, which remained healthy, and all uninfected animals showed no viral changes. The results point to the importance of virome composition in inflammation and the progression to AIDS.

However, the new data do not show whether carrying SIV leads to new viral infections, or whether immunosuppression as a result of being SIV-infected allows viruses previously present at undetectable levels to replicate to high levels, acknowledged Thackray. Thus, it’s not yet clear whether the viruses are triggering chronic immune system activation and thereby promoting pathogenesis, or merely taking advantage of a compromised immune system. Future research should probe these possibilities, as well as test human patients to see if HIV infection also correlates with virome changes.

The research also uncovered more than 30 previously undescribed virus species—and this is probably an underestimation. Some types of viruses were so diverse that “we just stopped counting,” said Thackray. Pathologist Guido Silvestri at Emory University, who was not involved in the study, is excited by the number of newly identified species. “In terms of viruses, we're just scratching the surface, because they're difficult to isolate with conventional methods,” he said. “We thought most viruses are pathogenic, but that's probably just a small minority.” Using new sequencing technologies, scientists “are finding viruses everywhere,” he added.

These same advancing technologies will also allow researchers to better discern the role of viruses in the progression of SIV, and possibly HIV, to AIDS, noted Thackray. These new methods “will give the power to tease out some relationship of components of the metagenome.”

Cracking Down on Vaccinations

A handful of US states are enacting laws that make it harder for parents to opt out of vaccinating their children against infectious diseases.

By Bob Grant | October 9, 2012

State legislatures across the US are trying to increase the number of children who receive vaccinations against disease by enacting laws that make opting out of those shots tougher for parents. California, Vermont, and Washington—states that allow parents to decline scheduled vaccinations for their children for personal or philosophical reasons—require parents opting out to provide proof that a health-care practitioner or representative of the state’s health department gave them scientific information about the risks and benefits of those vaccinations. State lawmakers in New Jersey and Arizona have floated ideas for similar legislation.

Even in the face of recent outbreaks of whooping cough and other diseases, vaccine exemption rates are rising across the nation. An average of 1.5 percent of US children entering kindergarten in 2010-2011 had an exemption, and rates in some states are even higher. “There really is a problem when you don’t have herd immunity so that you can stop the infectious diseases,” Washington Senator Karen Keiser (D) told Nature. The problem risks becoming worse in states, such as Kansas, Mississippi, Massachusetts, South Dakota, and West Virginia, that have recently tried to enact laws that permit philosophical exemptions. But states that have strengthened exemption requirements are already seeing positive results. Washington, for example, has seen kindergarten exemption rates drop to 4.5 percent this year from 6 percent last year.

Viral load will be no defence against prosecution for HIV exposure or transmission in Norway

Gus Cairns
Published: 20 October 2012

HIV campaigners reacted with dismay today to the issuing of a report by a Norwegian Commission on HIV and the Law which, while making one significant concession in the shape of allowing condom use as a defence, in some other ways strengthens the options the state has to prosecute individuals who infect, or expose others to, HIV.

Until now individuals were prosecuted in Norway under a 1902 law intended to be used against people who negligently or deliberately spread contagious diseases such as tuberculosis (TB) but which has, in practice, only ever been used in cases involving HIV, and only since 1991, apart from one isolated case in the 1930s.

A coalition of HIV activists had campaigned for the law to be revised, hoping that an examination of the law would lead to it restricting HIV transmission prosecutions to clearly deliberate ones or at least only to transmission rather than exposure, as has happened in some other countries such as The Netherlands and Denmark – which suspended prosecutions under its own criminal code last year. The occasion to do this was prompted by a revision of the 1902 act, the legislative framework for which was voted through in 2005.

In the event the document produced by the 12-person commission will make it easier rather than more difficult to prosecute cases of HIV transmission or exposure.

The commission’s report are only recommendations, but given that all recommendations were endorsed by a minimum nine-to-two majority, considerable pressure will be needed to change them.

By an eleven-to-one majority, the commission rejected one proposal, which was to abolish disease-specific legislation and to use the general law on assault, as is the case in the UK.

They specifically reject this as making prosecutions for HIV transmission or exposure too difficult, as Norway’s assault legislation requires proof of intent – and because it would make it too difficult to prosecute people who have behaved towards others “in a blameworthy, extremely indifferent or reckless manner.” In short, they wish to make it clear that the prosecution is for bad moral behaviour as much as it is for its effects.

The Commission also makes a clearer distinction between the “spread of disease” and the “transmission of disease” – the former applying to contagious diseases like flu and the latter largely to sexually transmitted diseases.

The most significant disappointment is that, by a nine-to-two majority, the commission decided to retain a criminal offence of HIV exposure, i.e. that transmission would not be necessary in order for there
to be a crime. They give public health reasons for retaining exposure as a crime, namely that if only transmission were a crime, the law would not act as enough of a disincentive. They say: “Only by ensuring that the penal provision also covers exposure to another person to the risk of infection will it promote a change in behaviour and thereby contribute to infection control”.

The commission, on the other hand, dismisses arguments that the law might have negative effects on public health, for instance by making people afraid to test or to disclose their status, by saying: “The Commission has found little scientific evidence of the effects of criminal regulation of infection transmission and exposure”.

The commission makes one major concession in the shape of condom use, saying that no offence would be committed “When proper infection control measures (such as use of a condom in connection with sexual intercourse) have been observed.”

It also makes a fairly significant concession in saying that a single case of exposure, without transmission, would probably now not be prosecuted, wishing to allow some latitude for what it calls “slip-ups”. However single exposures would still be crimes if transmission occurred or if there were other aggravating circumstances such as direct lying about HIV status.

The commission says that the condom defence would apply regardless of other risk factors such as the HIV-positive person’s viral load. This directly contradicts the recent judgement of the Canadian Supreme Court, which said that condom use alone was not a sufficient defence against prosecution as there was still a “realistic possibility” of infection: only in cases where condoms were used and the HIV-positive person had an undetectable viral load would HIV exposure without disclosure not be regarded as a crime.

The Norwegian commission, in contradistinction to Canada, does not regard undetectable viral load even as part of a valid defence. Nearly five years after the Swiss Statement that asserted that people with stable undetectable viral loads and no sexually transmitted infections could not transmit HIV, and 15 months after the results from the HPTN 052 study, which found that HIV treatment reduced the chance of infection between heterosexuals by 96%, they assert that “The knowledge available about the risk of infection at any given time associated with an HIV-positive person under medical treatment remains too uncertain to conclude that the description of the offence in the penal provision is not met.” They say that viral undetectability may be taken into consideration during sentencing, but not during prosecution: “The probability that the risk of infection is reduced may, depending on the circumstances, be given weight during sentencing.”

It is of note that, even though Norway has a small HIV epidemic concentrated overwhelmingly in gay men, most prosecutions have been of heterosexual transmission.

Finally, the commission makes mention of disclosure. The attitude toward disclosure in Scandinavian law is unusual as it regards assaults as offences against the state – against the body politic, if you like – and not as such against the individual. Harm is harm, therefore, even if one person has consented to the risk of harm.

The 1902 law does not mention disclosure and it has never been a valid defence: transmission or exposure are still indictable offences even if the partner is fully aware their partner has HIV. The only concession in this field is that transmission or exposure are not automatically indictable offences between ‘next of kin’, meaning spouses, which has included male/male couples since Norway legalised gay marriage in 2009. Next of kin have to specifically make a complaint and therefore in theory there would not be an indictment if they do not find out their partner has HIV.

The commission, for the first time, allows for a specific defence of disclosure, but one whose practicality is questionable: it says that if a partner (which doesn’t have to be a spouse) truly consents to the risk of infection via unprotected sex, then no offence is committed – but that to avoid unprovable assertions that partners assented to this risk, says that consent would only be valid if it is witnessed by a medical professional, presumably envisaging that serodiscordant couples would choose to make a clinic appointment to do this.

Louis Gay, the Norwegian activist who is publicly fighting a prosecution for a single case of oral sex – even though he disclosed and which, ironically, might not be indictable under the proposed new legislation – simply commented: “Welcome to my world”.

Indicted in March, Louis’ trial has now been postponed because his complainant – whose HIV has been shown not to come from Louis – has left the country.

Reference
Doctors in Egypt often won’t treat HIV-AIDS patients
By Nancy A. Youssef and Amina Ismail
McClatchy Newspapers
CAIRO—As the delivery date neared for the birth of her first child, Rose was stuck between her conscience – she didn’t want to lie – and the practical necessity of giving birth to a healthy child.

Rose thought about telling her doctor that she was HIV-positive – the routine blood tests her obstetrician had ordered didn’t screen for HIV – but she knew the risk of that: When she sent a friend to pretend that she was HIV-positive and pregnant, the doctor told the friend he didn’t deliver the babies of HIV patients.

So on her delivery date, she told the doctor she was a hypochondriac and that it was important to her that the doctors take extra precautions during her delivery.

“Every pregnant woman usually feels excited and can’t wait to get her baby delivered, except me; I was panicking,” she said. “It was a horrible feeling to go to a doctor and tell him that I am not infected. I felt dishonest.”

HIV education has become an international cause throughout Africa, where the rate of infection devastated many sub-Saharan nations but is being brought under control by concerted efforts on prevention and treatment. Similar efforts, however, are largely nonexistent in North Africa and the Middle East, and AIDS activists now worry that the rise of a conservative Islamic government in Egypt, where former longtime Muslim Brotherhood member Mohammed Morsi became the country’s first democratically elected president over the summer, will make matters worse.

AIDS is still considered a disease of homosexuals and prostitutes here. Doctors are taught that it’s a foreigner’s disease, and they receive little training in how to treat such patients. Most doctors refuse to treat HIV patients or to deliver their children. Egyptian officials continue to insist that there’s no AIDS problem here; to do otherwise would force the government to confront such taboo subjects as homosexuality, safe sex and what Muslim ethics say about how to treat the ill, however the disease is contracted.

“When the government becomes more religious, they believe AIDS is a punishment from God. But being religious starts with respecting human rights,” said Noor, Rose’s husband, who contracted AIDS from a blood transfusion when he was a child. “We are not a part of the revolution. They isolated us. We did not isolate them.”

Egypt’s attitude toward AIDS and HIV can be summed up in its movie industry. There have been only three films that featured HIV patients. In the first, when a man finds out that he’s HIV-positive, he kills himself. In the second, a man kills his HIV-positive son. The third, in which the protagonist toys with publicizing her HIV status, has had limited distribution.

Rose sheepishly explained, her veiled head bowed and looking at the ground as her son tried to teach himself to walk, that when she told her best friend early on that she was HIV-positive, she never heard from her friend again. Rose and Noor, who live in a five-story walk-up apartment, live in fear that their neighbors will learn of their infections. They agreed to share their story only if their real names weren’t used.

Rose’s family doesn’t know that she’s HIV-positive or that her first husband infected her eight years ago. They don’t know that Rose and Noor met at an AIDS seminar or how miraculous it is that their two young children are HIV-negative because Rose demanded cesarean births and didn’t breastfeed.

Every day Noor and Rose spend hours educating themselves, largely through the Internet, about the disease and how to get the medicine they need, all while hiding medicine and medical records in their home lest someone discover their secret. They talk about their condition only with other HIV patients, sometimes traveling hours to private seminars where patients reassure one another that they can’t spread the virus to their loved ones through touching or through sharing glasses of water.

HIV infections are climbing in only two regions of the world: Eastern Europe and the Middle East. The United Nations estimates that as many as 570,000 people in the Middle East have HIV or AIDS, 40 percent of them women. According to the United Nations, 70 percent of the men infected are married to women, often to hide their homosexuality. In Egypt, the Ministry of Health says there are 2,700 cases, but the true number is estimated conservatively at more than four times that – and growing.

“The world is talking about the beginning of the end of AIDS. We are not,” said Wessam not el Beih, the U.N.’s AIDS country director for Egypt.

According to one survey, 57 percent of doctors here think that HIV can be transmitted through a mosquito bite, according to a footnote in a U.N. report. Many patients, unaware of the symptoms or risks,
learn only by chance that they’ve been infected, when a blood test required for a visa or a medical procedure comes back positive.

The U.N. is leading the AIDS education effort here, and there have been efforts by individuals to bring attention to the issue. Last year, it provided some funding for the $1 million film about the woman who contemplated becoming the first person to admit on television that she was HIV-positive, based on a true story. She never had the chance; she died because she could not find a doctor to perform gallbladder surgery on her.

Ehab Abdel Rahman, the director of the HIV program at the Ministry of Health, balks at the suggestion that Egypt isn’t doing enough. He notes that in a country of nearly 90 million people, the number of cases is small. Patients receive the medicine they need. Any shortage is a shipping problem, not a social one. The blame, he said, lies with patients who try to diagnose and medicate themselves.

“We always ensure there isn’t any defective or shortage of medicine. It has never happened,” Rahman said. “Our goal is to have stigma-free hospitals.”

