April 2013 Epidemics and AIDS Update

**Heterosexuals Only: Hawaii Bill Limits Chlamydia Treatment**

*Honolulu Civil Beat*, (04.02.2013) Nathan Eagle

The state legislature of Hawaii is close to passing Senate Bill 655, which would allow physicians to prescribe antibiotics to the sexual partners of heterosexuals diagnosed with chlamydia, even if the partner declines a doctor’s exam (expedited partner therapy). As originally introduced by Sen. Josh Green (D-District 3), who is also an emergency room physician, the bill allowed doctors to prescribe expedited partner therapy for all residents of Hawaii. However, the Commerce and Consumer Protection Committee revised the bill to apply only to heterosexuals, based on a 2006 CDC report that recommended expedited partner therapy for same-sex couples “only as a last resort.”

There are not enough studies of the effectiveness of expedited partner therapy for same-sex couples to recommend the practice, according to the CDC study. Treatment for heterosexual partners consists of oral medications, whereas CDC recommends an injection for treatment for homosexuals with chlamydia.

Green stated that physicians would not give out syringes and injectable medications for same-sex expedited partner therapy.

In spite of CDC’s 2006 statement, expedited partner therapy has become increasingly prevalent across the United States; 32 states allow the practice, and it is potentially permissible in 11 other states. Expedited partner therapy is still a gray area in Hawaii state law; passage of Senate Bill 655 would clarify legality of the practice for physicians. Planned Parenthood of Hawaii supports passage of the bill.

The Democratic Party of Hawaii’s Gay, Lesbian, Bisexual, and Transgender Caucus will ask for an amendment eliminating the heterosexual restriction, according to spokesperson Jo-Ann Adams. CDC’s most recent data ranks Hawaii 22nd in the United States for chlamydia rates. Most of Hawaii’s cases occur among people ages 15 to 24. Chlamydia is more prevalent among Hawaiian women.

Hawaii’s House Consumer Protection and Judiciary committees plan to hear Senate Bill 655 next Monday, April 8.

**HIV Drugs Ease Inflammation in ‘Controllers’**

*MedPage Today*, (03.04.2013) Michael Smith

University of California at San Francisco researchers report that giving highly active antiretroviral treatment (HAART) to HIV “controllers”—people who maintain low levels of HIV plasma RNA without antiretroviral treatment—significantly reduced plasma RNA and chronic inflammation markers. Dr. Hiroyu Hatano stated the research team began the prospective 16-person study because the controllers showed signs of immune system activation and increased atherosclerosis.

Although members of the cohort had HIV for a median duration of 10 years, the participants had “robust” immune systems; the median plasma HIV RNA level was 77 copies per milliliter, and the median CD4 count was 615 cells per cubic millimeter of blood. Hatano reported that the cohort received raltegravir (Isentress) and a one-pill combination of tenofovir and emtricitabine (Truvada) for 24 weeks.

Variables measured in the study included plasma and cell-associated HIV RNA, proviral DNA in blood and gut-associated lymphoid tissue (GALT), and immune activation markers. Results indicated a significant decline in plasma HIV RNA and decreases in cell-associated RNA and GALT proviral DNA.

Scott Hammer, MD, co-chair of the 20th Conference on Retroviruses and Opportunistic Infections, declared that the finding would be unlikely to affect clinical practice because controllers do not ordinarily receive HAART, and there are other ways to control atherosclerosis. Taking HAART might upset the “delicate balance between the immune system and the viral load” of a controller. According to Hammer, pregnancy would be the only reason to give HAART to a controller.

Hatano said most of the study participants have opted to continue HAART, so it will be possible to report results after a longer period of treatment.

An abstract of the full report, “Prospective ART of Asymptomatic HIV+ Controllers,” was published online by the 20th Conference on Retroviruses and Opportunistic Infections at [http://www.retroconference.org/2013b/Abstracts8888/47981.htm](http://www.retroconference.org/2013b/Abstracts8888/47981.htm)

**New Light Shed On Common Sexually Transmitted Infection**

Apr. 2, 2013 — Research led by David H. Martin, MD, Professor and Chief of Infectious Diseases at LSU Health Sciences Center New Orleans, has found that a common sexually transmitted infection-causing parasite “cultivates” bacteria beneficial to it, changing thinking about which comes first-infection or bacteria. The researchers also discovered a previously unknown species of these bacteria.
The research was published ahead of print online in *Advance Access in the Journal of Infectious Diseases*, and was published online April 2, 2013 in Research Highlights in *Nature Reviews Urology*. *Trichomonas vaginalis* is a parasite and is a common sexually transmitted infection (STI) in women where it causes vaginal discharge, a higher rate of premature deliveries, and greater susceptibility to infection with the AIDS virus. Many women have this infection and do not know it.

It is known that a change in vaginal bacteria causes a problem known as bacterial vaginosis, and women with this condition are at increased risk of acquiring a trichomonas infection. The researchers wondered if, among women with bacterial vaginosis, there were unique bacterial communities which would make women more susceptible to infection with trichomonas.

"We discovered that there are two unique bacterial communities that are very strongly associated with trichomonas infection," notes Dr. Martin. "In part what is unique about these communities is high concentrations of bacteria known as mycoplasmas. In fact one of these is a completely unknown bacterium which we have named Mnola because it is a mycoplasma discovered in NOLA."

The mycoplasma associated with the other unique bacterial community is *Mycoplasma hominis*, a well known bacterial pathogen. The data indicate that women with trichomonas and this unique bacterial community suffer from worse disease than the other trichomonas-infected women. They have greater amounts of discharge and redness of the vaginal wall.

"We think that this group might also be at especially high risk for infection with HIV," adds Dr. Martin.

An especially interesting result of this research is that the evidence suggests that the trichomonas parasite is responsible in some way for the appearance these unique mycoplasma dominated bacterial communities.

"So instead of these unique communities predisposing a woman to infection as originally thought, we now believe that trichomonas takes on the role of a farmer in the vaginal environment by cultivating bacterial communities that are in some way beneficial to itself. Proving this hypothesis and figuring out how these bacteria interact with trichomonas will be the subject of future research," concludes Dr. Martin.

**Journal References:**

**Appendix Not Totally Useless**

The small organ evolved too many times for it to be an accident, but it’s still unclear what it does.

By Kate Yandell | February 15, 2013

The evolution of the appendix was not an accident, the *Huffington Post* reported. Researchers analyzed relatedness of the 50 out of 361 living mammalian species that have appendices. They found that the appendix had evolved independently 32 to 38 times and was lost only seven times, making it likely that it evolved for a reason.

The purpose of the appendix remains a mystery, however. While some scientists have thought must have originally evolved to aid in digestion, the study, published in the journal *Comptes Rendus Palevol* earlier this month (February 7), refutes that hypothesis.

The researchers came to this conclusion by analyzing the historical diets of the species that had evolved appendices. They found that the appearance of an appendix had no correlation with diet changes, indicating that despite being located in our gut, the appendix is not involved in digestion.

The paper’s authors support the hypothesis that the appendix may actually be a shelter for commensal gut bacterial during diarrheal disease. In the face of an infection, they may hide in the out-of-the-way appendix, preparing to return once the undesirable microbes have been flushed out.

But Randolph Nesse, a biologist at the University of Michigan, Ann Arbor, is not entirely convinced, maintaining the appendix’s purpose is still unknown. "One wonders why such a trait with such a function would not be universal," he told *The Huffington Post.*

**Comments**
Yeah, it’s totally useless... unless you consider the following to be of benefit:

1. Enhances synthesis of B vitamins and improves absorption of Calcium (bone building)
2. Protects against E. Coli infection
3. Improves lactose tolerance and digestibility of milk products
4. Reduces vaginal infection and yeast infection (candida)
5. Improves immune function
6. Promotes anti-carcinogenic activity
7. Helps prevent peptic ulcers caused by H. Pylori
8. Helps prevent and reduce acne
9. Helps with cholesterol metabolism
10. Helps improve nutritional value of foods
11. Protects against traveler’s diarrhea and speeds recovery after exposure
12. Helps with problems of constipation
13. Helps re-establish microflora after antibiotic use
14. May help lower allergic response
15. May help with recurring Urinary Tract Infection (UTI)
16. Helps with detoxification & colon cleansing
17. Helps produce natural antibiotics, like “acidophilus”
18. Helps alleviate bad breath
19. Ameliorates gynecologic dysfunction
20. Possess anti-tumorigenic activity
21. Helps the colonization within the intestinal, respiratory, and urogenital tract

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**From Toxins to Therapeutics**

Researchers are finding new drugs for chronic pain and autoimmune diseases by modifying animal venom-derived molecules that target the nervous and immune systems.

By Dan Cossins | March 19, 2013

Animal venoms are a veritable treasure trove of proteins and peptides fine-tuned by millions of years of evolution to kill or incapacitate both predator and prey. Usually delivered via injection—through an assortment of fangs, barbs, spines, and stingers—venom toxins evade the body’s defenses to seek out target cells, where they prevent blood cells from clotting, for example, or block ion channels on nerve cells to shut down or subvert their function.

Such high molecular specificity and potency has long made venom a promising source of drug candidates. More than 30 years ago, the US Food and Drug Administration approved the first venom-derived drug—a therapy for hypertension, called Capoten, copied from a pit viper venom peptide. A handful of venom-derived drugs have since been approved for cardiovascular disease, and in 2004, a venom-derived painkiller hit the market. Now, thanks to an increasing knowledge of the human nervous and immune systems, the pipeline from fang to pharmacy is expanding even further, with more pain medications and drugs that target autoimmune diseases such as multiple sclerosis and rheumatoid arthritis.

“We’re really at beginning of something exciting,” said Glenn King, a molecular biologist and spider venom researcher at the University of Queensland in Brisbane, Australia—“and it will get bigger over the next decade.”

**Targeting autoimmunity**

Perhaps the most compelling venom-derived drug currently in development comes from the sun anemone (*Stichodactyla helianthus*), which lives on reefs in the Caribbean and uses its soft green tentacles to stun shrimp with a cocktail of toxins. In the 1990s, a group of physiologists led by George Chandy at the University of California, Irvine, showed that one of these toxins, a peptide called ShK, is a potent inhibitor of a T lymphocyte potassium channel called Kv1.3, the up-regulation of which is implicated in autoimmune diseases.

To turn ShK into a useful therapeutic, however, the researchers had to make one important change. “ShK is great because it is very potent on kv1.3 channels, but the problem is that it blocks another potassium channel called kv1.1, found on neurons,” said Christine Beeton, a molecular biologist at Baylor College of Medicine who was part of the team that developed ShK-186. “You don’t want to inject [it] into humans knowing that it could block neurons, and not knowing what [that] could do.”
After studying ShK’s structure and functional properties, Beeton, Chandy, and colleagues tested almost 400 different synthetic derivatives of the compound. They settled on a version featuring an additional amino acid liked to the compound’s N-terminus, which ensures it does not block ion channels on cells other than T lymphocytes. The resulting synthetic peptide—called ShK-186 because it was the 186th version the researchers created—binds Kv1.3 channels with 100-fold greater potency than Kv1.1 channels, all but eliminating the potential for unforeseen side effects.

They later demonstrated in rodent models of multiple sclerosis (MS) that ShK-186 dramatically reverses paralysis. “It was absolutely remarkable to watch,” said Beeton. “We saw the disease almost completely go away.” And importantly, the drug did not broadly suppress the immune system, as treated animals were still able to fight off both chlamydia and influenza.

In December last year, Seattle-based biotechnology company Kineta completed Phase 1a human trials, testing for the safety of ShK-186 in healthy volunteers. Although the results are yet to be published, Beeton said the team was “very happy with the results,” and added that Phase 1b trials are due to begin this April. There is a long way to go before it hits the clinic, but ShK-186 currently holds great promise as a treatment for a range of autoimmune diseases, from MS to lupus and rheumatoid arthritis, said King. “ShK is one of the most exciting examples [of venom-derived drugs] at the moment. The implications are profound if it gets through.”

**Fighting pain with venom**

The first—and as yet, the only—approved venom-derived drug that acts on the nervous system is the painkiller Prialt, a chemically identical version of a peptide isolated from the cone snail (*Conus magus*). Approved in 2004, Prialt works is injected into the fluid around the spine, where it blocks a calcium ion channel in neurons and inhibits the cells’ ability to transmit pain signals to the brain.

But there are several promising leads for new venom-derived painkillers. Earlier this year, for example, researchers at the National Center of Scientific Research (CRNS) in Paris announced the discovery of two peptides isolated from black mamba venom that can block neuronal acid-sensing ion channels (ASICs), which play a key role in the pain pathway. In mice, these peptides—dubbed mambalgins—showed potent analgesic effects, as powerful as morphine, with no obvious toxicity. The peptides also induced less tolerance than morphine. The researchers are now developing mambalgins into a human pain therapeutic with the venom-focused pharmaceutical company Theralpha.

Another painkilling peptide, also under development by Theralpha, is derived from hannalgesin, a neurotoxin isolated from King Cobra (*Ophiophagus Hannah*) venom. Although the mechanism of action for this peptide—known as THA903—is not yet clear, pre-clinical studies have shown that it has a far stronger analgesic effect than morphine and, crucially, can be taken orally. “We drop a solution [of the peptide] under the tongue of the animal and within minutes you can find it in the blood,” said Manjunatha King of the National University of Singapore, who developed the hannalgesin-based peptide.

Meanwhile, other researchers are continuing to derive potential therapeutics from cone snails. *Conus catus*, for example, a close relative of Prialt’s source *C. magus*, yields a toxin that the Australia-based company Relevaré Pharmaceuticals has developed into an intravenous treatment called Leconotide. The drug blocks the same channel as Prialt and is currently in Phase 1 trials. And in January this year, Kineta announced that it has obtained the rights from the University of Utah’s Baldomero Olivera, who isolated the molecule that became Prialt, to advance a portfolio of drug candidates based on another snail venom-derived compound, Conotoxin Rg1a, for the treatment of chronic pain.

Moreover, these promising drug candidates are likely just the tip of the iceberg, researchers agree. It is estimated that less than 0.1 percent of the venom proteome of cone snails—thought to harbor around 100,000 peptides—has so far been tapped, and fewer than 0.01 percent of roughly 10 million active molecules found in spider venoms. But, Kini explained, “with the advent of technologies that enable proteomics and transcriptomics, it is becoming much easier to isolate and study toxins from venom found in miniscule quantities,” such as those yielded by spiders, scorpions, and cone snails—and even the nanoliters produced ticks and mosquitoes.

“There are thousands of venoms that we haven’t even looked at yet,” said Beeton, “so we have millions of molecules that are all potential drugs still to be explored.”

**Brain Activity Breaks DNA**

Researchers find that temporary double-stranded DNA breaks commonly result from normal neuron activation—but expression of an Alzheimer’s-linked protein increases the damage.
By Sabrina Richards | March 24, 2013

Double-stranded breaks in DNA—generally thought to be a severe form of damage—may simply be all in a day’s work for neurons, according to research published today (March 24) in *Nature Neuroscience*. Scientists studying mice reported that normal neuronal activation stimulated by exposure to new environments can cause temporary DNA breaks—suggesting that transient damage may be involved in learning and memory. Additionally, expressing a protein linked to Alzheimer’s disease exacerbates the damage, but blocking neuron activation can keep DNA breaks at a normal level, hinting at possible therapeutic strategy to prevent cognitive decline.

“It’s breathtaking work,” said Karl Herrup, a neurogeneticist at Rutgers University who was not involved in the research. DNA damage can be very dangerous to neurons, which aren’t readily replaced, so it seems likely that the cells must be getting something “worthwhile” from the breaks, said Herrup.

Neurologist Lennart Mucke at the Gladstone Institutes and the University of California, San Francisco, hit upon the arresting notion that severing and repairing DNA is “part and parcel” of normal brain activity in the course of his research on changes in genome stability in Alzheimer’s disease (AD), which is characterized by tangled clumps of amyloid β proteins and damaged neuronal DNA. Hoping to learn more about DNA damage associated with high amyloid levels in the brain, Mucke’s team chose to focus on double-stranded DNA breaks, which neuroscientists generally consider the most severe form of damage.

The team turned to a mouse model for AD, the J20 mouse, which expresses the human precursor of amyloid β (hAPP) at high levels. By 6 months, these mice exhibit deficiencies in learning and memory characteristic of AD. To detect double-stranded DNA breaks, the researchers looked for the gH2A.X variant of a specific histone protein, which is known to cluster at double-stranded breaks.

The researchers exposed J20 and wildtype mice to new cages to increase neuron activity. Surprisingly, after 2 hours in the novel environments, the number of gH2A.X-positive neurons spiked in the brains of both healthy and diseased animals, primarily in areas critical for memory formation and learning—suggesting that the brain activity itself was triggering DNA damage. Interestingly, the damage was resolved in wildtype mice within 24 hours back in their home cages, but the damage persisted in J20 mice. Furthermore, the damage was higher in J20 mice, which had up to three times as many gH2A.X-positive neurons—and the differences could be detected as early as 1 month, before the J20 mice began exhibiting cognitive symptoms. The results suggest that perhaps the high levels of amyloid in the brains of these mice was preventing DNA repair.

Mucke’s team tested whether reducing brain activity in J20 mice alleviated their double-stranded breaks, and found that J20 mice treated with an anti-epileptic drug for 1 month had normal levels of DNA damage.

It’s not yet clear what function, if any, these DNA breaks serve, acknowledged Mucke, whose lab is currently focusing on this question. Given that neuronal activation leads to changes in gene expression that enable animals to learn and form memories, it’s possible that the double-stranded DNA breaks enable these changes in some way. If so, “the challenge is how to integrate this into our way of thinking about not just neurobiology, but gene regulatory processes in general,” said Herrup.

Alternatively, the damage may simply be a side effect of other activation processes. Herrup also cautions that the assay used to confirm the double-stranded breaks may have in fact broken DNA that was simply rendered fragile by neuron activation-induced modifications.

But if the results hold up, Mucke says he sees therapeutic potential in the findings. It may be that “we can protect the neuronal genome inside nerve cells from amyloid damage by preventing abnormal excitatory activity using readily available anti-epileptic drugs,” he speculated.

It’s an attractive strategy, but Mark Mattson, a neuroscientist at the National Institute of Aging who did not participate in the research, cautioned that reducing neuronal activity could have negative consequences. Treating neurons with anti-epileptics been shown to reduce levels of brain-derived neurotrophic factor, which helps induce DNA repair, as well as neurotrophins important for keeping neurons healthy, he noted.

In the meantime, the findings are “just the beginning,” said Mucke. “We’ve raised more question than we’ve answered.”


Comments

Has anybody considered the impact of stress? I'm not a scientist but maybe an environmental change triggers possibility of change in dna, but done in a radical way it also increases stress, which is one of most destructive factors for our bodies?
We have made a quite stressful society and envirnoment to live in. And as I seen in many cases - negative emotions and stress block access to some memories, and memory overall (works the same way as we are forgetting bad things from our past). If our brain perceives our past as stressful, so it tries to "clean up" from it and then to "Mechanism of forgetting running for a long time builds a "habit" for brain, combined with dna changes without possibility (or "thinking space") to get around, leads to an increasing mess.

Hope it doesn't sound too stupid, and sorry if I made any mistakes in english, have a good day! :)

Sergio Stagnaro, Posts: 1, March 25, 2013
I find this article very interesting and fascinating. My Co-Authors and I can corroborate its conclusions in vivo, i.e., in humans. In addition, interestingly, we have demonstrated that, regarding, e.g., AD, there is an Inherited Real Risk of such a disorder, a flurry of environmental risk factors may act on, bringing about both mit-DNA and n-DNA specific breaking:

Marco Marchionni, Simone Caramel, Sergio Stagnaro, Inherited Real Risk of Alzheimer's Disease: bedside diagnosis and primary prevention, Frontiers in Neuroscience, in 

http://www.frontiersin.org/Aging_Neuroscience/10.3389/fnagi.2013.00013/full

CmdV

Taxpayer, Posts: 3, March 25, 2013
Wait. For awhile, we've been told to keep our minds active to stave off Alzheimer's Disease, and now we are told excessive brain activity in the presence of AD genes could be harmful! This report literally turns research on its head...

N K Mishra, Posts: 3, March 26, 2013
There may be stress-induced double strand breaks in neuronal DNA. But the question is: is this temporary or lasting or permanent? Does this break lead to realignment of genes or their inactivation?

wetopp, Posts: 1, March 27, 2013
One hopes they'll whole genome sequence several single nuclei from the memory region, ideally in human. Nerve cells know how to handle electrical currents, dsDNA is an electrical conductor with properties strongly dependent on local conditions inc DNA sequence. "Makes sense" that terminally differentiated neurons might find an alternative use for the information holding capacity of DNA to store memories. It would read out with the speed of light in DNA which is consistent with what we know about memory recall. Means there must be an electrical connection between the nerve cell membrane structures and the nucleus. Interesting to know if any transmission EM people have seen structures they can't explain in memory nerve cells.

Privacy and the HeLa Genome
European scientists have taken down the HeLa genome after publishing it without the consent of Henrietta Lacks's family.

By Kate Yandell | March 26, 2013
A team of European researchers earlier this month published the genome sequence of HeLa cells, the first cells to be grown immortally in culture. They have now taken the sequence down from repositories after hearing from the family of Henrietta Lacks, the woman from whom the cells were taken in 1951.

Rebecca Skloot, author of the 2010 book The Immortal Life of Henrietta Lacks, wrote on The New York Times: Opinion pages that the publication was in violation of the family's privacy, since the cells contain their genetic information.

"The Lacks family is proud of HeLa's contributions to society, and they don't want to stop HeLa research," she wrote. "But they do want to learn about the HeLa genome—how it can be used for the good of science while still protecting the family's privacy—so they can decide whether to consent to its publication."

Researchers originally took cervical tumor cells from Henrietta Lacks, a black woman in Baltimore, without her consent, and her children were later studied without explanation. A press release associated with the current study claimed that it was impossible to tell anything about the Lacks family from the sequence, but Skloot said this was untrue.

"That is private family information," Jeri Lacks-Whye, Henrietta Lacks' granddaughter, told Skloot. "It shouldn't have been published without our consent." By the time the researchers took the sequence down it had been downloaded at least 15 times.

Skloot argued that laws about using DNA sequences are outdated, since they were made at a time when it was not possible to get much information out of DNA, and since we will soon have access to even more detailed information than we have today. Francis Collins, head of the National Institutes of Health, agreed. "This latest HeLa situation really shows us that our policy is lagging years and maybe decades behind the science," he told Skloot. "It's time to catch up."

Comments

PPH, Posts: 5, March 26, 2013
What next? Are we to collect and deliver the tons of HeLa cells around the world to her family? Will her family talk to those cells? Read the cells bedtime stories? Shall we be forced to keep them alive as if they were a person?

Shall we be served with summons to hie ourselves to court to hear some lying attorney declaim how Henrietta's poor body has been violated with pipetters shoved into her broth? Will we be accused of raping her next? Her cancer was a cervical cancer! Will it be, "Oh, my god what a horror that poor soup broth has endured?"

