February 2012 Epidemics and AIDS Update

1. The Enigmatic Membrane (long)
2. Man sues strip club, government after contracting HIV
3. Fear-Resistance: How Worried Should We Be about "Totally Drug-Resistant"
4. Pediatricians Recommend HPV Vaccine for Boys, Too
5. HIV-Related Deaths Slow Economy
6. Acceptability and Feasibility of Rapid HIV Testing in an Adolescent Clinic Setting: Youth Testing Attitudes, Knowledge and Behaviors
7. Jordan Deports Five HIV-Positive Libyan Patients
8. Islamist Rebel Group Bans ICRC From Southern Areas Of Somalia Under Its Control
9. Poor Quality Vaccination Campaigns, Lack Of Government Commitment Helping Polio Spread In Chad
10. South African Government Officials Recall Defective Condoms
11. Men who have sex with men may now be the highest-risk group for HIV in Africa, IAVI study suggests
12. India Has Worst Child Mortality Gender Differential Worldwide, New U.N. Data Show
13. Mexico Sees Spike In Swine Flu After Two Years Of Low Transmission
14. Malaria kills nearly twice as many people than previously thought, but deaths declining rapidly
15. Sexually transmitted infections double in older population in 10 years
16. Human immune cells react sensitively to "stress"
17. Chaos in the Cell's Command Center
18. Coming Soon: Over-the-Counter Oral AIDS Test
19. Global Malaria Deaths Twice As High As Previously Estimated, IHME Study Suggests
20. New procedure repairs severed nerves in minutes, restoring limb use in days or weeks
21. Komen Reverses Move to Cut Planned Parenthood Funding
22. Do People with HIV Have to Tell Their Sex Partners? Supreme Court to Decide
24. Incidence of Sexually Transmitted Infections Among Hazardously Drinking Women After Incarceration
25. Panel Discussion Shows Heated Controversy Over H5N1 Research
26. WHO Disputes Study's Claims That Global Malaria Deaths Are Double Current Estimates
27. U.N. Supporting Yellow Fever Vaccination Campaigns In Cameroon, Ghana
28. Dispute Over Malaria Figures Highlights Lack Of Certainty In Data In Age Of 'Information Overload'
29. Why bad immunity genes survive
30. Odds of living a very long life lower than formerly predicted
31. Why Do Cells Age? Discovery of Extremely Long-Lived Proteins May Provide Insight Into Cell Aging and Neurodegenerative Diseases
32. Key to Immune Cell's 'Internal Guidance' System Discovered
33. HIV Experts Propose New Pathway for Conducting Phase 3 Drug Trials
34. What Really Fuels the HIV/AIDS Epidemic in Black America? (long)
35. Can Interfaith Research Partnerships Develop New Paradigms for Condom Use and HIV Prevention? The Implementation of Conceptual Events in Malawi Results in a 'Spiritualized Condom'
36. Al Jazeera Examines Unique Polio Eradication Campaign In Pakistan
37. Salk scientists use an old theory to discover new targets in the fight against breast cancer
38. Food Poisoning: Understanding How Bacteria Come Back from the 'Dead'
39. Use of some anti-HIV drugs during pregnancy linked to cleft lip and palate; investigators urge cautious interpretation of results
40. HIV treatment not advanced enough to dismiss full disclosure, court told
41. DNA Sequencing Helps Identify Cancer Cells for Immune System Attack
42. Secrets of Immune Response Illuminated in New Study
43. HIV Drugs Not Linked with Child Psychiatric Problems
44. Substance P Causes Seizures in Patients Infected by Pork Tapeworm
45. Most Lethal Known Species of Prion Protein Identified
46. New research reveals how protein protects cells from HIV infection
47. Tenofovir associated with increased risk of kidney disease
48. Controversy Over China Push to Eliminate Anonymous HIV Tests
49. SWAZILAND: Reaching out to gays for the first time
50. HIV rate way down thanks to condoms
51. Projected Life Expectancy of People with HIV According to Timing of Diagnosis
52. Archbishop: Don't Hand Out Condoms
53. Bird Flu Controversy An Opportunity To Set A Higher Tone For Public Debate
54. Diagnostics for viruses a step closer to reality
55. New molecule can tangle up DNA for more than 2 weeks
56. SIV infection may lead to increase in immune-suppressive Treg cells
57. Scientist Works to Detach Protein That HIV Uses as Protective Shield
58. Half of all new HIV transmissions in US may originate in undiagnosed individuals
59. Hepatitis C Survival on Inanimate Objects
60. Cost-effectiveness of HAART underestimated
61. Cash payments help cut HIV infection rate in young women, study finds
62. Femidoms still a taboo
63. CDC Warns Untreatable Gonorrhea Is on the Way
64. One Quarter Of Young Children Worldwide Suffer Effects Of Malnutrition, Save The Children Survey Shows
65. Seven Sahel Region Nations Declare Emergencies With At Least 12M People Threatened By Hunger
66. Contraceptive preferences among young Latinos related to decision-making 2-15-12
67. Oncolytic virus extends survival in medulloblastoma model
68. Diabetes may start in the intestines, research suggests
69. Prions Play Powerful Role in the Survival and Evolution of Wild Yeast Strains
70. Antibodies to Intracellular Cancer Antigens Combined With Chemotherapy Enhance Anti-Cancer Immunity
71. High prevalence of trauma among HIV-positive women in the US
72. UK guidelines on treatment of HIV in pregnancy give green light to efavirenz
73. Uganda: Government raid on LGBT-rights workshop
74. Results for viral load on Vacc-4x
75. HIV warning to women using injectable contraception
76. ESPN to Show Film on Johnson's HIV Disclosure
77. Effect of a Cash Transfer Program for Schooling on Prevalence of HIV and Herpes Simplex Type 2 in Malawi: A Cluster Randomized Trial
78. Countdown to the introduction of a norovirus vaccine
79. Nasty "Superbug" is Being Studied by UB Researchers
80. Light Shed On How Body Fends Off Bacteria
81. To Understand Chromosome Reshuffling, Look to the Genome's 3-D Structure
82. Severe nevirapine rash linked to slow clearance of drug
83. White House Holds LGBT Health Conference
84. 1 in 10 children face elevated risk of abuse, future PTSD, due to gender nonconformity
85. Protein That Sends 'Painful Touch' Signals Identified
86. Traitorous Immune Cells Promote Sudden Ovarian Cancer Progression
87. Live from the Thymus: T-Cells On the Move
88. Which Anti-HIV Drug Combinations Work Best and Why?
89. Anthrax-Killing Foam Proves Effective in Meth Lab Cleanup, Study Suggests
90. Hepatitis C surpasses HIV as a cause of death in the US
91. Sexual Compulsivity, Co-Occurring Psychosocial Health Problems and HIV Risk Among Gay and Bisexual Men: Further Evidence of a Syndemic
92. Russian Government's Censorship Of Websites With Harm Reduction Methods For Drug Users Helps Fuel HIV Epidemic, IPS Reports
93. India Still Faces Challenges In Efforts To Eradicate Polio
94. Evolution of staph 'superbug' traced between humans and food animals
95. Influenza vaccination of pregnant women helps their babies
96. Substantial number of HIV infections in UK-born patients acquired abroad
97. Norwegian HIV vaccine—Very modest results seen in recent clinical trial
98. France: Untested gay man found criminally liable for two previous partners' HIV acquisition
99. Oslo Declaration
100. Hepatitis C Deaths Up, Baby Boomers Most at Risk
101. Report: Myanmar Desperate for HIV and TB Drugs
102. Instant Infant HIV Diagnosis to Be Rolled Out in Rural Areas
103. Purdue Study Links Abstinence Programs, Academic Success
105. Cholera Epidemic Spreads In DRC, Efforts To Combat Disease Remain Underfunded, U.N. Reports
106. Scientific American Examines Gates Foundation Toilet-Design Initiative
107. Uncovered: Genetic cause of complex disease seen in Irish Traveller community
108. Theory of the 'rotting' Y chromosome dealt a fatal blow
109. In food form, some probiotics have a better chance to promote health
110. New way to tap largest remaining treasure trove of potential new antibiotics
111. How Cancer Cells Change Once They Spread to Distant Organs
112. The scientist who discovered Hepatitis C says he’s now discovered the vaccine
113. Getting Tough on Criminalisation
114. Abstinence and Birth Control in Sex Education Class?
115. Teachers Urged to Address Porn Factor
117. WHO Urging Afghans To Vaccinate Children For Measles Following Outbreak In Western Region
118. Researchers Begin Clinical Trial Of First Visceral Leishmaniasis Vaccine
119. Disarming the botulinum neurotoxin
120. Slamming the brakes on the malaria life cycle
121. Protein scouts for dangerous bacteria
122. Opinion: H5N1 flu is just as dangerous as feared, now requires action
123. New strategies for treatment of infectious diseases
124. Fat accumulation linked to cognitive impairment in patients with HIV
125. HIV Epidemic Feared on Ontario Reserves
126. Two New Analyses Raise Questions About Fatality Rate Of Bird Flu
127. South Sudan’s Army Calls For Concerted Efforts To Fight HIV/AIDS
128. Eradication Of River Blindness In Africa Is Feasible
129. Natural method for clearing cellular debris provides new targets for lupus treatment
130. In the Genes, but Which Ones? Studies That Linked Specific Genes to Intelligence Were Largely Wrong, Experts Say
131. Alzheimer’s, Parkinson’s, Certain Cancers: Correct Protein Folding Illuminated
132. Stronger Intestinal Barrier May Prevent Cancer in the Rest of the Body, New Study Suggests
133. Cell Energy Sensor Mechanism Discovered
134. RNA Chases Its Tail
135. Long Live the Y
136. New Kind of Cellular Suicide
137. Antimicrobial Cross-Resistance Risk
138. Immune Heat
139. C. diff Infection Source Unclear
140. Cellular Workout
141. Forced Feeding
142. Repeal of HPV Immunization Mandate Is Killed
143. Many African Men Fail to Get HIV Treatment
144. HIV Testing, Gay Community Involvement and Internet USE: Social and Behavioral Correlates of HIV Testing Among Australian Men Who Have Sex with Men
146. Florida’s AIDS Drug Program Has the Longest Waiting List in the United States
147. U.N. Helps Kick Off Polio Immunization Campaigns In Angola, Central African Republic
148. Novartis Defends Challenge To Indian Medicines Patent Law
149. IRIN Examines Potential Strategies To Fight Sleeping Sickness In Tanzania’s Rural Communities
150. Do parasites evolve to exploit gender differences in hosts?
151. Scientists discover new ‘off switch’ in immune response
152. Women decrease condom use during freshman year of college, study finds
153. Significant State-By-State Differences in Black, White Life Expectancy
154. Blood Mystery Solved: Two New Blood Types Identified
155. Gay Sex Legal, Says India Government
156. Maurice Tomlinson’s Countdown to Tolerance: The Cultural War Against Homosexuals is Heating Up
157. Mugabe admits losing cabinet to HIV and AIDS
158. New indicator diseases reveal hidden HIV
159. Utah House Passes Bill to Allow Schools to Skip Sex Education
160. Censorship and Dirty Needles Fuel HIV/AIDS Epidemic
161. Do Asian-American Women Who Were Maltreated as Children Have a Higher Likelihood for HIV Risk Behaviors and Adverse Mental Health Outcomes?
162. Exposed Persons Tested in Emory TB Case
The Enigmatic Membrane (long)
Despite years of research, the longstanding mystery of where the autophagosome gets its double lipid bilayers is not much clearer.
By Muriel Mari, Sharon A. Tooze, and Fulvio Reggiori | February 1, 2012

Cells live longer than their internal components. To keep their cytoplasm clear of excess or damaged organelles, as well as invading pathogens, or to feed themselves in time of nutrient deprivation, cells degrade these unwanted or potentially harmful structures, and produce needed food and fuel, using a process they have honed over millions of years. Known as autophagy, this catabolic process involves the selection and the sequestration of the targeted structures into unique transport vesicles called autophagosomes, which then deliver the contents to lysosomes where they are degraded by lytic enzymes. This conserved eukaryotic pathway plays a central role in a multitude of physiological processes, including programmed cell death, development, and differentiation. In addition, it plays a protective role against aging, tumorigenesis, neurodegeneration, and infection. Given all this, it is not surprising that an impairment of autophagy is correlated with various severe pathologies, including cardiovascular and autoimmune diseases, neuro- and myodegenerative disorders, and malignancies.

Despite significant advances over the last 20 years in the understanding of how this process works and what purposes it serves, there is a lingering question—how are autophagosomes formed? More specifically, where do their not one, but two lipid bilayers come from? Autophagosomes are not pre-built organelles that become active upon the induction of autophagy; they are made from scratch each time a cell needs to degrade one or more of its contents. And they are giant vesicles, with an average diameter of approximately 700–800 nanometers, which can further expand to accommodate large structures such as cellular organelles and bacteria, and which are made in large quantities under autophagy-inducing conditions. As a result, progression of autophagy requires a ready supply of lipids. This aspect of the process has intrigued researchers since the discovery of autophagy in the 1950s and '60s. Understanding the biogenesis of autophagosomes will provide information about how cells generate new compartments in response to internal and external cues, and will thus lead to a clearer conception of cell homeostasis.
Intrinsic to the question of the autophagosome's origin is the source of the lipids required to build the double-membrane vesicle and the way this supply is delivered. One major difficulty in addressing this question has been that autophagosomes contain no marker proteins that definitively link them to any known subcellular organelle, making it difficult to unveil their origins. Indeed, autophagosomes are distinct from all other organelles in the cell, both in structure and in protein composition. Recent advances in microscopic techniques and biochemical approaches have stimulated a series of studies investigating this issue, but the results are contradictory, at least at first glance, with different groups identifying evidence for contributions from the cell's plasma membrane, endoplasmic reticulum, mitochondria, and Golgi complex. From which of these organelles is the autophagosome derived, or could it be all of the above? The answer to this question is a prerequisite for understanding and manipulating...
the mechanism of autophagy. In turn, this knowledge is essential to the development of therapies or drugs that target this pathway to treat or even cure diseases in which autophagy is blocked or impaired.

**How autophagy works**

Autophagosome biogenesis and consumption can be divided into five discrete steps: induction, expansion, vesicle completion, fusion, and cargo degradation. The initial event upon induction is the formation of a membranous cistern called the phagophore, or isolation membrane. This compartment appears to be generated from what has been defined in yeast as the phagophore assembly site (PAS) or pre-autophagosomal structure, a putative early autophagosome precursor that is formed by the sequential association of at least a subset of Atg proteins, which are known to be specifically involved in autophagy. The subsequent expansion of the phagophore through the acquisition of additional lipids permits the engulfment of the intracellular material targeted for destruction. The double-membrane vesicle is completed when the inner and outer bilayers fuse to form two distinct membranes, one inside the other. Completed autophagosomes first fuse with endosomal structures to form amphisomes (an event that appears not to occur in yeast), and then with the mammalian lysosome or the yeast and plant vacuole, allowing the degradation of the inner vesicle and its cargo by acid hydrolases residing in these lytic compartments. Lastly, the basic metabolites generated from this catabolic processing of biological macromolecules are transported into the cytoplasm, where they are reused as either a source of energy or as building blocks for new proteins and lipids.

**Mixed membrane messages**

**THE ENDOPLASMIC RETICULUM**

The first organelle proposed as the source of autophagosomal membranes was the endoplasmic reticulum (ER), the compartment responsible for the production of the proteins and lipids that compose the cell. Morphological studies performed in the 1970s already indicated a possible functional link between autophagosomes and the ER, because these two organelles were often seen in close proximity. These observations were subsequently supported by immuno-ultrastructural analyses made by Bill Dunn of the University of Florida in 1990, in which integral membrane proteins of the rough ER were detected in both the inner and outer membranes of the autophagosomes.

More recently, using electron microscope tomography to study the three-dimensional organization of these organelles, two groups have confirmed and emphasized these pioneering observations by revealing the existence of a physical connection between the ER and the forming autophagosomes. In 2009, Mitsuko Hayashi-Nishino and colleagues at Osaka University in Japan performed 3-D reconstruction of cells expressing a mutant gene that causes defects in autophagosome formation, effectively pausing the process at the early stages of autophagosomal membrane formation (i.e., the phagophore stage). This analysis revealed that the ER and the growing phagophore are intimately associated, suggesting that the nascent autophagosome branches off from the ER. In fact, the rough ER was connected through a single point of contact to both the outer and inner membranes of the phagophore, supporting the notion that lipids could be supplied via direct transfer at the sites of membrane contact. It is unclear, however, whether phagophore membrane formation starts at the ER, or whether the membrane simply grows there after the process is initiated elsewhere. Päivi Ylä-Anttila of the University of Helsinki and co-workers obtained similar findings in a different cell type, but they have reported the existence of several points of contact between these two organelles.