But Omnia Kamal, a Morsi adviser on women’s issues and a member of the committee that’s charged with drawing up the country’s new constitution, offers a different view. In a nation plagued with economic programs and a litany of social issues, AIDS is not a priority, she said. There are more cases of hepatitis B and C, for example, which also need to be addressed.

“We have to start with economic issues, and then we will deal with social issues,” Kamal said. “For a proper democratic transition, you can’t start by changing everything right away.”

To be sure, there’s a connection between fixing the government and confronting social issues. Rahman said the government spent $8 million a year on AIDS prevention and medicine. But patients said they weren’t seeing the effects, and many think that the system, like most government institutions, is corrupt.

Amr Salama, the director of the movie “Asmaa,” about the woman contemplating publicly admitting that she has AIDS, had never met an HIV-positive patient when he started the project seven years ago. When he began working on the film as a 28-year-old, he feared that he’d contract the virus just by coming in contact with HIV patients.

It was on a train ride back from Alexandria, where he witnessed a furtive meeting of HIV patients, that he conceived of his film, after hearing scores of stories from people seemingly just like him, and he settled on the woman the group spoke about, who’d just died. She was an average Egyptian, a cleaner at the airport, who was forced to resign when her co-workers learned that she was HIV-positive. Before she died, despite the objections of her family, she thought about going public with her struggles.

Getting funding for the project was difficult. So was finding actors. He forced those who played HIV-positive patients to meet carriers of the virus. Those who played everyday Egyptians weren’t allowed to meet carriers, to keep them in character, he said. The government almost didn’t allow him to film a scene at the airport where Asmaa’s co-workers voted that she should resign, leaving money on the floor for her out of embarrassment over what they’d done. Even once permission was granted, Salama’s crew was allowed only limited time to film.

He rewrote the script more than 30 times, he said, the storyline evolving as he learned more about the issue. At one point, he featured a homosexual character, but he cut him out at the last minute, fearing the audience couldn’t handle it. In the film, Asmaa contracts the virus from her husband, who was infected when he was raped in prison. Through all the rewrites, the end of the movie stayed the same, Salama said: Asmaa appears on television and tells the audience, “When I die, it will be because of your illness, not mine.”

The first screening of the film was on Jan. 24, 2011, the day before the uprising here against the former regime of Hosni Mubarak began.

“Asmaa” was such a discovery for me. It was about finding a character I would have never met in real life,” Salama said. “It was about society. Society was one of the main characters of the film. It was the villain.”

The movie is hard to find here. It didn’t play at major movie houses. It isn’t part of the nation’s cinema lexicon. But Salama said he was optimistic that change was coming.

“We think if we say we have a problem it will smear the image of Egypt. If we do an awareness campaign, that means we have a problem,” Salama said. “We are in a period of self-evaluation. There is a dynamic happening. You can feel it in the air.”

So far, however, there’s no change within the medical community.

At Cairo’s Imbaba Hospital, a public facility, one doctor, Amir al Masry, said HIV patients arrived there daily. Many have treated themselves incorrectly, rendering the medication ineffective. Shortages are
only worse since Morsi was elected, Masry said: “There is no trust between the patient and the Ministry of Health. The patients accuse the ministry of stealing the money and the ministry accuses the patients of trying to draw sympathy.”

Even when HIV education reaches Egypt, the stigma is so widespread that it somehow stifles knowledge from disseminating. At Nehad Helmy’s women’s clinic, the examination room looks out to her office, where the wall is adorned with certificates of her HIV training. She first became interested as a master’s student, when no one would treat a pregnant woman who appeared at an Egyptian hospital with HIV in 1997. A hospital cleaning woman helped the woman deliver her baby, Helmy recalled, prompting her to begin studying HIV and pregnancy.

She and her husband moved to Holland, where doctors often specialize in HIV treatment. She earned one certificate after another, and she admired how patients there were treated like anyone else. Determined to bring that care to Egypt, she came home in 2009 and sought to open an AIDS clinic, but she couldn’t win government approval.

Now she’s afraid to advertise her HIV specialty for fear that no one else will visit her clinic. Instead, she treats HIV patients on the sly and sends test results to her friends in Holland for advice.

“There is no hope and no progress,” Helmy said. "Doctors think I am crazy for working on this.”

Perhaps because of that, the nation is peppered with people such as Noor, Rose and their friend Manal, who’s 34. Manal was applying for a visa to Saudi Arabia when she learned through a blood test that she was HIV-positive. When she begged her family to get tested for no reason in particular, they figured out her secret. For a time, Manal’s relatives feared that they could contract the virus just by touching her, and because of that Manal wasn’t always allowed to pick up her baby niece.

When she finally was allowed to hold the child, she moved to kiss her niece and a couple of drops of blood from a loose tooth fell out of her mouth onto the baby’s hand. Manal panicked and repeatedly scrubbed the spot, fearing that she’d spread the virus. She’s since learned more about the risks and has become a silent advocate within her home; her neighbors don’t know that she’s HIV-positive.

“People with HIV have a right to live,” she said.

Ismail is a McClatchy special correspondent.

SA antibody breakthrough ‘brings HIV vaccine closer’
by Tamar Kahn, 22 October 2012, 05:58
SOUTH African scientists have discovered how some people can make potent antibodies capable of neutralising strains of HIV, taking researchers a step closer to developing a vaccine.

A vaccine that prevents HIV infection has proven elusive for decades, partly because there are many different varieties of the rapidly evolving virus. One of the strategies scientists are exploring is how to produce a vaccine that prompts the body to make "broadly acting antibodies" that combat multiple strains of HIV.

Scientists have known for some time that about one in five people infected with HIV is capable of making these powerful antibodies after they have been infected for several years, but exactly how they arise has been a mystery.

But now a team of South African scientists has discovered that when the virus evolves to evade its host’s immune system by adding a sugar molecule to its surface, the host’s antibodies adapt to recognise the sugar in such a way they can kill nine of 10 known strains of HIV.

"We’re hoping we can use this information to develop a vaccine that prompts the body's immune system to make broadly neutralising antibodies,” said Penny Moore, lead author of a paper describing the discovery, published in the journal Nature Medicine on Sunday, and a senior scientist at the National Institute for Communicable Diseases (NICD).

The study is based on blood samples taken at regular intervals over several years from two women infected with HIV, enabling scientists to study how both the virus and the women’s antibodies have changed over time, she said.

The scientists found that a sugar molecule called a glycan, located at a specific point on the virus's outer protein coating labelled 332, prompted the immune systems of these women to make antibodies that killed 88% of HIV strains.

Unfortunately these broadly acting antibodies do not cure HIV, but they do stop it from infecting healthy cells, said Dr Moore. "They don’t help the people who develop them at all, because the virus is already established," she said.
The scientists found that the glycan at position 332 was present in about two thirds of HIV-C, the subtype circulating in Southern Africa.

This means a vaccine that targets just this glycan would be only partially effective, and suggests a vaccine would need to take aim at multiple weak points in the virus, said Dr Moore.

The study was conducted by a consortium from the Centre for Aids Programme of Research in South Africa (Caprisa), the NICD, the universities of Cape Town and KwaZulu-Natal, and the US universities of North Carolina and Harvard.

"Like all science, this study now needs to be replicated by other researchers," said consortium leader Prof Salim Abdool Karim, president of the Medical Research Council and co-director of Caprisa.

The discovery was welcomed by John Mascola, deputy director of vaccine research at the US National Institutes of Allergy and Infectious Diseases. He said: "Once we can see how (broadly neutralising antibodies) arise naturally, during infection, it becomes much more realistic to think that we can design vaccine strategies to induce similar neutralising antibodies."

Funding came from the Department of Science and Technology, the NIH, and the Bill and Melinda Gates Foundation. Prof Abdool Karim said the consortium would not patent its findings. "The knowledge we generate belongs to the world," he said.

**SOUTH AFRICA: Two women unlock possible key to HIV vaccine ****

JOHANNESBURG, 23 October 2012 (PlusNews)—Two South African women may have helped unlock the key to a vaccine to rid the world of one of its deadliest epidemics, according to new research released by South African HIV experts.

In 2005, an HIV-negative woman from the city of Durban enrolled in a study of acute HIV infection conducted by the Centre for the AIDS Programme of Research in South Africa (CAPRISA). Two years later, another HIV-negative woman in her early 20s, living in the rural township of Vulindlela, joined CAPRISA’s ground-breaking trial of the efficacy of an antiretroviral-based vaginal microbicide to prevent HIV infection.

Both women eventually contracted the virus and were placed on treatment. However, because they were part of large-scale clinical trials, researchers were able to follow them for years, discovering in the process that their bodies produce rare antibodies found in only one out of every five HIV patients, according to research published in the 21 October online edition of the journal Nature Medicine.

**Antibodies**

Everyone with HIV produces antibodies to the virus, but in most people these antibodies react only to the particular strain of HIV acquired. Wide variation in strains of HIV, caused by the virus’s ability to mutate, has been the biggest roadblock to vaccine development.

"HIV mutates incredibly fast, more so than perhaps any other virus," lead researcher Penny Moore told IRIN/PlusNews. “The virus that infects one person is very different from the virus that infects another.”

The women studied by CAPRISA, however, produced what are called “broadly neutralizing antibodies”, which can kill a wide range of HIV types across different individuals, overcoming regional variations in the virus. Antibodies taken from these women killed up to 88 percent of all types of HIV found worldwide, according to the study.

While broadly neutralizing antibodies were discovered three years ago, CAPRISA’s research is the first to uncover at least one way in which these antibodies work.

According to the study, the virus formed a layer of sugars to protect itself from the common, strain-specific antibodies of the two women. However, this layer of sugar proved to be what Moore calls the virus’s “Achilles heel.” The women were then able to produce broadly neutralizing antibodies that targeted and bonded with specific sugars, blocking the virus from infecting healthy cells.

According to CAPRISA director Salim Abdool Karim, these antibodies could be the key to developing an HIV vaccine.

“The holy grail of HIV prevention is a safe, effective HIV vaccine,” he told IRIN/PlusNews. “This discovery provides new clues on how vaccines could be designed to elicit broadly neutralizing antibodies.”

Researchers caution that a vaccine based on these antibodies is still years away and may come to consist of a series of different vaccines mimicking HIV infection, its progression and the body’s response. “[We’d want to see] if we could trick immune system to go through the same arms race it went through in these two women, without HIV infection,” Moore said.
The study was co-funded by the US government and South Africa’s Ministry of Science and Technology. While the South African government has not decided to patent this discovery, it is in the process of securing patents on CAPRISA’s tenofovir-based microbicide. If the microbicide is successful in follow-up trials, the government plans to begin local production of its active ingredient to ensure affordability and reduce dependence on foreign importers.

**A legacy**

At the Johannesburg launch of the research, South African Health Minister Aaron Motsoaledi congratulated researchers and acknowledged the women’s contributions.

“I wish to thank these women for allowing their experiences to be studied for the benefit of all us,” he told IRIN/PlusNews. “Sometimes, we forget about [study participants], but I think they are also scientists in one way or another. Without contributions like theirs, even the best idea cannot be tested.”

Unfortunately, the women’s antibodies have not delayed disease progression. One woman is doing well with HIV treatment, living with her partner and HIV-negative children in Durban. But the woman from Vulindlela died of extensively drug-resistant tuberculosis (XDR-TB) about a year ago, according to Karim, whose team hospitalized her for treatment.

XDR-TB is resistant to the most commonly used first-line TB drugs and at least half of the mostly commonly used second-line drugs. TB is the leading killer of HIV-positive people globally, and is one of South Africa’s leading causes of death.

“Such are the challenges we deal with on a daily basis in our country with HIV patients,” said Karim. “But her specimens, her virus, continue to inform our work and enable us to understand [HIV] so, in many ways, she’s left a lasting legacy.”

“Of the 34 million people living with HIV globally, two-thirds are in sub-Saharan Africa,” he added. “This is an African problem and... it’s unlikely that we’ll be able to eradicate this epidemic without a vaccine.”

**Simplifying HAART Regimen Fails to Maintain HIV-1 Viral Suppression**


A pilot study by Harold P. Katner, MD, of Mercer University School of Medicine in Macon, Ga., and colleagues assessed the durability of HIV-1 virologic suppression in persons who changed from a lopinavir/ritonavir-based triple highly active antiretroviral therapy (HAART) regimen once or twice a day to lopinavir/ritonavir monotherapy once daily. This was an observational cohort study to determine the proportion of subjects who sustained virologic suppression through the 48th week following their switch to the daily lopinavir/ritonavir monotherapy. Researchers presented the study at IDWeek 2012, a joint meeting of the Infectious Diseases Society of America (IDSA), the Society for Health and Epidemiology of America (SHEA), the HIV Medicine Association (HIVMA), and the Pediatric Infectious Diseases Society (PIDS).