Those cells aren't Henrietta, any more than the snot I blow (which has a few living cells in it) is me. There is no person, just a film of cells that can be induced to float around for short periods of time.

HeLa cells are LESS Henrietta than my snot is me. Why? Because it's a cancer. Those are the cancer cells that MURDERED their poor Henrietta. Those cells were and are a disease. No clone of those cells can be grown into a near duplicate of Henrietta.
Synthetic Vaccine Is Safer, More Stable
Scientists develop a safer vaccine for foot-and-mouth disease by reproducing the protein shells that encase the disease-causing virus.

By Dan Cossins | March 29, 2013

British researchers have created an entirely synthetic vaccine for the animal affliction foot-and-mouth disease, according to a study out this week in *PLOS Pathogens*. The vaccine comprises only a structural mimic of the protein shell of the virus that causes the disease, and thus contains no genetic material, rendering it unable to infect animals. The synthetic capsid has also been engineered for enhanced stability, so it lasts longer outside of cold storage and will therefore be easier to distribute in the poor, hot countries where foot and mouth is endemic.

The vaccine is expected to be available to farmers in 6 to 8 years, reported *Nature*. But if the method proves successful when scaled for commercial production, it could be used to create safer and more practical synthetic vaccines for human diseases caused by similar viruses, including polio, which remains a formidable problem in the developing world.

“This work will have a broad and enduring impact on vaccine development, and the technology should be transferable to other viruses from the same family,” study coauthor Dave Stuart, a structural biologist at the University of Oxford, told *BBC News*.

The research was carried out in response to an outbreak of foot-and-mouth that devastated farms in the United Kingdom in 2001. Almost 10 million livestock animals had to be put down, and a mass vaccination program followed. But 6 years later, a vaccine made from inactivated virus reverted to its infectious form and caused another outbreak.

Previous attempts to create a synthetic vaccine by making a recombinant version of the virus capsid failed primarily because the scientists were unable to make the complex shell structure strong enough; the synthetic shells simply fell apart too quickly to be useful. This time, however, Stuart and his colleagues were able to tweak the production process to reinforce the weak points and therefore make the empty capsids more stable.
The researchers then used X-ray crystallography to show that their synthetic capsids are almost exact replicas of the real thing, and demonstrated their ability to induce protective immunity in cattle for up to 34 weeks.

Mysterious Avian Influenza in China
Two people have died and five have fallen ill from the H7N9 virus.
By Kate Yandell | April 3, 2013
Two people died last month in Shanghai and one person from the nearby Anhui Province was reported to be in critical condition with a new strain of bird flu. Yesterday (April 2), the Chinese government announced that four more people had been hospitalized with the virus in the Jiangsu Province.

The virus has been identified as H7N9, a bird flu virus that has previously not shown much propensity for attacking humans. Prior to the recent Chinese cases, only one person had been confirmed dead of the virus, a Dutch vet who contracted the infection in 2003 during an outbreak on a poultry farm, 

ScienceInsider reported.

The epidemiology behind the current cases remains unclear. The infected people show no clear connections with each other, and only one of the four newly announced victims appear to have worked with poultry, the Chinese government said—a slaughterer who could have caught the virus from a bird.

Chinese officials have examined people who came in contact with the three original victims in Shanghai but said they had found no other cases, indicating that the virus is not transmissible between humans. But ScienceInsider said that the sons of an 87-year-old victim of the virus had gotten pneumonia around the time their father fell ill, and one of them had died, raising suspicions that they too had the virus.

Some in China wonder if the 16,000 dead pigs found mysteriously floating last month in rivers that supply Shanghai with water could be to blame, but the Chinese government said it had tested the pigs and found no signs of the virus. Malik Peiris, a University of Hong Kong virologist, told ScienceInsider that the pigs were an unlikely culprit: “It is not expected that any form of influenza would lead to such a huge die-off in pigs.”

Yi Guan, also a virologist at the University of Hong Kong, said that studying the viruses isolated from the infected people would explain more. “We haven’t carefully analyzed the virus sequences yet,” he told ScienceInsider. “So far we have very, very limited information.”

Big Data Opportunities for Global Infectious Disease Surveillance
Simon I. Hay, Dylan B. George, Catherine L. Moyes, John S. Brownstein
Published: April 2, 2013
Where Are the Diseases of Clinical Significance?
It is perhaps surprising to state that we have an extremely poor knowledge of the global distribution of the vast majority of infectious diseases [1]. A review of all infectious diseases of clinical significance has revealed it would be of public health benefit to map about half of these conditions; yet, astonishingly, only 2% (seven of 355) have been mapped comprehensively [2]. This geographical ignorance frustrates a variety of clinical, epidemiological, and public health aspirations.

Here we argue that this information gulf has serious implications for global public health surveillance and that too little attention is given to spatial epidemiology in international preparedness planning. Stated simply, how can we gauge the risk posed by new infectious disease outbreaks if we have only the crudest understanding of their natural geographical range? Additionally, how do we prioritise useful intelligence in the growing deluge of Big Data [3]–[5] if the contemporary geographical distribution of these infectious disease threats is unknown? We suggest that it should be a policy priority to improve the ability to triage spatially, infectious disease outbreak alerts [6],[7].

How Do We Map Infectious Diseases?
To explore the factors hindering progress, we need to consider how traditional methods are used to map disease. We illustrate this in Figure 1 using a schematic of the cartographic process applied recently to map dengue [8],[9]. The objective is to make a continuous map of the entire geographical range of a disease from a sample of locations where the disease has been observed [10],[11]. In the ecological literature this is described as identifying the fundamental niche of the target organism [12],[13]. In our application it is the fundamental niche of an infectious disease. It is rare for any organism or disease to
fully exploit all of the environmental space that is available to it, due to a whole host of evolutionary, biogeographical and ecological factors, so to help guide the mapping process we use evidence-based expert knowledge to demark the crude global limits of a disease—its definitive extent or realised niche.

Figure 1 shows the process used to generate a continuous data layer of disease risk, in this example dengue. The process starts with records of disease occurrence obtained from the literature [14], web reports [3], and GenBank [15] that are used to define the definitive extent of the disease [16] and to populate a database of occurrence points where the disease has been reported. Because it is rare for disease absence to be recorded, a common practice in niche mapping and modelling is to infer absences [17],[18]. The definitive extent and occurrence point data are used to infer plausible pseudo-absence points for further analysis [9].

To complete the process illustrated in Figure 1, a range of epidemiologically relevant environmental covariates are also assembled. These covariates, such as temperature and rainfall, must cover the area over which prediction is desired. Statistical techniques are then used to characterise points of presence and pseudo-absence against the range of covariates assembled [19],[20]. In this instance we favoured the Boosted Regression Tree technique due to favourable comparative reviews of performance, statistical flexibility, and community support evidenced by well documented and freely available R-code [19],[20]. These relationships are then used to predict the probability that the disease occurs at each location and thereby generate a risk map with a quantified measure of uncertainty.

Can We Use Big Data Approaches to Routinely Map All of These Infectious Diseases?
The process described above provides a continuous risk map in space that is static in time. Conversely HealthMap (www.healthmap.org) provides continually updated disease occurrence points but not continuous spatial data. Can we conceive of spatially continuous risk maps being updated in “real-time”—as frequently as new occurrence data are assimilated? The conceptual bridge of imagining spatial modelling as a continuous process in time is achieved simply by linking the output risk map back to the data inputs to create a feedback loop. This is important as it facilitates the novel step of spatial triage of new occurrence information (see below) and critically, the potential for multiple iterations of the map with continuous improvement by adding a machine learning element. This conceptual shift towards evolving maps, in combination with the increased availability of novel digital data sources [5],[22], is now dissected in the context of “Big Data.”

Big Data is a term used to describe information assemblages that make conventional data, or database, processing problematic due to any combination of their size (volume), frequency of update (velocity), or diversity (variety) [24]. These “volume, velocity, and variety” descriptors have proven useful themes with which to explore opportunities and challenges of Big Data [24] and are emulated here. Each

![Figure 1. A schematic overview of the process of predicting spatial disease risk.](image)
part of this mapping process can be radically improved with a Big Data approach, and the extent of the Big Data challenge is highlighted in Table 1. These challenges are discussed in turn.

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Table 1. An assessment of the challenges of using Big Data in disease mapping. doi:10.1371/journal.pmed.1001413.t001

It is well established that a huge amount of novel data are being generated that will make important contributions to temporal public health surveillance [5],[22]. The secondary use of passive search query and micro-blogging data as well as actively collected crowd-sourced data for disease surveillance has been well documented and validated for major public health events, including influenza and dengue epidemics [22],[23],[25]. Though these data sources demonstrate significant noise and require continual model fine-tuning, the sheer volume of health outcome related searches and personal accounts presents incredible new opportunities to monitor population health in real time. It is less well appreciated that this information could also be used to build definitive extents and databases on the occurrence of many diseases [2]. The volume, velocity, and variety of occurrence information from these sources will increase rapidly and transform our ability to create geographical baselines for a range of diseases. These novel data sources come with issues of reliability so it is important that the machine learning process is calibrated for known reporting bias and the triage process assigns a weighting to each data point as a measure of reliability. This weighting is an integral part of the niche mapping techniques used and feeds into the measure of uncertainty output for each location. An increasing proportion of these new data are geopositioned at source. Moreover, machine learning approaches to automate geo-positioning of disease reports [26], especially when combined with human oversight and crowdsourcing (outsourcing tasks online to volunteers) [27],[28], can further radically lower the logistical barriers to positioning this information.

In the era of satellite sensors, a diversity of epidemiologically relevant environmental information can be sourced globally at daily intervals [29]. Big Data volume, velocity, and variety challenges are involved in moving from the traditional processing of synoptic averages of covariates to harnessing a wider variety of temporally rich information that can be matched in time with the new occurrence information. This closer temporal matching of disease outbreaks with covariates may improve the accuracy of mapping models, allowing for the possibility of seasonally tailored geographic baselines and may help improve traditional temporal surveillance by facilitating early warning of epidemiologically relevant environmental changes.

Perhaps the most important development in relation to Big Data is the conceptual move from static to improving and evolving risk maps. Taking further our example of dengue mapping (Figure 1), the first evidence-based risk map generated can be used to help triage the information content of new reports before running the next map iteration. For example, disease reports located nearby existing records and with a high-predicted probability of occurrence are not alarming; we expect the disease to occur here from the history of reporting and the suitability of the environment. Furthermore, such reports will not substantially alter the risk map and are thus of low priority to analysts. Conversely, a disease outbreak far away from observed occurrence is alarming, and more so if it occurs in an area biologically suitable for the disease. It should be investigated and, if verified, contribute to improving next iterations of the map. It is easy to imagine how these automated learning processes, supervised by expert analysts, could be deployed in tandem for all diseases of concern, transforming our spatial intelligence, surveillance, and preparedness.

The Challenges Ahead

The biggest obstacles to incorporating a continuous spatial mapping component to routine biosurveillance will be demonstrating the feasibility and sustainability of this undertaking and engaging the audience. We have focussed here on applications for biosurveillance but it is important to emphasise the wider audiences. First, one should never underestimate the value of risk maps in helping to illustrate the extent of a public health problem [30]. Second, addressing the paucity of spatial information on infectious
disease distributions will transform our understanding of their environmental determinants and help radically improve our understanding of the factors that promote disease diversity \[31\] and emergence \[32\]. Third, a comprehensive atlas of contemporary distributions would be of considerable benefit to improve future assessments of the burden of disease \[33\]. The audience for risk maps that are continuous in time and space includes agencies who need to prioritise limited resources and respond to changing disease patterns, public and private R&D pipelines who need to assess value and plan research strategy, logistics groups who need to optimise the roll out of new interventions/treatments, and clinicians who want to accurately diagnose infectious diseases in local populations and returning travellers.

We have already argued that this mapping ambition is made tractable by automating many of the laborious steps in primary data acquisition and positioning. The Big Data revolution is already underway and harnessing the useful information in these new data sources will involve collaborations with computer scientists at the forefront of machine learning and with those who have had success in engaging communities \[27\]. The evidence shows that motivating people to devote some of their “cognitive surplus” to crowd sourcing is possible, so long as the products and benefits are immediately available to all for the common good. We have seen the rise of crowdsourcing influenza surveillance with participatory systems such as Flu Near You in the United States (www.flunearyou.org) and Influenzanet in the EU (www.influenzanet.eu), which now boast nearly 100,000 volunteers combined. From the outset all infectious disease data and derived maps should be made freely available to ensure engagement. This will also facilitate the uptake of new resources and their consideration by policy makers. Once the primary investment in the software platform is complete, and the community established, sustainability increases because demands for user inputs decrease as the software learns and the mapped outputs become increasingly stable. The ultimate vision is to democratisethe platform by providing the code to all interested authorities.

**Pandemic Influenza A Viruses Escape from Restriction by Human MxA through Adaptive Mutations in the Nucleoprotein**

Benjamin Mänz equal contributor, Dominik Dornfeld equal contributor, Veronika Götz, Roland Zell, Petra Zimmermann, Otto Haller, Georg Kochs, Martin Schwemmle

**Author Summary**

Influenza A viruses of avian or swine origin sporadically enter into the human population but do not transmit between individuals. In rare cases, however, they establish a new virus lineage in humans. The mechanisms by which invading viruses overcome the species barrier are not well understood, but multiple adaptations to the new host are required. Surprisingly little is known about adaptive mutations that overcome restriction factors of the intrinsic and innate host defense system. In this study, we have identified adaptive mutations in pandemic strains A/Brevig Mission/1/1918 and A/Hamburg/4/2009 that confer resistance to the interferon-induced antiviral factor MxA which is a dynamin-like large GTPase that recognizes the incoming viral nucleocapsids and blocks their function. The resistance-enhancing mutations changed several amino acids in the viral nucleoprotein which is the main nucleocapsid component. These mutations were sufficient to increase the pathogenicity of an avian influenza virus strain in a Mx-positive mouse model. Interestingly, the resistance-associated amino acids are counter-selected in circulating avian influenza strains, because they compromise general viral replication fitness. The present data indicate that the innate immunity factor MxA provides a barrier against zoonotic introduction of influenza A viruses and that adaptive mutations in the nucleoprotein must be carefully monitored.

**Gel safe and acceptable as approach to preventing HIV from anal sex**

PITTSBURGH, April 3, 2013 – A reformulated version of an anti-HIV gel developed for vaginal use was found safe and acceptable by HIV-negative men and women who used it rectally, according to a Phase I clinical trial published today in *PLOS ONE*. The study, led by researchers with the U.S. National Institutes of Health (NIH)-funded Microbicide Trials Network (MTN), tested a reduced glycerin formulation of tenofovir gel, and has spurred the development of an expanded safety study of the gel, expected to launch later this year.

Rectal microbicides, gel-based antiretroviral products applied into the rectum with the use of an applicator, are being developed as an approach for preventing or reducing the sexual transmission of HIV from unprotected anal sex. Researchers are working on developing rectal-specific products as well as reformulations of vaginal products, specifically, tenofovir gel.
The study, known as MTN-007, was the first to evaluate tenofovir gel reformulated with less glycerin, a common additive found in many gel-like products, in the hopes of making it better suited for use in the rectum. It began in October 2010 and enrolled 65 men and women at three sites – the University of Pittsburgh, University of Alabama at Birmingham and Fenway Health in Boston.

In MTN-007, study participants were randomly assigned to one of four study groups. Three of these groups were assigned to use one of the following products for a one-week period: a reduced glycerin formulation of tenofovir gel; a placebo gel containing no active ingredient; or a gel containing the spermicide nonoxynol-9. A fourth group did not use any gel but took part in all of the study-related procedures and tests, including physical and rectal exams.

Study results, preliminarily presented at a scientific meeting in 2012, indicated no significant differences in side effects among the three gel groups. Eighty percent of participants reported minor side effects related to the use of study products, and 18 percent reported moderate side effects. (Two study participants reported severe adverse events, but they were not related to use of the study products.) Participants’ adherence to the use of their assigned study products was high, with 94 percent using the products daily as directed. When asked about the likelihood that they would use the gel in the future, 87 percent of the participants who used the reformulated gel indicated they would likely use the gel again, compared to 93 percent of the placebo gel group, and 63 percent of the nonoxynol-9 gel group. In addition to assessing safety and acceptability, researchers also conducted gene expression testing, and noted changes in the activation of some genes in the reduced glycerin tenofovir gel group, which they will continue to assess in future rectal microbicide studies.

"We are very encouraged that the reformulated gel was quite safe, and that most people who used it said they would be willing to use it in the future," said Ian McGowan, M.D., Ph.D., co-principal investigator of the MTN and professor of medicine, Division of Gastroenterology, Hepatology and Nutrition and Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh School of Medicine. "These results have formed the basis for a follow-up study that should provide us with even more detailed information about the safety and acceptability of the gel."

Researchers are now in the final planning stages of a Phase II, multi-site trial of the reformulated gel called MTN-017 that will involve 186 men who have sex with men and transgender women at clinical sites in Peru, South Africa, Thailand, and the U.S., including Puerto Rico. Participants will cycle through three study regimens: reformulated tenofovir gel used daily, reformulated tenofovir gel used before and after anal sex, and daily use of the antiretroviral tablet Truvada®. MTN-017 will allow researchers to collect additional information about the gel’s safety and acceptability in the rectum, and compare it to the use of Truvada.

CONRAD developed the reduced glycerin formulation of tenofovir gel evaluated in MTN-007 and it differs from the formulation originally developed for vaginal use. Although the vaginal gel produced a significant antiviral effect when used in the rectum, it was found to cause gastrointestinal side effects in some study participants in an earlier study called RMP-02/MTN-006.

The vaginal formulation of tenofovir gel continues to be evaluated for preventing the transmission of HIV through vaginal sex in women. Ongoing is a Phase III trial called FACTS 001 that is testing its use before and after sex among women in South Africa. FACTS 001 hopes to replicate the results of CAPRISA 004, which found this regimen reduced the risk of HIV by 39 percent compared to placebo gel. The VOICE Study (Vaginal and Oral Interventions to Control the Epidemic), however, found daily use of the gel not effective among its study participants; most of the women did not use the product daily as recommended.

KS-associated IRIS common among people starting HIV therapy in Africa
Michael Carter
Published: 04 April 2013

Over 13% of people with HIV-related Kaposi’s sarcoma experience a worsening of disease after starting antiretroviral therapy, an international team of investigators report in the online edition of AIDS. This paradoxical worsening of disease was attributed to immune reconstitution inflammatory syndrome (IRIS) and was significantly more likely to occur among patients in southern Africa compared to those in the UK.

The authors believe their findings have important implications for HIV treatment strategies in southern Africa and also highlight the need for improvements in KS awareness among both clinicians and patients in resource-limited settings.
Kaposi’s sarcoma (KS) is the most common HIV-related cancer and is an important cause of illnesses and death in sub-Saharan Africa.

The introduction of effective HIV therapy in the late 1990s was accompanied by a substantial fall in KS incidence among people with HIV in the UK and similar countries. Moreover, treatment with antiretroviral drugs alone has been associated with complete or partial resolution of KS in up to 80% of patients.

However, there have been case reports of KS disease actually worsening in some patients after they started HIV therapy. Such deterioration is probably due to IRIS.

Investigators wanted to establish a clearer understanding of the incidence and risk factors for KS-associated IRIS among people with baseline KS at the time they started antiretrovirals.

They therefore examined the results from four observational cohorts involving a total of 436 people with HIV-related KS at the time they started antiretroviral therapy. Three of the cohorts were in sub-Saharan Africa (South Africa, Zimbabwe and Mozambique) and contributed 49% of participants. The remaining 51% were enrolled in the fourth cohort, which involved participants from London.

Common criteria were used to diagnose KS-IRIS across all four cohort studies. Two investigators had to agree the diagnosis and a separate investigator reviewed all cases.

There were significant differences between the participants enrolled in the African and the UK cohorts. Participants in the UK cohort were more likely to be male (95 vs 45%, p < 0.001) and were older at the time of KS diagnosis (39 vs 35 years, p < 0.001). The participants in London also had less severe disease (T1, poor prognosis = 62 vs 87%, p < 0.001) and were also less likely to have detectable KS viral load (58 vs 76%, p = 0.004). All the participants from the sub-Saharan African cohorts were of African ethnicity, as were 16% of participants who received care in London.

Median CD4 cell count at the time HIV therapy started was 196 cells/mm³ for the UK cohort and 138 cells/mm³ for the African cohorts (p < 0.001).

Treatment strategies differed between sub-Saharan Africa and the UK. Treatment consisted of antiretroviral therapy alone for all the participants in the African cohorts. Just over a third (34%) of the participants in London received chemotherapy in conjunction with HIV treatment.

Some 19 participants were lost to follow-up before completing three months of antiretroviral therapy. The remaining 417 individuals contributed a total of 104 person-years of follow-up. Overall, 58 participants (14%) developed a paradoxical KS-IRIS. The rate was 20% for participants in the African cohorts and 9% for participants in London.

Incidence was 7 cases per 100 person-months for patients in Africa compared to an incidence of 3 cases per 100 person-months for the UK patients. The investigators therefore calculated that incidence was 2.5 times higher in Africa compared to the UK.

Risk factors for the development of a KS-IRIS were initial treatment with antiretroviral therapy alone (p = 0.047), more advanced KS disease stage (p = 0.013), a HIV viral load above 100,000 copies/ml (p = 0.005) and detectable KS viral load (p = 0.015).

After the development of KS-IRIS, some 55% of participants received treatment with a combination of antiretroviral therapy and chemotherapy. The remaining participants received HIV treatment only.

Some 7% of patients had a complete response to treatment; 40% had a partial response; KS disease remained stable in 12% and 36% of individuals experienced disease progression, including 33% of patients who died.

All the participants in London had a complete or partial response compared to 23% of participants in sub-Saharan Africa.

The mortality rate was significantly higher among KS-IRIS patients compared to patients who did not have this paradoxical reaction (33 vs 11%, p < 0.001).

“Our results...highlight the relevance of KS-IRIS to mortality in SSA [sub-Saharan Africa], which is remarkably higher than for any other paradoxical IRIS event associated with major OIs [opportunistic infections], such as Cryptococcus or TB,” comment the authors.

Mortality risk factors were KS-IRIS (p < 0.001), not receiving chemotherapy (p = 0.029), a baseline CD4 cell count below 200 cells/mm³ (p = 0.05) and a detectable KS viral load at baseline (p = 0.069).

The investigators believe their findings have a number of “clinical and programmatic implications”. These include the continued scale-up of antiretroviral treatment in resource-limited settings and the initiation of treatment at a CD4 threshold of 350 cells/mm³.

The authors also believe that education surrounding KS needs to be improved in resource-limited settings and that there is an “urgent need” for global guidance on the management of KS and KS-IRIS.

Reference
April 3, 2013

Why HIV That Transmits Is More Infectious and Resilient

The individual HIV particles that succeed in transmitting between people are particularly resistant to the human immune response and are also structured to better access and enter immune cells, according to new research from Los Alamos National Laboratory and the University of Pennsylvania. The Penn researchers cloned virus from an acute, or recent, infection as well as viruses from people chronically infected and then compared the two.