Further support for the involvement of the ER in autophagosome formation comes from studying phosphatidylinositol-3-phosphate [PI(3)P], a lipid crucial for autophagosome formation. In 2008, researchers found that PI(3)P is enriched in specific regions of the ER where the autophagosomes have been observed breaking off under autophagy-inducing conditions. The same group also showed that cup-shaped structures they called omegasomes, which may be an autophagosome precursor (probably a phagophore expansion intermediate), emerge from these PI(3)P-rich subdomains. These findings have been corroborated by a new report revealing that Atg14L, a subunit of the complex involved in the synthesis of PI(3)P, is associated with the ER surface. Similarly, DFCP1, a protein mainly localizing to the ER, was found to be associated with both omegasomes and autophagosomal membranes connected to the ER.
Taken together, these data suggest that autophagosomes emerge from the ER. However, 30 percent of the autophagosome precursors observed in the 3-D tomography studies were not associated with the ER, raising the possibility that another membrane source for autophagosomes could exist.¹

**THE MITOCHONDRIUM**

In 2010, Jennifer Lippincott-Schwartz’s group at the National Institutes of Health in Bethesda proposed the outer membrane of the mitochondria as the main source of the autophagosomal lipid bilayers.² Their findings were obtained from extensive light-microscopy analyses of cells expressing fluorescently tagged marker proteins for autophagosomes and proteins localizing to the mitochondrial outer membrane. Under amino acid starvation conditions that initiate autophagy, these two sets of marker proteins were found to co-localize on nascent autophagosomes, suggesting a functional link between mitochondria and autophagosomes. The researchers also observed a potential direct physical connection between these two organelles, with autophagosomes growing in close proximity to mitochondria, leading the authors to propose that the mitochondria supply the forming autophagosomes with newly synthesized phospholipids.²⁻⁵ More recently, however, another group found that *Salmonella*-containing autophagosomal structures were negative for the same mitochondrial marker protein, indicating that mitochondrial lipids may not be involved in the biogenesis of all autophagosomes.⁹

Lippincott-Schwartz’s team also showed that the connection between the mitochondria and the ER is crucial for autophagosome formation. Mitochondria are normally associated with the ER through discrete points of contact that are known as the mitochondrial-associated membranes (MAMs). In the absence of MAMs, phospholipid biosynthesis is impaired, indicating their important role in the lipid exchange between ER and mitochondria. When MAMs are disrupted by knocking down one of the genes involved in their maintenance, starvation-induced autophagosomes are not formed.³ This observation has led to the hypothesis that the ER contribution as a membrane provider for autophagy could be as important as the mitochondrial one. Another possible interpretation, however, is that loss of the connection between the two organelles could lead to an impairment of several functions of the ER, which in turn could affect its contribution to phagophore or autophagosome biogenesis and/or expansion.

**THE PLASMA MEMBRANE**

Yet another possible contributor to the autophagosomal double membrane is the cell’s plasma membrane. In 2010, the laboratory of David Rubinsztein at the University of Cambridge reported that some vesicles forming from the plasma membrane are positive for the autophagosome marker Atg16L1, and fuse with like vesicles to create an early autophagosomal precursor, possibly a phagophore or an omegasome.¹⁰ Additional investigations from the same group have revealed that the maturation of Atg16L1-positive pre-autophagosomal vesicles requires their fusion via the action of a plasma membrane SNARE protein and its interacting partners. The involvement of plasma membrane SNAREs, which mediate vesicle fusion and exocytosis, in the early steps of autophagy has also been highlighted by studies in yeast. Additional support for a plasma membrane role in autophagosome biogenesis comes from the discovery that components of the exocyst—a tethering complex that acts in concert with SNAREs to mediate fusion of Golgi-derived vesicles with the plasma membrane—associate with nascent autophagosomes, and that they are essential for starvation-induced autophagy.
THE GOLGI APPARATUS

The potential involvement of the exocyst in autophagosome formation also raises the possibility of the Golgi apparatus being a potential source for autophagosomal membranes, as the exocyst complex is present in the Golgi as well as in vesicles derived from them. The Golgi is an organelle dedicated to posttranslational protein modifications and sorting. The work on yeast plasma membrane SNAREs has revealed that these proteins regulate the organization of organelles containing Atg9, a transmembrane protein essential for autophagy. In yeast, these organelles, which have been named Atg9 reservoirs, appear to be derived from the Golgi and play a central role in providing the initial membranes necessary to generate the phagophore. Even as early as the 1990s, the Golgi was implicated in autophagosome biogenesis in mammalian cells, as the growing phagophore, as well as complete autophagosomes, could be decorated with proteins that bind to sugar chains exclusively present on post-Golgi membranes. This concept has been recently reinforced by work in yeast, where it has also been shown that two complexes involved in membrane trafficking through the Golgi are essential for autophagy.

A single model?

While researchers have accumulated undoubtedly confusing evidence for the involvement of multiple organelles in the formation of autophagosomes, the resulting hypotheses are not mutually exclusive. Further research is required to sort out which organelles contribute to autophagosome biogenesis in which species under which conditions.

The apparent discrepancy between the conclusions reached by different laboratories on the origin of the autophagosomal membrane could be, in part, due to varying experimental approaches and techniques. More importantly, the different contributions could vary depending on the cell and tissue type and the conditions used to trigger autophagy, with cells deriving the membranes from the most suitable or expendable source. Thus, in a tissue with a defined function, in response to a specific stress stimulus, the growing autophagosome would be supplied with membranes from the most optimal reservoir: an organelle that could guarantee the delivery of a large amount of lipids, but whose depletion ideally would not adversely affect the function of the tissue. From a cursory look at the current available data, one might conclude that fasting animals utilize ER while nitrogen-starved yeast use Golgi, for example. However, accurate comparative studies are needed to determine whether such trends hold true for a wider variety of cell types and stress conditions.

Another possibility that should not be discarded a priori is that autophagosomes could be a mosaic of membranes derived from more than one organelle. For example, the phagophore could originate from one organelle, while additional lipid bilayers required for its expansion are acquired from another source. Having a spectrum of membrane sources to choose from could help ensure the availability of a large supply of lipids to sustain the progression of autophagy. One could imagine that a single intracellular organelle could not provide enough lipids to produce the multitude of autophagosomes generated during prolonged periods of starvation or stress.

Finally, it still remains to be determined whether the different organelles implicated so far in autophagosome biogenesis contribute to nonselective bulk autophagy or to selective forms of autophagy, such as mitophagy (selective degradation of mitochondria), pexophagy (selective degradation of peroxisomes), or reticulophagy (selective degradation of the ER). In this regard, the observation of ER or mitochondria connected to membranes of the phagophore, for example, could suggest that rather than contributing to autophagosome formation, these organelles are actually the object of the degradation process.

Autophagosomal membranes and drug therapies

Experimental evidence indicates that autophagosome biogenesis is probably a very complex process on several levels, including its regulation in response to different cellular and environmental cues, and the factors governing the choice of membrane sources.

Is there any therapeutic value in determining the origin of the autophagosomal membranes? We think that elucidating this process could ultimately provide new drug targets for the treatment of diseases that can be alleviated or cured by the activation of autophagy, including specific muscular dystrophies, persistent infections, and neurodegenerative disorders (ataxias, Huntington’s, and Parkinson’s diseases). Understanding the sources and processes by which the autophagosome’s lipid bilayers are delivered will
undoubtedly reveal critical new proteins and articulate their functions, allowing researchers to pinpoint specific parts of the pathway.

Importantly, autophagy has also been associated with cancer. For example, loss of one of the two copies of Beclin1/Atg6, a gene involved in autophagy, is often found in human breast, ovarian, and prostate cancers. Similarly, alterations of factors regulating the trafficking of the transmembrane protein Atg9 have been found to be a direct cause of tumorigenesis. These observations support the possibility that specific illnesses could be the phenomenological manifestation of a misregulation of lipid bilayer flux during autophagy. As a result, the factors modulating these pathways would be optimal targets for drugs aimed at restoring normal membrane supply and consequently proper progression of autophagy.

Conclusions and future directions
Since the discovery of autophagy, the membrane origin of the autophagosomes has been the subject of intense debate. Recent studies employing advanced technologies have confirmed and extended the pioneering ultrastructural observations and have provided some insights on the membrane origin of these unique vesicles. The diverse conclusions of the recent work, however, have not yet provided an unequivocal answer, but rather have raised new questions that now need to be addressed. The work on this topic has only just begun.

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References
9. J. Huang et al., “Antibacterial autophagy occurs at PI(3)P-enriched domains of the endoplasmic reticulum and requires Rab1 GTPase,” Autophagy, 7:17-26, 2011. e9

comments
☐ keepitlegal

Last paragraph of my prior comment got garbled. Let me try to state it more clearly.

Here's to focusing on research that informs us as to:

- How best to solve coping problems we can do something about; How to avoid blind forensic searching for evidence no longer in existence; and, How to attain the wisdom to know the difference (>:)

keepitlegal

It's refreshing to read open-minded evaluation of evidence so far, in any tributary of research. Instead of beginning with a beautiful model, and gerrymandering evidence to fit that beautiful model (as bio-evo theorists do) the article goes directly to what evidence we have so far, recognizes the questions raised by that evidence, and contemplates what might be pragmatic ways to test and rule out alternative ways what we now know might have come about in hopes we will someday rule out all but one.

This is science at its objective best.

Since we have no time machine, nor enough lifetimes to revisit every increment of Earth’s bio-history even if we had one, we must work forensically, long after incremental change by incremental change has had its inception trudging, as it were, upstream into the evolutionary past. It's as if we must exploring a stream by beginning at its mouth and working back to its source long after some of the tributaries have come and gone and the river of "what happened" has changed its course. Not only must we trace upstream, exploring one tributary after another but, also, we feel driven to guess where former tributaries may have dried up, and where new ones may have formed between then and now.

Probably the very best science can do, under such circumstances, is gain as much evidence as will provide us awareness of how things are now, and with that knowledge find ways to manipulate that in favor of advancing human coping (relieving or preventing as much as we can of pain, suffering, disease...)

If seeking to establish changes that occurred in the dim, distant past will help in the cause of human coping today and into the future, great. Hopefully, however, we aren't spending time fruitlessly trying to reconstruct a bio-evo past that may not be traceable.
Man sues strip club, government after contracting HIV
By Linda Nguyen, Postmedia News January 31, 2012

A man who is suing his ex-wife, Immigration officials, a doctor and a popular Toronto strip club after he contracted HIV will be in Ontario Superior Court Tuesday to hear if he can proceed with his $30 million lawsuit.

TORONTO — A Toronto man who found out nearly eight years ago that his Thai stripper wife had infected him with HIV has no one to blame but himself, the Ontario Superior Court heard Tuesday.

It is not reasonable for Canadian citizens to expect the government to be an "insurance" if they contract a disease after engaging in "risky" unprotected sex with an immigrant, argued Crown lawyer Marina Stefanovic in the Toronto court.

"The federal government and Immigration Canada has no room in people's bedrooms," she told Ontario Justice Carole Brown.

Percy Wilbert Whiteman is suing his ex-wife, Suwalee Iamkhong, the government, an immigration doctor and a popular Toronto strip club for $30 million, claiming negligence on the part of those parties led to his infection.

Whiteman, 36, claims the defendants did not take the necessary steps to find out that Iamkhong was HIV positive.

He also alleges that immigration officials put him at risk by not testing the 42-year-old Iamkhong for the human immunodeficiency virus when she immigrated to Canada in May 1995 on a special four-month work visa.

Stefanovic told the court that Iamkhong, who once worked as a prostitute, had "intentionally and criminally concealed her condition" from Citizenship and Immigration Canada. But even if she didn't, her having the disease did not preclude her eligibility to immigrate to Canada.

Even if they knew her status, officials would still have no "duty of care" obligation to notify Whiteman, said Stefanovic.

Citizenship and Immigration Canada only began mandatory HIV testing of all applicants 15 years and older in 2002.

Whiteman and Iamkhong met at the Zanzibar Tavern in downtown Toronto and were married from 1997 to 2004.

Whiteman only found out about his wife's HIV status when she was admitted to hospital in March 2004 with AIDS-like symptoms. He tested positive for the disease shortly after.

A lawyer for Dr. Martin Taylor, a designated medical practitioner named in the lawsuit, argued that it should be dismissed because it wasn't launched within a two-year limitation period, which started when Whiteman found out he was positive.

Whiteman didn't sue until 2008.

"(This is) a case that is clearly doomed to fail," said Taylor's lawyer, Chris Hubbard.

Furthermore, Taylor could not have been negligent towards Whiteman because they did not have a doctor-patient relationship. The two have never met.

In court documents, Whiteman alleges that the Zanzibar Tavern where his ex-wife was employed should've known about her disease and not have encouraged their sexual relationship.

Iamkhong was deported back to Thailand last year. Her lawyer was not present for the hearing Tuesday.

In August 2007, she was convicted of criminal negligence causing bodily harm for infecting Whiteman and not disclosing her status.

She had first tested positive for HIV in Hong Kong in 1994 after her first husband died of AIDS.

Throughout Tuesday's hearing, Whiteman appeared visibly frustrated.

Outside the courtroom, he said he was trying to deal with the proceedings and that his health is as good as it can be. He has not been in contact with his ex-wife for years.

The hearing continues Wednesday.

Fear-Resistance: How Worried Should We Be about "Totally Drug-Resistant" Tuberculosis?
An Indian clinic's claim of totally untreatedable TB ignited public fears, but experts say poor disease management is the real threat
By Erica Westly | January 30, 2012 | 3
A few weeks ago a clinic in Mumbai claimed to have identified a dozen patients with a strain of tuberculosis (TB) resistant to all known treatments. TB is a highly contagious lung infection that kills about 1.5 million people each year worldwide, according to the World Health Organization (WHO), so the development of a totally untreatable form of the disease would be cause for alarm. "It conveys that there is no hope, that not a single drug works," says Madhukar Pai, a tuberculosis researcher at McGill University in Montreal.

Fortunately, it does not appear that the Mumbai cases are completely untreatable. After evaluating the cases last week, India's Ministry of Health and Family Welfare reported that the patients actually had "extensively drug-resistant" tuberculosis, a form of the disease that is difficult to treat, but not incurable. Although three of the 12 patients have died, the other nine are reportedly being treated with antibiotics used to treat extensively drug-resistant TB, such as clofazimine and rifabutin.

Still, the case has prompted WHO to schedule a meeting in March to discuss the merits of creating a new "totally drug-resistant" category of tuberculosis. Most likely, "extensively drug-resistant," or XDR, will remain the top level of tuberculosis threat. For one thing, current laboratory tests for determining drug-resistant TB are not reliable enough to rule out all TB drugs conclusively, particularly three of the six classes of second-line drugs. "The tests aren't highly reproducible," says Peter Cegielski, head of the U.S. Centers for Disease Control and Prevention's drug-resistant TB program. "You can even get different results from the same patient specimen."

WHO cannot designate a new disease category without clear, quantifiable diagnostic criteria. For example, XDR-TB is defined as tuberculosis that is resistant to the main first-line TB drugs—rifampin and isoniazid—and to two or more of the second-line drugs for which there are reliable susceptibility tests.

There are also new tuberculosis drugs on the horizon, including two that will likely be available to patients in the next few years, making the timing of adding a "totally drug-resistant" TB category impractical.

That doesn't mean, however, that it is impossible for an untreatedable form of TB to exist. "It's reasonable to discuss it," Cegielski says. It also does not mean that public health workers can rest easy. Drug-resistant TB remains a huge problem worldwide. Not only does it take months or, in some cases, years to treat, but once drug-resistant strains develop, they can be passed from person to person.

What the recent Indian case really highlights, rather than the potential for total drug-resistance, is the need for consistent tuberculosis management worldwide, says Carole Mitnick, a public health researcher at Harvard University who specializes in the treatment of drug-resistant TB. "It reflects the lack of equal access to quality care and treatment," she says.

For example, tuberculosis medications are highly restricted in some countries, such as Brazil, but are more freely available in others. In India, where there are about two million new TB cases a year, it is possible to get some TB drugs from pharmacies without a prescription, says McGill's Pai, who is from India and has studied TB treatment there. "A lot of patients won't take the full course [of antibiotics], and then they start a new drug. That's the pattern that leads to drug resistance," he says. A study published in PLoS One last year found excessive private market sales of TB drugs in several countries, including India and Indonesia, implying misuse.

Pediatricians Recommend HPV Vaccine for Boys, Too

Pittsburgh Post-Gazette, (02.01.2012) Sally Kalson
The American Academy of Pediatrics today released a new recommendation calling for pre-teen and adolescent boys to be vaccinated against human papillomavirus, part of AAP's revised standard immunization schedule for youths.
The HPV vaccine already is recommended for girls in the same age range. Giving it to boys will protect them from HPV-linked oral and anal cancers and help prevent further transmission of the STD. AAP’s call follows a similar one made by CDC’s Advisory Committee on Immunization Practices in October.