A total of 13 individuals began lopinavir/ritonavir-based HAART therapy and maintained HIV-1 viral loads <75 copies/mL for 48 weeks before enrollment in the study; three failed screening—two due to elevated viral loads and one because of an inability to tolerate lopinavir/ritonavir daily. The research continued with 10 individuals, two female and six male African Americans and one male and one female Caucasian. Subjects were 27–53 years old, and the mean duration of their therapy before de-escalation was 252 weeks (105–413 weeks). Mean CD4 count at baseline was 338 cells/m³ (range 120–512 cells/m³). Subjects received frequent clinical, virologic, and immunologic monitoring.

One subject completed 48 weeks of daily lopinavir/ritonavir monotherapy and one withdrew at 22 weeks after experiencing two detectable viral loads five weeks apart. Four subjects had virologic failure, one of whom developed multiple nucleoside and protease inhibitor mutations. The study was terminated. None of the subjects reported severe adverse events.

**Migratory birds’ ticks can spread viral haemorrhagic fever**

[Published 2012-10-22]

A type of haemorrhagic fever (Crimean-Congo) that is prevalent in Africa, Asia, and the Balkans has begun to spread to new areas in southern Europe. Now Swedish researchers have shown that migratory birds carrying ticks are the possible source of contagion. The discovery is being published in the US Centers for Disease Control and Prevention journal Emerging Infectious Diseases.

[Crimean-Congo Haemorrhagic fever](https://www.cdc.gov) is a serious disease that begins with influenza-like symptoms but can develop into a very serious condition with high mortality (30%). The disease occurs in Africa, Asia,
and the Balkans but it has recently started to spread to new areas in southern Europe. It is caused by a virus that is spread by tick bites and common host animals are various small mammals and ungulates. Humans are infected by tick bites or close contact with contagious mammals.

Researchers have now studied the dissemination mechanisms of this potentially fatal disease. The study is multidisciplinary, with bird experts, tick experts, molecular biologists, virologists, and infectious disease physicians from Uppsala University and Uppsala University Hospital in collaboration with colleagues from the Swedish Institute for Communicable Disease Control, Kalmar and Linköping. Ornithologists and volunteers also helped gather birds.

During two spring seasons in 2009-2010, a total of 14 824 birds were captured at the two ornithological stations Capri (Italy) and Anticythera (Greece), on their way from Africa to Europe. A total of 747 ticks were gathered and analysed for the virus.

Some 30 different bird species were examined, and one species, the woodchat shrike, which winters in southern Africa and nests in Central Europe, proved to be a carrier of virus-infected ticks.

"This is the first time ticks infected with this virus have been found on migratory birds. This provides us with an entirely new explanation of how this disease, as well as other tick-borne diseases, has spread to new areas, where new mammal populations can be infected by the infected ticks," says Erik Salaneck, one of the authors of the study.

The Hyalomma tick, which spreads the disease, does not thrive in northern Europe, preferring warmer latitudes. But with a warmer climate, the boundary for both the tick species and the disease could move northward with the help of migratory birds.

The article will appear in print in December.


Probiotics Are Secret Weapon for Fighting Symptoms of the Common Cold in College Students, Study Suggests

ScienceDaily (Oct. 22, 2012) — College students are notoriously sleep-deprived, live in close quarters and lead stress-filled lives, making them especially susceptible for contracting colds and upper-respiratory infections. For these reasons, a team lead by researchers at the University of Medicine and Dentistry of New Jersey-School of Health Related Professions (UMDNJ-SHRP) selected this population to study the effects of probiotic supplementation on health-related quality of life (HRQL) during the common cold.

The study, led by Registered Dietitian Tracey J. Smith, an adjunct professor at UMDNJ-SHRP, randomized 198 college students aged 18 to 25 and living on-campus in residence halls at Framingham State University in Massachusetts. Groups received either a placebo (97 students) or a powder blend containing Chr. Hansen’s probiotic strains BB-12® and LGG® (101 students) for 12 weeks. Each day, students completed a survey to assess the effect of the probiotic supplementation.

Although there have been previous studies on the effect of probiotics on the duration of colds and severity of symptoms, this is the first study to investigate the effect of probiotic strains on HRQL during upper-respiratory infections, taking into account duration, symptom severity and functional impairment—all important factors of HRQL. "HRQL is subjectively assessed by the patient and most simply defined as ‘the component of overall quality of life that is determined primarily by the person’s health and that can be influenced by clinical interventions,’” Smith says.

An article detailing the results of the study was published in the October 2012 issue of the British Journal of Nutrition. "We know that certain probiotic strains support immune health and may improve health-related quality of life during upper-respiratory infections," says Smith. "This double-blind study assessed how probiotic supplementation affects the duration and severity of symptoms, and the impact of symptoms on the daily life of infected students."

The study found that while all students caught colds at roughly the same rate, the students who took the probiotic supplementation experienced:

- A duration of colds that was two days shorter (four days vs. six days)
- Symptoms that were 34% less severe and
- A higher quality of life that resulted in fewer missed school days (15 vs. 34 missed by students taking the placebo).

What makes probiotics so effective in treating symptoms of upper-respiratory infections? "Cold symptoms like a stuffy nose and sore throat are the body's inflammatory response toward a virus, not a direct action of the virus itself," explains Smith. "Probiotic microorganisms may soften your immune system's reaction by reducing your body's inflammatory response."
The Take-Away for the Public: "If cost is not an issue, then otherwise healthy persons who are especially stressed, sleep-deprived or living in close quarters [such as a college dormitory] could supplement daily during cold season with both LGG and BB12 to improve their quality of life if/when they do get a cold," says Smith. However she cautions that not all probiotics are created equal. "The study supports the combination of LGG and BB12—two very specific strains of probiotics. These two strains also are in a number of supplement-type products that are available over the counter," she says, "but consumers need to read the label to be sure that the product contains Lactobacillus rhamnosus GG [LGG] and Bifidobacterium animalis lactis BB12 [BB12]. There also are some yogurts that contain LGG and/or BB12 but check the labels, since companies change the probiotics strains often."

"People should also recognize that probiotics are not for everyone," Smith continues. "Those considering probiotic supplementation should consult with their physician first."

**Journal Reference:**
Tracey J. Smith, Diane Rigassio-Radler, Robert Denmark, Timothy Haley, Riva Touger-Decker. **Effect of Lactobacillus rhamnosus LGG® and Bifidobacterium animalis ssp. lactis BB-12® on health-related quality of life in college students affected by upper respiratory infections.** *British Journal of Nutrition, 2012;* : 1 DOI: 10.1017/S0007114512004138

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**Study to Identify Levels of Sucralose in Erie Beach Waters**
ScienceDaily (Oct. 23, 2012) — Faculty and student researchers at Mercyhurst University continue to investigate the presence of potentially harmful chemicals in the beach waters of Presque Isle State Park and have added a new one to their list: sucralose. A chlorinated form of sucrose found in artificial sweeteners, sucralose is used in an estimated 4,500 products ranging from Halloween candies to diet sodas.

Studies suggest that approximately 95 percent of ingested sucralose is not metabolized by the body and is excreted into the water supply, said Dr. Amy Parente, assistant professor of chemistry and biochemistry at Mercyhurst.

Many chlorinated compounds have been found to be toxic to humans and, while sucralose appears to have limited toxicity, the long-term effects of exposure have yet to be determined. Common practices aimed at removing contaminants from wastewater have not been shown to be successful at reducing levels of sucralose, Parente said.

Parente’s preliminary research has identified detectable levels of sucralose in local Lake Erie waters, which may pose concerns for the environment. She has received a grant from the Regional Science Consortium at the Tom Ridge Environmental Center to confirm these levels, with the ultimate goal of understanding the impact on the local aquatic ecosystem.

Sucralose in the water can have repercussions like altered water taste and biological health effects, she said. Another problem is that sucralose in the environment can provide a false signal for nutrient availability so organisms feeling that their food supply is adequate show decreased foraging behavior, which can ultimately affect their ability to survive.

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**City Leads U.S. in AIDS Cases**
*The Advocate (Baton Rouge),* (10.25.2012) Michelle Millhollon
The latest figures show the Baton Rouge metropolitan area as first and the New Orleans metropolitan area as fifth in the rate of AIDS cases in the United States. The Louisiana Commission on HIV/AIDS and Hepatitis C, which was formed to advise the governor on the viruses, met October 24, for the first time in more than two years. The commission failed to muster a quorum, but did review the grim statistics and discuss the commission’s future, specifically its role.

The statistics showed that new diagnoses of the HIV virus, which causes AIDS, are increasing in Louisiana. Also, the number of people infected is spreading from the metropolitan areas to other parts of the state. Other statistics presented: 18,502 people in Louisiana have AIDS or HIV as of June 30. Of those, 54 percent have AIDS. The number of people newly diagnosed with HIV in Louisiana increased by 12 percent from 2010 to 2011. Seventy-one percent of the newly diagnosed HIV patients were men. Seventy-four percent were black.

Some progress was made in between meetings. Louisiana succeeded in whittling down its wait list for people waiting to receive medications through the AIDS Drug Assistance Program (ADAP), due to the infusion of federal funding and the elimination of people who were not eligible. Also, the Division of Human Development and Services for Baton Rouge (DHDS) received a 6 percent increase in funding for the 2012 fiscal year, with awards increasing to $4.3 million. Raman Singh, chairman of the commission,
urged the group to meet more regularly to stop the serious problem of the large numbers of HIV/AIDs cases in Louisiana.

No More Needles! Scientists Develop Vaccine That Melts Under the Tongue


Researchers at the University of London have developed a new method for delivering vaccines directly into the bloodstream. Professor Simon Cutting of Royal Holloway, University of London, stated that instead of delivering the vaccine with a needle, vaccines based on Bacillus spores can be delivered as a nasal spray, an oral liquid or capsule, or a small soluble film placed under the tongue. Professor Cutting noted that these spores are exceptionally stable vaccines based on Bacillus and do not require cold storage, thus eliminating another issue with current vaccines. With oral vaccines, the fear of needles is no longer a deterrent to getting immunized, and the vaccine is safer to administer, particularly for countries where HIV is prevalent. Also, the vaccines will be more cost-effective to make and easier to keep fresh.

The technique was developed when researchers discovered they could use “good bacteria” to administer vaccines. Researchers found that Bacillus spores were perfect for transporting antigens, which cause the immune system to produce antibodies to protect against them. Professor Cutting has carried out trials to determine the effectiveness of Bacillus-based vaccines for diseases such as influenza, TB, and tetanus.

Fitchburg Man Gets 3 Years For Not Disclosing HIV to Sex Partners

Sentinel&Enterprise.com, (10.24.2012)

A Fitchburg, Mass., man who is HIV-positive and had unprotected sex with several partners without informing them that he was infected with the virus pled guilty to related charges and was sentenced to three years in prison on October 24. The Massachusetts man, who is now 20, was 19 when he was charged with three counts of assault and battery with a dangerous weapon and one count of statutory rape—one of his partners was only 13 years of age. According to the Fitchburg District Court documents, the statutory rape charge was reduced to indecent assault and battery on a child under 14, and one of the three charges of assault and battery with a dangerous weapon was dropped.

The Fitchburg man will spend three years in the Worcester House of Corrections, with credit given for the 199 days that he has already served during the time of his trial. After his release he will be on probation with monitoring until October 2017. Upon his release he has been ordered to stay away from his victims and cannot have any contact with children under 14. In addition he will be required to undergo counseling and submit a DNA sample to the state.

Antibiotics that only partly block protein machinery allow germs to poison themselves

Powerful antibiotics that scientists and physicians thought stop the growth of harmful bacteria by completely blocking their ability to make proteins actually allow the germs to continue producing certain proteins—which may help do them in.

The finding, by a team at the University of Illinois at Chicago College of Pharmacy, clarifies how antibiotics work and may aid in the discovery of new drugs or improve clinical therapy with existing ones. The study is published in the Oct. 26 issue of the journal Cell.

Among the most complex molecular machines in the cell are the ribosomes, responsible for churning out all the proteins a cell needs for survival. In bacteria, ribosomes are the target of many important antibiotics, says Alexander Mankin, professor and director of the UIC Center for Pharmaceutical Biotechnology, who led the study.

Mankin and his colleagues picked apart the process of protein synthesis inside the ribosome, comparing the action of the classic antibiotics erythromycin and azithromycin and newer drugs called ketolides, which are used to treat serious infections.

Surprisingly, the more powerful drugs were the more "leaky" in blocking the production of proteins. "We were shocked to discover that ketolides, which are known to be better antibiotics, allow for many more proteins to be made compared to the older, less efficient drugs," Mankin said. "We now believe that allowing cells to make some proteins could be much more damaging for a microbe than not letting it make any proteins at all."