Because HIV mutates so rapidly, the properties of the overall population of virus within an individual person changes significantly over time, meaning that it soon becomes different from the virus that initially caused the infection. There is also diversity in the viral population at any given time.

The investigators found that the transmitted viruses were more infectious and also had a more significant amount of what is known as envelope protein, which is a tool HIV uses to enter human immune cells. The transmitted HIV also had the capacity to thrive in the presence of alpha interferon, which belongs to a class of anti-viral immune cells called cytokines. When HIV first infects the body, the immune system reacts with a massive assault known as a “cytokine storm,” which eventually tapers as someone becomes chronically infected. By comparison, alpha interferon had a significant anti-viral effect against the cells cloned from the chronically infected people.

“The viruses that make it through transmission barriers to infect a new person are particularly infectious and resilient,” Los Alamos National Laboratory scientist Bette Korber said in a release. “Through this study we now better understand the biology that defines that resilience.”

Hepatitis A virus discovered to cloak itself in membranes hijacked from infected cells

CHAPEL HILL, N.C – Viruses have historically been classified into one of two types – those with an outer lipid-containing envelope and those without an envelope. For the first time, researchers at the University of North Carolina have discovered that hepatitis A virus, a common cause of enterically transmitted hepatitis, takes on characteristics of both virus types depending on whether it is in a host or in the environment.

“The whole universe of virology is divided into two types of viruses – viruses that are enveloped and viruses that are not enveloped. If you look at any basic virology textbook, it will say that these are categories that distinguish all viruses,” said lead researcher Stanley M. Lemon, MD, professor of medicine and a member of the UNC Lineberger Comprehensive Cancer Center and the Center for Translational Immunology.

In a paper published online in Nature on March 31, Dr. Lemon’s
team discovered that hepatitis A virus does not have an envelope when found in the environment, but acquires one from the cells that it grows in within the liver. It circulates in the blood completely cloaked in these membranes.

"What we have discovered is that a virus that has been classically considered to be 'non-enveloped', that is hepatitis A virus, actually hijacks membranes from the cells it grows in to wrap itself in an envelope. It steals membranes from the cell, as it leaves the cell, to cloak itself in this envelope that then protects it from antibodies. And that's really novel. No one has shown that previously for a virus. It really blurs that classic distinction between these two types of viruses," said Dr. Lemon.

Being enveloped in host membranes helps the virus to evade host immune systems and spread within the liver. Enveloped viruses are generally quite fragile in the environment, while non-enveloped viruses are harder outside of a host and can survive for longer periods between hosts. Dr. Lemon believes the dual nature of hepatitis A virus allows it to use the advantages of both virus types to enhance its survivability.

"What hepatitis A virus has done, and we don't totally understand how it has accomplished this, is to have the advantage of existing as a virus with no envelope and being very stable in the environment so it can be transmitted efficiently between people, but to wrap itself in a membrane to evade neutralizing antibodies and facilitate its spread within the host once it has infected a person," said Lemon. While no other virus has been shown to exhibit this particular behavior, Dr. Lemon said that it is likely that hepatitis A virus is not unique in its dual nature.

Hepatitis A is endemic in developing nations that lack modern sanitation and clean water. The virus is transmitted orally and then passed back into the environment through feces. By not needing its envelope to survive outside the host, the virus gains the ability of non-enveloped viruses to survive longer and be transmitted efficiently.

One major question raised by the finding is why the hepatitis A vaccine works so well to contain the infection. The vaccine, one of the most effective in use, was thought to elicit neutralizing antibodies that attack the virus in the blood. Since it is now known that the envelope surrounding the virus in the blood prevents this, the vaccine cannot work as previously thought.

"It makes us rethink completely the mechanism underlying the well-documented efficacy of hepatitis A vaccine. I think this is one of the most important things to come out of the study," said Dr. Lemon. The research at UNC was funded by the National Institute of Allergy and Infectious Diseases. Future studies will investigate the mechanisms behind the vaccine's effectiveness, Dr. Lemon said. While it was previously thought that vaccine-induced antibodies attacked the virus outside of the cell, the new findings suggest antibodies may actually be able to restrict viral replication within a cell.

"Understanding how this really good vaccine works will help us in the future to develop better vaccines for other viruses that we are having difficulty developing vaccines for," said Dr. Lemon.

Assessing Disease Surveillance and Notification Systems After a Pandemic

Apr. 3, 2013 — Significant investments over the past decade into disease surveillance and notification systems appear to have "paid off" and the systems "work remarkably well," says a Georgetown University Medical Center researcher who examined the public health response systems during the 2009 H1N1 influenza pandemic.

The findings are published online today in PLOS ONE.

After the Sept. 11 terrorist attacks in the U.S. and the potential threat of bioterrorism, many new advanced systems for disease surveillance and notification have been developed and implemented throughout the world. The goal of these systems is not only to detect a possible biological attack, but to characterize emerging pathogens so that a public health response can be implemented rapidly.

"You can't test these systems on a day-to-day basis," says the study's corresponding author, Michael A. Stoto, PhD, a professor in the department of health systems administration at Georgetown University School of Nursing & Health Studies, part of Georgetown University Medical Center. "The only way to test these systems is how they perform in a real public health emergency."

Stoto and his colleagues conducted a systematic and detailed review of the scientific literature, official documents, websites and news reports to construct a timeline of events for the 2009 H1N1 influenza pandemic, including the emergence and spread of the virus, local health officials' awareness and understanding of the outbreak, and notifications about the events and their implications.

Stoto’s analysis focused on three critical events: the identification of a novel viral subtype in two California children, the recognition that multiple disease outbreaks throughout Mexico were connected to
the two cases California cases, and the additional connection of about 100 New York City school children who had been to Mexico for spring break.

"Enhanced laboratory capacity in the U.S. and Canada led to earlier identification and characterization of the novel H1N1 strain," says Stoto, an expert on population health and public health assessment. "That recognition triggered national and global pandemic plans." He says tests were quickly developed to aid in surveillance and clinical decision-making and a vaccine was developed in time for the second H1N1 pandemic wave in fall 2009.

He also credits enhanced global notification systems that led to an earlier detection and characterization of the outbreak by "connecting the dots" between the cases in California, Mexico and New York City.

"The systems worked remarkably well," Stoto says, estimating that it might have been possible for the detection to be made a week sooner, though he says it's not likely that earlier detection would have changed the outcome. "Had the pandemic occurred as recently as 10 years ago, the delay could have been much greater," Stoto adds.

"What really made a difference in 2009 was that people from the U.S. and Mexico talked to each other through a formalized system of communication," he says. "I think taxpayers and policymakers want to know if the billions invested after 9-11 to prepare for a biological event is paying off. I think the answer is 'yes.' We've made significant progress in a short time."

Journal Reference:

Fighting Listeria and Other Food-Borne Illnesses With Nanobiotechnology
Researchers at Rensselaer Polytechnic Institute have developed a new method to kill deadly pathogenic bacteria in food handling and packaging. Using nature as their inspiration, the researchers successfully attached cell lytic enzymes to food-safe silica nanoparticles, and created a coating (seen up close in this scanning electron micrograph image) with the demonstrated ability to selectively kill listeria—a dangerous foodborne bacteria that causes an estimated 500 deaths every year in the United States.

(Credit: Rensselaer/Dordick)

Apr. 2, 2013 — Engineering researchers at Rensselaer Polytechnic Institute have developed a new method to kill deadly pathogenic bacteria, including listeria, in food handling and packaging. This innovation represents an alternative to the use of antibiotics or chemical decontamination in food supply systems.

Using nature as their inspiration, the researchers successfully attached cell lytic enzymes to food-safe silica nanoparticles, and created a coating with the demonstrated ability to selectively kill listeria—a dangerous foodborne bacteria that causes an estimated 500 deaths every year in the United States. The coating kills listeria on contact, even at high concentrations, within a few minutes without affecting other bacteria. The lytic enzymes can also be attached to starch nanoparticles commonly used in food packaging.
This new method is modular, and by using different lytic enzymes, could be engineered to create surfaces that selectively target other deadly bacteria such as anthrax, said Jonathan Dordick, vice president for research and the Howard P. Isermann Professor at Rensselaer, who helped lead the study.

This research, which combined the expertise of chemical engineers and material scientists, took place in the Rensselaer Center for Biotechnology and Interdisciplinary Studies and the Rensselaer Nanoscale Science and Engineering Center for the Directed Assembly of Nanostructures. Collaborating with Dordick were Rensselaer colleagues Ravi Kane, the P.K. Lashmet Professor of Chemical and Biological Engineering, and Linda Schadler, the Russell Sage Professor and associate dean for academic affairs for the Rensselaer School of Engineering.

"In this study, we have identified a new strategy for selectively killing specific types of bacteria. Stable enzyme-based coatings or sprays could be used in food supply infrastructure -- from picking equipment to packaging to preparation -- to kill listeria before anyone has a chance to get sick from it," Kane said.

"What's most exciting is that we can adapt this technology for all different kinds of harmful or deadly bacteria."

Results of the study are detailed in the paper "Enzyme-based Listericidal Nanocomposites," published today in the journal Scientific Reports from the Nature Publishing Group.

This most recent study builds upon the research team's success in 2010 of creating a coating for killing methicillin resistant Staphylococcus aureus (MRSA), the bacteria responsible for antibiotic resistant infections. While the previous coating was intended for use on surgical equipment and hospital walls, the development of a listeria-killing coating had the extra challenge of needing to be food-safe.

Dordick and the research team found their answer in lytic enzymes. Viruses that affect bacteria, called phages, inject their genetic material into healthy cells. The phage takes over a healthy cell, and in effect transforms the host cell into a little factory that creates more phages. Near the end of its life cycle, the original phage creates and releases lytic enzymes, which break down and make holes in cell walls of the infected bacteria. The manufactured phages escape through these holes and go on to infect other healthy cells.

Nature used lytic enzymes to break out of bacterial cells, Dordick said, and the researchers worked for years to exploit the same lytic enzymes to break into bacteria such as MRSA and listeria.

To stabilize the listeria-killing lytic enzymes, called Ply500, the researchers attached them to U.S. Food and Drug Administration-approved silica nanoparticles to create an ultra-thin film. The researchers also used maltose binding protein to attach Ply500 to edible starch nanoparticles commonly used in food packaging. Both Ply500 formulations were effective in killing within 24 hours all listeria at concentrations as high as 100,000 bacteria per milliliter -- a significantly higher concentration than normally found in food contamination situations.

"Starch is an inexpensive, edible material often sprayed into the packaging as a powder layer on meat product. We took advantage of the natural affinity of a maltose binding protein fused to Ply500, and biologically bound Ply500 to starch as a non-antibiotic, non-chemical agent for reducing the threat of listeria to our food supply," Schadler said.

Looking forward, the research team plans to continue investigating new methods for harnessing the power of lytic enzymes to selectively kill harmful bacteria.

Journal Reference:

New Instrument Will Quickly Detect Botulinum, Ricin, Other Biothreat Agents

Apr. 2, 2013 — Researchers at Sandia National Laboratories are developing a medical instrument that will be able to quickly detect a suite of biothreat agents, including anthrax, ricin, botulinum, shiga and SEB toxin.

The device, once developed, approved by the Food and Drug Administration and commercialized, would most likely be used in emergency rooms in the event of a bioterrorism incident.

"This is an unmet need for the nation's biodefense program," said Anup Singh, senior manager for Sandia's biological science and technology group. "A point-of-care device does not exist."

Sandia's work is funded by a recent grant -- nearly $4 million over four years -- from the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health. NIH has funded a number of recent projects at Sandia.

Sandia's biosciences and microfluidics program areas have continued to evolve with a string of notable projects, including:
MicroChemLab, a trailblazer in lab-on-a-chip technology, developed in the early 1990s
The "saliva device" and a follow-up technology, RapiDx, developed in the early-to-mid 2000s
SpinDx, the latest medical diagnostic tool developed at Sandia

"This will take things to the next level," said Singh. In addition to the broader suite of toxins and bacterial agents that the device would test for, the project includes comprehensive testing with animal (mouse) samples.

This is an important step, Singh said, since toxins may behave differently in live animals and humans than in laboratory blood samples. "We are getting closer and closer to translational elements of research, which involves testing in animal and clinical facilities. This is part of the maturation of our bioresearch activities at Sandia."

The project also will increase what SpinDx can do, he added. "When you look for bacterial agents, you don't want to rely solely on proteins because you won't get the detection sensitivity you need," explained Singh. "So we are also using other methods that may lead to better detection limits and additional confirmation."

The new NIH project includes collaborators with expertise in animal modeling as well as device manufacturing.

The University of Texas Medical Branch, with whom Sandia enjoys a years-long partnership, together with the U.S. Department of Agriculture's Western Regional Research Center in Albany, Calif., are providing Sandia with expert insight into toxins and diseases at animal lab facilities. Bio-Rad, a manufacturer and distributor of a variety of devices and laboratory technologies, is serving as a consultant on the project to evaluate plans for product development, assist with manufacturers' criteria on the device that is developed, and provide important feedback when a prototype is built.

Although the latest NIH award represents a continuing success story for Sandia's microfluidics/bioresearch work, Singh stresses that it was part of a thoughtful multi-year strategy.

"You've got to keep innovating and coming up with the next thing," he said. "Every technology has its lifecycle. As good as SpinDx is, we know there will be other technologies, better technologies that come along in the next few years. We have to continue to innovate to meet the needs of our customers, understand what other competing technologies are being designed to solve the problems and develop technologies that provide an improvement."

The need for diagnostic devices for biodefense is not going away, Singh said, since there are always new diseases springing up that lack good diagnostic assays.

"Plus, we want dual-use devices that combat both man-made and nature-made problems," he added. "We're not just going to wait for the next anthrax letter incident to happen for our devices to be used and tested; we want them to be useful for other things as well, like infectious diseases."

Expanding into those areas, he said, will keep Sandia's bioresearch efforts engaged for years to come. "That's where the value of the national labs really comes in," Singh said. "Our capabilities and culture are a very good fit for tackling long-term problems that require a sustained effort."

**The Judgment In Novartis v. India: What The Supreme Court Of India Said**

Published on 4 April 2013 @ 4:33 pm

Intellectual Property Watch

By Frederick M. Abbott

As part of a series of amendments to the India Patents Act that took effect on January 1, 2005, the Parliament of India adopted Section 3(d). This statutory provision has been in force for more than seven years. A challenge brought by Novartis to the constitutionality of the provision and to its compatibility with the WTO TRIPS Agreement (World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights) was rejected by the High Court at Madras in 2007. That judgment was not appealed. On 1 April 2013, the Supreme Court of India rendered judgment [pdf] on an appeal by Novartis against rejection by the India Patent Office of a product patent application for a specific compound, the beta crystalline form of imatinib mesylate. Imatinib mesylate is used to treat chronic myeloid leukemia and is marketed by Novartis as “Glivec” or “Gleevec”. Affirming the rejection, the Supreme Court confirmed that the beta crystalline form of imatinib mesylate failed the test of Section 3(d). The Court clarified that efficacy as contemplated under Section 3(d) is therapeutic efficacy.

This judgment has attracted worldwide press coverage. It has received severe criticism from a number of originator pharmaceutical companies, including Novartis, and from the US Chamber of Commerce, to the effect the judgment of the Indian Supreme Court has dealt a harsh blow against the future of
innovation, particularly in India. It is somewhat difficult to know why this decision interpreting Section 3(d) should come as a major surprise to anyone. Perhaps more important, it is difficult to understand what it is about the Supreme Court judgment that might so offend the sensibility of patent lawyers or government policymakers. The judgment is well-crafted, with close attention to the facts presented, and appears to take a balanced view of the matters brought before the Court. What did the Supreme Court of India say?

The case involves a substantial number of fairly complex technical issues, including some fairly complex legal issues. Without intending an injustice to that complexity, the main points made by the Court are these:

1. The express terms of the Patents Act as amended in 2005 reflect the considered judgment and will of the Indian Parliament as found in the legislative record. Section 3(d) was proposed by the Government with the stated purpose of addressing concerns raised by members of Parliament that the introduction of pharmaceutical product patent protection would substantially inhibit the availability of medicines for the population of India and developing countries more generally. Parliament sought to limit practices that might result in the grant of patents for insubstantial technological contributions. Parliament adopted in the Section 3(d) amendment, including the explanation, a requirement that patents for new forms of known substances should only be granted on the showing of a significant enhancement in known efficacy.

2. International legal rules accepted by India, in particular the WTO TRIPS Agreement, provide sufficient leeway or flexibility in the adoption of patenting standards to allow the approach adopted by the Indian Parliament.

3. The facts of this case involve certain transitional arrangements between the former pre-2005 Indian patent system which did not allow patents for pharmaceutical products, and the post-2005 regime under which such patents are permitted. For patent applications filed (with priority date) before 1 January 1995, a patent could not be secured in India for a pharmaceutical product. From 1995 to 2005, pharmaceutical product patent applications could be filed and held in a “mailbox”. A patent could be granted and become effective after 1 January 2005, based on a “mailbox application”.

4. In 1992, Novartis filed an initial patent application in the United States covering the drug “imatinib”, which patent application also covered pharmaceutically acceptable salts. It was subsequently granted a patent. Novartis applied for and received US Food and Drug Administration (FDA) approval for the marketing of a salt form of that drug called “imatinib mesylate”. The drug was placed on the market in that form in 2001.

5. In 1997, Novartis filed a patent application for a specific variation of the imatinib mesylate salt, the “beta crystalline” form. An examiner in the United States rejected this patent application, but the examiner was overruled by a Patent Office appeal board because the new crystalline form of the mesylate salt of imatinib involved a sufficient “manipulative step” under US patent law. The patent was granted for the United States.

6. In 1998, Novartis filed an application in India for this beta crystalline form. The application did not disclose any improvement in efficacy. However, when India adopted section 3(d) in 2005, Novartis undertook some studies to meet the statutory requirement to show enhanced efficacy.

7. The first issue before the Supreme Court was whether the mesylate salt form of imatinib had been disclosed, and was therefore publicly known, prior to 1997. On the basis of the documents, the Supreme Court found that it was. The mesylate salt was the form in which the drug was marketed. To satisfy the requirement of “enhanced efficacy” in section 3(d), comparison of the beta crystalline form had to be made with the already known mesylate salt. In light of this, the Indian Supreme Court found the efficacy studies reported by Novartis very odd. Novartis alleged that the beta crystalline form showed a 30% increase in “bioavailability” (based on tests in rats). But this 30% increase in bioavailability was not in comparison to the known and previously marketed mesylate salt form of the drug, which would ordinarily be soluble, but rather in comparison to the “free base” form of the imatinib drug that was not marketed because it was not soluble. So, Novartis did not compare its “new” form of salt to its “old” marketed form of salt, but rather to what it knew would be a much less bioavailable form. There was no evidence in the record as to how the new salt compared to the old salt even in terms of bioavailability.

8. The Supreme Court interpreted the meaning of “efficacy” in Section 3(d). It said that the new form of a drug must demonstrate an improvement in its therapeutic effect or curative property as compared to the old form in order to secure a patent. Novartis offered evidence that the beta crystalline form differed regarding certain properties relating to production and storage (e.g., heat stability). The
The Court held that these properties may be important from a storage point of view, but would not be relevant to showing “enhanced therapeutic efficacy”.

9. As previously noted, Novartis also presented evidence regarding increased “bioavailability”. The Court observed that “bioavailability” measures the level at which the drug is made available in the human body. The level of bioavailability may or may not have an influence on the therapeutic or curative effect of the drug. In this case, the Court held that such effect was not demonstrated.

10. The Court discussed at some length the meaning of therapeutic efficacy in respect to pharmaceutical products, and observed that there are different possible meanings. The definition may be limited only to action resulting in a curative effect, or it might be more broadly extended to cover improved safety or reduced toxicity. The Court decided to leave open what is the appropriate definition of enhanced (therapeutic) efficacy – the narrower or broader interpretation – because it did not need to reach that question in this case. Novartis had provided no evidence that the beta crystalline form of imatinib improved the therapeutic effect of the drug. There was nothing to measure. The Court did not say that a change in bioavailability may never result in enhanced efficacy. It said that the patent applicant needed to demonstrate that there was a resulting enhancement in efficacy.

11. At the very end of the decision, in requiring Novartis to pay the costs of the challengers, the Court said that it appeared that Novartis was in fact marketing an older form of the drug and not the beta crystalline version, and that it appeared that Novartis may have been trying to use a patent in India to cover a drug that it was not actually selling. It suggested that this showed Novartis “in rather poor light”.

The Supreme Court affirmed that India has adopted a standard of pharmaceutical patenting that is stricter than that followed by the US or the EU. For India, a patent applicant must not only show that a new form of known compound is different than an old form, but that the modification will result in an improvement in the treatment of the patient. There is in fact nothing new about such a standard. This was the approach followed by the US Patent Office up until a case decided by the Court of Appeals for the Federal Circuit, In re Brana, in 1995. Today, the Patent Office and Federal Circuit will approve patents for very minor modifications, supporting the practice known as “evergreening”. This is a very expensive proposition for US consumers because it allows the manufacturers to market and sell higher-priced patent-protected versions of their popular drugs.

The Federal Circuit rationalizes this practice, saying that allowing patenting without demonstration of significant therapeutic effect encourages the development of new compounds, therefore encouraging innovation. But, this is just a theory about the best time along a continuum for granting a patent. It may well be that granting patents after researchers have demonstrated that drugs will accomplish something significant in terms of curative effect will encourage researchers to concentrate on achieving desirable end results, rather than winning marketing games. The race will not be won by the first person who creates a new compound, but the first person who creates a new compound and shows that it is therapeutically significant.

The Indian Parliament, supported by the Supreme Court, has decided that Indian consumers should only pay for expensive patented products when those products represent a genuine advance over older versions. It is important to note what the Supreme Court did not say. It did not say that a new form of known compound may never be patented. It did not say that improving the bioavailability characteristics of the drug may never result in enhanced efficacy. It left open the question whether enhanced efficacy refers narrowly to curative effect, or more broadly to improved safety profile and reduced toxicity.

From a patent law standpoint, it is rather difficult to discern what about the Supreme Court’s decision strikes the US Chamber of Commerce, Pfizer or Novartis as some great threat to innovation or the long-term welfare of patients. It may put a damper on the profits of Pfizer or Novartis as they are less able to extend the life of patents by minor modifications that result in patients and public health systems paying more for drugs. But, one should be very careful of confusing the interests of the shareholders of Pfizer and Novartis with the interest of patients in the United States, Europe, India or Kenya. One might also be skeptical of claims from the industry that it will withdraw from the Indian market. Where there are profits to be made, the industry will be participating.

Botswana’s draconian Public Health Bill approved by Parliament, BONELA will challenge it as unconstitutional once President signs into law (Update 3)
Update: April 5th 2013
Very disappointing news from Botswana. The Public Health Bill – including all of its draconian provisions on HIV – has been approved by Parliament.