The three-shot HPV series is given over six months, with costs totaling around $360. Female vaccinations are covered by many private insurers due to inclusion on the routine vaccine schedule. Adding boys to the schedule likely will result in coverage as well.

Because HPV is linked to sexual activity, some critics worry that the vaccine against it could promote promiscuity. However, a CDC study on that issue showed no such effect, said Dr. Michael Brady, chair of AAP’s Committee on Infectious Diseases and chair of pediatrics at Nationwide Children’s Hospital in Columbus, Ohio.

“Given the amount of cancer in both genders, most people recognize the rationale,” said Brady. “Adding males from a cost-perspective was the right thing to do.”

“Boys who grow up to be men who have sex with men are at particular risk for HPV infection,” Brady added. “If you immunize only girls, you wouldn’t improve protection of that population.”


**HIV-Related Deaths Slow Economy**

*Inter Press Service*, (01.27.2012) Kristin Palitza

South Africa should have a population of 55 million citizens in 2012, but the toll of HIV/AIDS makes the figure closer to 50.6 million people, according to a new study by the South African Institute for Race Relations (SAIRR).

The research organization’s analysis used data from the Actuarial Society of South Africa and the South African Institute for Futures Research. It found almost one-third of all deaths in 2011 were AIDS-related. By 2025, the proportion of AIDS deaths is expected to rise 121 percent from the level in 2000, SAIRR said.

“The decrease of population growth has a negative impact on South Africa, because the group most affected by HIV and AIDS is aged between 15 and 49 years, which is the most productive part of the population,” said SAIRR researcher Thuthukani Ndebele. “If this age group continues to die early, we will see an acute social and economic impact throughout the country.”

SAIRR predicts the total number of South Africans living with HIV/AIDS will reach 6 million in 2015—double the number recorded in 2000.

In addition to reduced life expectancy and increased mortality, HIV/AIDS causes broader social ills such as orphanhood and child-headed households. UNICEF figures show that in 2009, 2 million South African children had lost one or both parents to the disease.

SAIRR is especially worried about the burden HIV/AIDS will have on the country’s public health system. In 2009, South Africa spent nearly 9 percent of its GDP on health, according to World Bank data. This percentage could increase in the near future. “Health budgets might have to increase even further, if government wants to prevent HIV/AIDS having an even more negative impact on the economy than it already has,” said Ndebele.

**Acceptability and Feasibility of Rapid HIV Testing in an Adolescent Clinic Setting: Youth Testing Attitudes, Knowledge and Behaviors**

*Journal of Adolescent Health Vol. 49; No. 6: P. 609-614*, (12.2011) Selin Tuysuzoglu, MD, MPH; Heath L. Corliss, MPH, PhD; Susan M. Fitzgerald, MSN, CPNP; Brian R. Abascal, MFA; Cathryn L. Samples, MD, MPH

The researchers undertook the current study to assess attitudes, knowledge, and behaviors regarding rapid HIV testing (RHT) among young people and to measure acceptability and feasibility of this testing in an adolescent clinic setting.

A 2007-08 project introduced free RHT at an urban, hospital-based clinic for adolescents and young adults in Boston. Patients and HIV testing clients were offered either free nonrapid tests or fingerstick RHT. A total of 127 youth completed an anonymous survey to assess their testing attitudes, knowledge, and behaviors. To determine associations with youth demographic characteristics and testing experience, an ordinal logistic regression model was used.
“Most participants valued rapid results. A minority desired confidentiality from parents and insurance providers,” the authors wrote. Older participants were more likely to know about testing methods (odds ratio: 1.25; CI: 1.04-1.51) and to plan for follow-up (OR: 1.43; CI: 1.14-1.81).

“Age, gender, and race were unrelated to testing facilitators such as rapidity, confidentiality, and cost, although younger clients were more likely to prefer noninvasive methods. Individuals with previous testing experience were more likely to say that they would contribute to expenses and value rapidity over cost,” the authors reported. “There was strong support for RHT among youth receiving HIV testing. Offering RHT to youth may facilitate routine testing. Future research should focus on increasing RHT access among diverse populations of youth.”

**Jordan Deports Five HIV-Positive Libyan Patients**
*Agence France Presse*, (01.31.2012)
A health ministry official said Tuesday that Jordan has deported five Libyan patients after learning they were HIV-positive. In the wake of months of fighting that ended the regime of Moamer Kadhafi in October, thousands of Libyans have undergone treatment in hospitals in Jordan and Greece. “The five people have been hospitalized in a private hospital in Amman,” the official said. “On Friday, health authorities found out that they were HIV-positive. They have been deported after a 72-hour quarantine.”

The official said the ministry “will impose more preventive measures to make sure all Libyans coming to Jordan are free of this disease.”

**Islamist Rebel Group Bans ICRC From Southern Areas Of Somalia Under Its Control**
The Islamist rebel group al-Shabab has banned the International Committee of the Red Cross (ICRC) from distributing food in southern areas of Somalia under its control, accusing the organization of delivering out-of-date food, the *Guardian* reports. "The new ban could deal a major blow to aid operations in the dangerous south of the country as the ICRC was one of only a few international agencies still able to operate there after al-Shabab banned 16 other groups last November," the newspaper reports. Famine continues to threaten 250,000 people in the region, according to the Guardian (Chonghaile, 1/31).

**Poor Quality Vaccination Campaigns, Lack Of Government Commitment Helping Polio Spread In Chad**
"Poor-quality emergency immunization campaigns and low routine polio immunization coverage are helping the polio virus to spread in Chad, with 132 cases reported in 2011—five times the number in 2010," IRIN reports. "More commitment is needed across the board, especially from local health authorities, to try to get immunizations right, say aid agencies," the news service adds.

"While a dysfunctional health system is linked to poor routine immunization coverage, 'the primary reason [for the upsurge] is operational,' said Oliver Rosenbauer, spokesperson for the Global Polio Eradication Initiative at WHO in Geneva," according to IRIN. The news service discusses reasons why some children are missed during vaccination campaigns, highlights the need for local-level government commitment and writes, "To ensure fewer children are missed, immunizers need to make better use of 'social data' to find out why and where a campaign is not working, says" Irina Dincu, WHO and UNICEF’s West Africa communication for development specialist (1/31).

**South African Government Officials Recall Defective Condoms**
Government health officials in Free State, South Africa, have recalled a lot of 8,700 boxes of condoms that were distributed free of charge at guesthouses, hotels, restaurants, and bars to celebrate the centenary of the African National Congress, *BBC News* reports (1/30). "The Free State Health Department says it is recalling the estimated 1.35 million condoms as a 'precautionary measure'—and urged the public not to panic," the BBC notes, adding, "They say they are still investigating claims that the condoms are porous."

"But the Treatment Action Campaign said no warning has been issued to people that they may have carried away defective condoms that could now cause them to unsuspectingly spread or contract HIV," the *Associated Press/Seattle Times* writes. The condom recall, the third recall in five years, "raises questions about the quality of some of the 425 million-plus condoms that the government gives away each year," according to the AP (Faul, 1/31).
Men who have sex with men may now be the highest-risk group for HIV in Africa, IAVI study suggests
Gus Cairns
Published: 01 February 2012

Men who have sex with men may now be at considerably higher risk of acquiring HIV than other at-risk groups such as female sex workers or young people of either sex, if findings by the International AIDS Vaccine Initiative (IAVI) of HIV incidence at two centres in Kenya can be generalised to other populations.

The study, which compared the Kenyan populations with a largely heterosexual group from South Africa, also found lower-than-expected HIV incidence amongst female sex workers and their clients. The researchers also found that recruiting MSM into the study was easier than expected, but note that there was a particularly high dropout rate in MSM.

They comment that while MSM “need urgent risk reduction interventions, and may be a suitable cohort for future HIV prevention studies,” because African MSM face considerably legal and social hurdles in coming forward, “careful consideration of the counselling and clinical needs, follow-up schedule and social support is vital to ensure continuing research participation.”

The study

The aim of the study was to collect data on HIV and STI incidence and risk factors in three populations in Kilifi, a district north of Mombasa, and the Kangemi district of Nairobi, both in Kenya, and from Gugulethu township in Cape Town in South Africa, the better to target HIV vaccine trials.

The researchers recruited 716 people in Mombasa, 653 in Nairobi and 465 in Cape Town. The researchers primarily used participants to recruit their peers in South Africa, where background HIV prevalence at 28% is ten times higher than in Kenya, but in Kenya recruited attendees at HIV testing centres, via outreach work in bars and brothels, and via ‘snowball’ sampling (asking members of a particular group to recruit others from the same group). The original idea had been to collect data on high-risk heterosexuals including sex workers but, as the researchers comment, “it quickly became apparent that MSM were willing to come forward and participate in HIV prevention research”.

Somewhat different monitoring and follow-up criteria were used in the three centres. In Cape Town participants were monitored monthly and followed up for one year while in the two Kenyan cohorts participants were monitored quarterly for two to four years. In Mombasa participants were examined for STIs at every visit but in Nairobi and Cape Town only examined if they had symptoms. As a result annual STI incidence was much higher in Mombasa (23%) than in the other two centres (3.7% and 4.4%).

The average age of participants was mid-20s (slightly older in Nairobi); nearly 70% were women in Cape Town, 50% in Nairobi and 36% in Mombasa. Participants in Capt Town were almost entirely heterosexual men and women and were not sex workers.

In Mombasa 56% of men (36% of the study population) was an MSM; 63% of men said they had sold sex (mainly to other men) and 54% had bought it. Three-quarters of female participants said they were female sex workers while one in 20 women said they had bought sex.

In Nairobi nearly all women defined as a sex worker and 85% of the men had bought sex; 22.5% of the men had had sex with other men and 33% defined as a male sex worker.

There was a high dropout rate in the study: 13% did not return after their enrolment visit, 37% altogether left the study prematurely. Annual attrition rates were 22% in Cape Town, 20% in Mombasa and 10% in Nairobi.

The results

HIV incidence was high in MSM in the Kenyan centres; annual incidence in MSM was 9.7% in Nairobi and 6.1% in Mombasa (there were only three individuals who said they were MSM in Capt Town, and none contracted HIV).

Annual HIV incidence in women was 3% in Cape Town, 2.7% in female sex workers and 2.3% in non-sex-workers in Mombasa, and only 0.4%—much lower than expected— in Nairobi. Annual HIV incidence in non-MSM men was 0.9% in Mombasa and zero in the other two centres.

In a multivariate analysis predictors of HIV infection included:

- No secondary education versus some: Hazard Ratio (HR): 3.34
- Genital ulcers, yes versus no: HR 4.48
- Paid for sex versus not: HR 0.17
- Receptive-only anal sex versus no anal sex (in men and women): HR 8.19
- Receptive and insertive anal sex versus none: HR 3.55
- Insertive-only anal sex versus none: HR 0.88 (non-significant)

Thus while receptive anal sex was very strongly associated with HIV infection, insertive anal sex was not. The finding that people who paid for sex were more than five times less likely to acquire HIV than people who did not was described as ‘unexpected’; the researchers suggest that people having paid-for sex may be more wary of HIV and STIs and more likely to use condoms.

The fact that HIV incidence in female sex workers was far lower than expected, especially in Nairobi, is likely due to decreasing background HIV prevalence and possibly more use of antiretrovirals. Higher condom use is a less likely explanation, because annual pregnancy rates remained high: the annual pregnancy rate was 18% in women in Nairobi, 14% in Cape Town and 11% in Mombasa.

This is some of the first data on HIV incidence in MSM in Africa, a continent where, as the researchers say, “the focus of prevention trials in adult Africans has largely been on heterosexual transmission.” They add that a recent UNAIDS report highlights the deficiencies in addressing the needs of MSM and comment that it “reinforces the importance of closing this gap from both a human rights and public health perspective.”

Reference

India Has Worst Child Mortality Gender Differential Worldwide, New U.N. Data Show
An Indian girl between the ages of one and five years old is 75 percent more likely to die than an Indian boy, giving the country the worst gender differential in child mortality in the world, according to new data released by the U.N. Department of Economic and Social Affairs, the Times of India reports. The "data for 150 countries over 40 years show that India and China are the only two countries in the world where female infant mortality is higher than male infant mortality in the 2000s," the newspaper writes (Shrinivasan, 2/1). In India, for every 100 deaths among females one to five years old, 56 males of the same age group die, whereas the global average is 111 male child deaths to every 100 female children, India Today notes. "Higher mortality among girls is a powerful warning that differential treatment or access to resources is putting girls at a disadvantage," the report said, according to the news service (2/1).

Mexico Sees Spike In Swine Flu After Two Years Of Low Transmission
"There have been 1,623 cases of all strains of flu in Mexico recorded so far for January, 90 percent of them H1N1 [swine flu]," compared to "about 1,000 flu cases in Mexico during all of last year," of which roughly 250 cases were swine flu, Health Secretary Salomon Chertorivski Woldenberg told reporters on Tuesday, the Associated Press reports. The news service notes, "Despite the spike, the number of cases is well within a normal flu season for Mexico, which can see from 5,000 to 11,000 incidents of all strains," Woldenberg said. "The low appearance of the H1N1 virus the past two years is one reason it's drawing so much media attention in Mexico," the AP writes, adding, "Public nervousness about H1N1 has been high since the first outbreak in spring 2009, when the virus initially appeared to have a high mortality rate and Mexican authorities closed restaurants, schools, museums, libraries, and theaters to stop its spread" (2/1).

Malaria kills nearly twice as many people than previously thought, but deaths declining rapidly
Despite assumptions that mainly young children die from the disease, 42 percent of 1.2 million deaths occur in older children and adults; anti-malaria drugs and insecticide-treated bed nets are driving mortality down
SEATTLE – Malaria is killing more people worldwide than previously thought, but the number of deaths has fallen rapidly as efforts to combat the disease have ramped up, according to new research from the Institute for Health Metrics and Evaluation at the University of Washington.

More than 1.2 million people died from malaria worldwide in 2010, nearly twice the number found in the most recent comprehensive study of the disease. IHME researchers say that deaths from malaria have been missed by previous studies because of the assumption that the disease mainly kills children under 5. IHME found that more than 78,000 children aged 5 to 14, and more than 445,000 people ages 15 and older died from malaria in 2010, meaning that 42% of all malaria deaths were in people aged 5 and older.

"You learn in medical school that people exposed to malaria as children develop immunity and rarely die from malaria as adults," said Dr. Christopher Murray, IHME Director and the study's lead author.
"What we have found in hospital records, death records, surveys and other sources shows that just is not the case."

The study also found that while the overall number of malaria deaths is higher than earlier reports, the trend in malaria deaths has followed a similar downward pattern. Starting in 1985, malaria deaths grew every year before peaking in 2004 at 1.8 million deaths worldwide. Since then, the number of deaths has fallen annually and, between 2007 and 2010, the decline in deaths has been more than 7% each year.

The new findings are being published today in The Lancet in "Global malaria mortality between 1980 and 2010: a systematic analysis." The work is part of an ongoing series being generated by the Global Burden of Diseases, Injuries, and Risk Factors 2010 Study. Global trends in child mortality, maternal mortality, breast cancer, and cervical cancer were released last year, and more trends will be released in the coming months.

Researchers say the biggest drivers of the decline in malaria deaths have been the scaleup of insecticide-treated bed nets and artemisinin-combination treatments (ACTs). This has been accomplished through the advent of the Global Fund to Fight AIDS, Malaria & Tuberculosis in 2001 and the creation of organizations focused on fighting malaria, such as the World Health Organization's Roll Back Malaria, Malaria No More and Nothing But Nets. Overall funding for malaria efforts grew from less than $0.25 billion annually in 2001 to more than $2 billion in 2009, according to IHME's latest estimates. IHME reported in September 2011 that homes owning at least one bed net were associated with a 23% reduction in child mortality.

"We have seen a huge increase in both funding and in policy attention given to malaria over the past decade, and it's having a real impact," said Dr. Alan Lopez, Head of the School of Population Health at the University of Queensland and one of the study's co-authors. "Reliably demonstrating just how big an impact is important to drive further investments in malaria control programs. This makes it even more critical for us to generate accurate estimates for all deaths, not just in young children and not just in sub-Saharan Africa."

One of the most important factors in identifying the new malaria estimates was the use of verbal autopsy data. In a verbal autopsy, researchers interview the relatives of someone who has recently died to identify the cause of death. IHME and collaborators around the world published a series of articles in a special edition of Population Health Metrics in August 2011 focused on advancing the science of verbal autopsy. Verbal autopsy data were especially important in India, where malaria deaths have been vastly undercounted in both children and adults. IHME found that more than 37,000 people over the age of 15 in India died from malaria in 2010, and the chances of someone dying from malaria in India have fallen rapidly since 1980.