The findings may point the way to better and more potent antibiotics, Mankin said. But he and colleagues are "thinking beyond just antibiotics."
"If a chemical can be designed that binds to the human ribosome and allows it to make good proteins but not bad ones, such as mutant enzymes or proteins that promote cancer, then such new drugs can treat many human maladies," he said.

Crime and Punishment: An International HIV Disclosure Dilemma
By Dave R.
October 25, 2012
This article originally appeared on PositiveLite.com, Canada's Online HIV Magazine. It is being reposted here in two parts.

There are times when many people outside the United States and Canada experience National Enquirer levels of disbelief at what's goes on in parts of North America in the field of sexual behavior and politics. The current criminalization of people with HIV who fail to tell their partners of their status is just such a moment in time. The sex may be safe and the viral load may be undetectable but you can still be charged with using your body and your virus as a murder or assault weapon, if you don't pre-warn that you're living with HIV.

Have lawmakers never heard of personal, sexual responsibility and the right to choose and refuse? Have thirty years of AIDS advertising been completely wasted? It appears that someone negative who has sex with someone positive will always (legally) be in the right if it comes to a dispute. Never mind that virtually everyone on the planet of sexual maturity knows by now, that the way to avoid disease is to have safe sex and the only safe way to be certain is to undergo an HIV test ten minutes before sex and even then, that person could have been infected in the last three months. After all that, they always have the choice whether to have sex or not! Of course I wouldn't include rape victims and other powerless persons; they are clearly cases apart. Yet, lawmakers in two of the supposedly most advanced and civilized societies in the world brush personal responsibility aside and automatically make the negative person the victim and the positive person the villain! Where's the balance? You could say that having HIV is the equivalent of being electronically tagged for the rest of your life as it is ... but they want to sentence you again and lock you away!

The whole subject of criminalizing people who have HIV and may or may not transmit it, is both a judicial and moral minefield. Sentences for transmission across the world range from a small fine, to life imprisonment or even worse in some countries. This shows how difficult fair legislation can be, especially when individual views and emotions clash with stigma and public health issues. However, to punish someone for having the virus; not transmitting it because of safe sex and undetectable viral loads and preferring not to tell the unharmed partner; is the world completely upside down! Exceptions to this may be those who genuinely set out to infect someone, or someone who infects through rape, or sexual assault but in the vast majority of cases this doesn't apply.

From a strictly personal point of view, it's just too jaw-dropping for words but I would hazard a guess that most people's reactions here in the Netherlands (including heterosexuals) would be ones of astonishment at the sheer unfairness of it all. Then I began to wonder if I wasn't perhaps jumping the gun with that reaction and decided to find out exactly what the legal situation here is regarding disclosure and the transmission of HIV. I also looked at other parts of the so-called First world to see if there is any form of universal consensus on the subject. Maybe knowing how other countries deal with the issue might bring some clarity? Certainly, it should highlight those administrations that are making politically influenced legal judgements, based on moral and populist sentiment, which stigmatize a single group.

It's a bit of a grey area here in the Netherlands. They work on the principle that if it isn't in the statute book, then it can't be illegal. However, there is no explicit law that either excuses HIV transmission, or finds non-disclosure not a problem. The highest judicial authority in the land (the Hoge Raad) has however, made several significant judgements since 1999 and have concluded in each case that it's practically impossible to prove intent when it comes to HIV. The Hoge Raad is quite willing to prosecute people who intentionally infect others but it finds that having HIV and keeping that information to yourself; combined with having unprotected sex is no reason at all to assume intent. Basically this means that although the police may wish to prosecute in these circumstances, it will never come to anything because the highest court in the land has ruled out any possible judicial consequences. It may sound somewhat "sitting on the fence" but it's about as pragmatic a ruling as you could find.
Believe me the ruling has been severely tested recently. In the years after 1999, a number of individuals were brought to court and prosecuted (on the grounds of attempted grievous bodily harm), only to have the cases overturned on appeal to the Hoge Raad. However, more recently the exact nature of this policy was tested when a number of barebackers in the north of the country were found to have been injecting drugged or drunken guests at parties with HIV-infected blood (an absolute exception by the way!). This was more or less conclusively proved and quite severe sentences (by Dutch standards) were issued. However, after successful appeals, parts of the case are again going to be reviewed because nobody can be certain that the "victims" hadn’t already contracted the virus through earlier, other means. They were after all, mainly seasoned party-goers. So you have a situation which highlights how shallow the North American prosecutions actually are. The defendants here had little to defend and had admitted their guilt in the face of evidence but whether they had actually infected their "victims" is almost impossible to prove, so therefore attempted murder, or grievous bodily harm becomes almost irrelevant. It's a system which looks at HIV in the most sensible and objective light possible at the highest possible levels. In 2005, the Dutch Cabinet even decided to avoid creating any law on the subject which may turn out to be unfair and unworkable in reality. So, in black and white terms, you may find someone taking you to court for infecting them with HIV but not knowing that they were positive but working through the legal system, that person will never be prosecuted without 100% proof that it was deliberately done.

Evidence of the success of pragmatism is that the HIV figures in the Netherlands are proportionately far smaller than in countries with more severe legal enforcement. It doesn’t stop here either; the teenage pregnancy figures are miniscule in comparison to the United States and drug use (and the social problems that ensue), are again proportionately a fraction of those in North America. For all those right wing political figures who see the Netherlands as the gateway to Hell and damnation; they could learn a lesson as to how pragmatic law making and social policies are not abused but social problems.

However (and this is a major point) these liberal policies based on common sense and fairness cannot be hijacked by future populist political leaders because the Netherlands always has a coalition government in power. The Christian democrats and other religious parties may not be happy about certain relaxations and what their instincts tell them are "immoralities" regarding sex but they can’t do a damned thing about it because their views are always tempered by the other moderate middle parties in the coalition. It has been this way for a long time and will remain this way for the foreseeable future, thanks to the political structures here. It can of course also be extremely frustrating because almost everything that's promised in election manifestos gets watered down in the compromises made after getting into power. However, its greatest advantage is that extremist views can never gain the upper hand. That word again; pragmatism! It has resulted in this country being one of the most relaxed about things people enjoy in life and one of the most socially balanced in the world. A large Islamic and therefore by nature, unbending population may affect things in the future but for now, the Netherlands is still one of the best places to be HIV positive in the world.

In France, the situation is fairly similar to that of the Netherlands in that there are no specific laws regarding HIV transmission. However, as in most countries, there have been individual cases which have helped shape both public opinion and judicial decision-making. Like the barebackers in the north of the Netherlands; one particular case caught the public imagination in 2004. A man called Christophe Morat was sentenced to six years imprisonment for failing to disclose his status to two women, both of whom became infected. One later committed suicide and largely due to this, Morat's appeal was rejected out of hand. The other woman is now a member of an action group (Femmes Positives) determined to get the French government to create a special law allowing women to prosecute former lovers. This widened the debate in France as to whether HIV positive people could be deemed either "victims" or "perpetrators" in the eyes of the law. Equally many argued that the concept of "equal responsibility" should remain, especially with regards to contraception. For the time being, the French, like the Dutch remain pragmatic about the problem, at least in the eyes of the law.

In 2011, the Danish government suspended one of the harshest laws in Europe concerning HIV transmission. Basically, just as we’re now seeing in the States and Canada, people could be found guilty even without infection; so negligent exposure to the possibility of infection was as equally punished as direct transmission. Fortunately, a serious lobby of medical experts, legal professionals and people living with the virus were able to persuade the government to look again; largely thanks to the success of HAART and the resulting unlikelihood of infection. In 2011, the laws were suspended and a thorough enquiry based on science and not stigma was implemented.
In 2010 in Germany, a case hit the headlines and was reported all across Europe. In 2009, Nadja Benaissa, a well-known pop singer was arrested after three men accused her of not revealing her HIV status before having sex. Only one subsequently tested positive. After that, she was released without anybody being sure why but early the following year she was arrested again and charged with one count of aggravated assault and two of attempted aggravated assault. Despite the fact that infecting someone with HIV carries a prison sentence of six months to ten years, she was given a two year suspended sentence. The lenient sentence was put down to the fact that she’d confessed to having the sex and not revealing her status and had apologized profusely for the harm caused;

"In those days I was careless ... I'm sorry from the bottom of my heart," she told the court. It was also taken into account that she was only seventeen at the time and she was tried in a juvenile court. This could be seen as an example of a court respecting the rule of law but looking beyond the cold hard facts, to examine the person they were dealing with and acting accordingly.

Yet there are examples of the other side of the coin. In 2004, it was claimed that Hans-Otto Schiemann, a 56 year old German, tried to infect nearly a hundred Thai women while living in Thailand. He had a self-confessed pathological hatred of Thai women (one of whom was his wife) so a motive was easy to spot. However, because there are no laws in Thailand to prosecute unprotected sex or its consequences, he was eventually deported back to Germany for outstaying his visa! Clearly the man had psychological problems because he ended up being deported for a second time after he was discovered in Thailand again. Here's a case (without knowing all the facts and evidence) for which the law probably was found wanting. The lack of a law meant that the man almost got off scot free—it's a very delicate balance!

A New Zealand case set the tone for dealing with these cases in that land. In 2005, a New Zealander had unprotected sex with his girlfriend and didn’t disclose his status. She initially told the man’s family that she was positive but it was a lie and she remained negative. However, charges were still brought against the man, of causing mental stress and trauma and he was sentenced to 300 hours of community service, six months supervision and $1000NZ costs to cover the girl’s therapy costs. He was in the end convicted of "criminal nuisance" which covers a multitude of sins. Unfortunately for him, another girl heard of the case and tried to bring a similar case to court. However, this case was dismissed because not only did she remain negative but he’d used a condom.

Were these pragmatic court judgements; or too severe; or too lenient? It shows how subjective the whole subject can end up being. I’m sure the court thought they were being both lenient and pragmatic but had the guy even committed a crime? To my mind it’s up for discussion.

In Australia, these laws tend to be more frequently applied and are termed, criminal acts that transmit, or risk transmitting, a serious disease (including HIV) plus recklessly endangering another person's life or causing grievous bodily harm. Depending on the state in which you live, penalties can range from a maximum of ten years, to life imprisonment. Here, transmitting HIV can be considered a breaking of both public health and criminal laws, thus compounding the penalty possibilities.

The UK’s laws in this area are based on "recklessly inflicting grievous bodily harm." This charge carries a maximum prison sentence of five years but certain factors must be established:

- The defendant did in fact infect their partner.
- The defendant was aware of the risk of transmission. In theory they may not have had a positive test, but they will have "known" they were infected.
- The complainant did not explicitly give informed consent to sex with an individual they knew had HIV.
- The defendant did not take steps to protect their partner—consistent condom use is a defense.

These seem on the face of it to be as reasonable as you can find on international statute books and in fact nobody has been prosecuted for intentional grievous bodily harm using HIV as a weapon. It's considered that the burden of proof is just too difficult and it is recognized that sex is actually a pretty inefficient way of transmitting HIV if someone intended to do it.

In 2010, the police in the UK themselves issued comprehensive guidance as to how to treat this subject both fairly and with sensitivity and reckless transmission prosecutions should only go ahead if there is new infection and evidence of intent. Furthermore, if someone living with HIV is taken into custody, their medication should not be interrupted and their confidentiality should be respected (a far cry from the name and shame tactics in North America!). In short, in the UK, you can be charged with assault or grievous bodily harm only if HIV transmission has occurred; not simply if there was no disclosure, nor if there was exposure to HIV but no transmission occurring.
Recently a UK gay man went to court in just such a case but was found not guilty after the defense successfully claimed that phylogenetic analysis (the establishment of both strain and source of HIV) could not prove that the man had deliberately infected the complainant. This use of science forms the basis of the appeals in the earlier mentioned Dutch case too. This seems to encouragingly show that the British authorities are implementing their own pragmatic conclusions. It also seems that more and more legal experts are realizing that the burden of proof in HIV transmission cases is extremely difficult; especially in cases of multiple sexual contact; which has to be both fairer for people with HIV and easier for the law to deal with.

However, at least fifteen people have slipped through the system in Great Britain and been sent to jail for up to ten years, (as in the case of an asylum seeker from Malawi). One can only hope that good intentions become reality and that enlightened thinkers win the day.

As far as the United States and Canada are concerned, the HIV criminalization cases there have been well documented; leading to various degrees of outrage from LGBT and HIV groups alike. Probably the best known is the homeless man who was given thirty five years for spitting at a police officer in 2008, with his saliva being declared a "deadly weapon." This in spite of the fact that nobody has ever proved that saliva is a medium for transmitting HIV and the fact that the officer didn’t contract HIV. This case was highlighted in the same year by South African judge, Edwin Cameron, in a speech about criminal transmission at the international AIDS conference of 2008.

"It stuns the mind that someone who has actually not harmed anyone, who has not actually damaged any property (or otherwise spoiled the world), could be locked away in these circumstances for 35 years. The inference that his HIV status played a pivotal role in sending him away for so long is unavoidable. In short: the man was punished not for what he did, but for the virus he carried."