**BONELA issued this press release** last week just prior to the vote.

MEMBERS OF PARLIAMENT (MPs) ARE THE ONLY ONES WHO CAN SAVE US FROM THE PROPOSED PUBLIC HEALTH BILL……IT IS IN THEIR HANDS

We knew that the Public Health Bill will be back in Parliament for further debate. However, we had anticipated that the Ministry of Health would heed calls made by stakeholders such as BONELA, UNAIDS, WHO, SALT, AIDS Alliance, ARASA, Ditshwanelo and other concerned Batswana and make amendments to the bill, particularly on the controversial, offensive and invasive provisions.

To our utter shock, the Ministry of Health intends to make no changes to the bill at all; even with the benefit of information on best practices availed to them. This to us; is a clear case of indifference and a deliberate plan to violate people’s rights.

BONELA and its stakeholders have done all that is possible to raise awareness, especially to the general public who would be affected by this law. It is now up to MPs to propose and vote on the amendments.

If MPs fail or decide not to discharge that constitutional mandate, as concerned stakeholders, we would know that our MPs are happy to see people’s rights being violated—that they are happy to see Batswana being tested for HIV without their consent, happy to give doctors sole mandates on deciding when and what to do with patients without consultations.

We would also know that MPs by failing to do their duty are happy to see litigants in court pleading not to be tested for HIV because their government want them to. Moreover, we would know that our MPs are happy to place responsibilities of sexual matters ONLY on those who are HIV positive by agreeing with forceful disclosure to all potential sexual partners by people living with HIV even if they are using protection.

Lastly, our MPs will be happy to see that whoever seeks dental services is required to do an HIV test before such services are meted.

It is therefore, in the hands of MPs to exercise their power to propose and vote for a sound Public Health bill. It is in your hands……

According to [this APA piece, published on Wednesday](#), the Bill was approved by parliament. BONELA is now waiting for Botswana President, Ian Khama, to sign the Bill into law before it can approach the High Court to challenge the offending clauses as unconstitutional.

Botswana’s Health Minister, Dr John Seakgosing, on Tuesday said the Public Health Bill, which seeks among other things, to isolate people who infect others with sexually-transmitted diseases such as HIV/AIDS, while knowing their status, will apply to Members of Parliament, cabinet ministers and even the president.

He explained to APA in an interview that the Bill that was passed last week, will not apply only to ordinary citizens.

According to Seakgosing, if the president, ministers and legislators are found to be infecting others carelessly, they will be brought before the courts where the magistrate will take a decision to isolate them from the public.

While he explained that the Bill does not seek to empower medical practitioners to force clients to undergo tests, but Clause 104 (3) (b) provides that “the director or a person authorised by him may where necessary and reasonable, require a person or a category of persons to undergo an HIV test”. Clause 104 (4) then provides that “where a person required to undergo a test under Clause 104 (3) refuses to do so, the director may apply to a magistrate for an order requiring that person to undergo the test.”

But some HIV/AIDS activists are up in arms saying the Bill will reverse the gains achieved in fighting the HIV scourge as it encourages discrimination.

AIDS advocacy group Botswana Network on Ethics Law and HIV/AIDS (BONELA) says it intends to take the government to court over the Public Health Bill that has been approved by parliament.

BONELA director, Uyapo Ndadi, said in an interview that his organisation is only waiting for President Ian Khama to sign the Bill into law before it can approach the high court to challenge certain clauses in it as they are unconstitutional.

**Update: December 14th 2012**
The Public Health Bill has been shelved until next February thanks to the advocacy against the “outrageous” HIV-related provisions (see below) spearheaded by the Botswana Network on Ethics, Law and HIV/AIDS (BONELA). That’s the good news this morning, according to Uyapo Ndadi, BONELA’s Executive Director:
I am happy to inform you that the outrageous Public Health Bill has been shelved, at least until next year February when parliament resumes business. Our collective advocacy has helped to thwart cabinet’s plans to have the bill passed into law during this sitting.

I am happy to further inform you that UNAIDS has also written to our government to remove the draconian provisions from the bill.

It is now hoped that in the intervening months, BONELA and other human rights advocates will add to the pressure created by UNAIDS to make the Government see that in order to save face internationally, they must either substantially rewrite the Bill or drop it completely.

**Update: December 11th**
Disappointing and worrying news today from BONELA:

Parliament yesterday voted in favour of passing the Bill from the 2nd reading stage to the Committee stage. Amendments to the Bill may be made at the Committee stage. It means that our efforts to get the Minister to withdraw the bill for lack of consultation have failed. Our hope now is that Parliament will remove from the bill the draconian parts of it.

A report in BOPA daily news highlights the debate yesterday

The Member of Parliament for Lobatse, Mr Nehemiah Modubule says he does not support the Public Health Bill in its current state. Debating the bill in parliament on Thursday, Mr Modubule said it should first be put into perspective, as some of the clauses are contradictory. He argued that they would have a hard time trying to amend such clauses if the bill passes to the committee stage. He noted that consultations with some stakeholders such as Botswana Network on Law and AIDS (BONELA) were not done. Furthermore, he said, the minister of health should have done justice to the bill by deferring it for further consultations, as some clauses touch on customs and practices of Batswana.

In his contribution, the MP for Moshupa, Mr Mokgweetsi Masisi supported the bill, arguing that prevention and control of diseases is not peculiar to Botswana, more so that new communicable diseases continue to emerge. Mr Masisi said the bill conforms to international practices in terms of public health, adding that consultations had been done and they should not delay the bill.

**Original post: December 10th**
On Friday, Botswana’s Parliament debated the proposed Public Health Bill which contains some shocking and regressive HIV-related provisions that, according to a strongly-worded press release from the Botswana Network on Ethics, Law and HIV/AIDS (BONELA) “have no place in a democratic and modern day Botswana..that are counter-productive, discriminatory, unconstitutional and barbaric.”

The relevant passages of the Bill are available to download here ([Botswana Public Health Bill 2012.pdf](Botswana Public Health Bill 2012.pdf), 1.4MB)

Some of the most problematic provisions as highlighted by BONELA, are below.

**Clause 104(3) b** – empowering medical practitioners to force their patients to undergo HIV tests without their consent.

The Director, or any person authorised by him or her, may, where necessary and reasonable require a person or a category of persons to undergo an HIV test.

**Clause 105 (2) b** – empowering doctors to test patients without their knowledge.

A medical practitioner responsible for the treatment of a person may conduct an HIV test without the consent of that person where — (b) the medical practitioner believes that such a test is clinically necessary or desirable in the interests of that person.

**Clause 109 (3)** – allowing surgeons or dentists to test a patient for HIV before deciding on whether to carry out a non-urgent procedure.

Where, in the opinion of a medical practitioner, nurse or dental practitioner, the surgical or dental procedure is not urgently required in respect of a person, the medical practitioner, nurse or dental practitioner may require the person to undergo an HIV test before carrying out that procedure.

**Clause 116 (1)** – mandating HIV disclosure to all potential sexual partners or care giver and allowing prosecution for placing another at risk.

A person who is aware of being infected with HIV or is carrying and is aware of carrying HIV antibodies shall — (a) take all reasonable measures and precautions to prevent the transmission of HIV to others; (b) inform, in advance, any sexual contact or care giver or person with whom sharp instruments are shared, of that fact; and (c) not place another person at risk of becoming infected with HIV.

**Clause 116 (7)** empowering doctors to disclose their patient’s HIV status to their sexual partner without their consent.

A medical practitioner who is responsible for the treatment of a person and who becomes aware that the person has not, after a reasonable opportunity [disclosed their HIV status] may, after consultation
with an approved specialist medical practitioner, inform any sexual contact or care giver of that person of the HIV or HIV antibody status of that person.

**Clause 116 (9-12)** - limiting the right to freedom of movement for people with HIV without sufficient legal checks and balances.

(9) The Director or any officer representing the Director may, in writing, apply to a magistrate for an order where the Director reasonably believes that a person infected with HIV — (a) is not complying with this Part; b) knowingly or recklessly places another person at risk of becoming infected with HIV without the knowledge of that person of the infected person’s HIV status; or (c) is likely to continue the behaviour referred to in paragraph (b). (10) For the purpose of subsection (9), a magistrate may make any or all of the following orders — (a) an order that the person infected with HIV undergo such medical and psychological assessment as the Minister determines; (b) an order imposing restrictions on the person for a period not exceeding 28 days; or (c) an order requiring that the person be isolated and detained by a person, at a place and in the manner specified in the order for a period not exceeding 28 days. (11) In making an order in respect of a person under subsection (10), a magistrate shall take into account the following matters — (a) whether, and by what method, the person transmitted HIV; (b) the seriousness of the risk of the person infecting other persons; (c) the past behaviour and likely future behaviour of the person; and (d) any other matter the magistrate considers relevant. (12) The Director may, in writing, apply to a magistrate to renew an order made under subsection (10) for a further period or periods not exceeding 28 days.

According to BONELA, the Bill appeared from out of the blue without any public consultation.

We are concerned by government attitude and tendency of introducing Bills in Parliament and debating them before engaging all stakeholders, including the civil society and Batswana as a whole. We know that the Botswana Health Professions Council is not aware of this Bill for they have not been consulted on it. As custodians of health we expect them to be intimately involved as this Bill is going to affect the way they work. This bill is significant in the lives of all of us and we therefore call upon [Minister of Health] Reverend Dr. John G.N. Seakgosing [contactable via phone on +26731363251] to withdraw it and if he refuses to, we urge MPs to reject it.

Although the Bill was discussed last Friday – and a copy of the Bill obtained only then – Parliament adjourned before voting, but will continue this week. Action, therefore, is urgently required.

**Highly Lethal Ebola Virus Has Diagnostic Achilles' Heel for Biothreat Detection, Scientists Say**

Apr. 5, 2013 — By screening a library of a billion llama antibodies on live Ebola viruses in the Texas Biomedical Research Institute’s highest biocontainment laboratory, scientists have identified a potential weakness in the make-up of these deadly agents that can immediately yield a sensitive test.

"Detecting single viral protein components can be challenging, especially at very low levels. However, most viruses are repetitive assemblies of a few components, called antigens, with some existing as polymers which present highly 'avid' targets for antibodies," said Texas Biomed virologist Andrew Hayhurst, Ph.D.

"Think of one pair of microscopic Velcro hooks where one hook is the viral antigen and the other is the antibody and it is a weak interaction. Have a thousand pairs of hooks and it makes a very powerful interaction... just like Velcro fasteners on hiking gear," Hayhurst explained.

The screening performed by Hayhurst and assistant Laura Jo Sherwood guided the selection of llama antibodies recognizing a polymer hiding within Ebola called nucleoprotein (NP). Remarkably, each antibody could be used in its own right to form a sensitive test for the Ebola NP, whereas most tests would require two different antibodies driving up costs and characterization times.

This research -- funded by National Institutes of Health (NIH), Defense Threat Reduction Agency Basic Science Program/Office of Naval Research and the Texas Biomedical Research Institute -- was published today in the journal *PLOS ONE*.

"Ebola NP is rather like a cob of corn displaying hundreds of kernels linked in a repetitive polymer, giving us the perfect molecular magnet to attract llama antibodies that can be assembled into highly avid assays based on a single antibody," Hayhurst said.

"Intriguingly, while using one antibody to polymers and aggregates has been put to use in neurodegenerative disease diagnostics for Parkinson’s, Alzheimer’s and other disorders, it has lagged behind in emerging viral diagnostics. We showcase its simplicity and effectiveness for viral threat detection here and it may well be useful for detecting other emerging viruses."
Journal Reference:

**Origami Condoms Radically Redesigns Almost Century-Old Latex Protection**

Posted: 04/08/2013 10:31 am EDT | Updated: 04/08/2013 2:01 pm EDT

Let's face it, for many people the classic latex condom is an unsensational product at best. And for nearly a century, no one really bothered to make that basic design any better.

But now a small business called Origami Condoms says it is ready to reinvent the condom and make it more appealing to use by taking a design tip from the Japanese art of paper folding. The secret? An accordion-like design.

"The latex condom was strictly protection. No one liked using it," Origami Condoms’ creator and company founder, Danny Resnic, told The Huffington Post. "We are trying to create a condom that feels great and is much closer to the real deal to encourage people to use them."

Traditional condom makers have long been trying to make the existing condom design more appealing with textures and even flavors. But Origami Condoms' breakthrough style -- which has condoms folded up rather than rolled up like its predecessors -- acts as a loose-fitting sheath when it’s in use and moves with the natural movement of the body. That means both participants will experience a lot more sensation during sex, Resnic said.

The company, which is based in Marina del Rey, Calif., has already snagged the attention of sexual health proponents as well as other major latex condom manufacturers who are interested in licensing the design, according to Resnic.

Last month the Bill and Melinda Gates Foundation called out the new condom company as a leading innovator for sexual health on its blog. "Origami Condoms provides an excellent example of a private enterprise focused on new condom design to promote consistent use by emphasizing the sexual experience," the blog post reads.

The foundation is also offering $100,000 to innovators to redesign the condom as part of a campaign for global health initiatives.

But interested parties may still have to wait awhile to get their hands on these innovative rubbers. Origami's condoms are still in clinical testing and will not be available for purchase until early 2015 at the soonest, Resnic said. The condom designs must first go through rigorous multi-phase testing before the company can apply for approval from the Food and Drug Administration.

Part of what makes the new design possible is its departure from latex, which is prone to breaking. Instead, Origami’s condoms are made from super-supple silicone, which allows the condom to be folded rather than rolled and to withstand more vigorous movement without tearing. (Check out the company's video for a demonstration of how they work.)

The danger of a torn condoms is something Resnic knows about only too well. In 1993 he was infected with HIV after a condom broke, he said. That event led Resnic, who has a professional background in design, to look at all the ways the traditional condom could be improved.

The new Origami Condoms design is not just about safety and pleasure, but also about speed, he said. In test groups, the new Origami Condoms could be put on in less than three seconds -- much faster than a traditional condom, which must be unrolled.

Origami is also working on a redesign of the female condom, which has faltered in popularity since it launched two decades ago. The company has also created the first condom to be designed exclusively for use in anal intercourse, Resnic said. These designs are also going through clinical testing.

The company has already received more than $3 million in funding for research and development, according to Resnic, and starting later this month, it will launch a fundraiser for an advertising campaign.
Even if these newfangled condoms do find their way to market, they won’t be cheap or subtle. Unlike today’s condoms, which can be squeezed into a wallet, these will be packaged in golf-ball-sized pods.

The company has not yet set a price point, but the condoms are likely to cost more than today’s goods. In one study conducted by Origami, participants said they would pay more than $7 per condom. Resnic is convinced that people will be willing to pay for the experience of using one.

“It’s a shift from protection to pleasure. Our focus is on making condom experience more pleasurable than anyone imagined possible," he said. "We almost didn’t want to call it a condom."

**Big Pharma Company Jacks Up Price of Overdose Life Saver by 1100%: Now, More People Will Die**

Naloxone is key to fighting overdose deaths, but sky-high prices threaten community distribution programs.

*April 8, 2013*

A remarkable thing happened in 2008: [drug overdose surpassed auto fatalities](http://www.bbc.com) as the leading cause of accidental death in the United States. Public health officials declared an epidemic, and communities united to battle this new enemy that had left a staggering body count in its wake. The people had a weapon, **naloxone**, an antidote that reverses opiate overdose, and programs began popping up across the country to provide training and free naloxone to people at risk for overdose. But then Big Pharma stepped in. The same year that naloxone became so critical to saving lives, one pharmaceutical company secured a monopoly on its production and jacked up the prices by 1100%.

The company, Hospira, claims its monopoly on injectable naloxone was unintentional. Naloxone has enjoyed price competition from manufacturers since it first came on the market in the 1960s, but in the early 2000s [manufacturers began closing](http://www.bbc.com) production lines without explanation. Hospira became the sole producer of injectable naloxone by default – a position it still holds today as no new manufacturers have stepped into the market. Generic, sterile injectables like naloxone can be difficult and costly to produce, and [low return on investment](http://www.bbc.com) is likely a deterrent to new manufacturers.

Whether Hospira maintains its grip on naloxone due to natural market forces or deliberate attempts to monopolize a product of increasing value to our over-prescribed nation, the price increases have been detrimental to overdose prevention programs. When costs blew up in 2008, threatening the sustainability of one of the largest naloxone distribution centers in the country, the Chicago Recovery Alliance, director Dan Bigg called Hospira to plead for a price break.

“One of Hospira’s marketing executives explained the rationale behind the increase,” says Bigg. “He told me that Hospira wanted to increase the average customer bill by 3-4%. Instead of raising all their prices and risk losing customers to the competition, they combed through their list of products and chose one item for a price increase so high as to cause the average bill to go up 3-4%.”

That product was naloxone.

In hindsight, naloxone was an obvious pick. Almost every doctor’s office and hospital across the country stocks naloxone. It is the only antidote for a growing public health crisis. And, of course, Hospira is the sole manufacturer, leaving customers no choice but to absorb the price increases if they want access to this life-saving medication.

Bigg has been lucky, as he was able to broker a deal with Hospira to buy naloxone at a reduced price, and he says Hospira is open to working with nonprofits to make naloxone more affordable. Unfortunately, other community programs may be too small to bargain for price breaks or don’t have a medical provider on staff who can order directly from a pharmaceutical company. According to Bigg, the bulk of naloxone customers -- hospitals and doctors’ offices -- aren’t complaining about the price hikes. Naloxone makes up such a tiny portion of their budgets, they might not even notice the extra cost. So, as with many things, the heaviest burden falls on those who can least afford it – small, community distribution programs that depend on inexpensive naloxone to keep saving lives. And these programs are closing.

Naloxone distribution programs are critical to overdose prevention; since 1996 they have handed out more than 53,000 naloxone kits and report over [10,000 overdose reversals](http://www.bbc.com). That’s 10,000 lives potentially saved – one for every five kits distributed. A [2013 study](http://www.bbc.com) on the effectiveness of naloxone distribution programs in Massachusetts reported a 27-46% reduction in overdose deaths in towns with a distribution center, even when adjusting for other factors. But according to Eliza Wheeler, member of a research team at the Harm Reduction Coalition that produced a [report](http://www.bbc.com) on naloxone distribution programs published by the CDC, in the past two years alone, almost 10% of the distribution programs have closed.
their doors. And when naloxone centers disappear, the remarkable declines in overdose deaths start to bounce back up.

**Study: Felons Banned from Food Stamps at Higher Risk of HIV**

*Connecticut Post (Bridgeport)*, (04.06.2013) Amanda Cuda

Researchers investigated whether convicted felons who are banned from accessing the Supplemental Nutrition Assistance Program (food stamps), Temporary Assistance for Needy Families, and other public food assistance are more likely to participate in behaviors that put them at risk for HIV infection. A law passed in 1966 bans those convicted of drug felonies from such food assistance. The researchers chose people recently released from prison in Texas, California, and Connecticut because these three states interpret the law differently. In Connecticut, persons who comply with their court sentences are eligible for benefits; in California, the ban only applies to individuals who have not completed a drug treatment ban; and Texas has a full ban without exceptions.

Researchers studied 110 people released from prison in these three states and determined whether they had a hard time getting access to food. Results showed that 91 percent of surveyed individuals reported food insecurity and 61 percent did not receive food assistance benefits. Those who got food stamps reported that the benefits were not enough to meet their needs. The 37 percent of participants who reported not eating for at least one full day in the past month were more likely to exchange sex for money and to use heroin, cocaine, or alcohol before sex than those who had at least one meal a day, thus increasing their risk of HIV and other STDs. However, the survey found no link between food insecurity among populations of recently released prisoners as a whole and HIV risk behaviors.

Even in states where persons with former drug convictions are allowed food assistance, food can be hard to come by. Among participants in such states who reported not having eaten for at least one day, only 10 percent said they were enrolled in the food stamp program and receiving enough aid to last a full month. Emily Wang, an assistant professor of internal medicine at Yale University School of Medicine and one of the researchers, stated that more research needs to be done on the subject of food security and people released from prison.


**Gel Safe and Acceptable as Approach to Preventing HIV from Anal Sex**

*Medical Xpress*, (04.03.2013)

US National Institutes of Health (NIH) researchers report that a reduced-glycerin formulation of tenofovir gel was safe and acceptable to HIV-negative women and men who used the anti-HIV gel rectally in a phase I clinical trial (MTN-007).

NIH is studying rectal microbicides inserted rectally via an applicator as a means of preventing sexual transmission of HIV. In addition to developing rectal-specific products, researchers reformulated a vaginal product, tenofovir gel, for rectal use. The original vaginal formulation caused gastrointestinal side effects when it was used rectally.

The 2010 MTN-007 study divided 65 men and women into four groups for the one-week trial. One group used a reduced glycerin formulation of tenofovir gel daily; one used a placebo gel daily; one used the spermicide nonoxynol-9 daily; and one group used no gel. All study participants underwent the same “study-related procedures and tests.” The three groups using gels reported no significant differences in side effects. Eighty percent had minor side effects, and only 18 percent reported moderate side effects. Compliance with daily use was high (94 percent), and 87 percent stated they would use the product again.

NIH plans a phase II multi-site trial (MTN-017) of the reformulated tenofovir gel in the United States, Thailand, South Africa, and Peru. The study will include 186 men who have sex with men and transgender women, all of whom will cycle through three regimens: daily use of tenofovir, use of tenofovir used before and after sex, and use of a daily antiretroviral pill (Truvada). The study will compare the reformulated tenofovir to Truvada and provide additional information about tenofovir gel safety.

The full report, “A Phase 1 Randomized, Double Blind, Placebo Controlled Rectal Safety and Acceptability Study of Tenofovir 1% Gel (MTN-007),” was published online in the journal PLoS ONE (2013; doi:10.1371/journal.pone.0060147).

**Five Japanese Drug Makers Form PPP To Accelerate Development Of Drugs, Vaccines For Infectious Diseases**

"Five Japanese pharmaceutical giants are teaming up with the Bill & Melinda Gates Foundation and Japan’s government to develop new medicines, vaccines, and diagnostics for infectious diseases in
developing countries," GENNews reports (4/8). "The Global Health Innovative Technology (GHIT) fund will see Takeda, Astellas, Daichi-Sankyo, Eisai and Shionogi partner with [the] non-profit Bill & Melinda Gates Foundation and the government to provide grants for research funding that will help tackle HIV, malaria, tuberculosis and neglected tropical diseases (NTDs)," according to PM Live (4/8). "This is the first [public-private partnership (PPP)] of its kind in Japan and will follow the model that has become the trend now in global medicine research," Japan Daily Press writes, adding, "Some groups have formed in Europe, including Innovative Medicines Initiative (IMI) which supports research into specific priority health areas like resistance to antibiotics."

"Kiyoshi Kurokawa, science adviser to the Japanese government and the GHIT Fund chair, said that the priority is to provide fast and impactful research with the spirit of collaboration," according to the news service (Torres, 4/8). "This initiative comes at a time when the [research and development (R&D)] landscape for neglected diseases is particularly in need of resources to guarantee that R&D is boosted in the long-term and that patients gain access to the fruits of that research,' said Dr. Bernard Pécoul, executive director of the Drugs for Neglected Diseases initiative (DNDi). 'We are delighted about the GHIT initiative,' he added," according to a DNDi press release (4/8).