Progress in fighting malaria can be seen everywhere. Countries such as Zambia and Tanzania have seen malaria deaths fall by more than 30% between 2004 and 2010. The progress being seen in Africa is especially significant, given that malaria deaths there accounted for a quarter of all deaths in children under 5 in 2010.

But the researchers warn that those gains could be reversed if global economic troubles continue to stifle funding efforts. IHME reported in December that growth in development assistance for health had slowed greatly between 2009 and 2011. The announcement by the Global Fund in November that it would cancel its next round of funding casts a cloud over the future of malaria programs, the researchers say.

"If the Global Fund is weakened, the world could lose 40% of all the funding dedicated to fighting malaria," said Stephen Lim, Associate Professor of Global Health at IHME and a co-author on the study. "That kind of loss of funding poses a definite threat to the health of people in countries with a high malaria burden, which in many cases are some of the poorest countries in the world. We need to think of ways to fill funding deficits in order to insure continued progress on malaria mortality."

Sexually transmitted infections double in older population in 10 years

Student BMJ editorial: Sexual health and the older adult

Sexually active adults aged 45 and over are being encouraged to pay more thought to safe sex in line with recent figures showing that STIs in 50-90 year olds have doubled in the past ten years.

In an editorial published in the Student BMJ, Rachel von Simson, medical student at King’s College London and Ranjababu Kulasegaram, consultant genitourinary physician at St Thomas' Hospital London, discuss research showing that 80% of 50-90 years olds are sexually active.

Statistics show an increase in cases of syphilis, chlamydia and gonorrhoea in the UK, USA and Canada in 45-64 year olds. There has also been an increase in cases of HIV with those aged 50 and over
accounting for 20% of adults accessing HIV care, an 82% increase on figures from 2001. This may however be down to HIV patients living longer, but new diagnoses of HIV in the over 50s have doubled between 2000 and 2009.

There has been little research on the reason behind the increase but it is thought that due to physical changes, older, post-menopausal women are more vulnerable to STIs. Furthermore, men on erectile dysfunction drugs are significantly more likely to be diagnosed with an STI within the first year of usage and in the year before starting the drug.

The authors suggest that GPs should take the opportunity to discuss safe sex with men seeking erectile dysfunction drugs as they have a high risk of contracting an STI. Telephone motivational interviewing has also been found to discourage involvement in unprotected sex.

The authors report that the UK is currently lacking in STI research in older adults and more needs to be done, but conclude that "doctors should maintain a low threshold for investigating sexually transmitted infections in older adults" and should encourage discussions regardless of the patient's age.

**Human immune cells react sensitively to "stress"**

*Scientists at the University Medical Center in Mainz prove multiple DNA repair defect in monocytes*

02.02.2012

Scientists working with Professor Bernd Kaina of the Institute of Toxicology at the Medical Center of Johannes Gutenberg University Mainz have demonstrated for the first time that certain cells circulating in human blood—so-called monocytes—are extremely sensitive to reactive oxygen species (ROS). They were also able to clarify the reason for this: ROS are aggressive forms of oxygen that are generated during states of "oxidative stress" and play a significant role in various diseases. However, ROS are also naturally produced by cells of the immune system, in particular by macrophages, in response to exposure to pathogens. Macrophages are, similar to dendritic cells, generated by monocytes, which happens when monocytes leave the blood stream and enter the tissue. The scientists show that both macrophages and dendritic cells are resistant to ROS, as opposed to their precursor cells, the monocytes. The Mainz team attributes this hypersensitivity of monocytes to multiple defects in DNA repair that are apparent in these cells. They assume that a sophisticated mechanism for regulating the immune response and preventing excessive ROS production is behind this phenomenon, which was observed for the very first time. Their work has been published in the leading scientific journal *Proceedings of the National Academy of Sciences*.

It is generally known that one of the undesirable effects of ionizing radiation and drugs used to treat cancer is an impairment of the immune system, which ceases to function properly. However, it is still unclear which immune system cells respond most sensitively following radio- and chemotherapy, and which cells are resistant. "This is the question we addressed in our current research project," explains Professor Dr. Bernd Kaina, Director of the Institute of Toxicology at the University Medical Center in Mainz. "We were able to demonstrate that human monocytes are hypersensitive to reactive oxygen species (ROS), while macrophages and dendritic cells derived from monocytes by cytokine maturation are resistant." The scientists observed this extreme sensitivity of monocytes after exposure to radiation, chemicals, and even oxidized low-density lipoprotein (oxLDL), which plays a role in atherosclerosis. All of the above resulted in the formation of intracellular ROS, which damages the DNA and leads to cell death or even malignant transformation. Specific immune system cells, particularly the macrophages, produce ROS in response to an invasion of the body by pathogens. Ideally, production of ROS should cease once the pathogens have been eliminated. There also need to be limitations on the quantity of ROS produced, as these can damage healthy cells in inflamed tissue as well. In fact, chronic infections, in which ROS are continuously being produced, are frequently linked to an increased susceptibility to cancer.

Why do monocytes react so sensitively to ROS? Kaina's team has successfully determined the cause of the hypersensitivity of monocytes to oxidative stress: The monocytes were unable to repair DNA following ROS-induced damage to their genetic substance. This is because these cells produce very low levels of certain important repair proteins called XRCC1, ligase III, PARP-1, and DNA-PK in medical jargon. "Monocytes are in fact defective as far as two important DNA repair systems are concerned, i.e. base excision repair and DNA double-strand break repair," explains Kaina. "Thus far, a general repair defect of this nature has been observed neither in the cells of the human body nor in experimental in vitro systems."
Professor Kaina assumes that the repair defect in monocytes plays an important role in the regulation of the immune response: To prevent excessive production of ROS by macrophages in the inflamed tissue and an overactivation of the immune response, monocytes, as precursor cells of the ROS-producing macrophages, undergo increased and selective destruction due to their extreme sensitivity to ROS. In turn, fewer monocytes mean fewer macrophages and consequently lower levels of ROS—all in all a sophisticated way of regulating the monocyte/macrophage/dendritic cell system. It is clear that this has potential clinical implications: In the case of chronic inflammatory diseases in particular, the body is in a state of imbalance and excessive amounts of ROS are produced, which results in damage to the genetic substance of the healthy cells and is a contributing factor to the onset of cancer. It is possible that this vicious circle could be interrupted by the selective elimination of monocytes in the inflamed tissue.

**Chaos in the Cell’s Command Center**

ScienceDaily (Feb. 1, 2012) — A defective operating system is never a good thing. Like computers, our cells depend on operating systems to drive normal functions. Gene expression programs comprise the software code our cells rely on, with each cell type controlled by its own program. Corrupted programs can trigger disease.

Cellular operating systems can be corrupted by viruses, mutations, or malfunctions that occur as cells change from one type to another. Unlike computers that can use one operating system for their entire existence, differentiating cells need to switch operating systems as they mature—from stem cell to, for example, nerve or muscle cell. In simple terms, differentiation requires two key steps: the genes active in the initial operating system must be deactivated; and the genes of the new cellular operating system must be turned on. If the switch is not flawless, a transitioning cell may die or be driven by a disease-causing program.

New research from Whitehead Institute scientists reveals the critical role one enzyme, lysine-specific demethylase 1 (LSD1), plays as embryonic stem cells differentiate into other cell types. Their research is published online this week in the journal *Nature*.

LSD1 was known to be critical to development, but little was known about the key role it plays during differentiation, when operating systems are switched.

"We knew that cells express a new set of genes when the operating switch occurs," says Steve Bilodeau, one of the Nature paper’s authors and a postdoctoral researcher in the lab of Whitehead Member Richard Young. "But this study shows it is also essential to shut off genes that were active in the prior cell state. If you don’t, the new cell is corrupted."

By investigating gene silencing during cell state transitions, Bilodeau and Warren Whyte, a Young lab graduate student and co-author of the Nature paper, redefined LSD1’s role and described a previously unknown mechanism for silencing genes.

When they looked at the embryonic stem cell operating system genes that must be turned off during differentiation, Whyte and Bilodeau found LSD1 poised on the stem cell genes’ enhancers, short bits of DNA that act as a landing pad for the proteins that enhance a gene’s transcription and ultimately its protein production. When LSD1 receives the signal that the stem cell is transitioning into a more differentiated state, the enzyme pops into action and silences the ESC genes’ enhancers. With their enhancers no longer operational, transcription of the stem cell genes is silenced, shutting down the stem cell operating system. As this occurs, other mechanisms switch on the cell’s new operating system.

"This reveals the critical function of LSD1 in cell differentiation," says Whyte. "The enzyme decommissions the stem cell enhancers, thus allowing the new cell to function entirely within the parameters of the new operating system."

Although the work focuses on one enzyme’s job in normal cells, Young sees broader implications. LSD1 is a member of a class of molecules that regulate both gene activity and chromosome structure, so the findings about LSD1 could give insight into how related regulators function. Also, knowing how a mechanism operates in normal cells provides a solid foundation for teasing apart what is going wrong in abnormal cells.

"This new knowledge brings us one important step closer to understanding defective operating systems in diseases such as cancer," says Young. "And this may give us a new angle on drug development for these diseases."

**Journal Reference:**

Coming Soon: Over-the-Counter Oral AIDS Test

*Crain’s New York Business*, (02.01.2012) Gale Scott

In January, Bethlehem, Pa.-based OraSure Technologies submitted a final module of clinical test results supporting its application to sell the OraQuick rapid HIV test to the public. Food and Drug Administration approval could come this year. The test uses oral fluid or blood; it currently is used widely in clinical settings.

To assess issues regarding at-home rapid HIV testing, Columbia University researchers conducted a study in which they offered the OraQuick test in an office setting to men who have sex with men, then interviewed them about their attitudes toward it. More than 80 percent said they would use the kit to test themselves or their sexual partners, according to Alex Carballo-Díéguez, Timothy Frasca, and colleagues at the HIV Center for Clinical and Behavioral Studies at the New York State Psychiatric Institute.

In general, however, there was little agreement about how to raise the subject with a partner or how to handle an unexpected positive result. Some men talked about making the test a condition of forgoing condom use; others said the test might be a signal that a relationship had advanced beyond casual status.

Opponents of at-home testing worry about how users would react if the test is positive. “There’s a lot of potential opposition, and clinics might not be crazy about direct access in a private setting with no personnel with them if they get a positive result,” Carballo-Díéguez said. The study’s participants gave different reactions to this scenario: Some said they would offer sympathy; a minority said they would leave at once.

In a follow-up study to the paper they published this week in the *Journal of Sex Research*, the authors are distributing rapid test kits for use at home and asking testers to report on their experiences.

Global Malaria Deaths Twice As High As Previously Estimated, IHME Study Suggests

"Malaria is killing more people worldwide than previously thought, but the number of deaths has fallen rapidly as efforts to combat the disease have ramped up, according to new research from the Institute for Health Metrics and Evaluation (IHME) at the University of Washington" published in the *Lancet* on Thursday, an IHME press release reports. "More than 1.2 million people died from malaria worldwide in 2010, nearly twice the number found in the most recent comprehensive study of the disease," the press release states (2/2). The study, funded by the Bill & Melinda Gates Foundation, "used new data and new computer modeling to build a historical database for malaria between 1980 and 2010," BBC News notes (Bowdler, 2/2).

"IHME researchers say that deaths from malaria have been missed by previous studies because of the assumption that the disease mainly kills children under five," the press release states, and notes that the researchers found "more than 78,000 children aged five to 14, and more than 445,000 people ages 15 and older died from malaria in 2010, meaning that 42 percent of all malaria deaths were in people aged five and older" (2/2). A *Lancet* editorial accompanies the study. "We believe urgent technical and policy analyses must be initiated by WHO ... to review these new data and their implications for malaria control programs. This opportunity needs to be grasped with urgency and optimism," the editorial states (2/4). Additional coverage of the study is available from ABC News, BBC News, GlobalPost, the Globe and Mail, the Guardian, the Guardian’s "DataBlog," KLPU 88.5’s "Humanosphere," the Los Angeles Times’ "World Now," NPR’s "Shots," and the Washington Post.

New procedure repairs severed nerves in minutes, restoring limb use in days or weeks

**Team apply new procedure to rapidly induce nerve regeneration in mammals**

American scientists believe a new procedure to repair severed nerves could result in patients recovering in days or weeks, rather than months or years. The team used a cellular mechanism similar to that used by many invertebrates to repair damage to nerve axons. Their results are published today in the *Journal of Neuroscience Research*.

"We have developed a procedure which can repair severed nerves within minutes so that the behavior they control can be partially restored within days and often largely restored within two to four weeks," said Professor George Bittner from the University of Texas. "If further developed in clinical trials this approach would be a great advance on current procedures that usually imperfectly restore lost function within months at best."
The team studied the mechanisms all animal cells use to repair damage to their membranes and focused on invertebrates, which have a superior ability to regenerate nerve axons compared to mammals. An axon is a long extension arising from a nerve cell body that communicates with other nerve cells or with muscles.

This research success arises from Bittner’s discovery that nerve axons of invertebrates which have been severed from their cell body do not degenerate within days, as happens with mammals, but can survive for months, or even years.

The severed proximal nerve axon in invertebrates can also reconnect with its surviving distal nerve axon to produce much quicker and much better restoration of behaviour than occurs in mammals.

"Severed invertebrate nerve axons can reconnect proximal and distal ends of severed nerve axons within seven days, allowing a rate of behavioural recovery that is far superior to mammals," said Bittner.

"In mammals the severed distal axonal stump degenerates within three days and it can take nerve growths from proximal axonal stumps months or years to regenerate and restore use of muscles or sensory areas, often with less accuracy and with much less function being restored."

The team described their success in applying this process to rats in two research papers published today. The team were able to repair severed sciatic nerves in the upper thigh, with results showing the rats were able to use their limb within a week and had much function restored within 2 to 4 weeks, in some cases to almost full function.

"We used rats as an experimental model to demonstrate how severed nerve axons can be repaired. Without our procedure, the return of nearly full function rarely comes close to happening," said Bittner.

"The sciatic nerve controls all muscle movement of the leg of all mammals and this new approach to repairing nerve axons could almost-certainly be just as successful in humans."

To explore the long term implications and medical uses of this procedure, MD's and other scientist-collaborators at Harvard Medical School and Vanderbilt Medical School and Hospitals are conducting studies to obtain approval to begin clinical trials.

"We believe this procedure could produce a transformational change in the way nerve injuries are repaired," concluded Bittner.

Komen Reverses Move to Cut Planned Parenthood Funding

 Reuters, (02.03.2012) David Morgan; Anna Yukhananov
The Susan G. Komen for the Cure foundation released a statement Friday reversing its earlier decision to cut funding to Planned Parenthood as part of new rules tightening grant eligibility.

The foundation, the world's largest breast cancer charity, announced earlier in the week it would cease funding breast cancer screening grants to Planned Parenthood, which provides a variety of services including STD testing, cancer screenings, reproductive care, sex education, and abortion. Komen said its revised eligibility guidelines exclude groups under investigation by authorities, and Planned Parenthood is the subject of a probe by US Rep. Cliff Stearns (R-Fla.), who opposes abortion.

Local Komen chapters and many foundation supporters denounced the decision, and a social media protest campaign was in full swing by Thursday. That night, the Komen board convened for a special meeting on the issue.

“We want to apologize to the American public for recent decisions that cast doubt upon our commitment to our mission of saving women’s lives,” said a statement from the foundation’s board of directors and founder Nancy Brinker.

New funding criteria will be amended to “ensure that politics has no place in our grant process.” The guidelines will make clear that an organization under investigation only will be disqualified if the probe is “criminal and conclusive in nature and not political.”

Do People with HIV Have to Tell Their Sex Partners? Supreme Court to Decide

Canadian Press, (02.05.2012) Chinta Puxley
Canada’s Supreme Court on Wednesday will hear two cases regarding whether it is a crime for people with HIV to not tell their sexual partners about the infection when the risk of transmission is low. A 1998 ruling on the issue has been interpreted differently by judges across Canada.

In the first case, the Manitoba Court of Appeal overturned four convictions tied to one man’s failure to disclose his infection to sex partners. The court noted that some sex partners lacked exposure to “significant risk.” The man was on antiretroviral therapy and used condoms in some encounters, and none of his partners tested HIV-positive, the court said.
Nevertheless, each uninfected sex partner was exposed to the chance of infection, the province is arguing before the Supreme Court. "It does not matter that the chance of this occurring is small, the law aims to stop people from taking that chance," the province said. "The choice whether to assume this risk must ... lie with the person assuming the risk, not the person imposing it," it added.