There's little more that you can politely add to that statement. The sentence was inhumane and brutal and justified on the grounds of nothing but hearsay, fear and possible political influence. It certainly had no basis in scientific fact. The fact remains that in most states of the United States, a person living with HIV can be charged and found guilty of reckless endangerment, or assault with a deadly weapon (i.e. the HIV virus) if criminal intent can be proved. Unfortunately, the fact also remains that it is far too easy to "prove" criminal intent largely on the grounds of circumstantial evidence and often pure stigmatism.

One of the worst and most cruel aspects of US state legislation is that, despite official guidelines that call for confidentiality; all states are now implementing so-called "name-based reporting" where people's personal details can be handed over to the police by their medical providers. This exposes them from day one to public scrutiny if their case comes to court. What happens when that person is removed from the system? Do his or her medical details and stigmatizing labels get expunged at the same time? I seriously doubt it—the authorities like to keep tabs on you.

In Canada, as most readers will know, it has been against the law since 1998 not to disclose your status and more than 130 people have been charged with sexual assault since that date. Canada is still the only country in the world to have convicted someone of murder for transmitting the virus and apparently, three quarters of Canadians believe someone should be imprisoned for not disclosing their HIV status. It beggars belief frankly but hopefully a few of the legal challenges that seem to be in the pipeline will be successful and bring a little sanity to the proceedings. Not only that; a successful challenge, with a clear explanation and public statement, will go some way to changing public attitudes about legal responsibility and HIV. Politicians can sway the public and vice versa but when the spiral of moral opinion and political mood and therefore legislation, shifts away from the facts, there are inevitably victims as a result.

It seems to me essential that all judicial bodies need to be made fully aware of the most up to date scientific knowledge about HIV transmission. They also need to be aware of the consequences of their legal decisions for people wondering whether to disclose or not. Furthermore, they need to know the risks of spreading the virus even further, if disclosure just becomes too dangerous for normal well-meaning people. Medical records need to be legally protected to ensure confidentiality and the police need to know exactly what they're dealing with and how many factors are involved. This is all happening in some countries but progress is still slow and when nations like the USA and Canada turn the clocks back on the basis of what is perceived as public moral outrage and convict through stigma, then the life sentence that comes with having HIV can turn into a sentence depriving you of your freedom as well.

In 2011, the Global Forum on MSM and HIV stated in their conclusions that:

**Policy makers, parliamentarians and advocates should take necessary steps to:**

1) Repeal laws that criminalize or punish consensual same-sex behaviors among adults, preferred gender identities and non-conforming gender expressions so that everyone, irrespective of sexual orientation, sexual identity, gender identity or gender expression can realize their basic health and
human rights, including access to HIV-related and other health services without fear of ridicule, blackmail, harassment, arrest or violence.

2) Repeal laws that criminalize HIV non-disclosure, exposure or transmission, which are often used as proxies for human rights abuses against gay men and other MSM and which have absolutely no public health value.

Furthermore, in July, 2012 the Global Commission on HIV and the Law recommended the following:

_To ensure an effective, sustainable response to HIV that is consistent with human rights obligations:_

2.1. Countries must not enact laws that explicitly criminalize HIV transmission, HIV exposure or failure to disclose HIV status. Where such laws exist, they are counterproductive and must be repealed. The provisions of model codes that have been advanced to support the enactment of such laws should be withdrawn and amended to conform to these recommendations.

2.2. Law enforcement authorities must not prosecute people in cases of HIV non-disclosure or exposure where no intentional or malicious HIV transmission has been proven to take place. Invoking criminal laws in cases of adult private consensual sexual activity is disproportionate and counterproductive to enhancing public health.

2.3. Countries must amend or repeal any law that explicitly or effectively criminalizes vertical transmission of HIV. While the process of review and repeal is under way, governments must place moratoria on enforcement of any such laws.

2.4. Countries may legitimately prosecute HIV transmission that was both actual and intentional, using general criminal law, but such prosecutions should be pursued with care and require a high standard of evidence and proof.

2.5. The convictions of those who have been successfully prosecuted for HIV exposure, non-disclosure and transmission must be reviewed. Such convictions must be set aside or the accused immediately released from prison with pardons or similar actions to ensure that these charges do not remain on criminal or sex offender records.

This whole issue shows how much we still have to fight for in this world and how divided the world actually is regarding attitudes to HIV. I always assumed that despite the plethora of extremist views that can exist in North America; when it came to HIV and AIDS, we could at least rely on Americans and Canadians to lead the way in enlightened thinking and scientific advance. To discover that their systems of law applying to HIV have reverted to medieval practice in order to persecute small groups of people in medical need, is a shock that undermines a great deal of trust in the world order.

Other countries in the first world are by no means perfect; after all it is a crime to expose another person to HIV, or transmit HIV to them _in over 60 nations_ but it seems that common sense and fairness play a much greater role in interpreting the law in many other lands. Actually, in the whole of the European Union, only Poland and Latvia have _specific_ laws relating to HIV disclosure and transmission. One thing I’ve learned is that a government of coalition is much less likely to be swayed by moral hysteria than the two party systems that rule much of the Western world: perhaps the Netherlands is not such a bad place to live after all!

Finally, when it comes to the great argument as to whether to disclose or not; I personally wonder if there’s not an argument for saying that HIV positive people should have the legal _right_ to remain silent and _not_ disclose if they don’t want to. The burden of responsibility should then fall on the HIV negative participant to protect him or herself. Everyone then has the choice whether to state beforehand; "yes I want you to wear a condom," or "no I don’t and I fully understand the risks." That way, more people may get tested because there’s no legal sanction if they turn out to be positive. In fact the responsibility for self-protection from HIV should be everyone’s, given the knowledge everyone now has. I somehow doubt if the statistics of HIV transmission would change one way or the other but at least people living with the virus wouldn’t be living in fear of being punished twice.

_There have been many excellent articles on this subject both here and elsewhere and if I’m repeating (or even unwittingly contradicting) things that have been said by for instance, Edwin Bernard and others on this site, please forgive me. This is a personal view on the issue from someone learning about it for the first time._

References/Further Information:

- [Risks, Rights & Health](#)
- [Specialist Submission to the Global Commission on HIV and the Law: Men Who Have Sex With Men (MSM)](#)
- [Prison for Man With HIV Who Spit on a Police Officer](#)
- [Canada: Supreme Court Makes Bad HIV Disclosure Law Worse](#)
Feinstein Institute researchers discover that bean used in Chinese food could protect against sepsis

MANHASSET, NY – Researchers at The Feinstein Institute for Medical Research have discovered that a bean commonly used in Chinese cuisine protects against the life-threatening condition sepsis. These findings are published in the current issue of Evidence-based Complementary and Alternative Medicine (eCAM).

It has been found that a deoxyribonucleic acid (DNA) protein, HMGB1, mediates inflammation. Inflammation is necessary for maintaining good health – without inflammation, wounds and infections would never heal. However, persistent and constant inflammation can damage tissue and organs, and lead to diseases such as sepsis. Sepsis affects approximately 750,000 Americans each year, 28 to 50 percent of whom die from the condition, and costs the nation’s healthcare system nearly $17 billion annually. It is a potentially life-threatening complication of an infection or injury, and occurs when chemicals released into the bloodstream to fight the infection trigger inflammation throughout the body. The result is that organs become damaged, including liver, heart, lungs, kidney, and brain. If excessive damage occurs, it may be irreversible. Therefore, it is important to identify ways in which persistent and constant inflammation can be halted.

Neutralizing the protein HMGB1 protects against persistent and constant inflammation that results in damage to tissue and organs. Haichao Wang, PhD, and his colleagues, including Shu Zhu, MD and PhD, and Andrew E. Sama, MD, at the Feinstein Institute found that extract from mung bean (Vigna radiata), a bean native to India and commonly used in Chinese food and traditional medicine, reduced the release of HMGB1, thereby increasing survival rates in mice from 29.4 percent to 70 percent (P < 0.05).

"Many traditional medicinal herbs have been successfully developed into effective therapies for various inflammatory ailments, and now we have validated the therapeutic potential of another medicinal product, mung bean extract," said Dr. Wang. "Demonstrating that mung bean extract has a positive effect on septic mice shows promise that this bean can also have a positive effect on septic humans – of course, additional studies are required to prove the safe and effective use in humans."

Influenza vaccine may reduce risk of heart disease and death

Flu shot may reduce risk of a major cardiac event by 50 percent and cardiac deaths by 40 percent

Getting a flu shot may not only protect you from getting sick, it might also prevent heart disease.

Two Toronto-based researchers presented studies at the 2012 Canadian Cardiovascular Congress which found that the influenza vaccine could be an important treatment for maintaining heart health and warding off cardiovascular events like strokes and heart attacks.

Dr. Jacob Udell, a cardiologist at Women’s College Hospital and the University of Toronto, and his team from the TIMI Study Group and Network for Innovation in Clinical Research looked at published clinical trials on this subject, dating back to the 1960s.

"For those who had the flu shot, there was a pretty strong risk reduction," says Dr. Udell. The flu vaccine provided an approximate 50 per cent reduction in the risk of a major cardiac event (heart attack, stroke, or cardiac death) compared with placebo after one year of follow-up. A similar trend was seen for the flu vaccine reducing death from any cause (approximately 40 per cent).

The influenza vaccine reduced cardiovascular events and cardiovascular death in people with or without heart disease.

The combined studies examined a total of 3,227 patients, with an almost equal split between patients with and without established heart disease. Half of the participants were randomly assigned to receive flu vaccine and those that did not typically received a placebo vaccine.

Dr. Udell says these results provide support for current guideline recommendations for influenza vaccination of individuals with a prior heart attack, but for a different reason than simply reducing flu risk. And although it was encouraging to see a reduction in non-fatal cardiac events, he believes a large, lengthier multi-national study would comprehensively demonstrate the vaccine’s effectiveness to reduce fatal cardiac events and save lives.

"A large study that was international in scope and representative of patients such as those in North America and Canada in particular could help answer this question," he says.
This research could also potentially boost use of the vaccine, which Udell believes is still woefully low. "The use of the vaccine is still much too low, less than 50 per cent of the general population; it’s even poorly used among health care workers," he says. "Imagine if this vaccine could also be a proven way to prevent heart disease."

An Ipsos Reid survey conducted by B.C. and Quebec Lung Associations this year found that 36 per cent of Canadians reported having received a flu shot in 2011.

And according to the Public Health Agency of Canada’s National Advisory Committee on Immunization (NACI), the 2008 Adult National Immunization Coverage Survey found that vaccination rates for adults 18 to 64 years of age with a chronic medical condition is low at 35 per cent.

It also found that non-institutionalized seniors aged 65 and older have higher coverage, at 66 per cent.

According to the NACI, rates for both groups have declined somewhat since their 2006 survey and fall short of the 80 per cent national targets for influenza vaccine coverage in adults under age 65 with chronic conditions and in seniors.

People with ICDS who get the shot have fewer adverse events The second study, conducted by cardiology Drs. Ramanan Kumareswaran and Sheldon Singh from Sunnybrook Health Sciences Centre examined the use of the influenza vaccine in patients with implantable cardiac defibrillators or ICDs.

"Anecdotes suggest that patients have more ICD shocks during flu season. We were trying to figure out what we can do to reduce the amount of shocks in (our clinic’s) ICD population during the flu season," says Dr. Kumareswaran.

Patients with ICDs that had appointments at the Sunnybrook Hospital ICD clinic between September 1st 2011 and November 31st 2011 completed a survey that identified their demographics, health status, if they received a flu shot in the past year and opinions towards the vaccine.

The patients’ health charts were reviewed to determine all ICD therapies in five months preceding the 2011 flu season (June to October) and for three months during the 2010-2011 flu season (December to March).

A total of 230 patients with an average age between 70 and 74 completed surveys with 179 (78 per cent) patients reported receiving the vaccination in the previous year. Just over 20 per cent did not receive the vaccine.

The patients who did not receive the flu vaccine had a trend toward experiencing more ICD therapies on average. Specifically, 10.6 per cent of patients who received the vaccine received at least one ICD therapy during flu season compared to 13.7 per cent of patients who did not receive the influenza vaccine.

"What is interesting is that if this is consistent over time, it could be of significant benefit to our patient population who already have compromised survival to start with," says Dr. Singh.

"We would like to look at this on a larger scale to determine whether or not our results can be replicated. We’re in the process to determine how best to do that.” An ICD is a small battery-powered electrical impulse generator implanted in patients who are at risk of sudden cardiac death.

The device is programmed to detect cardiac arrhythmia and correct it by delivering a jolt of electricity or increasing the heart rate to restore a healthy rhythm once an irregular beat has been detected.