08 April 2013 - 16H48

South Africa rolls out new single dose AIDS drug

AFP - South Africa's health minister on Monday launched a new single dose anti-AIDs drug which will simplify the world's biggest HIV treatment regime to just one life-saving pill a day.

The three-in-one combination anti-retroviral (ARV) was secured at a record-low price and will cost the state 89 rand a month ($10, eight euros) per patient.

"Before 2010, we were buying the most expensive ARVs in the world. Now we are a country where the ARVs are the cheapest in the world," said Health Minister Aaron Motsoaledi.

"It means we can increase the number of people on treatment," he added during a visit to the township of Ga-Rankuwa, about 35 kilometres (22 miles) northwest of the capital Pretoria.

After years of refusing to roll out ARVs, South Africa now has 1.9 million people on treatment among its 5.6 million HIV-positive population, which is the world's largest.

The new pill will be introduced this month to positive pregnant women and breastfeeding mothers, people co-infected with TB, and to new ARV patients.

Patients already on treatment will be assessed by doctors to start switching later this year.

"You're just going to take it once, and it's just going to be less pill burden," said patient Andrew Mosani.

"People are tired (of) taking many drugs on a day to day basis."

The pill also had fewer side effects and was easy to swallow, he added.

The South African National AIDS Council welcomed the treatment shift, saying it hoped it would encourage patients to stay on treatment.

"This is simplifying the way patients have become used to taking ARV treatment," said the council's CEO Fareed Abdullah.

"We have come a very long way since the advent of anti-retrovirals. At one point, patients used to take up to 16 pills a day," he added.

South Africa once refused to roll out ARVs under former president Thabo Mbeki but now has the largest anti-retroviral (ARV) programme in the world.

The scaling up of treatment has seen the number of pregnant women passing on HIV to their babies brought down to less than three percent.

Life expectancy has also shot up by six years to 60 over the past few years.

One-in-Four Deaths in Pregnancy Due to HIV in Worst-Affected Countries

AIDSMAP, (04.09.2013) Carole Leach-Lemens
Researchers from the London School of Hygiene and Tropical Medicine report that the risk of pregnancy-related death is eight times higher for HIV-infected women than for uninfected women. In sub-Saharan countries with high HIV prevalence, one in four pregnancy-related deaths can be attributed to HIV. The study authors based their conclusions on a systematic review of 23 studies that had collected data on the risk of pregnancy-related death among uninfected and HIV-infected women.

Many of the 23 studies were conducted in areas of the world where a "verbal autopsy" from family members is the most common form of death report. Most of the HIV-infected women in the 23 studies
were not taking antiretroviral therapy and were in an “advanced stage” of the disease. Little is known about the effects of HIV on pregnancy; it is not clear whether HIV causes more complications for pregnant women or whether pregnancy triggers the HIV progression.

The review compared death during pregnancy and the postpartum period among HIV-infected women and uninfected women to calculate the relative risk of death and the prevalence of HIV, and then used the pooled relative risk data from the meta-analysis to predict the effect of HIV on pregnancy-related death at the population level. This calculation method removes assumptions about HIV being related to or coincidental to pregnancy. Severe anemia and TB can cause maternal death and HIV-related death indirectly. Study authors suggest that future studies focus on identifying HIV-related deaths from “verbal autopsies.”

Previous estimates of pregnancy-related death among HIV-infected women were not based on empirical data and did not distinguish between pregnancy-related deaths and maternal death that was incidental to the pregnancy.


**Reuters Examines Debate Among Non-Profit Groups Over Anti-Prostitution Pledge Law**

"A Supreme Court case that challenges a law requiring anti-prostitution policies for HIV/AIDS programs seeking federal money has generated a split among non-profit groups that counsel sex workers overseas," Reuters reports. "The case involves a 2003 law that bars funding for groups that work on HIV/AIDS prevention but do not have a policy opposing prostitution and sex trafficking," the news service writes, adding, "It has pitted two non-governmental organizations that operate programs overseas, backed by umbrella organizations representing others like them, against 46 organizations that have sided with the federal government in defending the law." Reuters continues, "The organizations challenging the provision on First Amendment grounds do not want to take a stand on prostitution. They say the law interferes with their work providing advice and counseling to prostitutes about the risks of HIV infection."

"The court on April 22 will consider whether the requirement, which has not been enforced since a 2006 injunction, is valid under the U.S. Constitution," according to Reuters. "Some entities that receive funding, including the World Health Organization, were exempted from the provision," the news service notes. Reuters recounts the history of the law and quotes several representatives of organizations on both sides of the issue. UNAIDS "supports the groups challenging the law," Reuters notes, adding, "It has filed a brief ... noting that programs 'work best when they involve, and do not stigmatize, the affected populations'" (Hurley, 4/10).

**China Reports Additional Deaths From H7N9; Scientists Work To Uncover Source**

"China reported two more fatalities from a new strain of avian flu [H7N9] on Tuesday, bringing the death toll to nine, and raised the total number of infections by four to 28 as the government renewed efforts to combat the spread of the disease," the Wall Street Journal reports (Tejada/Burkitt, 4/9).

However, Reuters reports "31 confirmed cases of the virus, all in eastern China, according to data from the National Health and Family Planning Commission" (Sweeney et al., 4/10). "Chinese authorities say they do not know how the virus is spreading, though it is believed the infection is passing from birds to humans," Agence France-Presse writes (Savadove, 4/9). "Scientists urgently want to find out which sources are stoking the human infections that result in flu-like symptoms and, in most reported cases, severe pneumonia," Nature reports, adding, "So far, investigations of the cases remain largely inconclusive: some patients had contact with poultry or other animals just before falling ill, whereas others had not" (Butler, 4/9). "All possible steps to monitor and contain the spread of the H7N9 influenza virus in China are being taken by local authorities," a WHO spokesperson said on Tuesday, the U.N. News Centre reports (4/9).

**Disease Burden From Air Pollution Underestimated, U.N. Reports**

"Air pollution is an underestimated scourge that kills far more people than AIDS and malaria and a shift to cleaner energy could easily halve the toll by 2030, U.N. officials said on Tuesday” at a conference in Oslo focusing on new development goals for the post-2015 development agenda, Reuters reports. "A 2012 World Health Organization (WHO) study found that 3.5 million people die early annually from indoor air pollution and 3.3 million from outdoor air pollution," the news service notes, adding, "The data, published..."
as part of a global review of causes of death in December 2012, were an upwards revision of previous figures of 1.9 million premature deaths caused by household pollution a year and 1.3 million outdoors, [Maria Neira, the WHO's director of public health and environment,] said" (Doyle, 4/9). "Ground-level ozone pollution was estimated to cause an additional 200,000 premature deaths every year, the [U.N. Environment Programme (UNEP)] said in a press release," the U.N. News Centre writes (4/8).

"By comparison, U.N. reports show there were about 1.7 million AIDS-related deaths in 2011 and malaria killed about 660,000 people in 2010," according to Reuters. "Investments in solar, wind or hydropower would benefit both human health and a drive by almost 200 nations to slow climate change, blamed mainly on a build-up of greenhouse gases in the atmosphere from use of fossil fuels, [officials at the conference] said," the news service writes. "Almost 200 governments have agreed to work out by the end of 2015 a deal to combat climate change," but "negotiations have stalled, partly because of economic slowdown and divisions between nations about how to share out the burden of cuts," Reuters notes.

**Scientists use nature against nature to develop an antibiotic with reduced resistance**

A new broad range antibiotic, developed jointly by scientists at The Rockefeller University and Astex Pharmaceuticals, has been found to kill a wide range of bacteria, including drug-resistant *Staphylococcus* (MRSA) bacteria that do not respond to traditional drugs, in mice. The antibiotic, Epimerox, targets weaknesses in bacteria that have long been exploited by viruses that attack them, known as phage, and has even been shown to protect animals from fatal infection by *Bacillus anthracis*, the bacteria that causes anthrax.

Target selection is critical for the development of new antimicrobial agents. To date, most approaches for target selection have focused on the importance of bacterial survival. However, in addition to survival, the Rockefeller scientists believe that molecular targets should be identified by determining which cellular pathways have a low probability for developing resistance.

"For a billion years, phages repeatedly have infected populations of bacteria, and during this period of time they have identified weaknesses in the bacterial armor," says senior author Vincent A. Fischetti, professor and head of the Laboratory of Bacterial Pathogenesis and Immunology. "We're taking advantage of what phage have 'learned' during this period for us to identify new antibiotic targets that we believe will escape the problem of resistance found for other antibiotics."

The path to identification of this new target spanned more than seven years of effort. Fischetti and his colleagues used a phage-encoded molecule to identify a bacterial target enzyme called 2-epimerase, which is used by *Bacillus anthracis* to synthesize an essential cell wall structure. In 2008, Fischetti's lab, with Rockefeller's Erec Stebbins and his colleagues in the Laboratory of Structural Microbiology, solved the crystal structure of this enzyme. Based on this work, the researchers identified a previously unknown regulatory mechanism in 2-epimerase that involves direct interaction between one substrate molecule in the enzyme's active site and another in the enzyme's allosteric site. Fischetti and his colleagues chose to target the allosteric site of 2-epimerase to develop inhibitory compounds, because it is found in other bacterial 2-epimerases but not in the human equivalent of the enzyme.

Through the collaboration with Astex, an inhibitor of 2-epimerase named Epimerox was developed. Raymond Schuch, a former postdoctoral researcher in Fischetti's lab, tested the inhibitor in mice infected with *Bacillus anthracis*. He found that not only did Epimerox protect the animals from anthrax, but the bacteria did not develop resistance to the inhibitor. The researchers also found that Epimerox was able to kill methicillin-resistant *Staphylococcus aureus* (or MRSA) with no evidence of resistance even after extensive testing. Their work was published this week in *PLOS One*.

"Since nearly all Gram-positive bacteria contain 2-epimerase, we believe that Epimerox should be an effective broad-range antibiotic agent," says Fischetti. "The long-term evolutionary interaction between phage and bacteria has allowed us to identify targets that bacteria cannot easily change or circumvent. That finding gives us confidence that the probability for developing resistance to Epimerox is rather low, thereby enabling treatment of infections caused by multi-drug-resistant bacteria such as MRSA. It is a very encouraging result at a time when antibiotic resistance is a major health concern."

**Researchers Engineer 'Protein Switch' to Dissect Role of Cancer's Key Players**
At top is a structural model of uniRapR domain which binds small molecule rapamycin. The bottom left depicts inactive state of the protein of interest modified with uniRapR domain. Binding of rapamycin and uniRapR reactivates the protein (bottom right).

(Credit: Image courtesy of University of North Carolina School of Medicine)
April 10, 2013 — Researchers at the University of North Carolina at Chapel Hill School of Medicine have "rationally rewired" some of the cell’s smallest components to create proteins that can be switched on or off by command. These "protein switches" can be used to interrogate the inner workings of each cell, helping scientists uncover the molecular mechanisms of human health and disease.

In the first application of this approach, the UNC researchers showed how a protein called Src kinase influences the way cells extend and move, a previously unknown role that is consistent with the protein’s ties to tumor progression and metastasis.

"This rationally designed control of protein conformations represents a breakthrough in computational protein design,” said senior study author Nikolay Dokholyan, PhD, a professor of biochemistry and biophysics. "We now have a new tool for delineating the activities of various proteins in living cells in a way that was never before possible."

The research was published online ahead of print in the Proceedings of the National Academy of Sciences. In the study, Dokholyan created a "switch" that would make a protein wobbly and unable to do its job unless it was flipped "on" by a drug called rapamycin, which would stabilize the protein and let it perform its function.

The approach is a simpler and more reliable version of a protein engineering system pioneered three years ago by Dokholyan and Klaus Hahn, professor of pharmacology at UNC, called rapamycin regulated or RapR. In the old approach, the switching mechanism depended on two proteins and the drug. The first protein -- the one the researchers wanted to study -- was given the RapR modification and put in cells in tissue culture. The second protein was placed in the cells as well, but simply floated around until the addition of drug caused it to latch on to the modification in the first protein and turn it on. The problem with the approach was that some cells would have a lot of the first protein and less of the second, or vice versa.

"It became the Achilles heel of the technique, because there was variability in the results due to the different ratios between the proteins," said Hahn. "What Dokholyan was able to do, which was extremely challenging from a protein engineering standpoint, was to combine the two parts into one."

Dokholyan and his colleagues took the two proteins and broke them apart into their individual components, structures called alpha helices and beta sheets. They then rewired them together to make a whole new protein where the parts could interact with each other. When researchers compared this system, called uniRapR, with the previous approach, they found the new one gave cleaner, more reliable and more consistent results.

They then applied the technique to study Src kinase, a protein involved in the metastasis or spread of tumor cells. Scientists had postulated that Src kinase plays a role in cell motility, but previous methods have not allowed them to isolate its activity from other similar proteins.

Working both in cultured human cells and in the model organism zebrafish, the researchers showed that turning on Src causes the cell to extend its edges as part of cell movement. Now that they have dissected the role of one protein, the researchers plan to look at a variety of other kinases to understand their roles in the development, progression, and spread of cancer.

**Journal Reference:**

**New Way to Clear Cholesterol from the Blood**
April 10, 2013 — Researchers at the University of Michigan have identified a new potential therapeutic target for lowering cholesterol that could be an alternative or complementary therapy to statins.

Scientists in the lab of David Ginsburg at the Life Sciences Institute inhibited the action of a gene responsible for transporting a protein that interferes with the ability of the liver to remove cholesterol from the blood in mice. Trapping the destructive protein where it couldn’t harm receptors responsible for removing cholesterol preserved the liver cells’ capacity to clear plasma cholesterol from the blood, but did not appear to otherwise affect the health of the mice.

In the research, published April 9 in the online journal *eLife*, scientists found that mice with an inactive SEC24A gene could develop normally. However, their plasma cholesterol levels were reduced by 45 percent because vesicles from liver cells were not able to recruit and transport a critical regulator of blood cholesterol levels called proprotein convertase subtilisin/kexin type 9. PCSK9 is a secretory protein that destroys the liver cells' receptors of low-density lipoprotein-LDL, the so-called "bad cholesterol" -- and prevents the cells from removing the LDL.
"Inhibiting SEC24A or PCSK9 may be an alternative to statins, and could work together with statins to produce even greater effects," said Xiao-Wei Chen of the Ginsburg lab, the first author on the paper. "Also, they might be effective on patients who are resistant to or intolerant of statins."

Initial studies of anti-PCSK9 therapies in humans have shown that eliminating PCSK9 can lower cholesterol dramatically and work with statins like Lipitor to lower it even further. The Ginsburg lab's research points to a new area for study: rather than inhibiting PCSK9 itself, perhaps future therapies could block the transport mechanism that allows the destructive protein to reach the LDL receptors.

The paper, "SEC24A deficiency lowers plasma cholesterol through reduced PCSK9 secretion," explains the mechanism by which cells transport PCSK9. Vesicles transport proteins in the cell; the Ginsburg lab's research focused on a specialized type of vesicle packaged by the Coat Protein Complex II, which regulates the metabolism of cholesterol, among many other things. These vesicles selectively transport cargo proteins including PCSK9.

Without those LDL receptors (LDLR), liver cells are not able to remove LDLs from the bloodstream, so protecting the LDLR from PCSK9 would allow the receptors to continue to remove cholesterol.

"Without SEC24A, much of the PCSK9 couldn't make its way out of the cells to destroy the LDLR, which then clears cholesterol from the blood," Chen said.

The part of the vesicle that selects which proteins to transport is SEC24. By blocking SEC24A gene, the researchers disabled the vesicle's selection of PCSK9. The destructive protein remained trapped within the cells, leaving the LDLR intact and enabling the liver to clear the body of cholesterol that otherwise could accumulate in arteries.

"We have no reason at this point to expect that this strategy will be any better than anti-PCSK9 therapy for treating high cholesterol, but it would be another alternative approach, and it's hard to predict which drugs will work the best and be the safest until we actually try them out in people," Ginsburg said.

Journal Reference:

'Shadow Biosphere' theory gaining scientific support
By Robin McKie, The Observer
Saturday, April 13, 2013 20:51 EDT

Never mind aliens in outer space. Some scientists believe we may be sharing the planet with 'weird' lifeforms that are so different from our own they're invisible to us.

Across the world's great deserts, a mysterious sheen has been found on boulders and rock faces. These layers of manganese, arsenic and silica are known as desert varnish and they are found in the Atacama desert in Chile, the Mojave desert in California, and in many other arid places. They can make the desert glitter with surprising colour and, by scraping off pieces of varnish, native people have created intriguing symbols and images on rock walls and surfaces.

How desert varnish forms has yet to be resolved, despite intense research by geologists. Most theories suggest it is produced by chemical reactions that act over thousands of years or by ecological processes yet to be determined.

Professor Carol Cleland, of Colorado University, has a very different suggestion. She believes desert varnish could be the manifestation of an alternative, invisible biological world. Cleland, a philosopher based at the university's astrobiology centre, calls this ethereal dimension the shadow biosphere. “The idea is straightforward,” she says. “On Earth we may be co-inhabiting with microbial lifeforms that have a completely different biochemistry from the one shared by life as we currently know it.”

It is a striking idea: We share our planet with another domain of life that exists “like the realm of fairies and elves just beyond the hedgerow”, as David Toomey puts it in his newly published Weird Life: The Search for Life that is Very, Very Different from Our Own. But an alternative biosphere to our own would be more than a mere scientific curiosity: it is of crucial importance, for its existence would greatly boost expectations of finding life elsewhere in the cosmos. As Paul Davies, of Arizona State University, has put it: “If life started more than once on Earth, we could be virtually certain that the universe is teeming with it.”

However, by the same token, if it turns out we have failed to realise that we have been sharing a planet with these shadowy lifeforms for eons, despite all the scientific advances of the 19th and 20th centuries, then we may need to think again about the way we hunt for life on other worlds. Robot spacecraft – such as the Mars rover Curiosity – are certainly sophisticated. But what chance do they have of detecting alien
entities if the massed laboratories of modern science have not yet spotted them on our own planet? This point is stressed by the US biologist Craig Venter. As he has remarked: “We’re looking for life on Mars and we don’t even know what’s on Earth!”

The concept of a shadow biosphere was first outlined by Cleland and her Colorado colleague Shelley Copley in 2006 in the International Journal of Astrobiology, and is now supported by many other scientists, including astrobiologists Chris McKay, who is based at Nasa’s Ames Research Centre, California, and Paul Davies.

These researchers believe life may exist in more than one form on Earth: standard life – like ours – and “weird life”, as they term the conjectured inhabitants of the shadow biosphere. “All the microorganisms we have detected on Earth to date have had a biology like our own: proteins made up of a maximum of 20 amino acids and a DNA genetic code made out of only four chemical bases: adenine, cytosine, guanine and thymine,” says Cleland. “Yet there are up to 100 amino acids in nature and at least a dozen bases. These could easily have combined in the remote past to create lifeforms with a very different biochemistry to our own. More to the point, some may still exist in corners of the planet.”

Science’s failure to date to spot this weird life may seem puzzling. The natural history of our planet has been scrupulously studied and analysed by scientists, so how could a whole new type of life, albeit a microbial one, have been missed? Cleland has an answer. The methods we use to detect micro-organisms today are based entirely on our own biochemistry and are therefore incapable of spotting shadow microbes, she argues. A sample of weird microbial life would simply not trigger responses to biochemists’ probes and would end up being thrown out with the rubbish.

That is why unexplained phenomena like desert varnish are important, she says, because they might provide us with clues about the shadow biosphere. We may have failed to detect the source of desert varnish for the simple reason that it is the handiwork of weird microbes which generate energy by oxidising minerals, leaving deposits behind them.

The idea of the shadow biosphere is also controversial and is challenged by several other scientists. “I think it is very unlikely that after 300 years of microbiology we would not have detected such organisms despite the fact that they are supposed to have a different biochemistry from the kind we know about today,” says Professor Charles Cockell, of the UK Centre for Astrobiology at Edinburgh University. “It is really quite unlikely,” adds Cockell, whose centre will be officially opened this week at a ceremony in Edinburgh.

Ways need to be found to determine whether or not the shadow biosphere exists, says Dimitar Sasselov, professor of astronomy at Harvard University and director of the Harvard Origins of Life Initiative. “If you want a clue you can count up the amount of carbon that is emitted by living things – cows, sheep, grass, plants, forests and all the planet’s bacteria. When you do, you find there is a discrepancy of around 5% when you compare the amount given off from Earth’s standard biosphere and the amount you find in the atmosphere.”

In other words, there is slightly too much carbon dioxide in the atmosphere than can be explained by the emissions of standard lifeforms on Earth. There could be an error in these calculations, of course. Alternatively, the shadow biosphere could be responsible for this excess, says Sasselov. “There is plenty of room for a shadow biosphere. That is clear. Certainly, it is not true, as some allege, that we have strong evidence to show that it does not exist. In fact, the opposite is true: we do not have good enough evidence to dismiss it.”

A key point to note is that scientists – although describing the inhabitants of the shadow biosphere as weird – still assume they will be carbon-based entities. Complex chemistry based on other elements, such as silicon, is possible, they acknowledge but these alternatives cannot create the vast range of organic materials that carbon can generate. In other words, the shadow biosphere, if it exists, will almost certainly be inhabited by carbon life, albeit of an alien variety.

“Billions of years ago, life based on different types of carbon biochemistry could have arisen in several places on Earth,” says Cleland. “These varieties would have been based on different combinations of bases and amino acids. Eventually, one – based on DNA and on proteins made from 20 amino acids – formed multicellular entities and became the dominant form of life on Earth. That is why we find that life as we know it, from insects to humans and from plants to birds, has DNA as its genetic code. However, other lifeforms based on different bases and proteins could still have survived – in the shadow biosphere.”

A different prospect is highlighted by Sasselov, who points out that a complex organic chemical can come in two different shapes even though they have the same chemical formula. Each is a mirror-image of the other and are said to have a different chirality. “Amino acids are an example,” says Sasselov. “Each comes in a right-handed version and a left-handed version. Our bodies – in common with all other
lifeforms — only use left-handed versions to create proteins. Right-handed amino acids are simply ignored by our bodies. However, there may be some organisms, somewhere on the planet, that use only right-handed amino acids. They could make up the weird life of the shadow biosphere.”

But how can scientists pinpoint this weird life? Microbes are usually detected in laboratories by feeding nutrients to suspected samples so they grow and expend. Then the resulting cultures can be analysed. A weird lifeform — such as one made only of proteins formed out of right-handed amino acids — will not respond to left-handed nutrients, however. It will fail to form cultures and register its existence.

One solution to this problem is being pursued by Sasselov and colleagues’ Harvard Origins of Life Initiative. They are building an artificial cell — or bionic system — made only of right-handed components including right-handed DNA and right-handed ribosomes. “If there are right-handed lifeforms out there, many of them will be viruses — which will attempt to hijack the DNA of our bionic cells,” adds Sasselov.