Prosecutors are making similar arguments for the second case, which was overturned by Quebec's Court of Appeal on grounds that the odds of HIV transmission at the time were low. A sweeping responsibility for disclosure would unfairly strip those infected of their right to privacy, say lawyers for the two defendants with HIV. In addition, it could discourage people from testing and seeking treatment, endangering those with HIV as well as the public. Condom use and low viral loads should factor into the law, which should reflect more clearly what constitutes "significant risk," they argue. "We submit that only the actual intentional transmission of the virus should be criminalized, as in most of the Commonwealth countries," they say.

**Uganda Launches Plan to Eliminate Mother-to-Child Transmission of HIV/AIDS by 2015**

*Xinhua News Agency*, (02.01.2012)  Samuel Okiro; Yuan Qing

Uganda has launched a new HIV/AIDS prevention strategy for the elimination of mother-to-child transmission of HIV by 2015, a senior ministry of health official said Wednesday. Objectives include adopting of a more cost-effective treatment regimen, improving health infrastructure, and increasing women’s access to family planning.

Uganda’s HIV prevalence among pregnant women is 6.5 percent, which amounts to 90,000 HIV-positive pregnant women annually, said Zainab Akol, program manager at the AIDS Control Program. About 25,000 babies are infected each year. “We in the ACP and our partners are fully determined to eliminate mother-to-child transmission of HIV in the next five years,” Akol said.

Uganda began offering ARVs to prevent mother-to-child HIV infections in 2000, and it introduced a combination regimen to the program in 2006. However, delivery of the drugs has not been consistent—a problem the new plan aims to address.

Of the nearly 1.2 million people who have HIV in Uganda, more than 200,000 were infected perinatally; the majority are women; and 10 percent are children under age 15, Akol said. As part of its prevention strategy, Uganda’s AIDS information center will implement a circumcision campaign targeting males ages 15-59.

**Incidence of Sexually Transmitted Infections Among Hazardously Drinking Women After Incarceration**

*Women's Health Issues Vol. 22; No. 1: P. e1-e7*, (01.02.2012)  Michael D. Stein; Celeste M. Caviness; Bradley J. Anderson

“At the time of incarceration, women have a high prevalence of sexually transmitted infections (STI),” wrote the authors, who noted that women remain at high risk for new infections in the months following community release. In the current report, the team assessed the rates and predictors of incident chlamydia, gonorrhea, and trichomoniasis after incarceration in a sample of hazardously drinking women.

The study involved a total of 245 incarcerated women; the participants self-reported behavioral data. At baseline and three- and six-month time points, vaginal swabs were collected and tested for chlamydia, gonorrhea, and trichomoniasis. Treatment was provided in response to all positive tests.

The participants comprised 175 Caucasians (71.4 percent), 47 African Americans (19.2 percent), 17 Hispanics (6.9 percent) and six women of other ethnic origins (2.4 percent). The researchers estimated the STI incidence rate to be 30.5 new infections per 100 person-years (95 percent confidence interval, 21.3-43.5). “Number of male sex partners reported during follow-up was a significant (z=2.16; p=.03) predictor of STI; each additional male sex partner increased the estimated hazard of STI by 1.26,” according to the results.

“Incarcerated women who are hazardous drinkers are at high risk for STI in the months after their return to the community. In addition to testing and treatment during incarceration, post-release rescreening, education, partner treatment, and follow-up are recommended,” the authors concluded.
Panel Discussion Shows Heated Controversy Over H5N1 Research

"The controversy over research about potentially dangerous H5N1 viruses heated up [Thursday night] in a New York City debate that featured some of the leading voices exchanging blunt comments on the alleged risks and benefits of publishing or withholding the full details of the studies," CIDRAP News reports. "The debate, sponsored by the New York Academy of Sciences, involved two members of the biosecurity advisory board that called for 'redacting' the two studies in question to delete details, along with scientists who want the full studies published and representatives of Science and Nature, the two journals involved," the news service adds (Roos, 2/3).

"The panel discussion, which seemed tense from the start, threatened to turn into a shouting match midway through the evening when one panelist lobbed a verbal attack at another," Scientific American's "Observations" blog writes. The blog highlights a number of comments made during the debate and references several papers that have been published on the issue (Gorman, 2/3).

WHO Disputes Study's Claims That Global Malaria Deaths Are Double Current Estimates

The WHO has disputed a study published last week in the Lancet "that claims nearly twice as many people are dying of malaria than current estimates," VOA News reports. The WHO "says both its estimates of malaria deaths and those of the Lancet study are statistically the same for all groups in all regions," with one exception, VOA writes, noting, "WHO spokesman Gregory Hartl says there's a notable statistical difference in regard to children over five and adults in Africa."

According to VOA, "He says the two groups used different methodologies and different sources of data in arriving at their conclusions," and "says it is important to look more carefully at the sources and the quality of data before arriving at conclusions." Hartl "says the emphasis of malaria work in the future will aim to improve diagnostic testing, surveillance and vital statistic registration," the news service writes, adding, "Despite these disputed claims, Hart says both the WHO and Lancet study agree that global death rates from malaria are falling due to better treatment, prevention and control measures" (Schlein, 2/3).

U.N. Supporting Yellow Fever Vaccination Campaigns In Cameroon, Ghana

Following an outbreak of the mosquito-borne yellow fever virus in Cameroon that has infected at least 23 people and killed at least seven people, U.N. and local officials are working to vaccinate "1.2 million people considered at high risk of contracting yellow fever, which has no cure," the U.N. News Centre reports. "The U.N. Central Emergency Response Fund (CERF), the International Coordinating Group on Yellow Fever Provision (YF-ICG)—which includes WHO and the U.N. Children's Fund (UNICEF)—and the public-private partnership known as the GAVI Alliance are funding the vaccination campaign," the news service writes. In Ghana, YF-ICG is working with the European Community Humanitarian Office (ECHO) to plan a vaccination campaign after at least three cases of yellow fever have been reported in the north of the country, the U.N. News Centre notes (2/3).

Dispute Over Malaria Figures Highlights Lack Of Certainty In Data In Age Of 'Information Overload'

In this post in TIME World's "Global Spin" blog, TIME's Africa bureau chief Alex Perry examines questions surrounding an Institute for Health Metrics and Evaluation (IHME) study published in the Lancet on Friday that suggests "malaria kills almost twice as many people a year as previously believed," writing, "If correct, at a stroke that overturns medical consensus, makes a nonsense of decades of World Health Organization (WHO) statistics—the official malaria numbers—and plunges the current multibillion-dollars anti-malaria campaign, and the push to reach a 2015 deadline for achieving the eight Millennium Development Goals, into grave doubt."

Perry notes, "WHO disputed the new figures, saying IHME had used unreliable verbal testimony, rather than clinical autopsies, to arrive at its figure," and "the IHME claims that if the WHO did measure the trend correctly, it woefully underestimated the size of the problem." He concludes, "Some people look at these statistical about-turns and smell a rat. They conclude that aid workers and health campaigners manipulate figures for their own purposes: to give the impression of a crisis in a fundraising drive or make out that a catastrophe has been averted when it comes to performance assessments. ... But the disputed malaria figures would seem to reveal a different truth. In a world that sometimes seems wondrously connected, and where people worry about information overload, it's a sobering thought that, more often than we'd like, we really don't know what's going on out there" (2/6).
Why bad immunity genes survive
Utah study implicates arms race between genes and germs
SALT LAKE CITY, Feb. 6, 2012 – University of Utah biologists found new evidence why mice, people and other vertebrate animals carry thousands of varieties of genes to make immune-system proteins named MHCs – even though some of those genes make us susceptible to infections and to autoimmune diseases.

"Major histocompatibility complex" (MHC) proteins are found on the surface of most cells in vertebrate animals. They distinguish self from foreign, and trigger an immune response against foreign invaders. MHCs recognize invading germs, reject or accept transplanted organs and play a role in helping us smell compatible mates.

genes, and why the ones that cause susceptibility to diseases are being maintained and not eliminated," says biology Professor Wayne Potts. "They are involved in a never-ending arms race that causes them, at any point in time, to be good against some infections but bad against other infections and autoimmune diseases."

By allowing a disease virus to evolve rapidly in mice, the study produced new experimental evidence for the arms race between genes and germs – known technically as "antagonistic coevolution." The findings will be published online the week of Feb. 6, 2012, in the journal Proceedings of the National Academy of Sciences.

Potts, the senior author, ran the study with first author and former doctoral student Jason Kubinak, now a postdoctoral fellow in pathology. Other co-authors were biology doctoral student James Ruff, biology undergraduate C. Whitney Hyzer and Patricia Slev, a clinical assistant professor of pathology. The research was funded by the National Science Foundation and the National Institute of Allergy and Infectious Diseases.

Theories for the Diversity of Immune-System MHC Genes
Most genes in humans and other vertebrate have only one or two "alleles," which are varieties or variants of a single gene. Although any given person carries no more than 12 varieties of the six human MHC genes, the human population has anywhere from hundreds to 2,300 varieties of each of the six human genes that produce MHC proteins.

"The mystery is why there are so many different versions of the same [MHC] genes in the human population," Kubinak says, especially because many people carry MHCs that make them susceptible to many pathogens (including the AIDS virus, malaria and hepatitis B and C) and autoimmune diseases (including type I diabetes, rheumatoid arthritis, lupus, multiple sclerosis, irritable bowel disease and ankylosing spondylitis).

Scientists have proposed three theories for why so many MHC gene variants exist in vertebrate animal populations (invertebrates don't have MHCs), and say all three likely are involved in maintaining the tremendous diversity of MHCs:

- An organism with more MHC varieties has a better immune response than organisms with fewer varieties, so over time, organisms with more MHCs are more likely to survive. However, this theory cannot explain the full extent of MHC diversity.
- Previous research indicates people and other animals are attracted to the smell of potential mates with MHCs that are "foreign" rather than "self." Parents with different MHC variants produce children with more MHCs and thus stronger immune systems.
- Antagonistic coevolution between an organism and its pathogens. Kubinak says: "We have an organism and the microbes that infect it. Microbes evolve to better exploit the organism, and the organism evolves better defenses to fight off the infection. One theory to explain this great diversity in MHC genes is that those competing interests over time favor retaining more diversity."

The Arms Race between Germs and MHC Genes
"You naturally keep genes that fight disease," Kubinak says. "They help you survive, so those MHC genes become more common in the population over time because the people who carry them live to have offspring."
Pathogens – disease-causing viruses, bacteria or parasites – infect animals, which defend themselves with MHCs that recognize the invader and trigger an immune response to destroy the invading pathogen. But over time, some pathogens mutate and evolve to become less recognizable by the MHCs and thus evade an immune response. As a result, the pathogens thrive. MHCs that lose the battle to germs become less common because they now predispose people who carry them to get sick and maybe die. It was thought such disease-susceptibility MHC genes eventually should vanish from the population, but they usually don’t.

Why? While some of those MHCs do go extinct, others can persist, for two reasons. First, some of the now-rare MHCs gain an advantage because they no longer are targeted by evolving microbes, so they regain an ability to detect and fight the same germ that earlier defeated them – after that germ mutates yet again. Second, some of the rare MHCs can mount an effective immune response against completely different microbes.

How the Study was Performed; Implications of the Findings
The researchers studied 60 mice that were genetically identical, except the mice were divided into three groups, each with a different variety of MHC genes known as b, d and k, respectively.

A mouse leukemia virus named the Friend virus was grown in tissue culture and used to infect two mice from each of the three MHC types. The fast-evolving retrovirus grew within the mice for 12 days, attacking, enlarging and replicating within the spleen and liver. Virus particles in the spleen were collected, and the severity of illness was measured by weighing the enlarged spleen.

Then, virus taken from each of the first three pairs of mice (b, d and k) was used to infect another three pair of mice with the same MHC types. The process was repeated until 10 pairs of mice in each MHC type were infected, allowing the virus time to mutate.

In this first experiment, the biologists showed they could get the Friend virus to adapt to and thus evade the MHC variants (b, d or k) in the mouse cells it attacked.

Next, the researchers showed that the virus adapted only to specific MHC proteins. For example, viruses that adapted to and sickened mice with the MHC type b protein still were attacked effectively in mice that had the type d and k MHCs.

In the third experiment, the researchers showed that pathogen fitness (measured by the number of virus particles in the spleen) correlated with pathogen virulence (as measured by spleen enlargement and thus weight). So the virus that evaded MHC type b made mice with that MHC sicker.

Together, the experiments demonstrate "the first step in the antagonistic coevolutionary dance" between a virus and MHC genes, Potts says.

Potts says the findings have some important implications:

- The use of antibiotics to boost productivity in dairy herds and other livestock is a major reason human diseases increasingly resist antibiotics. Selective breeding for more milk and beef has reduced genetic diversity in livestock, including their MHCs. So breeding more MHCs back into herds could enhance their resistance to disease and thus reduce the need for antibiotics.
- Because their populations are diminished, endangered species have less genetic diversity, making them an easier target for germs. Potts says it would be desirable to breed protective MHCs back into endangered species to bolster their disease defenses.
- Genetic variation of MHCs in people and other organisms is important for limiting the evolution and spread of emerging diseases. In effect, Potts and colleagues created emerging diseases by making a virus evolve in mice. "It’s a model to identify what things change in viruses to make them more virulent and thus an emerging disease."

Odds of living a very long life lower than formerly predicted
Research just published by a team of demographers at the social science research organization NORC at the University of Chicago contradicts a long-held belief that the mortality rate of Americans flattens out above age 80.

It also explains why there are only half as many people in the U.S. age 100 and above than the Census Bureau predicted there would be as recently as six years ago.

The research is based on a new way of accurately measuring mortality of Americans who are 80 years of age and older, an issue that has proven remarkably elusive in the past. The work will be significant in arriving at more accurate cost projections for programs such as Social Security and Medicare, which are based in part on mortality rates.
The research, done by Leonid A. Gavrilov and Natalia S. Gavrilova, and published in the current edition of the *North American Actuarial Journal*, is based on highly accurate information about the date of birth and the date of death of more than nine million Americans born between 1875 and 1895. The data is publicly available in the Social Security Administration Death Master File. "It is a remarkable resource that allowed us to build what is called an extinct birth cohort that corrects or explains a number of misunderstandings about the mortality rate of our oldest citizens," said Leonid Gavrilov.

A stark example of the problem of estimating the number of people over 100 came recently when the U.S. Census Bureau revised sharply downward the number of living centenarians. Six years ago, the bureau predicted that by 2010 there would be 114,000 people age 100 or older. The actual number turned out to be 53,364. The projection was wrong by a factor of two.

The newly published paper, titled "Mortality Measurement at Advanced Ages: A Study of the Social Security Administration Death Master File," explains the discrepancy and is likely to make a difference in the way mortality projections for the very old are done in the future.

The key finding is straightforward—the rate of mortality growth with age of the oldest Americans is the same as that for those who are younger. The research reveals that mortality deceleration, the long-held belief that the mortality rate flattens out above age 80, does not take place.

Anne Zissu, chair of the Department of Business NYC College of Technology/CUNY, said the research provides "an essential tool" for developing models on seniors' financial assets. Zissu said the research "will alter our financial approach to this valuation of mortality/longevity risk. Demographers and financiers need to work on this issue together, and their models must adapt to each other."

The mortality rate for people between the ages of 30 and 80 follows what is called the Gompertz Law, named for its founder, Benjamin Gompertz, who observed in 1825 that a person’s risk of death in a given year doubles every eight years of age. It is a phenomenon that holds up across nations and over time and is an important part of the foundation of actuarial science.

For approximately 70 years, demographers have believed that above age 80 the Gompertz Law did not hold and that mortality rates flattened out. The work done by the Gavrilovs, a husband-and-wife team, reveals that the Gompertz Law holds at least through age 106, and probably higher, but the researchers say mortality data for those older than 106 is unreliable.

The Gavrilovs say the extinct birth cohort of people born between 1875 and 1895, which they built using the Social Security Administration Death Master File, reveals beyond question that the mortality rate of people in that cohort aligns with the Gompertz Law.

"It amazes me that the Gompertz model fits so well nearly 200 years after he proposed it. I like the approach of using extinct cohorts methods on SSA DMF (Social Security Administration Death Master File) data by month and the use of male-female ratios to test the quality of the data at advanced ages," said Tom Edwalds, Assistant Vice President, Mortality Research, for the Munich American Reassurance Company.

Prior estimates of the number of centenarians in the United States were made in less direct ways that were subject to error. They depended, for example, on people self-reporting their age in the U.S. Census, which is less reliable than having actual birth and death data.
**Why Do Cells Age? Discovery of Extremely Long-Lived Proteins May Provide Insight Into Cell Aging and Neurodegenerative Diseases**

ScienceDaily (Feb. 3, 2012) — One of the big mysteries in biology is why cells age. Now scientists at the Salk Institute for Biological Studies report that they have discovered a weakness in a component of brain cells that may explain how the aging process occurs in the brain.