About 5,000 Canadians get ICDs every year and there are about 100,000 Canadians who currently have them. (Most Canadians with advanced heart disease are potential candidates for ICDs.)

Heart and Stroke Foundation spokesperson Dr. Beth Abramson says these studies strengthen National Advisory Committee for Immunization recommendations for the use of the influenza vaccine in those at high risk of developing influenza related complications, such as patients with heart disease or diabetes, and those who have close contact with those at high risk of developing complications.

"In addition to leading a heart healthy life, having an annual flu shot could be another easy way to help prevent cardiac events," she says.

Dr. Abramson notes that the Heart and Stroke Foundation recommends an influenza vaccination for those at high risk of influenza-related complications or hospitalization (including people with heart conditions, those with diabetes, people over 65 years of age, people with a BMI at or above 40 and children or adults treated with ASA). It is also recommended for people who are most likely to transmit influenza to high risk individuals (family members, friends, coworkers, healthcare provider and caregivers).
Test developed to detect early-stage diseases with naked eye
Prototype ultra sensitive disease sensor developed

Scientists have developed a prototype ultra-sensitive sensor that would enable doctors to detect the early stages of diseases and viruses with the naked eye, according to research published today in the journal *Nature Nanotechnology*.

The team, from Imperial College London, report that their visual sensor technology is ten times more sensitive than the current gold standard methods for measuring biomarkers. These indicate the onset of diseases such as prostate cancer and infection by viruses including HIV.

The researchers say their sensor would benefit countries where sophisticated detection equipment is scarce, enabling cheaper and simpler detection and treatments for patients.

In the study, the team tested the effectiveness of the sensor by detecting a biomarker called p24 in blood samples, which indicates HIV infection.

Professor Molly Stevens, from the Departments of Materials and Bioengineering at Imperial College London, says:

"It is vital that patients get periodically tested in order to assess the success of retroviral therapies and check for new cases of infection. Unfortunately, the existing gold standard detection methods can be too expensive to be implemented in parts of the world where resources are scarce. Our approach affords for improved sensitivity, does not require sophisticated instrumentation and it is ten times cheaper, which could allow more tests to be performed for better screening of many diseases."

The researchers in today's study also tested samples for the biomarker called Prostate Specific Antigen (PSA), which is an early indicator for Prostate Cancer. The team say the sensor can also be reconfigured for other viruses and diseases where the specific biomarker is known.

The sensor works by analysing serum, derived from blood, in a disposable container. If the result is positive for p24 or PSA, there is a reaction that generates irregular clumps of nanoparticles, which give off a distinctive blue hue in a solution inside the container. If the results are negative the nanoparticles separate into ball-like shapes, creating a reddish hue. Both reactions can be easily seen by the naked eye.

The team also report that the sensor was so sensitive that it was able to detect minute levels of p24 in samples where patients had low viral loads, which could not be diagnosed using existing tests such as the Enzyme-linked Immunosorbent Assay (ELISA) test and the gold standard nucleic acid based test.

Dr Roberto de la Rica, co-author of the study from the Department of Materials at Imperial College London, adds: "We have developed a test that we hope will enable previously undetectable HIV infections and indicators of cancer to be picked up, which would mean people could be treated sooner. We also believe that this test could be significantly cheaper to administer, which could pave the way for more widespread use of HIV testing in poorer parts of the world."

The next stage of the research will see the team approaching not-for-profit global health organisations, which could provide strategic direction and funding for manufacturing and distributing the sensor to low income countries.

Mechanism found for destruction of key allergy-inducing complexes, Stanford researchers say

STANFORD, Calif. — Researchers have learned how a man-made molecule destroys complexes that induce allergic responses — a discovery that could lead to the development of highly potent, rapidly acting interventions for a host of acute allergic reactions.

The study, which will be published online Oct. 28 in *Nature*, was led by scientists at the Stanford University School of Medicine and the University of Bern, Switzerland.

The new inhibitor disarms IgE antibodies, pivotal players in acute allergies, by detaching the antibody from its partner in crime, a molecule called FcR. (Other mechanisms lead to slower-developing allergic reactions.)

"It would be an incredible intervention if you could rapidly disconnect IgE antibodies in the midst of an acute allergic response," said Ted Jardetzky, PhD, professor of structural biology and senior investigator for the study. It turns out the inhibitor used by the team does just that.

A myriad of allergens, ranging from ragweed pollen to bee venom to peanuts, can set off IgE antibodies, resulting in allergic reactions within seconds. The new inhibitor destroys the complex that tethers IgE to the cells responsible for the reaction, called mast cells. Severing this connection would be the holy grail of IgE-targeted allergy treatment.
The first time a potential allergen enters the body, some people respond by making allergen-specific IgE antibodies. These antibodies stick around long after the initial allergen is cleared from the body. Most of the antibodies get snagged by IgE-specific receptors called FcRs, which are exposed on the surface of mast cells. The mast cells are then primed to react the next time a person encounters the allergen.

Dissociation of this IgE-FcR interaction is a sought-after goal of allergy treatment for a good reason: IgE-coated mast cells are grenades of histamine, and re-encountering the allergen is equivalent to pulling out the clip. When an allergen makes a return visit, it binds to the pre-loaded IgE on the mast cell surface, triggering the release of inflammatory mediators — including histamine — that promote the allergic response. As allergy sufferers are well aware, these nasty reactions can occur within a matter of seconds. In a severe allergic response, sudden anaphylactic shock and death can be the result.

The key to actively disabling the allergic response lies in the separation of IgE from the FcRs on the surface of mast cells. But separating these dangerous couples is a tall order because their interaction is extremely stable — sensitizing the mast cells for weeks. Currently available treatment using omalizumab (an anti-IgE antibody sold under the trade name Xolair) can block new interactions between IgE and FcR, but it is not designed to pry the molecules apart once they’ve formed a bond on the surface of a mast cell. So Xolair can dampen the allergic response, but as stated on the product’s website: “Xolair is not a rescue medicine and should not be used to treat sudden asthma attacks.”

While simply blocking IgE binding is helpful for some allergy sufferers, when it comes to the rapid quenching of an acute allergic response, “what you’d really like to do is get rid of it,” said Jardetzky. Along with scientists at the University of Bern, his team discovered that an engineered protein inhibitor called DARPin E2-79 stripped IgE from the mast cell receptor. Using this inhibitor, “an interaction that normally lasts for hours or days in terms of its stability is stripped off in a matter of seconds,” said Jardetzky.

DARPin E2-79 is one of a family of engineered inhibitors containing protein-binding regions called ankyrin repeats. While Jardetzky’s group was using structural biology and biophysical approaches to probe the weak spots in the IgE-FcR interaction, scientists at the University of Bern were tinkering with DARPins that dampened IgE’s disastrous effects. The collaboration of the two groups resulted in the characterization of DARPin E2-79, an inhibitor that goes beyond mere blockade to actively disassemble the IgE-FcR power couple.

Jardetzky’s group solved E2-79’s structure and used this information to model its interaction with the IgE-FcR pair. Then, using sensitive biochemical techniques that detect step-by-step binding interactions between molecules, the teams were able to tease out the mechanism that the inhibitor uses to break the IgE-FcR bond.

The researchers found that E2-79 hastens the separation of the two molecules by taking advantage of a moment of weakness in the relationship between IgE and FcR. IgE maintains its interaction with FcR using two contact points, and occasionally one of these points releases while the other one keeps the pair together. Normally this brief looseness isn’t enough to separate the couple, but E2-79 can swoop into the small space between them, effectively driving the couple apart.

While E2-79 is the first molecule to display these IgE stripping characteristics, Jardetzky hopes that this work will stimulate the discovery of smaller compounds capable of working even more efficiently. Drug developers generally expect large macromolecules like E2-79 to be less potent than small molecule inhibitors and unlikely to be able to disrupt complexes, so the fact that E2-79 worked so well was a surprise. Small molecules are more amenable to oral administration, and are easier and cheaper to manufacture than large macromolecules. “Now we’re in the hunt for a small molecule that could have this kind of activity. That would be the real hit,” said Jardetzky.

The discovery of E2-79’s mechanism of IgE inhibition could lead to rapid discoveries from other labs as well. Now that scientists know what mechanism to look for, they may be inspired to dig back through freezers full of IgE inhibitors that were identified years ago, said Jardetzky. In the light of techniques described in this study, perhaps once-neglected inhibitors will show new promise in the treatment of allergic disease.

**Dysentery Epidemic Killed Many in the 1700s-1800s in Sweden**

ScienceDaily (Oct. 25, 2012) — In the 1700s-1800s, dysentery was a disease causing many deaths. In fact, in some areas in Sweden 90 percent of all deaths were due to dysentery during the worst outbreaks. A new doctoral thesis in history from the University of Gothenburg, Sweden, presents demographic and medical history of the disease.
Dysentery, or rödsot as it used to be called in Swedish, remains a major problem in developing countries. In the Western world, however, the disease is almost gone. Yet prior to the decline in infectious diseases among causes of death in the 1800s, Sweden was at times struck very hard by the disease, with catastrophic consequences.

'The disease had detrimental effects, but the geographical differences were significant. For example, 90 percent of all deaths in a parish could be due to dysentery in some years, while nearby parishes were left practically unaffected,' says the author of the thesis, Helene Castenbrandt.

Castenbrandt studied how the disease struck Sweden during the period 1750-1900, with a focus on changes over time as well as regional and local differences. Jönköping County was used as a case study. Besides demographic data, she also used parish registers, maps, newspapers, reports from medical district officers and other information written down by doctors.

Many historians have described dysentery as a regularly recurring and not very serious disease. Cholera and smallpox are often described as the most devastating epidemic diseases of that era. But Castenbrandt's results beg to differ.

'My study points to dysentery as very epidemic in nature. The disease struck communities extremely hard at times. It flared up quite irregularly and the patterns of transmission differed from one outbreak to the next.'

Using Jönköping County as an example, the study clearly shows the vast differences in dysentery mortality within the same county. The pattern of transmission for the three most severe outbreaks in 1773, 1808 and 1857 shows that although the disease spread across almost the entire county, there were some clusters with extremely high mortality. However, the hardest hit parts of the county varied.

The thesis also analyses the reasons behind the presence and disappearance of the disease. The results point to complex links between possible explanations such as sanitary conditions and population concentrations for example in connection with wars.

'It is likely that many factors interacted, which makes it difficult to identify one single reason why dysentery emerged and disappeared. I hope future studies will be able to explore these links,' says Castenbrandt.

Far from Random, Evolution Follows a Predictable Genetic Pattern
ScienceDaily (Oct. 25, 2012) — Evolution, often perceived as a series of random changes, might in fact be driven by a simple and repeated genetic solution to an environmental pressure that a broad range of species happen to share, according to new research.

Princeton University research published in the journal Science suggests that knowledge of a species' genes—and how certain external conditions affect the proteins encoded by those genes—could be used to determine a predictable evolutionary pattern driven by outside factors. Scientists could then pinpoint how the diversity of adaptations seen in the natural world developed even in distantly related animals.

"Is evolution predictable? To a surprising extent the answer is yes," said senior researcher Peter Andolfatto, an assistant professor in Princeton’s Department of Ecology and Evolutionary Biology and the Lewis-Sigler Institute for Integrative Genomics. He worked with lead author and postdoctoral research associate Ying Zhen, and graduate students Matthew Aardema and Molly Schumer, all from Princeton’s ecology and evolutionary biology department, as well as Edgar Medina, a biological sciences graduate student at the University of the Andes in Colombia.

The researchers carried out a survey of DNA sequences from 29 distantly related insect species, the largest sample of organisms yet examined for a single evolutionary trait. Fourteen of these species have evolved a nearly identical characteristic due to one external influence—they feed on plants that produce cardenolides, a class of steroid-like cardiotoxins that are a natural defense for plants such as milkweed and dogbane.

Though separated by 300 million years of evolution, these diverse insects—which include beetles, butterflies and aphids—experienced changes to a key protein called sodium-potassium adenosine triphosphatase, or the sodium-potassium pump, which regulates a cell's crucial sodium-to-potassium ratio. The protein in these insects eventually evolved a resistance to cardenolides, which usually cripple the protein's ability to "pump" potassium into cells and excess sodium out.

Andolfatto and his co-authors first sequenced and assembled all the expressed genes in the studied species. They used these sequences to predict how the sodium-potassium pump would be encoded in each of the species' genes based on cardenolide exposure.
Scientists using similar techniques could trace protein changes in a species' DNA to understand how many diverse organisms evolved as a result of environmental factors, Andolfatto said. "To apply this approach more generally a scientist would have to know something about the genetic underpinnings of a trait and investigate how that trait evolves in large groups of species facing a common evolutionary problem," Andolfatto said.

"For instance, the sodium-potassium pump also is a candidate gene location related to salinity tolerance," he said. "Looking at changes to this protein in the right organisms could reveal how organisms have or may respond to the increasing salinization of oceans and freshwater habitats."