“When they do that they will leave evidence of their existence. Essentially we are building honey traps to catch any right-handed viruses that might live in the shadow biosphere and so reveal their existence.”

Other scientists suggest a different approach — by looking at Earth’s most inhospitable ecological niches: hot vents on the seafloor, mountaintops, highly saline lakes, Antarctic ice sheets and deserts. Standard lifeforms, mainly bacteria, have been found in these places but only a few. Some niches, researchers speculate, may prove to be just too inhospitable for standard life but may just be tolerable enough to support weird life. Microscopic studies would reveal their existence while standard culture tests would show they had a different biochemistry from standard lifeforms.

And a promising example is provided by the desert varnish proposed as a target by Cleland and backed by David Toomey in Weird Life. “No laboratory microbiologist has been able to coax bacteria or algae to make desert varnish,” he states. “It is also possible that the stuff is the end result of some very weird chemistry but no one has been able to reproduce that either.” So yes, these sites could provide proof of the shadow biosphere’s existence, he argues.

Not surprisingly, Cleland agrees. “The only trouble is that no one has yet got round to investigating desert varnish for weird life,” adds Cleland. “I confess I find that disappointing.”

**Reports Of H7N9 Cases, Deaths Continue From Across China**

“Two more people have died in China from a new strain of bird flu, raising the death toll from the virus to 13, state media reported Sunday,” the Associated Press reports. “A total of 11 new cases were reported Sunday — including two in a central province that previously had been unaffected,” the news service notes (4/14). "On Saturday, Xinhua reported that a seven-year-old girl in the capital city of Beijing was the first person to contract bird flu outside of the eastern region," AlJazeera writes (4/14). "The girl is in stable condition at a local hospital, [Beijing’s health bureau] said," the Wall Street Journal notes (Tejada, 4/12). "Up until Saturday, when Beijing officials reported the capital's first case of H7N9, all cases had been in Shanghai and other areas of eastern China," the AP writes in a separate article, adding, "On Sunday, officials announced the first two cases in central Henan province, which is next to Beijing" (4/14). "By Sunday night, there had been 60 confirmed human infections with the H7N9 avian influenza virus, two weeks after it was publicly identified by Chinese health authorities," according to the Financial Times (Rabinovitch, 4/14). "Experts fear the prospect of such viruses mutating into a form easily transmissible between humans, which would have the potential to trigger a pandemic," Agence France-Presse notes (4/14). "There are no reported cases outside the country, according to the World Health Organization (WHO)," BBC News writes (4/13).

"Chinese authorities moved over the weekend to take new measures to stop the spread of the flu, with Beijing city officials closing live poultry markets and ordering medical agencies to stock up on medication such as Tamiflu," the Wall Street Journal notes in a separate article, adding, "At a briefing on Sunday, Michael O’Leary, the World Health Organization’s representative to China, said further spreading is expected based on what officials know about the disease" (Chin, 4/14). "'There’s no way to predict how it will spread but it’s not surprising if we have new cases in different places like we do in Beijing,' he told reporters," BBC News writes in a separate article (4/14). "While the spread of the virus to an area outside the Shanghai region suggests a wider footprint of the H7N9 virus, health officials have emphasized that there have yet to be any confirmed cases of human-to-human transmission, which would suggest a mutation to a more virulent form of the virus," according to the New York Times (Mullany, 4/13). "Here in the U.S., the [CDC] has beefed up resources to deal with the outbreak," NPR’s Shots blog writes, noting, "The agency received a vial of H7N9 from China Thursday so it could develop tests and vaccines against
the virus" (Doucleff, 4/12). "Flu labs around the world are developing vaccine seed strains to serve as a template for bulk immunization production, should it be required," Bloomberg News adds (4/15).

**Pakistani Taliban Deny Responsibility For Attacks On Polio Workers**
"The Pakistani Taliban on Friday denied any involvement in attacks on polio workers, which have killed 21 people since December, but confirmed it opposed the vaccination as ‘un-Islamic,’" Agence France-Presse reports. Ehsanullah Ehsan, a spokesperson for the umbrella group Tehreek-e-Taliban Pakistan (TTP), told AFP, "We have no link with the attacks on polio teams," the news agency notes. "We have very strong reservations against anti-polio vaccines because they are un-Islamic and bad for the health," he added, according to AFP. "The umbrella militant faction last year banned polio vaccinations in the tribal region of Waziristan, alleging the campaign was a cover for espionage," the news agency writes, adding, "Rumors about vaccines being a plot to sterilize Muslims have also dogged efforts to tackle the highly infectious disease in Pakistan, one of only three countries where it remains endemic." Afghanistan and Nigeria are the other two countries, AFP notes (4/13).

**Production Of Synthetic Artemisinin An Attack Against Farmers Currently Growing The Plant**
"On Thursday, the founder of Amyris Biotech triumphantly announced production of 70 million doses of the anti-malarial compound artemisinin," Jim Thomas, research program director for ETC group, a technology watchdog that works with farmers' organizations, writes in The Guardian's "Poverty Matters" blog. "This sounds like good news for poor people but may be a step backwards -- the start of a new high-tech assault on farmers," he continues, noting, "Until this week, artemisinin for drugs was sourced entirely from the delicate leaves of artemesia annua (sweet wormwood), following sustained efforts to develop artemesia growing as doubly beneficial: a source of livelihood for African and Asian farmers, and a public health good." He adds, "What makes Amyris' breakthrough significant is that its version has never been near a wormwood shrub. It comes from an industrial vat of bioengineered yeast."

"Vat-grown artemisinin is highly attractive to large pharmaceutical companies such as Sanofi Aventis," as "[t]hey will now avoid the complexity of sourcing from thousands of farmers and 20,000 hectares (50,000 acres) in Kenya, Tanzania, Madagascar, Mozambique, India, Vietnam and China," Thomas writes. "As for artemesia farmers, this announcement is an assault on their livelihoods," he adds. But Jay Keasling, the key synthetic biologist behind the project, "argues that putting artemesia growers out of business accompanies a laudable public health move: some growers sell to producers of questionable artemisinin monotherapies, which in turn may give rise to artemisinin resistance," he notes, adding, "Farmers are unfortunate collateral damaged." Thomas states, "Unfortunately, far from an isolated story, today's artemisinin threat is just an opening salvo in a volley of potentially damaging market disruptions involving [synthetic biology (synbio)]," concluding, "In the fight between people and microbes, bioengineered microbes may have just opened up a new economic line of attack" (4/12).

**Excess Vitamin E Intake Not a Health Concern, Study Suggests**
Apr. 15, 2013 — Despite concerns that have been expressed about possible health risks from high intake of vitamin E, a new review concludes that biological mechanisms exist to routinely eliminate excess levels of the vitamin, and they make it almost impossible to take a harmful amount.

No level of vitamin E in the diet or from any normal use of supplements should be a concern, according to an expert from the Linus Pauling Institute at Oregon State University. The review was just published in the Journal of Lipid Research.

"I believe that past studies which have alleged adverse consequences from vitamin E have misinterpreted the data," said Maret Traber, an internationally recognized expert on this micronutrient and professor in the OSU College of Public Health and Human Sciences.

"Taking too much vitamin E is not the real concern," Traber said. "A much more important issue is that more than 90 percent of people in the U.S. have inadequate levels of vitamin E in their diet."

Vitamin E is an antioxidant and a very important nutrient for proper function of many organs, nerves and muscles, and is also an anticoagulant that can reduce blood clotting. It can be found in oils, meat and some other foods, but is often consumed at inadequate dietary levels, especially with increasing emphasis on low-fat diets.

In the review of how vitamin E is metabolized, researchers have found that two major systems in the liver work to control the level of vitamin E in the body, and they routinely excrete excessive amounts. Very
high intakes achieved with supplementation only succeed in doubling the tissue levels of vitamin E, which is not harmful.

"Toxic levels of vitamin E in the body simply do not occur," Traber said. "Unlike some other fat-soluble vitamins such as vitamins A and D, it’s not possible for toxic levels of vitamin E to accumulate in the liver or other tissues."

Vitamin E, because of its interaction with vitamin K, can cause some increase in bleeding, research has shown. But no research has found this poses a health risk.

On the other hand, vitamin E performs many critical roles in optimum health. It protects polyunsaturated fatty acids from oxidizing, may help protect other essential lipids, and has been studied for possible value in many degenerative diseases. Higher than normal intake levels may be needed for some people who have certain health problems, and smoking has also been shown to deplete vitamin E levels.

Traber said she recommends taking a daily multivitamin that has the full RDA of vitamin E, along with consuming a healthy and balanced diet.

Journal Reference:

Circumcision reduces HIV risk by changing penis ‘biome’, says study
By David Ferguson
Tuesday, April 16, 2013 11:47 EDT
A study released Tuesday says that circumcision significantly reduces men’s chances of being infected by HIV by changing the microbiome of the penis. According to a paper in the American Journal of Microbiology, a reduction of the number of anaerobic bacteria present on the penis appears to play a role in reducing the rate of infection.

In the study, researchers from the Translational Genomics Research Institute (TGen) in Flagstaff, Arizona and at George Washington University in Washington, D.C. studied the effect of circumcision on the types of bacteria that live under the foreskin before and after the procedure via swab cultures taken from a large sample group of adult Ugandan men.

By one year after circumcision, the total bacteria population in the area had dropped significantly. Anaerobic bacteria, organisms that thrive in conditions with little or no oxygen, particularly declined.

Scientists have shown that circumcision reduces the risk of HIV infection in men by 50 to 60 percent as well as reducing incidences of human papillomavirus and herpes simplex type 2, but the biological processes involved remained a mystery.

It could be, some scientists said, that the anatomy of the circumcised penis makes it less vulnerable to infection. Other scientists argued that the benefits of circumcision are conferred by way of changing the native bacteria population on and around the foreskin. The new study points toward the latter theory.

“There was a dramatic and significant change in the penis microbiome as a result of male circumcision,” study author Dr. Lance Price told the website MedicalXpress.com. “From an ecological perspective, it’s like rolling back a rock and seeing the ecosystem change. You remove the foreskin and you’re increasing the amount of oxygen, decreasing the moisture — we’re changing the ecosystem.”

He continued, “From a public health perspective the findings are really interesting because some of these organisms that are decreasing could cause inflammation. We’re used to thinking about how disrupting the gut microbiome can make someone more susceptible to an infection. Now we think maybe this disturbance [in the penile microbiome] could be a good thing — could have a positive effect.”

The evidence suggests that high levels of foreskin bacteria could make the body more vulnerable to sexually transmitted viral infections. One theory says that high bacterial loads activate cells in the foreskin called Langerhans cells, which would normally be tasked with defending the body from outside infections. Instead, the cells end up binding with HIV and ferrying it past the body’s lines of defense and straight into the system. Reducing the bacterial load on the head of the penis could keep these Langerhans cells from turning traitor.

Price sees the potential in these results for developing non-surgical alternatives to circumcision.

“The work that we’re doing, by potentially revealing the underlying biological mechanisms, could reveal alternatives to circumcision that would have the same biological impact. In other words, if we find that it’s a group of anaerobes that are increasing the risk for HIV, we can find alternative ways to bring down those anaerobes,” he said, thereby decreasing the risk of infection.
Circumcision study supports HIV theory

Researchers say the foreskin can shelter troublesome bacteria, so its removal may bolster the immune system to keep the AIDS virus at bay.

By Monte Morin, Los Angeles Times
April 15, 2013, 11:16 p.m.

Circumcision is known to reduce a man’s risk of HIV infection by at least half, but scientists don’t know why. A new study offers support for the theory that removing the foreskin deprives troublesome bacteria of a place to live, leaving the immune system in much better shape to keep the human immunodeficiency virus at bay.

Anyone who has ever lifted a rock and watched as the earth beneath it was quickly vacated by legions of bugs and tiny worms would be familiar with the principle, said study leader Dr. Cindy Liu: After the foreskin is cut away, the masses of genital bacteria that once existed beneath it end up disappearing.

"It’s the same as if you clear-cut a forest,” said Liu, a pathologist at the Translational Genomics Research Institute in Flagstaff, Ariz. "The community of animals that once lived in that forest is going to change.”

Of particular note is that circumcision undercuts anaerobic bacteria, the microbes that thrive in oxygen-deprived environments, she said. By reducing the number of anaerobic bacteria, the body’s immune cells may be better able to destroy the virus — and less likely to fall prey to its Trojan horse-style of attack, the authors suggest.

Liu and her colleagues present their case in a paper published Tuesday in the journal mBio.

Numerous studies conducted over the last two decades have shown that male circumcision reduces the risk of HIV infection in men who have heterosexual intercourse by 50% to 60%. Some researchers have speculated that the foreskin is prone to tearing, giving the virus more routes of entry. Others have argued that removal of the foreskin simply reduces the surface area available to be infected.

Liu and coauthor Lance Price, a professor of environmental health sciences at George Washington University in Washington, suspected it had to do with the bacterial species that inhabit the coronal sulcus, the shallow groove behind the head, or glans, of the penis.

To establish a possible connection, study authors enrolled 156 Ugandan men in a randomized trial in which half of them were circumcised and the other half were not.

Study participants ranged in age from 15 to 49. While the prospect of undergoing circumcision as an adult might not appeal to many American men, 5,000 Ugandan males volunteered for the study. In a region where 1 in 6 people are infected with HIV, circumcision’s "powerful potential” to reduce the risk of infection was strong motivation, said coauthor Dr. Aaron Tobian, a health epidemiologist and pathologist who teaches at Johns Hopkins University School of Medicine.

On average, there was an 81% reduction in bacteria in the circumcised men one year after surgery, the researchers reported. Some of the biggest drops were recorded for anaerobic bacteria, they said.

Bacteria on the coronal sulcus fell by more than 33% in the circumcised men, Liu said.

Interestingly, the men in the uncircumcised control group also experienced a reduction in bacteria, but not to the degree that the circumcised men did, Liu said. This was probably because of health and hygiene information that was given to all study participants.

"That's not an uncommon outcome," she said. "Just being in a trial can confer some benefits."

The study only examined the effect of circumcision on reducing or altering bacterial colonies on the penis. Further research must be done to draw a direct connection between these changes in the microbiome and subsequent HIV infection.

However, the study offers strong support for the idea that bacteria — particularly anaerobic bacteria — can cause inflammation that will trigger the body’s immune system and summon a variety of cells to fight a threat. Among those fighters are T4 cells, which are infected by HIV. The virus needs those cells to survive and replicate over time.

The study authors argue that the large populations of bacteria in uncircumcised men attract these T4 cells, giving the virus a means of entry during intercourse with an infected person. However, circumcised men are much less likely to mobilize these susceptible cells; therefore, the virus can be destroyed by other types of immune cells.

Dr. Alexandra Levine, chief medical officer at the City of Hope Cancer Center in Duarte, said scientists have long been searching for the connection between circumcision and reduced HIV infection. The authors of the new study make a convincing argument, she said.
"This is an important paper in beginning to document what the reason might be," said Levine, who was not involved in the research. "Their data are convincing to me."

Price said that colleagues were already working on follow-up studies. If the connection can be proved, there might be less-invasive ways of altering bacterial populations that do not rely on circumcision.

"As a society, we’ve gotten used to thinking about alterations to the microbiome as having negative outcomes," said Price, who is married to study leader Liu. "We think about the person who takes antibiotics in the hospital and ends up with an infection in their gut because we’ve knocked out the natural microbiota. But here’s a situation where we’re flipping that notion on its head. The disturbance of the microbiome could have a positive effect."

The Facts About Bacterial Meningitis for Gay Men in San Francisco

Magnet Medical Director Chris Hall, MD, gives us the facts about bacterial meningitis and what guys in our community need to know. Check back here for more updates as we learn them.

What is bacterial meningitis?
Meningitis is an inflammation of the delicate membranes that cover the brain and spinal cord. One form of bacterial meningitis, caused by Neisseria meningitidis (or meningococcus), is uncommon but potentially fatal and should always be viewed as a medical emergency. As many as 10-15% of cases lead to death, sometimes within 24 hours, and a significant number of those with who contract the infection have serious complications.

How is it transmitted?
It is transmitted from person-to-person through droplets of respiratory or throat secretions. Close contact—such as kissing, sneezing or coughing on someone, or living in close quarters with an infected person—facilitates the spread of the disease. Droplet spread (versus airborne spread) generally takes place at a range of three feet or less, and prolonged contact generally is required for infection to occur.

What are the symptoms?
The most common symptoms are a stiff neck, high fever, sensitivity to light, confusion, severe headache, and vomiting. Rash may also occur. The symptoms usually develop within three to seven days of infection. Antibiotic treatment is effective, but it must be given without delay once meningococcal disease is suspected.

What if I start to feel symptoms?
If you suspect that you or someone you know has meningitis, seek medical care right away. Early, aggressive treatment of bacterial meningitis can prevent serious complications and death. Preventive oral antibiotic therapy for close contacts of confirmed cases is available and highly effective.

Is there a vaccine?
Yes. If you are concerned about potential future exposure, you should get vaccinated. You can see your primary care physician, the Adult Immunization and Travel Clinic in San Francisco, or a local Walgreens pharmacy. The vaccine typically costs between $130 and $160 without insurance, and two doses separated by two months are required for people who are HIV-positive.

Is there an elevated risk of bacterial meningitis for gay men, based on recent cases discussed in the media?
The overwhelming majority of meningococcal meningitis cases in the United States are sporadic and isolated—only a small percentage of cases are linked to an outbreak. However, an outbreak of bacterial meningitis in gay men and other men who have sex with men (MSM) in New York has been tracked since 2010, with 22 cases identified through April 2013, leading to seven deaths. These individuals were affected at 60 times the incidence rate, compared to that expected in the overall population. Fifty-five (55) percent of the cases were among HIV-positive individuals, and African Americans were disproportionately affected. The individuals shared risk factors that included meeting sex partners through social media. For this reason, the New York City Department of Health has issued advisories recommending that all sexually active gay and other MSM be vaccinated. Since that time, other health departments have advised vaccinations for those gay men traveling to New York City who might be sexually active while there. On April 13, 2013, a West Hollywood man died of meningococcal meningitis, raising concern that a similar pattern of illness might be observed in the Los Angeles area.

Have we seen any concerning cases of bacterial meningitis among gay men in San Francisco or the Bay Area?
Public health officials in San Francisco and Alameda Counties are closely monitoring the situation here in the Bay Area. To date, there are no concerning cases or signs of local clusters or cases specifically linked to
those in either New York City or Los Angeles. Therefore, a community-wide vaccination program has not been initiated.

Gay men are encouraged to discuss risk and advisability of vaccination with a health care provider. Should concerning cases arise in the Bay Area, recommendations will be updated to reflect what is known. San Francisco AIDS Foundation continues to work closely with local public health officials to promote the health and safety of gay and other MSM in San Francisco who might be affected by this potential health threat.

**HIV is not a crime! Accountability demanded for scientists who provide ‘expert’ testimony supporting HIV criminalization**

Posted on **April 14, 2013** by AAN

Saturday, April 13, 2013 – At the Canadian Association of HIV/AIDS Researchers conference in Vancouver AIDS ACTION NOW! led people living with HIV, researchers, and doctors to stand in solidarity and call for members of the Canadian HIV research community to stop acting as paid expert witnesses on the side of Crown prosecutors in HIV non-disclosure trials.

Over 50 demonstrators stood behind a sign that said: “HIV is not a crime. AIDS Profiteering is” during Dr. Robert Remis’ abstract presentation. Dr. Remis is a prominent epidemiologist who is responsible for Ontario’s provincial epidemic surveillance, and is also a paid expert witness for the Crown in many HIV non-disclosure trials.

AIDS activists have been increasingly angered at the perceived conflict of interest practiced by this scientist and that he financially benefits off the lives of people who are prosecuted in relation to HIV non-disclosure. In one case, Remis’ testimony in the pre-trial led to charges being increased from assault to aggravated assault. Remis is also a member of the Canadian Association of HIV/AIDS Researchers and was a abstract reviewer for the conference’s Epidemiology and Public Health Sciences track.

Jessica Whitbread of AIDS ACTION NOW! stated, “We are calling on HIV scientists and doctors to take a moral stand and stop perpetrating HIV stigma against those of us living with HIV. If we are to end stigma and HIV criminalization we need to act in our own movement first.”

The protest was silent and strong with members leaving their seats in the front row to come and join the demonstration. One member of the audience who joined the demonstration stated, “When I looked back I saw a dense wall of fierce women activists and it gave me the chills to know how powerful they were. Then I got up and joined them.” Another member of the protest said: “We need to stand for something or else we will compromise for anything.”

Demonstrators handed out a flyer that said:

**Dear Doctor,**

It’s your duty to actively oppose the criminalization of people living with HIV.

Use your title and platform to promote science, reason, and social justice. Speak out against the further marginalization of populations you serve and study.

Criminalization perpetuates stigmatizing misinformation, fear, and hatred. Testifying in support of prosecution appeases oppression. You know that this miscarriage of justice contradicts science and public health so retaliate.

Strongly advocate for universal access to HIV education, testing, and treatment, and say NO to the criminal prosecution of people living with HIV!

Sincerely,

Integrity

**A New Phase in the HIV Epidemic Among MSM**

*In San Francisco, HIV incidence did not increase between 2004 and 2011 among men who have sex with men, despite ongoing risk behavior.*

In cities with large populations of men who have sex with men (MSM), the incidence of HIV infection in MSM rose during the late 1990s and early 2000s, despite increased prevention efforts and widespread use of antiretroviral therapy (ART). Now, researchers have investigated the possibility of another phase in the HIV epidemic among MSM.

Using data from the National HIV Behavioral Surveillance system, the investigators compared risk behavior characteristics among MSM in San Francisco in 2004, 2008, and 2011. Men were enrolled from a random sampling of venues and completed an interviewer-administered survey. Of those who were
enrolled and interviewed, most underwent serologic testing (386 of 386 [100%] in 2004, 507 of 521 [97.3%] in 2008, and 478 of 510 [93.7%] in 2011).

Between 2004 and 2011, significant decreases occurred in the rates of unrecognized HIV infection (21.7% vs. 7.5%; \( P = 0.025 \)) and methamphetamine use during the preceding year (22.8% vs. 11.9%; \( P < 0.001 \)), together with a significant increase in the proportion of HIV-uninfected MSM receiving testing during the preceding 6 months (44.1% vs. 57.8%; \( P < 0.001 \)). ART use also increased: in 2004, 71.2% of HIV-infected MSM reported ever using ART, whereas in 2011, 88.2% reported current receipt. No changes were seen in HIV prevalence (24.0% and 23.0%), or in history of gonorrhea infection or having multiple sex partners during the preceding year. HIV incidence did decrease, from 2.6% to 1.0% per year, but the difference was not statistically significant.

**Comment:** These data are cautiously encouraging with regard to the potential effects of interventions to decrease new HIV infections, including (1) using ART as prevention, (2) increasing HIV testing to minimize unrecognized HIV infections, and (3) continuing efforts to modify risk behaviors. Some data suggest that knowledge of one's HIV serostatus can affect risk behaviors, and making HIV testing a routine part of care may be an easy way to decrease transmission. However, even though HIV incidence seemed not to increase in the present study despite ongoing high-risk behavior, other recent studies have produced different findings (JW AIDS Clin Care Mar 25 2013).