The scientists discovered that certain proteins, called extremely long-lived proteins (ELLPs), which are found on the surface of the nucleus of neurons, have a remarkably long lifespan.

**or less, the Salk Institute researchers identified ELLPs in the rat brain that were as old as the organism, a finding they reported February 3 in Science.**

The Salk scientists are the first to discover an essential intracellular machine whose components include proteins of this age. Their results suggest the proteins last an entire lifetime, without being replaced.

ELLPs make up the transport channels on the surface of the nucleus; gates that control what materials enter and exit. Their long lifespan might be an advantage if not for the wear-and-tear that these proteins experience over time. Unlike other proteins in the body, ELLPs are not replaced when they incur aberrant chemical modifications and other damage.

Damage to the ELLPs weakens the ability of the three-dimensional transport channels that are composed of these proteins to safeguard the cell's nucleus from toxins, says Martin Hetzer, a professor in Salk's Molecular and Cell Biology Laboratory, who headed the research. These toxins may alter the cell's DNA and thereby the activity of genes, resulting in cellular aging.

Funded by the Ellison Medical Foundation and the Glenn Foundation for Medical Research, Hetzer’s research group is the only lab in the world that is investigating the role of these transport channels, called the nuclear pore complex (NPC), in the aging process.

Previous studies have revealed that alterations in gene expression underlie the aging process. But, until the Hetzer lab’s discovery that mammals’ NPCs possess an Achilles' heel that allows DNA-damaging toxins to enter the nucleus, the scientific community has had few solid clues about how these gene alterations occur.

"The fundamental defining feature of aging is an overall decline in the functional capacity of various organs such as the heart and the brain," says Hetzer. "This decline results from deterioration of the homeostasis, or internal stability, within the constituent cells of those organs. Recent research in several laboratories has linked breakdown of protein homeostasis to declining cell function."

The results that Hetzer and his team just report suggest that declining neuron function may originate in ELLPs that deteriorate as a result of damage over time.

"Most cells, but not neurons, combat functional deterioration of their protein components through the process of protein turnover, in which the potentially impaired parts of the proteins are replaced with new functional copies," says Hetzer.

"Our results also suggest that nuclear pore deterioration might be a general aging mechanism leading to age-related defects in nuclear function, such as the loss of youthful gene expression programs," he adds. The findings may prove relevant to understanding the molecular origins of aging and such neurodegenerative disorders as Alzheimer's disease and Parkinson's disease.

In previous studies, Hetzer and his team discovered large filaments in the nuclei of neurons of old mice and rats, whose origins they traced to the cytoplasm. Such filaments have been linked to various
neurological disorders including Parkinson's disease. Whether the misplaced molecules are a cause, or a result, of the disease has not yet been determined.

Also in previous studies, Hetzer and his team documented age-dependent declines in the functioning of NPCs in the neurons of healthy aging rats, which are laboratory models of human biology.

Hetzer's team includes his colleagues at the Salk Institute as well as John Yates III, a professor in the Department of Chemical Physiology of The Scripps Research Institute.

When Hetzer decided three years ago to investigate whether the NPC plays a role in initiating or contributing to the onset of aging and certain neurodegenerative diseases, some members of the scientific community warned him that such a study was too bold and would be difficult and expensive to conduct. But Hetzer was determined despite the warnings.

Journal Reference:

Key to Immune Cell's 'Internal Guidance' System Discovered ****
ScienceDaily (Feb. 5, 2012) — University of British Columbia researchers have discovered the molecular pathway that enables receptors inside immune cells to find, and flag, fragments of pathogens trying to invade a host.

The discovery of the role played by the molecule CD74 could help immunologists investigate treatments that offer better immune responses against cancers, viruses and bacteria, and lead to more efficient vaccines.

The findings were recently published in Nature Immunology.

"This could ultimately lead to a blueprint for improving the performance of a variety of vaccines, including those against HIV, tuberculosis and malaria," says UBC biologist Wilfred Jefferies, whose lab conducted the study. "This detailed understanding of the role of CD74 may also begin to explain differences in immune responses between individuals that could impact personalized medical options in the future."

CD74 is an important piece of cellular machinery inside dendritic cells—which regulate mammalian primary immune responses. Dendritic cells possess specialized pathways that enable them to sense and then respond to foreign threats. Until now no one has been able to piece together the circuitry which enables a cellular receptor—Major Histocompatibility Class I (MHC I)—inside the cells to find and 'collide' with foreign invaders.

The key finding of this work is the discovery of the guiding role played by CD74 to link MHC I receptors to compartments containing invading pathogens within the immune cell. This sophisticated circuit allows the immune cell to recognize and signal the presence of a pathogen in the body and to alert T immune fighter cells. The T-cells respond by dividing and attacking infected cells, destroying the pathogen.

Jefferies' team used 'knock-out' mice that had been genetically modified to lack the CD74 function to uncover the role of the molecule. The team—which includes research associate Genc Basha, postdoctoral fellow Anna Reinicke, graduate students Kyla Omilusik and Ana Chavez-Steenbock1, undergraduate student Nathan Lack, and technician Kyung Bok Choi—then confirmed their findings using biochemical analysis.

Jefferies is a professor with UBC’s departments of Microbiology and Immunology, Zoology, and Medical Genetics and with UBC's Michael Smith Laboratories and Biomedical Research Centre. He is also a member of the Centre for Blood Research and the Brain Research Centre at UBC.

Journal Reference:
Genc Basha, Kyla Omilusik, Ana Chavez-Steenbock, Anna T Reinicke, Nathan Lack, Kyung Bok Choi, Wilfred A Jefferies. A CD74-dependent MHC class I endolysosomal cross-presentation pathway. Nature Immunology, 2012; DOI: 10.1038/ni.2225

HIV Experts Propose New Pathway for Conducting Phase 3 Drug Trials ***
New Approach Intended to Remove Barriers to Innovation in Drug Development
WASHINGTON, DC (February 7, 2012) – As the war on HIV/AIDS begins its fourth decade, medical researchers, pharmaceutical manufacturers, patient advocates and government regulators face a new and unexpected scientific challenge: how to demonstrate the safety and efficacy of promising new antiretroviral drugs when the two traditional study designs – the superiority trial and the non-inferiority trial – are no longer useful in showing improvements in both “treatment experienced” patients and those who have never received drug therapy (treatment-naïve patients).
Because this challenge could have a dampening effect on what is now a robust drug development pipeline for HIV, the Forum for Collaborative HIV Research has just released a new scientific paper that lays out a substantially different approach for conducting Phase 3 HIV clinical trials.

Published in the journal *AIDS*, the paper summarizes the insights of specialists from the Food and Drug Administration, European Medicines Agency, academia, the patient advocacy community and industry that overcoming the current difficulties in conducting new HIV drug trials requires moving from the large-scale study model to a new approach where clinical improvements are demonstrated through a sequence of short, step-wise efficacy and safety studies.

“Despite the many valuable antiretroviral drugs now available to treat HIV, new antiretrovirals can bring important benefits, such as fewer side effects, less frequent dosing and a lower risk of drug resistance. That is why overcoming the barriers to innovation in HIV drug development is so critical,” said Veronica Miller, Ph.D., Director of the Forum and one of the authors of the paper. “Our paper offers a new pathway for regulatory approval of promising new HIV drugs and reflects the best thinking of the top experts in the field.”

The new pathway described in the paper calls for a multi-phased study design, which includes:

- A short study (10-14 days) comparing the investigational compound versus placebo, with the patient’s current failing regimen as background, to evaluate short-term efficacy in viral load reduction
- A follow-on study where all participants receive the investigational drug (at a single or different doses) and are assessed at 24 weeks to evaluate dose response, safety, durability of initial response and development of resistance
- The possibility of a second comparative safety trial in patients with a minimum of two active drugs available where participants are randomized to the investigational agent plus a new optimized background regimen of antiretroviral drugs versus patients on a new optimized background regimen plus placebo

Intended to preserve innovation in HIV drug development, the new proposed pathway focuses specifically on trials in multi-drug resistant patients, where rates of accrual into HIV clinical trials have declined precipitously, due largely to the increasing use of boosted protease inhibitors and the overall enhanced potency and efficacy of antiretroviral regimens. From 2006 to the present, the rate of patient recruitment for trials of treatment-experienced participants with multiple drug resistance has fallen from 1.15 per month to 0.02 per month even though sponsors are using an ever increasing number of study sites and countries. For these patients, the new approach of a short, step-wise superiority trial allows sponsors to demonstrate efficacy before the risk of developing resistance to the new drug or additional resistance to the old drugs can take place.

These new options are not as promising for conducting studies in treatment-naïve patients, where results of both superiority and non-inferiority trials are difficult to interpret. With superiority trials, the challenge is that current first-line antiretroviral regimens produce viral suppression rates exceeding 90 percent in this patient population, making these studies impractical. With non-inferiority trials, the problem is that true differences between drug regimens can be difficult to interpret. For these reasons, there is no consensus on the utility of studying investigational agents in this patient population, although scientists, regulators and drug sponsors recognize these HIV drugs may offer treatment-naïve patients better tolerability or reduced long-term safety risks than currently available options.

Reflecting the realities of today’s environment, the new paper notes the availability of a wide range of antiretroviral agents – 26 unique antiretroviral drugs (plus alternative formulations and fixed-dose combinations) from six different therapeutic classes – which collectively have produced viral suppression rates of between 70 percent and 90 percent. But the paper also reflects the growing problem of drug resistant strains of HIV and the ongoing need for new treatment options. Accordingly, the proposed changes in HIV trial design are intended as a pathway for regulatory approval of promising new drugs that will address multi-drug resistant virus while also offering patients advantages in safety and tolerability for patients.

What Really Fuels the HIV/AIDS Epidemic in Black America? (long)

From The Body
February 6, 2012
For the past 15 years, we have been bombarded with images and media attention that have blamed the "down-low brotha"—the closeted gay man who sleeps with both men and women—for the HIV epidemic in black America. Meanwhile, numerous studies have debunked those claims. Yes, there are closeted gay black men, but the reality is that so much more is at play when it comes to why African Americans account for only 14 percent of the U.S. population but make up almost half of all newly diagnosed HIV cases each year.

Take a look at what HIV advocates from across the country say is really worsening the epidemic in the African-American community.

Poverty

Ingrid Floyd, Executive Director, Iris House, New York
Poverty fuels the HIV epidemic due to its impact on all aspects of life, including income, housing, education, nutrition, access to health care—and the list goes on. In the African-American communities where poverty rates are even higher, there exists a greater gap in all of these areas that fuels the inability to negotiate, feel empowered, get educated on HIV and get tested.

Let’s be real: If I can’t afford my next meal or next month’s rent, do you think I’m going to make a big deal about using condoms? Because the man that’s taking care of me is taking care of her too.

No, I have too much else to deal with.

But there is hope. Many community organizations are now targeting these communities to conduct HIV testing and connect those who test positive, or are lost to care, to medical treatment. Even though we cannot always directly impact the poverty levels in these communities, we can impact the availability of testing and education resources.

Injection Drug Use

Allen Kwabena Frimpong, Capacity Building Advisor, Harm Reduction Coalition, New York
According to the CDC, the number of new HIV infections among the sub-populations most affected are lowest among black males and females who inject drugs. Two factors that contribute to these relatively low numbers are: One, our white counterparts use drugs more than we do—despite the fact that we disproportionately carry the health, social and economic costs associated with the harms from drug use and punitive drug policies.

Two, the advent of syringe exchange programs has also driven down the number of new infections among African Americans—though we know anecdotally, and through research, that there are barriers to African Americans accessing syringe exchange programs given law enforcement practices that racially profile and target them.

We know incarceration is a driver of HIV. We know lack of employment and education drives people to participate in "street economies," and we know that participation in these economies has harmful consequences in our communities and continues a cycle that does not encourage people to be empowered enough to protect themselves and their loved ones against HIV. It’s for these reasons that a harm reduction approach, and a drug policy agenda that ends the criminalization of people who use drugs, will be vital in ensuring that African-American communities don’t bear the brunt of the health, social and economic costs associated with harms like HIV infection.

Gender Inequality

Deon Haywood, Executive Director, Women With a Vision, New Orleans
As long as we have economically repressive policies in this country, we’re going to have women at risk for HIV. As we often say, HIV can affect anybody, but it’s particularly hard on women who are poor.

Policies that target African-American women on welfare—like Temporary Assistance for Needy Families, which in some states requires a negative drug test to qualify for assistance—put women at an economic disadvantage that can leave them vulnerable to violence, and to HIV, through possibly unprotected "survival sex" and whatever other activities they need to engage in so that they and their families can survive.

In today’s economy, where so many people are struggling, to target and penalize people who may have smoked marijuana, rather than providing job training, education, or even recovery services, seems a misplacing of priorities.
And when it comes to access to reproductive health care: Budget cuts routinely shut down state-run family-planning clinics, leaving women with no place to go for regular checkups, to learn about their bodies and what to do with them, how to keep themselves healthy. Furthermore, national reproductive-justice struggles often do not take into account the issues of greatest concern to poor women.

Low Health Literacy
Bethsheba Johnson, G.N.P.-B.C., A.A.H.I.V.S., Associate Medical Director, St. Hope Foundation, Houston

Health literacy is the ability to use written materials to function in health care settings and to maintain one's health and the skills needed to advocate for and request needed clarification. However, a shocking number of Americans, especially those of color, are lacking these skills. Previous research suggests that a low level of health literacy is an underlying factor that explains racial disparities in the prevalence and incidence of HIV/AIDS.

For HIV-positive individuals, it can be extremely difficult to navigate the health care system. For example, there can be difficulty in taking and refilling prescriptions, scheduling a referral, understanding test results and lifestyle modification messages, completion of forms for care, and adherence to medications. Meanwhile, I have had many patients that couldn't read at a level necessary to function. How can you refill a prescription if you can't read it? Or those persons who don't understand how to complete their ADAP or Medicaid Part D forms?

In terms of prevention, the messages we're sending to educate the community on the importance of HIV prevention must be culturally sensitive AND tailored to the health literacy level of the masses. Evidence-based messages on multimedia (Internet, social media groups, written materials, provider-patient interaction) need to be designed to reach those at highest risk for infection.

Homophobia
Kenyon Farrow, Communications Manager, Housing Works, New York

Homophobia is a major factor that's driving HIV rates in black communities. We're told we're worthless by the churches we attend. Black LGBT youth are not getting a comprehensive sex education in schools that includes sexuality across the spectrum, so it's irrelevant to them. Twenty-five to 40 percent of homeless youth are LGBT, and a disproportionate number are black. Is it any wonder that new infections among men who have sex with men (MSM) are highest among black MSM ages 13 to 29?

But homophobia also makes straight black people vulnerable to HIV infection. As long as black women are only worried about if their boyfriends and husbands aren't bisexual, then they're less likely to consider practicing safer sex with heterosexual men, which is the overwhelming reason why black women are contracting HIV—from heterosexual men—but we don't hear that on black radio or in Tyler Perry movies.

Untreated and Undiagnosed STDs
Claire Simon, Communications Manager, Co-Founder/Co-Director, Young Women of Color HIV/AIDS Coalition, New York

Undiagnosed and untreated sexually transmitted diseases (STDs) are known to increase the chances of one being infected with HIV because they suppress your immune system, making you more vulnerable to seroconverting. The CDC estimates that there are approximately 19 million new STD infections each year—almost half of them among young people 15 to 24 years of age. In a 2008 report, the CDC found that one in two African-American girls has had at least one STD.

It's also important to note that many STDs have no signs or symptoms, especially among men, and with symptoms or not, the disease can be passed on to a sex partner.

Practicing safer sex (using condoms during every sexual encounter/act each and every time), getting screened every three to six months for undiagnosed and untreated cases of HIV/STDs, and engaging in partner notification services if you are diagnosed with an STD may contribute to decreased transmission or burden of disease in the community.

Lack of Access to Quality Health Care
Hilary Beard, Author of Health First! The Black Woman's Wellness Guide, Philadelphia

Black people are disproportionately uninsured, and when you don’t have insurance, it means there is no co-pay; you have to pay for that appointment out of your own pocket. And if you cannot afford insurance or don't have a job that offers any, it's a serious financial strain. You might be inclined to skip appointments, put them off and not get the necessary tests that you need, not take your meds because you cannot afford them, or split your pills in half or take them every other day. This can set into motion a whole chain of events.
In terms of HIV, not having access to health care can mean that people are not getting tested with the frequency that they should, and if they are suffering from other chronic diseases that lower their immune system, they can even become more susceptible to becoming infected with and passing on HIV to someone else. All of which happens with people being completely unaware that they are even positive. So it's nothing malicious, or intentional or promiscuous, because HIV can happen between loving monogamous partners where someone is completely unaware that they are infected with HIV, because they haven't gotten tested.