Jianzhi Zhang, a University of Michigan professor of ecology and evolutionary biology, said that the Princeton-based study shows that certain traits have a limited number of molecular mechanisms, and that numerous, distinct species can share the few mechanisms there are. As a result, it is likely that a cross-section of certain organisms can provide insight into the development of other creatures, he said.

"The finding of parallel evolution in not two, but numerous herbivorous insects increases the significance of the study because such frequent parallelism is extremely unlikely to have happened simply by chance," said Zhang, who is familiar with the study but had no role in it.

"It shows that a common molecular mechanism is used by many different insects to defend themselves against the toxins in their food, suggesting that perhaps the number of potential mechanisms for achieving this goal is very limited," he said. "That many different insects independently evolved the same molecular tricks to defend themselves against the same toxin suggests that studying a small number of well-chosen model organisms can teach us a lot about other species. Yes, evolution is predictable to a certain degree."

Andolfatto and his co-authors examined the sodium-potassium pump protein because of its well-known sensitivity to cardenolides. In order to function properly in a wide variety of physiological contexts, cells must be able to control levels of potassium and sodium. Situated on the cell membrane, the protein generates a desired potassium to sodium ratio by "pumping" three sodium atoms out of the cell for every two potassium atoms it brings in.

Cardenolides disrupt the exchange of potassium and sodium, essentially shutting down the protein, Andolfatto said. The human genome contains four copies of the pump protein, and it is a candidate gene for a number of human genetic disorders, including salt-sensitive hypertension and migraines. In addition, humans have long used low doses of cardenolides medicinally for purposes such as controlling heart arrhythmia and congestive heart failure.

The Princeton researchers used the DNA microarray facility in the University's Lewis-Sigler Institute for Integrative Genomics to sequence the expression of the sodium-potassium pump protein in insect species spanning three orders: butterflies and moths (Lepidoptera); beetles and weevils (Coleoptera); and aphids, bed bugs, milkweed bugs and other sucking insects (Hemiptera).

The researchers found that the genes of cardenolide-resistant insects incorporated various mutations that allowed it to resist the toxin. During the evolutionary timeframe examined, the sodium-potassium pump of insects feeding on dogbane and milkweed underwent 33 mutations at sites known to affect sensitivity to cardenolides. These mutations often involved similar or identical amino-acid changes that reduced susceptibility to the toxin. On the other hand, the sodium-potassium pump mutated just once in insects that do not feed on these plants.

Significantly, the researchers found that multiple gene duplications occurred in the ancestors of several of the resistant species. These insects essentially wound up with one conventional sodium-potassium pump protein and one "experimental" version, Andolfatto said. In these insects, the newer, hardier versions of the sodium-potassium pump are mostly expressed in gut tissue where they are likely needed most.

"These gene duplications are an elegant solution to the problem of adapting to environmental changes," Andolfatto said. "In species with these duplicates, the organism is free to experiment with one copy while keeping the other constant, avoiding the risk that the new version of the protein will not perform its primary job as well."

The researchers' findings unify the generally separate ideas of what predominately drives genetic evolution: protein evolution, the evolution of the elements that control protein expression or gene duplication. This study shows that all three mechanisms can be used to solve the same evolutionary problem, Andolfatto said.

Central to the work is the breadth of species the researchers were able to examine using modern gene sequencing equipment, Andolfatto said.
"Historically, studying genetic evolution at this level has been conducted on just a handful of ‘model’ organisms such as fruit flies,” Andolfatto said. "Modern sequencing methods allowed us to approach evolutionary questions in a different way and come up with more comprehensive answers than had we examined one trait in any one organism.

"The power of what we've done is to survey diverse organisms facing a similar problem and find striking evidence for a limited number of possible solutions," he said. "The fact that many of these solutions are used over and over again by completely unrelated species suggests that the evolutionary path is repeatable and predictable."

**Journal Reference:**

**Glycoprotein N of Human Cytomegalovirus Protects the Virus from Neutralizing Antibodies**

**Abstract**
Herpes viruses persist in the infected host and are transmitted between hosts in the presence of a fully functional humoral immune response, suggesting that they can evade neutralization by antiviral antibodies. Human cytomegalovirus (HCMV) encodes a number of polymorphic highly glycosylated virion glycoproteins (g), including the essential envelope glycoprotein, gN. We have tested the hypothesis that glycosylation of gN contributes to resistance of the virus to neutralizing antibodies. Recombinant viruses carrying deletions in serine/threonine rich sequences within the glycosylated surface domain of gN were constructed in the genetic background of HCMV strain AD169. The deletions had no influence on the formation of the gM/gN complex and *in vitro* replication of the respective viruses compared to the parent virus. The gN-truncated viruses were significantly more susceptible to neutralization by a gN-specific monoclonal antibody and in addition by a number of gB- and gH-specific monoclonal antibodies. Sera from individuals previously infected with HCMV also more efficiently neutralized gN-truncated viruses. Immunization of mice with viruses that expressed the truncated forms of gN resulted in significantly higher serum neutralizing antibody titers against the homologous strain that was accompanied by increased antibody titers against known neutralizing epitopes on gB and gH. Importantly, neutralization activity of sera from animals immunized with gN-truncated virus did not exhibit enhanced neutralizing activity against the parental wild type virus carrying the fully glycosylated wild type gN. Our results indicate that the extensive glycosylation of gN could represent a potentially important mechanism by which HCMV neutralization by a number of different antibody reactivities can be inhibited.

**Global Burden of Human Brucellosis: A Systematic Review of Disease Frequency**

**Abstract**
Background
This report presents a systematic review of scientific literature published between 1990–2010 relating to the frequency of human brucellosis, commissioned by WHO. The objectives were to identify high quality disease incidence data to complement existing knowledge of the global disease burden and, ultimately, to contribute towards the calculation of a Disability-Adjusted Life Years (DALY) estimate for brucellosis.

Methods/Principal Findings
Thirty three databases were searched, identifying 2,385 articles relating to human brucellosis. Based on strict screening criteria, 60 studies were selected for quality assessment, of which only 29 were of sufficient quality for data analysis. Data were only available from 15 countries in the regions of Northern Africa and Middle East, Western Europe, Central and South America, Sub-Saharan Africa, and Central Asia. Half of the studies presented incidence data, six of which were longitudinal prospective studies, and half presented seroprevalence data which were converted to incidence rates. Brucellosis incidence varied widely between, and within, countries. Although study biases cannot be ruled out, demographic, occupational, and socioeconomic factors likely play a role. Aggregated data at national or regional levels do not capture these complexities of disease dynamics and, consequently, at-risk populations or areas may be overlooked. In many brucellosis-endemic countries, health systems are weak and passively-acquired official data underestimate the true disease burden.

Conclusions
High quality research is essential for an accurate assessment of disease burden, particularly in Eastern Europe, the Asia-Pacific, Central and South America and Africa where data are lacking. Providing formal
epidemiological and statistical training to researchers is essential for improving study quality. An integrated approach to disease surveillance involving both human health and veterinary services would allow a better understanding of disease dynamics at the animal-human interface, as well as a more cost-effective utilisation of resources.

Fungal Meningitis From Injection of Contaminated Steroids

A Compounding Problem

Lucy E. Wilson, MD, ScM; David Blythe, MD, MPH; Joshua M. Sharfstein, MD

Injections of contaminated steroids lead to a deadly outbreak of meningitis. Investigations reveal that a compounding pharmacy manufactured the steroids under unacceptable conditions. Newspaper reports document significant gaps in oversight by state and federal agencies, and public health officials call for stronger controls.

The year is 2002. According to the San Francisco Chronicle, “the case of Doc’s Pharmacy illustrates how doctors, as well as their patients, are unaware of the risks inherent in pharmacy compounding.”

Not long after, the Kansas City Star reviews a series of compounding-related injuries and deaths from across the country. A pharmaceutical industry executive is quoted by the paper as saying, “It is just a matter of time before somebody makes a grossly contaminated product and scores of people die. . . . People will then be asking, ‘Why did this happen?’”

Almost exactly a decade later, at the end of September 2012, the Maryland Department of Health and Mental Hygiene receives a call from the Centers for Disease Control and Prevention (CDC). Seven Maryland outpatient facilities have received suspect lots of methylprednisolone acetate injection from the New England Compounding Center. Working with these facilities and other clinicians to identify affected patients reveals that at least 17 Marylanders have meningitis and 1 has died.

As of October 25, this outbreak has reached 18 states, causing 328 cases of serious fungal infection, including 323 cases of meningitis, 5 cases of peripheral joint infection, and 24 deaths. Thousands of additional patients have undergone lumbar punctures and other invasive diagnostic procedures. Tens of thousands are living in fear that they could become seriously ill at any moment.

Managing the crisis has required an intensive response by federal, state, and local public health officials. With an evolving spectrum of fungal illness caused by Exserohilum and potentially Aspergillus, Cladosporium, and other species, CDC experts have developed and modified working case definitions, diagnostic recommendations, and treatment guidelines. The CDC’s emergency operations center has assisted states in contacting thousands of patients. The Food and Drug Administration (FDA) has focused its attention on the conditions at the New England Compounding Center, overseeing an increasing series of recalls. On October 18, the FDA announced that unopened vials from implicated lots tested positive for Exserohilum, the same fungus identified in meningitis cases.

Health departments across the nation have coordinated local activities in emergency response mode. These efforts include investigating reports of possible cases, providing guidance to physicians on diagnosis and treatment, sharing information with the CDC and with other states, and analyzing data to better define the risk associated with exposure. State health departments have also organized outreach to scores of clinics and tens of thousands of exposed patients to assess symptoms, encourage vigilance, and answer questions.

There are many questions. Patients already affected with chronic pain syndromes ask how they can identify new or worsening symptoms and endure the stress of medical evaluation and the complicated logistics of the health care system. Physicians want to know whether it is possible to reassure anxious callers who may have received one of the more than 3000 products made by the New England Compounding Center, when few clinics are able to track which lots were administered to specific patients. And everyone wants to know: Why did this happen?

According to the International Association for Compounding Pharmacists, there are an estimated 7500 compounding pharmacies in the United States, and 1% to 3% of all prescriptions are compounded. Unlike pharmaceutical manufacturers, compounding pharmacies do not have to demonstrate the safety and efficacy of their products or adhere to manufacturing and labeling standards. Only about 2% participate in the industry’s voluntary accreditation program.

State pharmacy boards provide inconsistent oversight, with few having the resources to address complex manufacturing issues or to police improper behavior. Efforts by the FDA to oversee compounding pharmacies have been thwarted by court action and political opposition; nonetheless, the agency has issued consumer advisories and sought to retain authority over pharmacies that function as large-scale manufacturers by, for example, selling compounded drugs to clinics without requiring patient-
specific prescriptions. In the case of the New England Compounding Center, however, oversight efforts failed to prevent harm.

Many compounded products, produced at a small scale, are necessary for specific situations in clinical medicine. Other compounded products, however, pose substantial risk and may provide little benefit. The large-scale compounding of sterile medications otherwise available from FDA-approved manufacturers is especially concerning. Discussions with physicians who ordered in bulk from the New England Compounding Center indicate that some centers did so to save money over FDA-approved products. Other physicians believed that preservative-free methylprednisolone would be less likely to cause complications such as chemical arachnoiditis. There was also the mistaken view that compounded products were safer than the FDA-approved versions, on the grounds that some FDA-approved products carried warnings against epidural use, whereas certain compounded versions did not.

In 2002, the San Francisco Chronicle noted that compounders see a business opportunity in drug shortages. A decade later, this opportunity remains. The trade association Professional Compounding Centers of America, whose motto is “Compound With Confidence,” recruits pharmacists with the statement, “At one time, all medications were compounded.” The association goes on to say that “compounding has experienced a renaissance as modern technology and innovative techniques and research have allowed more pharmacists to customize medications to meet specific needs.”

The debacle at the New England Compounding Center, however, indicates that compounding has yet to fully emerge from the Dark Ages. Congressional hearings will call attention to the need to stop certain high-risk compounding practices and more closely oversee those that remain. Legislation clarifying FDA’s authority and empowering the agency to establish national standards for compounding, including adverse event reporting, should follow. State agencies should serve as partners in oversight and enforcement. Physicians and patients should routinely discuss the potential risks of using compounded products, particularly in the rapidly expanding world of pain management. All compounding pharmacies must take responsibility for the quality of what they produce.

The meningitis outbreak of 2012 exposes how far the health care system still needs to go to protect patients from unsafe products. Fortunately, there is reason for hope. The urgent and coordinated response to the crisis, involving clinicians and public health officials across the country, has helped to inform and protect the public. If only a fraction of this energy can be applied to the task of prevention, the compounding problem could be fixed. Ten years from now, the problems associated with this outbreak should be more than just another chapter in the book of drug compounding tragedies. Instead, it should be remembered as the moment public health and the health care system came together to write a different ending.