— Sonia Nagy Chimienti, MD

Published in Journal Watch HIV/AIDS Clinical Care April 12, 2013

**Citation(s):**

**Misconduct By Zimbabwe U.N. Official Might Have Worsened 2008 Cholera Outbreak, U.N. Tribunal Finds**

South Africa’s Mail & Guardian examines the findings of a recent U.N. tribunal that found misconduct by the former head of the U.N. Development Programme office in Zimbabwe, which led to the 2009 wrongful dismissal of the head of the U.N.’s Office for the Coordination of Humanitarian Affairs after he warned about the potential for a cholera epidemic. "The U.N. said [Agostinho] Zacarias, now the UNDP’s resident coordinator in South Africa, failed poor Zimbabweans by opting to protect the image of Zanu-PF," President Robert Mugabe’s ruling party, according to the newspaper.

"In 2008, rocked by galloping inflation and an economic meltdown, Harare was unable to provide water to residents in its high-density townships for months, leading to the cholera outbreak," but Zacarias "was unable or unwilling to take measures to combat cholera -- which affected about 100,000 people in 2008," despite warnings from Georges Tadonki, the Mail & Guardian continues. The newspaper describes the details of the case, saying it raises questions about the country’s response to a typhoid outbreak last year, and adds, "Civil society organizations that spoke to the Mail & Guardian but did not want to be named because they work closely with the U.N. or receive funding from it, said the ruling raises questions about what the U.N. will do if the events of 2008 repeat themselves ahead of the looming elections" (4/12).

**Haiti cholera mutations could lead to more severe disease**

**Strain is evolving to be more like virulent 1800s cholera**

CHICAGO --- The cholera strain that transferred to Haiti in 2010 has multiple toxin gene mutations that may account for the severity of disease and is evolving to be more like an 1800s version of cholera, reports a new Northwestern Medicine study.

The strain, "altered El Tor," which emerged around 2000, is known to be more virulent and to cause more severe diarrhea and dehydration than earlier strains that had been circulating since the 1960s. This study reports the altered El Tor strain has acquired two additional signature mutations during the past decade that may further increase virulence.

In addition, these newly discovered signature mutations documented in the study further link the Haitian cholera epidemic to the strain from Nepal.

The paper will be published April 16 in the journal mBio.

The new Northwestern study suggests the strain with multi-signature toxin gene mutations may trigger a unique pattern of infection accounting for the severity of disease noted during the Haiti cholera outbreak.
"The cholera strain from the 1800s epidemic did the same thing," said Karla Satchell, the senior author of the paper and an associate professor of microbiology-immunology at Northwestern University Feinberg School of Medicine. "That strain also modified its toxin genes and the cholera got worse.”

Satchell has spent her career studying a single toxin of the bacterium that causes cholera, MARTX, which helps the bacteria block the body’s immune defense so cholera can colonize the gut. She closely followed genomics research conducted to track the Haiti epidemic, curious to see how her toxin was affected. She was shocked to see it had completely mutated out of existence.

"Oh, my!" she recalls thinking. "My toxin has been booted out of this key strain." She postulates that this may have affected the behavior of the mutated strain in disease.

Satchell and colleagues analyzed publicly available genomic sequencing data and found this new cholera strain had accumulated some curious genetic changes during its global spread. First, the main cholera toxin that causes the diarrhea acquired genetic changes that converted the toxin to a form similar to that produced by strains prevalent during the historic cholera epidemics of the 1800s.

Surprisingly, this new strain next acquired a genetic lesion that inactivated the MARTX toxin, previously recognized to be important for evading the immune system. A third as yet uncharacterized genetic mutation in the cholera toxin followed, suggesting a mutation emerged in the cholera toxin to compensate for the loss of MARTX.

These mutations occurring in the same strain indicate that the bacterium interacts differently with the immune system than previous strains.

"Perhaps this results in the bacterium more successfully evading early detection after a person accidently drinks cholera infected fluids," Satchell said. "Interestingly, these multiple mutations in important proteins that specifically contribute to disease could explain why this strain is causing more severe disease, although the contribution of each mutation to human infection remains to be studied."

Previously published research on the Haiti cholera strain noted the change in the bacterium’s DNA and tracked its origin to Nepal, but scientists didn't ask how the changes affected the bacterium’s function. In addition, scientists had believed the bacterial strains responsible for the "new wave" of cholera that engulfed Haiti and first began spreading in 2000 were functionally identical to most other strains prevalent in the environment.

Satchell's finding further confirms the strain infecting Haiti likely originated in Nepal, consistent with the conclusion from the whole genome analysis and public health studies. Strains with this unique signature of a cholera toxin with three genetic changes coupled with loss of MARTX has spread only in a very defined geographical area including India where it was first detected in 2007. It has spread through Bangladesh, Cameroon, Nepal and then into Haiti and the Dominican Republic in 2010. Even though other strains are nearly identical and barely distinguishable at the genetic level, only this very small group of isolates share this unique signature, verifying from a functional viewpoint that the strain that moved to Haiti likely originated in Nepal.

"What we discovered is that the bacterial strains responsible for the 'new wave' of cholera are not all functionally identical with minor modification as previously thought, nor are they similar to most other strains prevalent in the environment, but, in fact, the strain with multi-signature toxin gene mutations may instigate a unique pattern of infection accounting for the severity of disease noted during the Haiti cholera outbreak," Satchell said.

How Does Acupuncture Work? The Science behind the Therapy Is Explored in a Special Issue of Medical Acupuncture

New Rochelle, NY, April 16, 2013—Even as medical acupuncture is increasingly being validated as an effective treatment for a broad range of medical conditions, what has been missing is an understanding of the basic science and mechanisms of action of this age-old method of healing. A special issue of Medical Acupuncture, a peer-reviewed journal published by Mary Ann Liebert, Inc., publishers presents a series of articles by authors from around the world who provide diverse and insightful perspectives on the science and physiologic responses underlying medical acupuncture. The issue is available on the Medical Acupuncture website.

“Understanding acupuncture in the same manner that we understand the mechanism of action and pharmacokinetics of a particular drug will, similarly, enable us to match treatments better with conditions,” states Guest Editor Richard F. Hobbs, III, MD. “The net effect will be improved outcomes,” he writes in his editorial “Basic Science Matters.”
In the editorial “Basic Science: Mysteries and Mechanisms of Acupuncture,” Richard Niemtzow, MD, PhD, MPH, Editor-in-Chief of Medical Acupuncture, a retired Air Force Colonel and current Director of the USAF Acupuncture Center, Joint Base Andrews, Maryland, suggests that natural events have scientific explanations and that “the two explanations—one scientific, the other environmental—might both elucidate how acupuncture works.”

The issue includes a Review article by John Longhurst, MD, PhD, University of California, Irvine, entitled “Acupuncture’s Cardiovascular Actions: A Mechanistic Perspective.” The article describes how acupuncture’s effects on cardiovascular function can decrease elevated blood pressure, improve blood flow, and relieve pain.

Steven Harte, PhD and colleagues from the University of Michigan (Ann Arbor) and Massachusetts General Hospital and Harvard Medical School (Boston, MA) report the results of a study aimed at understanding the differences in patient responses to traditional vs. sham acupuncture. They used pressure-pain testing to identify patients who may be less likely to respond to sham acupuncture based on levels of neurotransmitters in the brain. The study is described in the article “Pressure Pain Sensitivity and Insular Combined Glutamate and Glutamine (Glx) Are Associated with Subsequent Clinical Response to Sham But Not Traditional Acupuncture in Patients Who Have Chronic Pain.”

Keith Spaulding, ND, MAC and coauthors assessed the electrophysiological differences between actual and nearby (or sham) acupuncture points in the article “Acupuncture Needle Stimulation Induces Changes in Bioelectric Potential.”

About the Journal
Medical Acupuncture, the Official Journal of the American Academy of Medical Acupuncture, is an authoritative peer-reviewed journal published bimonthly in print and online that presents evidence-based clinical articles, case reports, and research findings that integrate concepts from traditional and modern forms of acupuncture with Western medical training. Tables of content and a sample issue may be viewed on the Medical Acupuncture website.

Climate and Environmental Changes Affect the Occurrence of Diseases Transmitted Between Animals and Humans

Apr. 15, 2013 — How are human and animal diseases in general affected by the climate becoming "wilder, wetter and warmer"? Solveig Jore's doctoral research shows that the tick Ixodes ricinus has spread over larger geographical areas in Norway and that climate and environmental changes, access to host animals and demography affect tick distribution in Norway. Furthermore, local climatic conditions can have a decisive influence on the ability of the tick to spread dangerous viruses. The climate can also play a role in the spread of gastrointestinal infections.

The effects of climate changes are the easiest to detect and are probably most pronounced near the geographical distribution limits of the infection or for the vector which carries the infection. Norway represents the northern distribution limit in Europe for the tick Ixodes ricinus and is therefore well suited as a location for investigating how climate changes affect the distribution of this tick.

By correlating different sources of data on tick distribution, we find that occurrences of the commonest species of tick in Norway (I. ricinus) have been reported considerably further north and higher up in mountainous regions than was formerly the case. The distribution pattern of I. ricinus has changed substantially over the last 50 years and we can now expect to find this tick as far north as Harstad, which is 400 km further north than previous records. The tick has also been detected at altitudes as high as 700-800 metres above sea level. This means that there is an increased risk of humans and animals becoming infected and falling ill in new areas of the country.

The occurrence of the viral disease tick-borne encephalitis (TBE) has been documented in several parts of Norway for the first time. Research shows that the occurrence of the TBEV virus responsible for TBE in infected areas is at an equivalent level to that shown in other European studies. Jore examined the relationship between the distribution of the virus in the tick and microclimatic conditions at seven different collection points along the southern coast of Norway. Her findings suggest that the degree of humidity in the air can have a decisive effect on how this virus can survive/reproduce in the tick and then be transmitted to humans via tick bites.

Jore discovered a strong connection between a higher prevalence of ticks and changes in certain climatic factors, overgrown vegetation, an increase in the number of deer and the number of farms with ruminants.

The analyses carried out in this study underline the importance of taking into account seasonal fluctuations in climatic variables and not just average changes. Since the current changes in the climate...
are expected to increase the fluctuations in certain variables (i.e. changes in extreme values), Jore's doctoral research emphasises how important it is to focus on this aspect when evaluating the effects of climate changes and when modelling for the distribution of the disease.

Campylobacteriosis is the most common bacterial cause of gastrointestinal disease in humans in Norway and Europe, and chicken is believed to be a main source of infection in humans. The occurrence of this disease in humans and chickens was studied in six European countries and in all the countries, there were clear seasonal and correlated variations in both types of the disease, with the highest incidence occurring in the summer. These variations may be due to the changes in temperature themselves, or to factors influenced by temperature changes in the summer season.

**Alternative Way to Explain Life's Complexity Proposed**

Apr. 12, 2013 — Evolution skeptics argue that some biological structures, like the brain or the eye, are simply too complex for natural selection to explain. Biologists have proposed various ways that so-called 'irreducibly complex' structures could emerge incrementally over time, bit by bit. But a new study proposes an alternative route.

Instead of starting from simpler precursors and becoming more intricate, say authors Dan McShea and Wim Hordijk, some structures could have evolved from complex beginnings that gradually grew simpler -- an idea they dub "complexity by subtraction." Computer models and trends in skull evolution back them up, the researchers show in a study published this week in the journal *Evolutionary Biology*.

Some biological structures are too dizzyingly complex to have emerged stepwise by adding one part and then the next over time, intelligent design advocates say. Consider the human eye, or the cascade that causes blood to clot, or the flagellum, the tiny appendage that enables some bacteria to get around. Such all-or-none structures, the argument goes, need all their parts in order to function. Alter or take away any one piece, and the whole system stops working. In other words, what good is two thirds of an eye, or half of a flagellum?

For the majority of scientists, the standard response is to point to simpler versions of supposedly 'irreducibly complex' structures that exist in nature today, such as cup eyes in flatworms. Others show how such structures could have evolved incrementally over millions of years from simpler precursors. A simple eye-like structure -- say, a patch of light-sensitive cells on the surface of the skin -- could evolve into a camera-like eye like what we humans and many other animals have today, biologists say.

"Even a very simple eye with a small number of parts would work a little. It would be able to detect shadows, or where light is coming from," said co-author Dan McShea of Duke University.

In a new study, McShea and co-author Wim Hordijk propose an alternative route. Instead of emerging by gradually and incrementally adding new genes, cells, tissues or organs over time, what if some so-called 'irreducibly complex' structures came to be by gradually losing parts, becoming simpler and more streamlined? Think of naturally occurring rock arches, which start as cliffs or piles of stone and form when bits of stone are weathered away. They call the principle 'complexity by subtraction.'

"Instead of building up bit by bit from simple to complex, you start complex and then winnow out the unnecessary parts, refining them and making them more efficient as you go," McShea said.

A computer model used by co-author Wim Hordijk supports the idea. In the model, complex structures are represented by an array of cells, some white and some black, like the squares of a checkerboard. In this class of models known as cellular automata, the cells can change between black and white according to a set of rules.

Using a computer program that mimics the process of inheritance, mutation, recombination, and reproduction, the cells were then asked to perform a certain task. The better they were at accomplishing the task, the more likely they were to get passed on to the next generation, and over time a new generation of rules replaced the old ones. In the beginning, the patterns of black and white cells that emerged were quite complex. But after several more generations, some rules 'evolved' to generate simpler black and white cell patterns, and became more efficient at performing the task, Hordijk said.

We see similar trends in nature too, the authors say. Summarizing the results of previous paleontological studies, they show that vertebrate skulls started out complex, but have grown simpler and more streamlined. "For example, the skulls of fossil fish consist of a large number of differently-shaped bones that cover the skull like a jigsaw puzzle," McShea said. "We see a reduction in the number of skull bone types in the evolutionary transitions from fish to amphibian to reptile to mammal." In some cases
skull bones were lost; in other cases adjacent bones were fused. Human skulls, for example, have fewer bones than fish skulls.

Computer simulations like Hordijk's will allow scientists to test ideas about how often 'complexity by subtraction' happens, or how long it takes. The next step is to find out how often the phenomenon happens in nature.

"What we need to do next is pick an arbitrary sample of complex structures and trace their evolution and see if you can tell which route they proceeded by, [from simple to complex or the opposite]. That will tell us whether this is common or not," McShea added.

**Journal Reference:**

**Mathematics Provides a Shortcut to Timely, Cost-Effective Interventions for HIV**

Apr. 15, 2013 — Mathematical estimates of treatment outcomes can cut costs and provide faster delivery of preventative measures.

South Africa is home to the largest HIV epidemic in the world with a total of 5.6 million people living with HIV. Large-scale clinical trials evaluating combination methods of prevention and treatment are often prohibitively expensive and take years to complete. In the absence of such trials, mathematical models can help assess the effectiveness of different HIV intervention combinations, as demonstrated in a new study by Elisa Long and Robert Stavert from Yale University in the US. Their findings appear in the *Journal of General Internal Medicine*, published by Springer.

Currently 60 percent of individuals in need of treatment for HIV in South Africa do not receive it. The allocation of scant resources to fight the HIV epidemic means each strategy must be measured in terms of cost versus benefit. A number of new clinical trials have presented evidence supporting a range of biomedical interventions that reduce transmission of HIV. These include voluntary male circumcision -- now recommended by the World Health Organization and Joint United Nations Programme on HIV/AIDS as a preventive strategy -- as well as vaginal microbicides and oral pre-exposure prophylaxis, all of which confer only partial protection against HIV. Long and Stavert show that a combination portfolio of multiple interventions could not only prevent up to two-thirds of future HIV infections, but is also cost-effective in a resource-limited setting such as South Africa.

The authors developed a mathematical model accounting for disease progression, mortality, morbidity and the heterosexual transmission of HIV to help forecast future trends in the disease. Using data specific for South Africa, the authors estimated the health benefits and cost-effectiveness of a "combination approach" using all three of the above methods in tandem with current levels of antiretroviral therapy, screening and counseling.

For each intervention, they calculated the HIV incidence and prevalence over 10 years. At present rates of screening and treatment, the researchers predict that HIV prevalence will decline from 19 percent to 14 percent of the population in the next 10 years. However, they calculate that their combination approach including male circumcision, vaginal microbicides and oral pre-exposure prophylaxis could further reduce HIV prevalence to 10 percent over that time scale -- preventing 1.5 million HIV infection over 10 years -- even if screening and antiretroviral therapy are kept at current levels. Increasing antiretroviral therapy use and HIV screening frequency in addition could avert more than 2 million HIV infections over 10 years, or 60 percent of the projected total.

The researchers also determined a hierarchy of effectiveness versus cost for these intervention strategies. Where budgets are limited, they suggest money should be allocated first to increasing male circumcision, then to more frequent HIV screening, use of vaginal microbicides and increasing antiretroviral therapy. Additionally, they calculate that omitting pre-exposure prophylaxis from their combination strategy could offer 90 percent of the benefits of treatment for less than 25 percent of the costs.

The authors conclude: "In the absence of multi-intervention randomized clinical or observational trials, a mathematical HIV epidemic model provides useful insights about the aggregate benefit of implementing a portfolio of biomedical, diagnostic and treatment programs. Allocating limited available resources for HIV control in South Africa is a key priority, and our study indicates that a multi-intervention HIV portfolio could avert nearly two-thirds of projected new HIV infections, and is a cost-effective use of resources."

**Journal Reference:**
New Technique to Deliver Life-Saving Drugs to the Brain

Researchers from the Herbert Wertheim College of Medicine at Florida International University (FIU) report developing a novel technique that uses magneto-electric nanoparticles (MENs) to deliver antiretroviral therapies to HIV-infected brain cells. According to Professor Madhavan Nair, PhD, a natural filter prevents most substances from passing into the brain. As a result, more than 99 percent of HIV therapies, such as AZTTP, go to the lungs, liver, and other organs, leaving reservoirs of HIV hidden in the brain.

Nair and Professor Sakhrat Khizroev, PhD—an electrical engineer and physicist—developed a technique that binds AZTTP to a MEN that is inserted into a monocyte/macrophage cell and injected into the body. Next, the team uses a magnet to draw the MEN into the brain, where a low electrical current triggers release of the drug. Magneto-electricity then guides the drug to its target. The team has successfully tested the technique in a laboratory setting, and will soon begin the next phase of testing.

Khizroev anticipates that the technique also might be useful for treating other neurological diseases, such as Parkinson’s, Alzheimer’s, epilepsy, muscular dystrophy, meningitis, chronic pain, and cancer.

Indian Drug Supplier Cuts Price Of 5-In-1 Childhood Vaccine For GAVI Alliance;

Groups Highlight World Immunization Week
"The cost of immunizing children in developing countries with a five-in-one vaccine is set to fall after a deal by an Indian supplier to slash the price it charges the GAVI global vaccines group," Reuters reports. "GAVI said on Thursday that Biological E would sell the pentavalent shot for $1.19 per dose, compared to a 2012 weighted average price of $2.17, saving it up to $150 million over the next four years," the news service writes, noting the five-in-one vaccine "protects against diphtheria, tetanus, whooping cough, hepatitis B and Haemophilus influenzae type B (Hib)." The news service adds, "The agreement between Biological E and the GAVI Alliance, which funds bulk-buy vaccination programs for poor nations, highlights the growing role of India's low-cost drugs sector in supplying products around the world," noting, "India's staunch support for its generics sector has led to clashes with Western pharmaceutical companies, most recently following a high-profile defeat for Novartis in a cancer drug patent case this month" (Hirschler, 4/17).

In similar news, a joint press release from the WHO, UNICEF, the GAVI Alliance and the Bill & Melinda Gates Foundation notes that, in advance of World Immunization Week, which begins April 20, "global experts are highlighting strategies to further advance progress on the Global Vaccine Action Plan that was endorsed by the World Health Assembly, 2012." According to the press release, "Better supply and logistics systems are essential to reach the estimated 22 million children in developing countries who are still not protected from dangerous diseases with basic vaccines, according to a special immunization issue published today by Vaccine." The press release adds, "Articles in the special supplement also underline the need to improve understanding about the health benefits of immunization" (4/18).

International Research Team Casting Wide Net In Search For H7N9 Source, Transmission Routes
"Another case of bird flu has been reported in China, taking the total infection count to 83 people, as health authorities inside and outside the country try to determine how to stop its spread," CNN reports. "Seventeen people have died from the H7N9 strain of the virus which, while common in birds, hadn't been detected in humans before the first cases were reported in March," the news agency writes (Whiteman, 4/18). "Authorities haven't confirmed human-to-human transmission of the disease, though the government-controlled Beijing Daily reported yesterday that 40 percent of those sick have had no contact with poultry," Forbes notes, adding, "Encouragingly, a seven-year-old girl diagnosed with the flu last week checked out of a Beijing hospital [this week]. She is one of five people released from hospitals after being treated" (Flannery, 4/17).

"Understanding how the virus is spreading is a goal of international and Chinese experts assembled by the World Health Organization as they begin a weeklong investigation Friday," the Associated Press reports (4/18). "China is investigating four possible cases of human-to-human transmission of a deadly bird flu that has killed 17 people but so far there was 'no sustained' evidence of transmission between..."
people, the [WHO] said on Thursday," the New York Times notes. "As investigators looked at the possibility of human transmission, there was mounting concern that the new virus ... may not originate in birds but in other animals and in environmental sources, [a] WHO spokesman said," the newspaper writes (Perlez, 4/18). The international research team "is examining 'family clusters' of people infected with the virus, a top health official was quoted as saying," Reuters notes (Wee, 4/18).

Women With HIV Who Breastfeed Exclusively Longer Than 4 Months Have Lower Risk Of Transmitting Virus To Infants, Study Shows

"The amount of HIV in an infected mother’s breast milk spikes when weaning begins, according to a study published [Wednesday] in Science Translational Medicine," Nature reports. "The findings are likely to add urgency to efforts to ensure that infected mothers without access to formula take antiretroviral drugs throughout and beyond the time that they wean their infants," the journal writes (Wadman, 4/17). "To test whether breastfeeding routines affect the levels of HIV in breast milk, the researchers tested nearly 1,000 women and their infants in Lusaka, Zambia, over 24 months," the Los Angeles Times' "Science Now" blog writes, adding, "The women were divided into two groups -- one that weaned their babies abruptly after four months, and one in which the women continued to breastfeed as long as they chose." According to the blog, "HIV-infected mothers who breastfed exclusively longer than the first four months after birth had less risk of transmitting the virus to their babies through their milk, researchers said" (MacVean, 4/17).

"The milk from women who ... stopped breastfeeding abruptly contained markedly higher levels of HIV than did milk from the women who continued to breastfeed exclusively," Nature notes. "The current practice of giving mothers one to two weeks of antiretroviral therapy after weaning may not be enough, the authors say, given that weaning is a stop-and-start, often protracted, process in real life," according to the magazine (4/17). "Our results have profound implications for prevention of mother-to-child HIV transmission programs in settings where breastfeeding is necessary to protect infant and maternal health," the researchers wrote, GlobalPost notes (Peterson, 4/17). "WHO guidelines suggest that where HIV treatments are used, mothers should breastfeed their infants to at least 12 months," Bloomberg Businessweek writes, adding, "And if antiretroviral drugs are unavailable, women can still breastfeed for at least the first six months" (Ostrow, 4/17).