**Mass Incarceration**

**Tracie Gardner, Founder and Director, Women's Initiative to Stop HIV NY, New York**

When looking at the incidence of many STDs, particularly HIV, they are concentrated in poor, segregated neighborhoods that are characterized by high rates of incarceration. Inner-city populations of African Americans and Latinos account for almost two-thirds of the 2.2 million Americans in prison nationwide, and two disturbing trends are increasingly present in these communities.

When talking about incarceration and HIV, the main myth to explain this relationship is that when men go to prison they contract HIV there and then bring it back into the community. And this is not really the case. Mass incarceration removes men from a community and the person left behind chooses another partner, who also may be sleeping with other people in the community (aka multiple concurrent sexual partnerships). When widespread, this behavior creates an efficient, effective pattern for introducing and maintaining an STD through a network of sexual relationships.

And so as we find ourselves with poverty and joblessness leading to crime, we will continue to see HIV flourish, especially with a broken health care system. HIV is a disease of LOCATION. Behavior is not enough to explain the disproportionate effect on black and Latino communities.

**Lack of Comprehensive Sex Education**

**Kellee Terrell, News Editor, TheBody.com, New York**

Thanks to former Presidents George Bush and Bill Clinton, since 1997, our federal government has invested almost 1.5 billion in abstinence-only education, while numerous studies have shown that these programs are completely ineffective in delaying sex. And in the end, what this means is that our youths have not received the crucial information that they need to protect them and ward off unwanted pregnancies and STDs, including HIV.

And despite President Obama channeling more federal funds to comprehensive sex education, this does not mean that most schools across the country are incorporating these lessons into their curriculum or that these lessons are LGBT friendly.

That's sad, because knowledge is power. You cannot protect yourself if you don’t know how or understand why you need to. And while there are many factors that contribute to why HIV diagnoses are on the rise among black youth, it’s clear that a lack of information is part of that complex problem. When it comes to this disease and other reproductive health issues, our young people just don’t know what they need to.

We need to shift our mentality from looking at sex education as something that encourages our youths to have sex—which it doesn't, because they are having sex anyway—to understanding it as arming our children with what they need to fight for their health. Without it, our children pay the price with their lives.

**Late Testing**

**David Malebranche, M.D., Associate Professor, Emory University School of Medicine, Atlanta**

Late HIV testing among black Americans is a contributor to the current HIV racial disparity in America. Many believe that a lack of testing is the cause, but in fact, black Americans have the highest HIV testing rates among any racial/ethnic group in the country. The issue is not “if” we get HIV testing or not, but rather "when" this testing takes place.

Similar to other chronic disease issues such as high blood pressure, cancer screening, diabetes and heart disease, HIV testing is a byproduct of poor overall health care access. In many situations, we are much more likely to use an emergency room as our primary care provider. And this is mostly a reflection of larger societal issues such as poverty, lack of health insurance, transportation, institutional stigma, work schedules, and racism and cultural incompetency among providers.

These factors may influence our behaviors and how we choose to prioritize our health, receive medical or public health messages, and follow recommendations by medical providers.

Yes, "to test or not to test" for HIV is subject to a number of different, very specific factors such as fear of disease, discrimination and community stigma, not to mention the individual-level impact a positive
HIV test may have on personal decisions of disclosure and sexual behavior with partners. But if the foundation of health care that is available to us is shaky, talking about HIV testing will be a moot point if we can't even access and have positive experiences in the settings that often provide these testing services.

**Can Interfaith Research Partnerships Develop New Paradigms for Condom Use and HIV Prevention? The Implementation of Conceptual Events in Malawi Results in a 'Spiritualized Condom'**

*Sexually Transmitted Infections Vol. 87: P. 611-615, (12..2011)*

The aim of this intervention research study was to engage senior leaders of faith-based organizations (FBOs) in Malawi in a participatory process to construct an interfaith theology of HIV/AIDS,” the authors wrote. The process was created to enhance faith community leaders’ capacity to respond more effectively to the HIV/AIDS pandemic.

An evidence-driven combination of ethnographic and participatory action research methodologies was employed. During the four-year project, conceptual events—“innovative participatory action research processes”—were held, bringing together health service providers, policy makers, and a non-governmental organization in partnership with FBOs and grassroots faith-based communities.

An interfaith theology of HIV/AIDS emerged from the facilitated dialogue. This resulted in “the proposition that a ‘spiritualized condom’ endorses a ‘theology of protecting life,’” the authors wrote. The following convictions supported this proposition:

*Life is sacred and should be protected.*
*Killing or murder is a “greater sin” compared to the “lesser sin of infidelity.”*
*Protecting the innocent is a moral and religious requirement.*
*Condoms potentially can prevent the death of an innocent person.*
*Condom use should be encouraged, even in the context of marriage.*

“Clinicians, non-governmental organizations, health service providers, and policy makers, assisted by health social scientists, can successfully partner with FBOs and their leaders to 1) modify and transform faith-based understandings of HIV risk and 2) bring about attitudinal behavior changes that help to address the challenges association with HIV/AIDS,” the researchers concluded.

**Al Jazeera Examines Unique Polio Eradication Campaign In Pakistan**

In this video report, *Al Jazeera* examines polio eradication efforts in Pakistan, writing, “[I]n an unusual effort to eliminate the disease, health workers are stopping vehicles at a busy toll booth outside Islamabad to administer free polio vaccination drops to children under the age of five.” The video recounts a "promise" made by Pakistan's prime minister last month to eliminate new polio infections in the country by the end of the year and provides commentary by Shahnaz Wazir Ali, assistant to the prime minister on social affairs, and Dennis King of UNICEF Pakistan about the target, current infection rates, and ongoing eradication efforts (Tyab, 2/6).
Salk scientists use an old theory to discover new targets in the fight against breast cancer

Similarities between genetic signatures in developing organs and breast cancer could predict and personalize cancer therapies

La Jolla, CA—Reviving a theory first proposed in the late 1800s that the development of organs in the normal embryo and the development of cancers are related, scientists at the Salk Institute for Biological Studies have studied organ development in mice to unravel how breast cancers, and perhaps other cancers, develop in people. Their findings provide new ways to predict and personalize the diagnosis and treatment of cancer.

In a paper published February 3 in *Cell Stem Cell*, the scientists report striking similarities between genetic signatures found in certain types of human breast cancer and those of stem cells in breast tissue in mouse embryos. These findings suggest that cancer cells subvert key genetic programs that guide immature cells to build organs during normal growth.

"Stem cells in a healthy developing embryo have a GPS system to alert them about their position in the organ," says Geoffrey Wahl, a professor in Salk's Gene Expression Laboratory, who led the research. "The system depends on internal instructions and external signals from the environment to tell the stem cell what to do and where to go in the body. It stimulates the stem cells to grow and form more stem cells, or to change into different cells that form complex organs, such as the breast. Our findings tell us that this GPS system is broken during cancer development, and that may explain why we detect stem-like cells in breast cancers."

The relationship between cancer and embryonic tissues was first proposed in the 1870s by Francesco Durante and Julius Cohnheim, who thought that cancers originated from cells in adults that persist in an immature, embryonic-like state. More recently, scientists including Benjamin Spike, a co-first author on the current work and post-doctoral fellow in the Wahl lab, have discovered that tumors often contain cells with stem cell characteristics revealed by their genetic signatures.

As a result, many scientists and physicians are pursuing ways to destroy stem-like cells in cancer, since such cells may make cancer more resistant to treatment and may lead to cancer recurrence. The Salk scientists are now characterizing the stem-like cells in certain forms of breast cancer to arrest their growth.

Studying the genetic activity of organ-specific stem cells is very difficult because the cells are very rare, and it is hard to separate them from other cells in the organ. But, by focusing on tissue obtained from mouse embryos, the Salk researchers were able for the first time to identify and isolate a sufficiently large number of fetal breast stem cells to begin to understand how their GPS works.

The Salk scientists first made the surprising finding that these fetal breast stem cells were not fully functional until just prior to birth. This observation suggested that a very special landscape is needed for a cell to become a stem cell. The breast stem cells at this late embryonic stage were sufficiently abundant to simplify their isolation. This enabled their genetic signature to be determined, and then compared to that of the stem-like cells in breast cancers.

The signatures of the breast stem cells in the fetus were stunningly similar to the stem-like cells found in aggressive breast cancers, including a significant fraction of a virulent cancer subtype known as "triple-negative." This is important as this type of breast cancer has until now lacked the molecular targets useful for designing personalized therapeutic strategies.

"The cells that fuel the development of tumors in the adult are unlikely to 'invent' entirely new patterns of gene expression," says Benjamin Spike. "Instead, some cancer cells seem to reactivate and corrupt programs that govern fetal tissue stem cell function, including programs from their neighboring cells that constitute the surrounding fetal stem cell landscape, or microenvironment."

The discovery of the shared genetic signatures provides a new avenue for scientists to explore the links between development and cancer. By uncovering new biological markers, the scientists hope to develop tests that individualize treatment by showing how the GPS system of a tumor operates. This should help doctors to determine which patients may benefit from treatment, and the correct types of treatment to administer.
Doctors are already using drugs, such as Herceptin, that specifically target malfunctioning genetic pathways in tumors, but no such therapies are currently available for certain aggressive forms of the disease, such as the triple negative subtype.

Although triple negative cancer cells lack the three critical genetic markers that are currently used to guide breast cancer treatment, the scientists’ analysis suggests a strong reliance on signaling through pathways similar to those that affect fetal breast stem cell growth.

They found that the fetal breast stem cells are sensitive to a class of targeted therapies that already exists, so these therapies might also work in triple negative breast cancers. Laboratory studies and clinical trials are currently underway to test this possibility.

"Substantial effort is being expended to personalize cancer treatment by gaining a better understanding of the genetics of an individual patient's cancer," Wahl says. "Our findings offer a way to discover new targets and new drugs for humans by studying the primitive stem cells in a mouse."

**Food Poisoning: Understanding How Bacteria Come Back from the 'Dead'**

*Coloured Transmission Electron Micrograph of Salmonella Typhimurium. (Credit: Paul Gunning and Roy Bongaerts, IFR)*
ScienceDaily (Feb. 2, 2012) — *Salmonella* remains a serious cause of food poisoning in the UK and throughout the EU, in part due to its ability to thrive and quickly adapt to the different environments in which it can grow. New research involving a team of IFR scientists, funded by BBSRC, has taken the first detailed look at what *Salmonella* does when it enters a new environment, which could provide clues to finding new ways of reducing transmission through the food chain and preventing human illness.

Bacteria can multiply rapidly, potentially doubling every 20 minutes in ideal conditions. However, this exponential growth phase is preceded by a period known as lag phase, where no increase in cell number is seen. Lag phase was first described in the 19th Century, and was assumed to be needed by bacteria to prepare to exploit new environmental conditions. Beyond this, surprisingly little was known about lag phase, other than bacteria are metabolically active in this period. But exactly what are bacteria doing physiologically during this period?

To fill in this knowledge gap researchers at IFR, along with colleagues at Campden BRI, a membership-based organisation carrying out research and development for the food and drinks industry, have developed a simple and robust system for studying the biology of *Salmonella* during lag phase. In this system, lag phase lasts about two hours, but the cells sense their new environment remarkably quickly, and within four minutes switch on a specific set of genes, including some that control the uptake of specific nutrients.

For example, one nutrient accumulated is phosphate which is needed for many cellular processes, and a gene encoding a phosphate transporter was the most upregulated gene during the first four minutes of lag phase. The cellular uptake mechanisms for iron were also activated during lag phase, and are needed for key aspects of bacterial metabolism. This increase in iron leads to a short term sensitivity to oxidative damage. Manganese and calcium are also accumulated in lag phase, but are lost from the cell during exponential growth.

This new understanding of *Salmonella* metabolism during lag phase show how rapidly *Salmonella* senses favourable conditions and builds up the materials needed for growth. This study was carried out by two BBSRC-CASE studentships, which were partially funded by Campden BRI.

**Journal Reference:**

Use of some anti-HIV drugs during pregnancy linked to cleft lip and palate; investigators urge cautious interpretation of results

**Michael Carter**
Published: 09 February 2012

US investigators have identified a possible association between the use of antiretroviral therapy during pregnancy and an increased risk of having a baby with a cleft lip or palate. The study, published in the January edition of *Cleft Palate-Craniofacial Journal*, found preliminary evidence seven anti-HIV drugs may increase the risk of this birth abnormality.

However, the investigators emphasise that their their findings are far from definitive. “Our report, although the first to report this signal, is merely a starting point; further investigations on these drugs’ side effects are required to follow.”

Appropriate use of antiretroviral therapy during pregnancy can reduce the risk of mother-to-child transmission of HIV to below 1%.

However, it is important to understand the possible risks associated with the use of anti-HIV drugs during pregnancy. The protocols of clinical trials routinely exclude pregnant and nursing mothers. Therefore, investigators scrutinised the Food and Drug Administration’s (FDA’s) Adverse Events Reporting System (AERS) to see if therapy with antiretrovirals during pregnancy increased the risk of cleft lip or palate.

Data from April 2004 to October 2009 were examined by the researchers. They calculated crude reporting odds ratios (ROR) to detect potential associations between specific antiretroviral drugs and the birth abnormality.

“Readers should be cognizant of the fact that the RORs calculated in this study should not be interpreted as definitive measure of the associations’ strength without further validation in well-controlled and prospective or retrospective epidemiological studies,” write the authors.

A total of 26 cases of cleft lip or palate that were possibly associated with the use of HIV therapy during pregnancy were identified.
Six of these cases involved exposure to efavirenz (Sustiva, also in the combination pill Atripla), which had a ROR of 196.01 (95% CI, 85.89-447.32). In addition, five cases were reported in the context of 3TC (Epivir) therapy (ROR = 60.23; 95% CI, 24.53-147.89); three after nevirapine (Viramune) treatment (ROR = 27.59; 95% CI, 8.75-86.99); five following the use of lopinavir/ritonavir (Kaletra) during pregnancy (ROR = 26.47; 95% CI, 10.78-64.67); and three cases of the defect were reported after maternal use of Combivir (3TC/AZT), providing a ROR of 24.94 (95% CI, 7.91-78.62).

Elevated RORs were also apparent for Trizivir (3TC/abacavir/AZT) and nelfinavir (Viracept).

“Our report is the first to detect a possible association between cleft lip and palate development and...antiretroviral drugs,” write the investigators. However, they do not view their results as definitive and point to studies “of antiretroviral use during pregnancy that fail to show a statistical association with cleft lip and palate.”

The authors also note that the abnormality is believed to have a number of risk factors, including both genetic and environmental causes. “Our analyses report crude RORs and do not control for important confounders such as personal characteristics, diet, genetics, and so forth.”

They therefore conclude, “further studies should be performed to assess the relative safety of these drugs and the specific conditions or potential synergies that might lead to the development of cleft lip and palate.”

Reference

HIV treatment not advanced enough to dismiss full disclosure, court told
By Linda Nguyen, Postmedia News February 8, 2012
OTTAWA — Medical treatment for HIV has not advanced enough to preclude the duty for someone infected with the virus to not disclose their status to a sex partner, the Supreme Court of Canada heard Wednesday.

"We’re not there yet," Manitoba Crown attorney Elizabeth Thomson told the nine-justice panel. "The threat of HIV is not theoretical. The threat is still real."

The country’s highest court is hearing an appeal involving two people living with the human immunodeficiency virus, who recently were acquitted by appeal courts of aggravated assault and sexual assault charges for not disclosing their HIV status.

Thomson told the panel that a person living with HIV should always disclose because it is still a disease that is chronic, incurable and has the potential to lead to death.

She said an unknowing partner could never truly give consent when they don’t know the extent of the risk they are taking in terms of contracting the virus.

"You must tell prospective partners if what you bring to the table can cause significant harm," said Thomson.

Quebec Crown attorney Caroline Fontaine also added that the criminal law is meant to protect the public at large, even if it means singling out people infected with HIV.

"An HIV-infected person’s sex life cannot be like everyone else’s," she said.

This is the first time the Supreme Court has reviewed non-disclosure legislation since 1998.

HIV/AIDS advocates argue that since then, someone with HIV is no longer as infectious as they used to be if they take regular anti-viral medication, thus lowering the risk for transmission.

But Fontaine argued that changing the law to reflect estimates of someone’s viral load, and risk of transmission is akin to basing it on "moving targets" and would be "dangerous."

"The fact of remains, HIV is fatal," she said. "Life with HIV has improved but it is still fatal."