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Hospitalizations and Mortality Associated With Norovirus Outbreaks in Nursing Homes, 2009-2010

Context Norovirus outbreaks are common among vulnerable, elderly populations in US nursing homes.
Adverse birth outcomes more frequent in women exposed to ART during pregnancy, largest-ever study confirms

Carole Leach-Lemens
Published: 30 October 2012

Among HIV-infected women in Botswana, starting combination antiretroviral therapy during pregnancy was associated with an increased risk for adverse birth outcomes, including pre-term delivery, small for gestational age, stillbirth and neonatal death, researchers report in the largest study of birth outcomes to date among HIV-positive women with access to ART in pregnancy.

The study is published in the advance online edition of the *Journal of Infectious Diseases.*

Increased risk for adverse birth outcomes was also seen among HIV-positive women exposed to ART started before they became pregnant, compared to all HIV-positive women.

Maternal HIV infection was significantly associated with an increased risk for stillbirth, pre-term delivery, small for gestational age and neonatal death, with adjusted odd ratios (AORs) ranging from 1.3 to 1.8, Jennifer Y Chen and colleagues write in this analysis of over 33,000 records of women delivering at six government hospitals over a two-year period.

In an accompanying editorial, Heather Watts and Lynne Mofenson note such adverse pregnancy outcomes are not surprising since HIV-positive women are additionally at increased risk for co-infections, including tuberculosis and malaria, which are also associated with adverse pregnancy outcomes.

Importantly, “The pathogenesis of preterm delivery among all women and the potential increased risk among HIV-infected women are not well understood.”

In resource-rich settings, Watts and Mofenson note, the effect of pre-term delivery on infant death and disease may be limited because of the level of care available. However, in resource-poor settings any increased risk for pre-term delivery because of ART “could have enormous impact, because options for care of preterm infants [are] limited and millions of HIV-infected women become pregnant each year”.

Conflicting findings from studies, mostly in resource-rich settings, may be the result of small sample size, differences in population and exposure categories and availability of care and treatment before delivery, note the authors.

To address these limitations, they undertook the largest surveillance study to date and restricted their analyses to ART exposure at conception, or to a time-limited comparison of ART with zidovudine during pregnancy with similar opportunities for outcomes. Comparisons were adjusted for CD4 cell count.
In all analyses, ART exposure was significantly associated with adverse birth outcomes, independent of CD4 cell count. Yet the association appeared greater in those with CD4 cell counts over 200, leading Watts and Mofenson to suggest that not all outcomes could be the result of women on ART with more advanced illness.

These findings support previous studies in West Africa and Botswana showing a link between ART and pre-term delivery.

Watts and Mofenson acknowledge the appeal of the programmatic and operational advantages of the recent guidance from WHO for resource-poor settings of using a single ART regimen for the lifelong treatment of all HIV-positive women and prevention of mother-to-child transmission (Option B+). Additionally, this approach will ensure women with more advanced illness can be treated without waiting for CD4 cell counts.

Nonetheless, implementation of this strategy, they add, critically requires monitoring the rate of HIV-free survival and infant HIV infection because an increase in pre-term delivery in resource-poor settings may lead to increased infant death, undermining the benefits of preventing mother-to-child transmission.

The increased risk for pre-term delivery with women starting combination ART compared to zidovudine treatment is concerning, they note. Triple-drug ART was associated with a significantly elevated risk of pre-term delivery (AOR 1.4), small for gestational age (AOR 1.5) and stillbirth (AOR 2.5), when compared to exposure to zidovudine prophylaxis alone. There was also an increased rate of neonatal death (1.9% compared to 0.8%, p=0.002) among this group; CD4 count made no difference.

The authors note that, while the severity of pre-term delivery and small for gestational age may reflect the rate of neonatal death, it may also differ by the level of obstetrical and neonatal care.

Yet Watts and Mofenson note it is unclear how this difference will translate into overall infant mortality. They cite a previous study that showed twice the risk of pre-term delivery in women with CD4 counts over 200, randomised to zidovudine, lamivudine and lopinavir/ritonavir compared to zidovudine, lamivudine and abacavir, but no differences in infant hospitalisation or death by six months of age.

Watts and Mofenson stress the need for more data on the potential benefits and risks of combination ART and zidovudine; the efficacy of both options is equivalent (assuming appropriate use) in women not needing treatment for their own health (those with CD4 cell counts at or above 350 cells/mm$^3$).

Watts and Mofenson highlight the clear benefit of combination ART among women with CD4 cell counts under 350 “because 92% of maternal mortality and 88% of perinatal and breastfeeding transmission occur in this group, and these rates can be reduced with the prompt start of ART. Any increased risk of PTD would need to be very high to outweigh benefits for this group of women.”

Watts and Mofenson advocate for conducting surveillance of rates of adverse events to determine the best ART regimen for use in pregnancy for maternal and infant health.

Distinguishing between the causes of pre-term birth can help focus research into the pathogenesis of pre-term delivery in HIV-positive women, they suggest.

Finding hypertension to be a strong predictor for all adverse birth outcomes, the authors advocate for prioritising management of hypertension in pregnancy for all high-risk women, including those receiving ART.

The authors conclude, “although these data are observational they...underscore the need for further research into potential mechanisms by which ART may affect birth outcomes as well as investigation of the safest antiretroviral regimens for use during pregnancy...As more women gain access to ART during pregnancy [in resource-limited settings] additional efforts are needed to identify those at high risk for adverse outcomes and provide intensified support systems that address modifiable risk factors...in pregnancy.”

References
Traditional risk factors predict neurocognitive impairment in people with HIV
Michael Carter
Published: 31 October 2012

Neurocognitive impairment in people with HIV – loss of memory, poor concentration and declining mental ability – is most likely to be happening for the same reasons as in the wider population, and the risk of impairment does not appear to be associated with HIV infection, a French cohort study has found.

Older age, anxiety and depression, cardiovascular disease and a history of brain injury were strongly associated with neurocognitive impairment, which was detected in 59% of a cohort of French people with HIV.

“Most of the cases were related to non-HIV-related determinants,” comment the authors. “The high prevalence of NCI [neurocognitive impairment] observed in our cohort was neither associated with incomplete viral suppression nor current nor nadir CD4 count. Furthermore, we did not find any association with the current cART [combination antiretroviral therapy] regimen.”

There is considerable interest in the frequency and causes of neurocognitive impairment in people with HIV.

Some studies have suggested that the majority of people, even in the era of modern antiretroviral treatment, have some form of impairment.

However, much of the existing research is limited because it was conducted in highly selected groups of participants who often had pre-existing cognitive complaints.

Researchers in southern France therefore designed a study involving a broad spectrum of people receiving routine HIV care.

To be eligible for the study, participants were required to be aged over 18 and medically stable. Recruitment took place between 2007 and 2009 and a total of 400 people joined the study.

Their neurocognitive function was assessed using standardised tests, which were administered by trained psychologists. Information was also gathered from medical records regarding known risk factors for neurocognitive impairment, such as older age, level of educational attainment, cardiovascular disease, mental health problems such as depression and a history of head injury.

Approximately half the participants also had an MRI scan to see if there was an association between neurocognitive function and atrophy of grey matter in the brain.

The participants had a median age of 47 years and 79% were men. Most (89%) were taking antiretroviral therapy, and 93% of these people had a viral load below 500 copies/ml. Current median CD4 cell count was 515 cells/mm$^3$ and the median nadir CD4 cell count was 260 cells/mm$^3$.

Approximately a fifth (19%) of participants had high cholesterol, 4% had a history of cardiovascular disease and 29% were co-infected with hepatitis B or hepatitis C virus.

Neurocognitive testing found a high prevalence of impairment (59%). This was asymptomatic in 20% of participants and mild in 31%; 7% had HIV-associated dementia.

People with impairment were significantly older (p = 0.02), and were more likely to have other health complaints, including a history of cardiovascular disease (p = 0.01), elevated cholesterol (p = 0.04), a history of stroke, brain trauma or neurological disease (p < 0.001), depression (p < 0.001), anxiety (p < 0.001), diagnosis with an AIDS-related neurocognitive condition (p < 0.001), or lower levels of education (p < 0.001).

After controlling for confounding factors, the investigators found that a number of traditional risk factors were associated with an increased risk of impairment.

These included lower levels of education, a history of cardiovascular disease, high cholesterol, anxiety, depression, a history of neurological disease or trauma, and diagnosis with an AIDS-defining neurological disease. No HIV-related factor such as CD4 cell count, viral load, duration of infection with the virus, or use of antiretroviral therapy had a significant association with the risk of impairment.

When the investigators restricted their analysis to the 192 participants without anxiety, depression, a history of brain damage and who also had a higher level of education, they found that only 19% had symptomatic impairment. Restricting analysis further to people without a history of cardiovascular disease reduced the prevalence to just 10%.

The authors believe their results have clinical significance and show the importance of screening for cardiovascular disease, anxiety and depression and when detected, offering appropriate treatment.

The results of the MRI scans showed that people with impairment had significantly lower grey matter volume (p = 0.006). This remained the case after exclusion of participants with the neurological manifestations of AIDS and a history of head trauma (p = 0.03).
“Our study shows for the first time in a large sample a strong association between a reduced volume of grey matter and any stage of NCI,” comment the investigators. “Such results are important for better understanding HIV-associated neurocognitive disorders since they suggest that the cognitive defects in HIV-infected patients are not only due to the functional changes in neural circuitry but could also be the consequence of macrostructural brain lesions.”

They conclude: “All together, our findings suggest that, in patients that are well controlled for HIV infection, cardiovascular and psychiatric disease, in addition to any brain damage including neuroAIDS, and low level of education are related to NCI...screening for cognitive impairment should be accompanied by screening for cardiovascular and psychiatric co-morbidities, in particular depression and anxiety disorders.”

Reference

U.N. Agencies Publish 'Atlas' Linking Climate, Health
"Two U.N. agencies on Monday presented a new tool to map health risks linked to climate change and extreme weather conditions, enabling authorities to give advance warnings and act to prevent 'climate-sensitive' diseases from spreading," Agence France-Presse reports (10/30). "As the world's climate continues to change, hazards to human health are increasing," according to the "Atlas of health and climate," published jointly by WHO and the World Meteorological Organization (WMO), a press release from the agencies states (10/29). "Climate variability and extreme conditions such as floods can trigger epidemics of diseases, such as diarrhea, malaria, dengue, and meningitis-diseases, which cause death and suffering for millions of people," VOA News writes (Schlein, 10/29).

"Though the data or conclusions aren't necessarily new, the way in which they are presented may sharpen governments' ability to respond to the threats posed by rising temperatures and changing climate," the Associated Press notes (10/29). "Using graphs, charts and bullet points, the Atlas can be used as a guide for decision makers on how to prevent such diseases, WHO Director-General Margaret Chan told reporters in Geneva, speaking alongside WMO chief Michel Jarraud," AFP adds (10/30). "But the Atlas authors say they still have a long way to go to make such warnings global and reliable," IRIN writes, adding, "We have good real-time weather data, but that is not the case with health data," said Geoff Love, WMO's director of weather and disaster risk reduction" (10/30).

Drug-Resistant Malaria Spreading In Asia, Experts Warn
"Drug-resistant malaria is spreading in Asia, experts warned as a high-level conference opened Wednesday with the aim of hammering out an action plan to strengthen the region's response," Agence France-Presse reports. "Resistance to the drug used everywhere to cure the life-threatening disease has emerged in Cambodia, Thailand and Myanmar," Richard Feachem, director of global health at the University of California, San Francisco and former head of the Global Fund to Fight AIDS, Tuberculosis and Malaria, said, according to the news service. "The danger is that at some time this resistance may break out of Southeast Asia and crop up in Africa," he added, AFP writes. Feachem spoke ahead of the "Malaria 2012: Saving Lives in the Asia-Pacific" conference in Sydney, which "will seek consensus on the actions needed to strengthen the region's response to malaria," according to AFP (Coorey, 10/31).

Experimental HIV Test Might Help Improve Diagnosis, Treatment In Developing Countries
"Scientists have come up with a test for the virus that causes AIDS that is 10 times more sensitive and a fraction of the cost of existing methods, offering the promise of better diagnosis and treatment in the developing world," Reuters reports. "The test uses nanotechnology to give a result that can be seen with the naked eye by turning a sample red or blue, according to research from scientists at Imperial College in London published in the journal Nature Nanotechnology," the news agency writes (Wickham, 10/28). "The test can be configured to a unique signature of a disease or virus—such as a protein found on the surface of HIV," and if the marker is present, a chemical reaction causes a blue result and a red result if the marker is not present, according to BBC News. "Early testing showed the presence of markers of HIV and prostate cancer could be detected," BBC News notes, adding, "However, trials on a much larger scale will be needed before it could be used clinically" (Gallagher, 10/28).