Why does smallpox vaccine shield some, not others? It's in the genes, Mayo finds

ROCHESTER, Minn. -- How well people are protected by the smallpox vaccine depends on more than the quality of the vaccination: individual genes can alter their response, Mayo Clinic research shows. The findings, gathered using sophisticated genomic screening, appear in today's online issue of the journal Genes and Immunity.

"We were looking into the intercellular reactions that occur when vaccinated and unvaccinated persons are exposed to and infected with smallpox virus. We were able to use blood samples taken directly from vaccinated patients," says senior author Gregory Poland, M.D., director of the Mayo Clinic Vaccine Research Group. "We could see what would happen based on exposing a mixed-cell peripheral blood cell population to the vaccinia virus."

While worldwide vaccination is believed to have eradicated smallpox, the highly contagious and sometimes fatal illness remains a bioterrorism concern.

Researchers studied 44 participants from Mayo Clinic and the Naval Health Research Center who had received the smallpox vaccine in the previous 48 months. Two samples were prepared from each of the 44, one uninfected and one that was infected with vaccinia, a smallpox-like virus. RNA (ribonucleic acid, molecules that represent the DNA makeup) from the samples was then tested in the high-speed sequencing facilities at Mayo Clinic's Center for Individualized Medicine. Genetic differences were found between people with robust protective antibodies and those with lower immunity from smallpox.

Dr. Poland says this individualized medicine approach and its findings offer researchers new targets for developing tests to determine if a person should receive a specific vaccine, but also an opportunity to develop new vaccines to benefit non-responders.

Tell me where you're from and I'll tell you what tastes you prefer

The country of residence is a fundamental factor in taste preferences
Children love fatty and sugary foods. Or do they? New research contradicts the idea that all children under the age of ten have the same taste in food and highlights the importance of the country of residence, culture and age in these preferences.

**SINC**

Until now the scientific community believed that children’s favourite foods were chips, sweets and sugary drinks, the very foods that are the most damaging to their health.

However, a new study published in the ‘Food Quality and Preference’ journal concludes that this hypothesis is not entirely true after analysing whether or not all children have the same preference for sugar and fat, considered to be a cause of excess weight and obesity for all ages. During the research, which forms part of the Identification and prevention of Dietary and lifestyle induced health Effects In Children and infantS (IDEFICS) project, the flavour preferences of more than 1,700 children between six and nine years old from eight European countries (Italy, Estonia, Cyprus, Belgium, Sweden, Germany, Hungary and Spain) were examined.

Using sensory tests, the authors were able to determine the children’s taste for fat, sugar, salt and monosodium glutamate, a flavour enhancer that corresponds to the fifth basic taste, known as ‘umami’.

"The results were surprising", Silvia Bel-Serrat, the only Spanish co-author of the study who works in the University of Zaragoza, explained to SINC. "Although we often tend to think that children share a common predisposition towards fats and sugar, we observed that the preferences of children from different countries were not at all similar."

**German and Cypriots in relation to biscuits**

More than 70% of the German children preferred biscuits with added fat compared to only 35% of the children from Cyprus. Conversely, the majority of the German children preferred plain apple juice, while the Swedish, Italian and Hungarian children opted for the version with added sugar or flavours.

"This means that flavour preferences are influenced by cultural factors, but we also see that these tastes are developed in a similar way as children grow up", stated Anne Lanfer, the study's main author and researcher at the Institute for Prevention Research and Epidemiology in Bremen (Germany). Thus, in all eight countries the older children had a higher preference for sugar and salt than the younger ones.

The research team also assessed whether tastes varied according to the child’s gender, taste threshold, parent's level of education, feeding patterns during their early years, time spent watching television and parents' use of food as a reward.

The results showed that there was no link between these factors and the preference for sugar, fat, salt and umami among the children, despite the fact that an influence on flavour preference had previously been attributed to such factors.

**Refining prevention**

The researchers believe the study has important implications. "There is a tendency to undertake uniform dietary prevention programmes across European countries. However, flavour preferences vary from one country to another and the same programme will not be equally effective in all countries," Lanfer pointed out.

For example, promoting the consumption and distribution of apple juice with no added sugar would be more effective in Germany, where there is a high level of acceptance, than in Hungary, where the majority of children prefer juice with added sugar. Furthermore, knowing that children’s preferences change as they grow older, "there is still hope that children's flavour preferences are not stable and can be influenced by their parents and the surrounding environment", the authors concluded.

**Reference:**

Anne Lanfer, Karin Bammann, Kolja Knof, Kirsten Buchecker, Paola Russo, Toomas Veidebaum, Yiannis Kourides, Stefaan de Henauw, Dénes Molnar, Silvia Bel-Serrat, Lauren Lissner, Wolfgang Ahrens. "Indicadores de las preferencias de sabor en niños europeos: Estudio IDEFICS". *Food Quality and Preference* 27 (2013) 128

**Scientists Throw New Light On DNA Copying Process**
Apr. 18, 2013 — Research led by a scientist at the University of York has thrown new light on the way breakdowns in the DNA copying process inside cells can contribute to cancer and other diseases.

Peter McGlynn, an Anniversary Professor in the University's Department of Biology, led a team of researchers who have discovered that the protein machines that copy DNA in a model organism pause frequently during this copying process, creating the potential for dangerous mutations to develop. The research, which is published in the Proceedings of the National Academy of Sciences (PNAS), involved scientists at the School of Medical Sciences at the University of Aberdeen, where Professor McGlynn worked previously, the Centre for Genetics and Genomics at the Queen's Medical Centre, University of Nottingham and the Memorial Sloan-Kettering Cancer Center, New York.

The project focused on a bacterium called Escherichia coli which is a powerful model for studying the DNA copying process, the study of which has revealed many aspects of DNA metabolism in more complex organisms such as humans.

Professor McGlynn, who was one of 16 Chairs established at York to mark the University's 50th Anniversary, says: "Our work demonstrates that when organisms try to copy their genetic material, the copying machines stall very frequently which is the first step in formation of mutations that, in man, can cause cancers and genetic disease.

"We have analysed what causes most of these breakdowns and how, under normal circumstances, cells repair these broken copying machines. Just as importantly, our work reveals that efficient repair of these breakdowns is very important to avoid corruption of the genetic code."


Health Experts In China Working To Identify Source, Transmission Routes Of H7N9 Flu Virus

"Fifteen global and Chinese health experts are on a mission in Beijing and Shanghai to learn more about the H7N9 bird flu virus that has killed 17 people and sickened 70 others, said Dr. Michael O'Leary, head of WHO's office in China," the Associated Press reports (Wong, 4/19). "The first human case was identified three weeks ago, and the rapid compilation of human cases since then has public health officials in China and scientists from around the world scrambling to identify the source of the infection and prevent further spread," the San Francisco Chronicle notes (Allday, 4/18). "As the number of cases of [the] deadly strain of bird flu rises in China, health officials there are investigating the possibility that the disease has spread from human to human," the Globe and Mail writes (Andreatta, 4/18).

"China is investigating four possible cases of human-to-human transmission of [H7N9], but so far there has been 'no sustained' evidence of transmission between people, the [WHO] said Thursday," according to the New York Times (Perlez, 4/18). "Chinese authorities are attempting to identify the bird reservoir that is the source of the disease so they can reduce human exposure to it," The Lancet adds (Alcorn, 4/20). "The government is urging people to move quickly to head off the spread of the disease, most importantly closing down chicken markets," the Washington Post notes (Mufson, 4/17). However, "[m]ore than 50 percent of patients infected with [H7N9] had no contact with poultry, the World Health
Organization said on Friday, further raising questions about whether the virus was transmitted between humans,” Reuters reports (Rajagopalan/Kelland, 4/19).

**Sofosbuvir Offers High Cure Rate For Two Hepatitis C Subtypes**

Sofosbuvir, a new drug, is offering impressive cure rates for Hepatitis C patients with two subtypes of the disease - genotypes 2 and 3, according to researchers led by Weill Cornell Medical College.

Approximately 1 in every 4 hepatitis C patients in the USA has one of these two subtypes.

Sofosbuvir, which is much safer than Interferon, offered more effective treatment for the majority of patients involved in a Phase 3 clinical trial. The participants had no other treatment options, the scientists reported in *NEJM* (New England Journal of Medicine).

Interferon can have serious side effects, including loss of vision, sepsis, heart failure, and leucopenia (a decrease of white blood cells).

The following response rates were reported after three months therapy with sofosbuvir combined with ribavirin:

- 93% among those with genotype 2
- 61% among participants with genotype 3

Several drugs being tested for hepatitis C were published in the online edition of *NEJM* (April 23, 2013 edition). This issue of the journal coincides with the International Liver Congress 2013 in Amsterdam, the Netherlands.

Study leader, Dr. Ira Jacobson, chief of the Division of Gastroenterology and Hepatology and Vincent Astor Distinguished Professor of Medicine at Weill Cornell Medical College, said:

"The new sofosbuvir therapy offers a much-needed alternative to standard therapy with interferon, which can cause significant side effects for hepatitis C patients.

"We have dreamed for years of being able to eliminate interferon from our hepatitis C regimens and this study is one of several that are finally bringing us very close to realizing that goal."

The POSITRON trial included 207 participants. The patients either had not responded to interferon, were unwilling to use it, or unable to tolerate it, in spite of there being no other treatment options available.

Dr. Jacobson said "This new treatment represents a paradigm shift in the way that hepatitis C is going to be treated. We are achieving the same or higher cure rates in many patients with sofosbuvir, compared to interferon, and we are doing it in half the time with a drug that has a remarkable safety profile."

The authors estimate that up to 50% of hepatitis C patients are either unable to use interferon or refuse to use it. They see Sofosbuvir as an extremely promising treatment for these patients. They believe that potent antiviral drug combos will eventually replace interferon use for the majority of patients with hepatitis C.

Sofosbuvir interferes with the hepatitis C virus' ability to replicate. It also makes it more difficult for drug resistance to occur. Sofosbuvir has yet to be approved by the Food and Drug Administration (FDA). The four clinical trials, the results of which were published in *NEJM*, were used to support the regulatory filing of the medication by Gilead Sciences Inc., the makers of sofosbuvir.

**About hepatitis C**

Globally, about 170 million people are infected with hepatitis C; the disease kills 350,000 people annually. According to US statistics, approximately 4 million Americans are infected with hepatitis C. Often patients have no symptoms, so the majority of hepatitis C infected people don’t know they are infected.

Hepatitis C, if left untreated, can progress to cirrhosis, liver cancer and liver failure.

The hepatitis C Virus spreads by contact with infected blood, such as injection drug use, sexual contact or through blood transfusions.

Of the 7 major genotypes of hepatitis C, 1, 2 and 3 are the most common. In the USA, genotype 1 is the most common, while the most prevalent in Europe are genotypes 2 and 3. In the Indian subcontinent genotype 3 is the most common.

**The POSITRON Trial**

75% (207) of all the patients in the POSITRON trial were randomly selected to receive a sofosbuvir and ribavirin combo, while the rest (71) were given a placebo treatment. All of the participants either had not responded to interferon or refused to use it. Dr. Jacobson said "This mirrors what happens frequently in
the clinic. Between 15 and 30 percent of patients with hepatitis C genotype 2 or 3 infections do not have a response to interferon therapy and do not have alternate treatment options."

Participants were enrolled at sixty-three sites in New Zealand, Canada, Australia and the USA. The study should that the response rates were:

- 78% among the sofosbuvir plus ribavirin patients
  - 93% among those with genotype 2
  - 61% among the genotype 3 patients
  - 81% among patients without cirrhosis
  - 61% among those with cirrhosis
  - 0% among the placebo patients

**The FUSION Trial**

This trial was led by Dr. David R. Nelson from the University of Florida at Gainesville. The results were incorporated into this *NEJM* manuscript publication. The trial tested the sofosbuvir plus ribavirin combo in hepatitis C patients with genotypes 2 or 3 who had not responded to interferon treatment.

Patients were tested at 12 and 16 weeks of therapy. The findings showed that the longer people were on the sofosbuvir combo, the higher their cure rate was, regardless of genotype. However, the difference seen in genotype 3 was "highly significant".

- For those with hepatitis C genotype 2, there was a response rate of 86% at 12 weeks and 94% at 16 weeks.
- For genotype 3 patients, there was a response rate of 30% at 12 weeks and 62% at 16 weeks.

Dr. Jacobson said: "Given the absence to date of alternative therapies for patients with genotype 2 or 3 who have failed interferon therapy or for whom it is not an option, treatment with the new sofosbuvir regimen offers a vast improvement. But the optimal duration of treatment for genotype 3 patients, in order to maximize their chance of cure, remains undefined. It could be longer than 16 weeks."

Further studies will decide what the optimum treatment duration for those with genotype 3 should be. Additional studies will also determine whether different sofosbuvir combos might shorten treatment times.

**Fighting Schistosomiasis Would Help Reduce HIV Incidence, Researchers Say**

"The transmission of HIV in sub-Saharan Africa could be slashed if efforts are made to combat the spread of the waterborne disease schistosomiasis by providing clean water, sanitation and health education," *SciDev.Net* reports. Schistosomiasis can cause genital ulcers in women, making them more susceptible to HIV infection, the news service notes. "To test whether schistosomiasis infections could be reduced in a cost-effective manner, researchers from Norway, South Africa and the United States plugged epidemiological and clinical data from Zimbabwe into a mathematical model," *SciDev.Net* reports, adding, "They found that community-based interventions -- providing universal clean water, sanitation and education, as well as the drug praziquantel to treat schistosomiasis in children -- would be a cost-effective way of cutting the two infections at between $725 and $1,000 per individual over a period of 20 years." The news service continues, "And because these interventions can reduce schistosomiasis and HIV transmission, as well as diarrheal disease and bacterial infections caused by infected water, they should be economically attractive to policymakers, the researchers write in *Proceedings of the National Academy of Sciences (PNAS)*" (Nakkazi, 4/23).

**Polio Can Be Eradicated Using Lessons From Smallpox**

"With only 223 wild poliovirus cases in five countries in 2012, the paralytic disease has been knocked down to just a handful of small reservoirs. Recognizing this historic opportunity to achieve eradication, we have enthusiastically joined more than 400 scientists from 80 countries to sign the *Scientific Declaration on Polio Eradication*," Larry Brilliant, president and CEO of the Skoll Global Threats Fund, and William Foege, a senior fellow in the Bill & Melinda Gates Foundation's Global Health Program -- both of whom "served more than three decades ago on the team that eradicated smallpox, the only other human disease to be wiped from the planet" -- write in a *Scientific American guest blog*. "Through the declaration, we are endorsing a clear path -- not just an aspiration -- to bring an end to polio: the new *Eradication and Endgame Strategic Plan*," developed under the auspices of the Global Polio Eradication Initiative (GPEI), they state. "We see in the polio endgame plan the same hallmarks of success that guided smallpox eradication to completion," they continue.
First, there "is a relentless focus on pulling out the roots of the disease, no matter how challenging the circumstances," Brilliant and Foege write. Second, the plan leaves room for "creative problem-solving" and "spectacular innovation," such as GIS mapping technology that allows for the tracking of missed areas in vaccination campaigns, they note. Third, the polio eradication effort is "learning from setbacks," they state, adding, "We are encouraged that the polio effort is taking a page from smallpox by continually reviewing where past approaches have been insufficient." They continue, "Perhaps the most important way in which polio eradication builds on smallpox is by following up after a country eliminates the disease by building systems for other national health priorities." The authors conclude, "Now, the global community must meet its collective responsibility to ensure implementation of the plan, including fully funding it upfront and promoting shared accountability. By working together, we will soon relegate polio -- alongside smallpox -- to the history books" (4/22).

Fighting Bacteria With New Genre of Antibodies
Apr. 24, 2013 — In an advance toward coping with bacteria that shrug off existing antibiotics and sterilization methods, scientists are reporting development of a new family of selective antimicrobial agents that do not rely on traditional antibiotics.

Their report on these synthetic colloid particles, which can be custom-designed to recognize the shape of specific kinds of bacteria and inactivate them, appears in the Journal of the American Chemical Society.

Vesselin Paunov and colleagues point out that many bacteria have developed resistance to existing antibiotics. They sought a new approach -- one that bacteria would be unable to elude by mutating into drug-resistant forms. Their inspiration was the antibodies that the immune system produces when microbes invade the body. Those antibodies patrol the body for microbes and bind to their surfaces, triggering a chain of events in which the body's immune system attacks and destroys the microbes.

Paunov's team describes development and successful tests of synthetic colloid particles, called "colloid antibodies." Colloids are materials in which tiny particles of one material are dispersed in another material. Milk is a colloid in which globules of fat are spread throughout water and other materials. The colloid antibody particles are shells packed with a killing agent. They are designed to recognize and bind to specific bacteria.

Laboratory experiments showed that the colloid antibodies attached to and inactivated only their intended targets without harming other cells. "We anticipate that similar shape selective colloid antibodies can potentially become a powerful weapon in the fight against antibiotic-resistant bacteria," say the researchers. "They can also find applications as non-toxic antibacterial agents, preventing growth of harmful bacteria in various formulations."

Journal Reference:

HIV-Positive Patient Wins Suit Over Doc’s “Unreasonable Fear”
Posted April 29, 2013 in Your Personal Rights by Josh Crank
A California appeals panel has reversed a lower court verdict denying the claims of an HIV-positive woman whose surgery was canceled at the last minute by an anesthesiologist who was worried he might contract the disease.

Plaintiff Maureen K. developed a painful hernia and scheduled reparative surgery in 2009, three years after being diagnosed HIV-positive. With the consent of her immunologist, Maureen stopped taking her anti-retroviral (ARV) medications two months before the procedure because they were causing negative side effects.

The surgeon who approved the procedure, Dr. Constanze Rayhrer, did so with knowledge of Maureen’s medical history, HIV status and the fact that she was not taking ARVs. But when anesthesiologist Dr. Theodore Tuschka arrived in the preoperative room and saw Maureen’s medical chart, he announced that he would not participate in the surgery because, according to court filings, “he wanted to keep himself safe and the people that he works with safe.”

Tuschka wrote on Maureen’s medical chart: “Patient with HIV positive off medications two months. Suggest workup by treating physician documenting viral loads and infectious status. Hopefully patient will be on meds or have documented nonviremic state for the safety of the operating room personnel.”
Maureen’s attorney called the note the “smoking gun” because it demonstrated that Tuschka cancelled the operation solely for his own safety and that of the operating room staff, not out of any concern for Maureen’s health.

**Unruh Civil Rights Act**
Humiliated, Maureen sued Tuschka for violating the Unruh Civil Rights Act, a California law that broadly prohibits discrimination based on sex, race, religion, national origin, sexual orientation, disability, medical condition and other bases. The suit went to trial, during which Dr. Rayhrer testified that adherence to “universal precautions” protects all operating room staff from blood-borne diseases.

After both parties rested their cases, Tuschka’s attorney requested a special jury instruction regarding the definition of “disability,” despite not disputing a pretrial brief by Maureen’s attorney that considered her disabled status as an undisputed issue. The trial judge granted the special instruction over the plaintiff’s objection and also ordered the jury to determine whether Maureen had “a ‘physical disability’ based on her HIV status.”

The jury determined that Maureen was not disabled.

**Jury Decision ‘Defies Common Sense’**
On appeal, a panel of judges ruled that the trial court “prejudicially erred” by asking the jury to decide whether Maureen was disabled, noting that in California, “a person with HIV is disabled as a matter of law.”

“No medical doctor should have liability for refusing to perform a procedure that he or she believes will harm the patient,” Justice Kenneth R. Yegan wrote. “That is not what happened here. Here, an HIV-positive patient was denied medically necessary surgery because an anesthesiologist unreasonably feared for his own safety and that of the operating room staff.”

“Even with recent advances in treatment, HIV/AIDS remains a devastating, progressive illness for which there is no known cure,” Yegan continued. “Therapies such as ARV medications may delay its progression, but nothing can permanently alleviate the many symptoms and side effects experienced by those who are living with this condition. It defies common sense to say that an incurable illness marked by the progressive and ultimately total destruction of the immune system is not an actual disability.”

**Broad Protections Against Discrimination**
The Unruh Civil Rights Act dates back to 1959 and has been amended to specifically protect additional classes like sexual orientation. The California Supreme Court has held that the protections are **not restricted to the specified classes**, interpreting the law as prohibiting all arbitrary and intentional discrimination.

“The Unruh Civil Rights Act bars all California businesses from discriminating in providing services, including medical services,” said Department of Fair Employment and Housing Director Phyllis Cheng. “The Unruh Act incorporates the Fair Employment and Housing Act’s broad definition of disability, which since 2000 has expressly identified HIV/AIDS as a disability.”

**7 States Trying to Gut Sex Ed and Promote Abstinence**
*The Week*, (04.29.2013)
In 2013, at least seven states have proposed stopping comprehensive sex education in favor of an abstinence-based or anti-abortion approach. The seven states are Arkansas, Kansas, Montana, North Carolina, North Dakota, Ohio, and Texas. Congress also has proposed legislation, with one bill espousing abstinence legislation and another in favor of pro-sex education. The American Sexual Health Association has said that 50 percent of sexually active Americans will have an STD by the age of 25.

**International Networks of Gay Men Unite to Fight HIV**
*PrideSource*, (04.23.2013)
Major regional networks of men who have sex with men (MSM) and the Global Forum on MSM and HIV ( MSMGF) have united to advocate for increased HIV prevention funding and access to services for gay and other MSM. Partners in the consortium include the Asia Pacific Coalition on Male Sexual Health, the African Men for Sexual Health and Rights, Asociacion para la Salud Integral y Ciudadania en America Latina y el Caribe, the Caribbean Vulnerable Communities Coalition, the European Coalition on Male
Health, and MSMGF. The consortium will work to coordinate the work of human rights organizations and HIV service providers worldwide.

Although HIV prevalence is much higher among MSM worldwide, only two percent of global HIV funding goes to MSM programs, according to Dr. George Ayala, executive director of MSMGF. Recent data indicate HIV prevalence among MSM is 15 percent in South Asia, 18 percent in sub-Saharan Africa, 25 percent in the Caribbean, 15 percent in Latin America, and 6.6 percent in Central Asia and Eastern Europe.

Ayala stated that MSM-led grassroots organizations often are best at providing HIV services. However, they often face hostility because of homophobia, and they lack funding and capacity-building support. Ayala stated that the consortium members will be well-positioned to hear concerns of grassroots organizations and to provide technical assistance with community-based research and to advocate for policy changes and increased funding.

The coalition’s priority issues include advocating to assure funding from the Global Fund is apportioned according to the disease burden, establishing a “global emergency response system” to support MSM activists, and documenting LGBT-led organizations’ roles in responding to HIV among MSM.