A lawyer for Clato Maboir, the Winnipeg HIV-positive man central in these cases, told the panel that the law should not continue to penalize those carrying the virus if they take steps in lowering their viral count and have no intention of transmitting the disease by not disclosing to their sex partner.

Arguments from a number of interveners in these cases, including the Canadian HIV/AIDS Legal Network, the Criminal Lawyers' Association and the B.C. Civil Liberties Association, was to resume Wednesday afternoon.

Every seat in the courtroom was taken for the hearing and an overflow room was packed. A small group of protesters was outside the courthouse giving speeches and holding up placards on the issue.

The interveners argued that Canada’s stance on HIV disclosure has resulted in people being afraid to disclose their status over fear of prosecution and at times, afraid even to have their condition diagnosed.
Since 1998, it is estimated that 130 people living with HIV have been charged by the criminal courts for non-disclosure. In 2009, Johnson Aziga became the first person in Canada to be convicted for first-degree murder for not telling a number of women he had the virus, including two who later died of AIDS-related cancers.

**DNA Sequencing Helps Identify Cancer Cells for Immune System Attack**

ScienceDaily (Feb. 8, 2012) — DNA sequences from tumor cells can be used to direct the immune system to attack cancer, according to scientists at Washington University School of Medicine in St. Louis.

The research, in mice, appears online Feb. 8 in *Nature*.

The immune system relies on an intricate network of alarm bells, targets and safety brakes to determine when and what to attack. The new results suggest that scientists may now be able to combine DNA sequencing data with their knowledge of the triggers and targets that set off immune alarms to more precisely develop vaccines and other immunotherapies for cancer.

"We already have ways to identify specific targets for immunotherapy, but they are technically challenging, extremely labor-intensive and often take more than a year to complete," says senior author Robert Schreiber, PhD, the Alumni Professor of Pathology and Immunology at the School of Medicine and co-leader of the tumor immunology program at the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine. "These difficulties have stood in the way of developing personalized immunotherapies for cancer patients, who often require immediate care for their disease. To our knowledge, this is one of the first studies to show that the faster methods provided by DNA sequencing can help. That opens up all kinds of exciting possibilities."

Scientists have long maintained that the immune system can recognize cancer as a threat either on its own or with the help of vaccines or other immunotherapeutic treatments, which help alert the immune system to the danger posed by cancers. Once the cancer is recognized, the immune system should develop the capacity to attack growing cancer cells until either the tumor is eradicated or the immune system’s resources are exhausted.

Schreiber and his colleagues have shown that interactions between the immune system and cancer are more complex. Their theory, called cancer immunoediting, suggests that some of the mutations in tumor cells are very easy for the immune system to recognize as a threat. If the immune system detects these mutations in cancer cells, it attacks until they are destroyed.

At that point, the cancer may be eliminated. But it’s also possible that the cancer can be "edited" by the immune system, resulting in the removal of all the cells containing the critical easily recognized mutations. The remaining tumor cells can continue to grow or enter into a period of dormancy where they are not destroyed but are held in check by the immune system.

For the new study, Schreiber and his colleagues wanted to define the genetics of tumors that had yet to interact with the immune system. To do so, they induced tumors in mice with disabled immune systems. They collaborated with Washington University's Genome Institute scientists, who sequenced the cancer cells’ genes.

"Until very recently, this work would have been impractical because of the costs involved," Schreiber says. "But the technology has improved and prices have come down, and now it’s possible to obtain this genetic information for a few thousand dollars instead of a million."

By comparing genetic data from cancer cells and normal cells, scientists identified 3,743 mutations in the genes of the tumor cells. Next, they turned to an online database of protein sequences likely to be recognized by a key immune system sensor. This helped them narrow their focus to a few mutated genes whose altered proteins seemed most likely to trigger immune system attacks. One of these mutated proteins, an altered form of spectrin-beta2, was present in all tumor cells that were attacked by the immune system and in none of the cells that were ignored.

Researchers cloned this mutant gene and put it into other mouse tumor cells that lacked the mutation. When transplanted into mice with normal immunity, the tumor cells that made the mutant spectrin-beta2 protein were attacked and eliminated by immune cells.

"Many of the cancer genome projects now under way are looking for the 'driver' mutations, or the mutations that cause the cancers," Schreiber says. "Our results suggest there may be additional information in the sequencing data that can help us make the immune system attack cancers."

Schreiber calls the spectrin-beta2 mutation identified in the study "low-hanging fruit," noting that it’s such a red flag to the immune system that its presence normally leads the immune system to assault cancer cells without any prompting from immunotherapy.
He and his colleagues are currently sequencing DNA in tumors grown from mice with normal immune systems to see if they can identify mutations that are not as readily discernible to the immune system. "The idea would be to make a vaccine that helps the immune system recognize and attack six or seven of these mutated proteins in a cancer," he says. "Therapeutically, that could be very helpful."

**Journal Reference:**

**Secrets of Immune Response Illuminated in New Study**
*ScienceDaily* (Feb. 9, 2012) — When disease-causing invaders like bacteria infect a human host, cells of various types swing into action, coordinating their activities to address the threat.

In new research appearing in this month's issue of the journal *Nature Immunology*, Roy Curtiss, director of the Center for Infectious Diseases and Vaccinology at the Biodesign Institute at Arizona State University, along with international collaborators, investigates the coordination of a particular type of immune response, involving the release of IFN-λ—a cell-signaling protein molecule known as a cytokine.

Molecules like IFN-λ have long been recognized as vital weapons in the immune system's arsenal against viral, bacterial and parasitic pathogens, as well as tumors. They are known as interferons—named for their ability to interfere with the functioning or replication of infectious agents. Communication between cells enabled by interferons can trigger the protective defenses of the immune system, which will attempt by various means to eradicate the infectious pathogen.

"The inception of this study was based on studies conducted in collaboration with the Richard Strugnell group at the University of Melbourne when it was shown that flagella produced by S. Typhimurium—and especially by a mutant generated by Shifeng Wang in our group, that hyper produced the flagellin—were superior in inducing a cascade in host cells leading to the production of NFκB," a protein complex that plays a key role in regulating the immune response to infection.

The cytokine IFN-λ is produced by a type of lymphocyte known as a memory CD8+ T cell. Memory T cells are a vital part of the adaptive immune system. Typically, they are activated and induced to proliferate when they come in contact with a specific antigen produced by the infectious agent and recognized by the T cell's antigen receptor. After their initial encounter with the unfamiliar invader, memory T cells survive in the host in an inactive state, "remembering" the cognate antigen to which they are related. Should they re-encounter this antigen, they can speedily mount a response, liberating IFN-λ.

An understanding of how IFN-λ release is regulated and the complex pathways involved in the production of this key cytokine remains incomplete. The current study demonstrates that the release of
IFN-λ by memory T cells can also occur without the activation of these cells by direct contact with the disease antigen. In this way, memory CD8+ T cells also contribute to the host’s innate immune response.

The mechanism for this antigen-independent immune response is the focus of the current study. The team’s results significantly advance the understanding of such pathways and their subtle regulation, and may stimulate new biomedical approaches to interfering with and disabling disease-causing intruders.

In the new study, the group found that the antigen-independent production of IFN-λ by memory T cells relies on another cell type, known as splenic dendritic cells. Such cells contain so-called NOD-like receptors (NLRs). The NLRs are able to sniff out pathogen-associated molecular patterns. When they sense these distinctive patterns, the NLRs sound the alert.

While their more familiar cousins, the TOLL-like receptors, sense pathogen-associated molecular patterns in the extracellular space, NLRs sense pathogenic traces in the intracellular compartments. Further, once NLR’s have successfully detected their target, they assemble large protein complexes in the dendritic cell, known as inflammasomes.

In the case of bacterial invasion, the NLR inside the splenic dendritic cell is triggered when it senses flagellin—a protein associated with bacterial flagellum. The NLR then assembles the inflammasome complex, which produces two key pro-inflammatory interleukins—IL-1 and IL-18. It is the second of these that will migrate from the dendritic cell to the memory CD8+ T cell, triggering the release of IFN-λ. Figure 1 graphically describes this process.

In the current study, antigen-independent secretion of IFN-λ by memory CD8+ T cells was demonstrated in mice infected with the intracellular pathogen Salmonella Typhimurium. The response could be detected as soon as 2 hours post-infection—the NOD-like receptors representing the earliest response to pathogenic invasion. Further, by using strains of S. Typhimurium deficient in flagellin, the group showed impaired IFN-λ secretion by CD8+ T cells.

Intriguingly, the group also found a robust IFN-λ response when dendritic cells were presented with heat-killed S. Typhimurium or even with the injection of purified flagellin alone—powerful evidence that the dendritic cell inflammasome assembled by the NOD-like receptor’s sensing of flagellin was sufficient to induce IFN-λ production in memory CD8+ T cells. This flagellin-induced response was also demonstrated for two other pathogens: Yersinia and Pseudomonas.

The study also confirmed the hypothesis that production of IL-18 in dendritic cells, following inflammasome formation, generated the production of IFN-λ by attaching to a specific receptor-adaptor on the memory CD8+ T cells, which the group identified. The authors speculate that a particular inflammasome known as NAIP5 in splenic dendritic cells is responsible for sensing flagellin and initiating the cascade of events leading to IFN-λ production in CD8+ T cells.

Previous research had suggested a mechanism for S. Typhimurium to transfer flagellin into the cell from the extracellular medium, through the pathogen’s specific secretion system. This is considered critical, as many bacteria are non-pathogenic and indeed, important to the host. An inflammasome response to these so-called commensal bacteria could therefore have disastrous consequences, triggering an inappropriate autoimmune response.

Experiments also demonstrated that not all bacterial flagellins are recognized by the inflammasomes—E. coli flagellins, for example, are not. The reasons for this have yet to be fully explored. The team further speculates that the inflammasome system and its NOD-like receptors may have evolved not only to deal with pathogenic invaders but to carefully regulate the balance of commensal bacteria, keeping populations of healthy microbes in check.

The study was the fruit of a multi-institute collaboration, co-authored by researchers from Department of Microbiology and Immunology, The University of Melbourne, Australia; Department of Biochemistry, University of Lausanne, Epalinges, Switzerland; Department of Infectious Diseases & Pulmonary Medicine, Charité University Hospital, Berlin, Germany and the Ludwig Institute of Cancer Research, Heidelberg, Australia.

As Curtiss explains, the group’s research findings lay the groundwork for future investigation: “We are now incorporating the findings from the current study to design a superior recombinant attenuated Salmonella vaccine strain with greatly enhanced ability to induce a CD8-dependent cellular immunity against viral, parasitic and bacterial pathogens in which a CD8 response is critical for successful control.”

**Journal Reference:**
HIV Drugs Not Linked with Child Psychiatric Problems

Reuters, (02.07.2012) Julie Steehuysen

Antiretroviral therapy does not appear to increase the risk of psychiatric problems in children with HIV, a new study suggests. Scientists have been worried about high rates of psychiatric and academic problems in children with HIV.

"The question that is coming up is, 'Why do they have so many issues? Is it their HIV, is it their antiretrovirals or is it other factors?" said study author Dr. Sharon Nachman of Stony Brook University in New York.

In an earlier study, Nachman and colleagues found that children with HIV and those with an HIV-positive family member had similarly high rates of psychiatric problems, suggesting environmental stressors. The new study analyzed data on 319 HIV-infected children and adolescents ages six to 17 enrolled in the International Maternal Pediatrics Adolescent AIDS Clinical Trials Group study in the United States and Puerto Rico.

One-third of the children had at least one psychiatric disorder, such as depression or attention-deficit hyperactivity disorder (ADHD). However, no link was found between antiretroviral therapy and any psychiatric problem.

"It wasn't the antiretrovirals," Nachman said. "It didn't matter which antiretrovirals the kids used. Those didn't predict or prevent a kid from getting a psychiatric illness" or having social or academic problems, she said.

In looking at markers of the severity of the disease, such as CD4 cell levels and viral loads, the results were mixed. Children with a lower CD4 percentage at baseline had less severe depression. Those with high viral loads at baseline had more severe depression. Children with the most severe disease at baseline did worse on cognitive tests of executive functioning, such as remembering a sequence of numbers, Nachman said.

"It appears if you had a high viral load at a younger age or a low CD4 percentage, you did get a hit on your brain" in terms of executive function, Nachman said. The study did not prove cause and effect, but it suggests HIV infection could affect the brain, she said.


Substance P Causes Seizures in Patients Infected by Pork Tapeworm

ScienceDaily (Feb. 9, 2012) — A neuropeptide called Substance P is the cause of seizures in patients with brains infected by the pork tapeworm (Taenia solium), said Baylor College of Medicine researchers in a report that appears online in the open access journal PLoS Pathogens.

"Neurocysticercosis or the tapeworm parasitic infection in the brain, is the major cause of acquired seizures," said Dr. Prema Robinson, assistant professor of medicine—infectious diseases, and corresponding author of the report. "It is particularly important to understand the source of these seizures in order to develop ways to treat and prevent them."

Substance P is a neuropeptide (a small protein−like molecule involved in neuron−to−neuron communication.) It is produced by neurons, endothelial cells (the cells that line blood vessels) and cells involved in host defense. Discovered in the 1930s, it has long been recognized as a pain transmitter. However, in recent years, it has also been found to play a role in many other functions.

Inflammation of the brain

Robinson realized that Substance P is involved in inflammation and wondered if it might be involved in seizure activity.

Robinson and her colleagues—including one from Tufts Medical Center in Boston—found Substance P in autopsies of the brains of patients who had the tapeworm infection. They did not find Substance P in uninfected brains.

"As long as the parasite is alive, nothing happens," said Robinson. However, once the worm dies, the body responds with chemicals that recruit immune system cells to the site of infection, causing inflammation. Her studies showed that the cells that produce Substance P are found mainly in areas of inflammation near the dead worms.

Animals injected with Substance P alone or with extracts from the areas of inflammation (granulomas) near the worms in infected mice suffered severe seizures, she said.

When the rodents received the drug that blocks the Substance P receptor, they did not have seizures, she said.
In addition, mice that lacked the Substance P receptor did not have seizures even when injected with the extracts of granulomas from infected mice. In addition, granuloma extracts from mice that lacked the cells that make Substance P did not induce seizures.

**Medications block receptor**

These findings have implications for people, who often suffer seizures during treatment for the tapeworm infection, she said. As the worms die, inflammatory cells rush to the scene and the seizures begin. There are medications known to block the receptor for Substance P. These medications may prove to be the most effective means of treating and preventing seizures in these patients.

Robinson plans to look at the role Substance P may play in other diseases associated with seizures such as cancer and tuberculosis.

**Journal Reference:**


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**Most Lethal Known Species of Prion Protein Identified**

Scientists from the Florida campus of The Scripps Research Institute have identified a single prion protein that causes neuronal death similar to that seen in “mad cow” disease, but is at least 10 times more lethal than larger prion species.

This toxic single molecule or “monomer” challenges the prevailing concept that neuronal damage is linked to the toxicity of prion protein aggregates called “oligomers.”

The study was published this week in an advance, online edition of the journal *Proceedings of the National Academy of Sciences*.

“By identifying a single molecule as the most toxic species of prion proteins, we’ve opened a new chapter in understanding how prion-induced neurodegeneration occurs,” said Scripps Florida Professor Corinne Lasmézas, who led the new study. “We didn’t think we would find neuronal death from this toxic monomer so close to what normally happens in the disease state. Now we have a powerful tool to explore the mechanisms of neurodegeneration.”

In the study, the newly identified toxic form of abnormal prion protein, known as TPrP, caused several forms of neuronal damage ranging from apoptosis (programmed cell death) to autophagy, the self-eating of cellular components, as well as molecular signatures remarkably similar to that observed in the brains of prion-infected animals. The study found the most toxic form of prion protein was a specific structure known as alpha-helical.

**New Paths to Explore**

In addition to the insights it offers into prion diseases such as “mad cow” and a rare human form Creutzfeldt-Jakob disease, the study opens the possibility that similar neurotoxic proteins might be involved in neurodegenerative disorders such as Alzheimer’s and Parkinson diseases.

In prion disease, infectious prions (short for proteinaceous infectious particles), thought to be composed solely of protein, have the ability to reproduce, despite the fact that they lack DNA and RNA. Mammalian cells normally produce what is known as cellular prion protein or PrP; during infection with a prion disease, the abnormal or misfolded protein converts the normal host prion protein into its disease form.

Lasmézas explains that prion diseases are similar to Alzheimer’s and other protein misfolding diseases in that they are caused by the toxicity of a misfolded host protein. Recent work, as reported in *The New York Times*, also found that diseases such as Alzheimer’s resemble prion diseases by spreading from cell to cell.

The new study adds another twist. “Until now, it was thought that oligomers of proteins are toxic in all these diseases,” Lasmézas said. “Since we found for the first time that an abnormally folded monomer is highly toxic, it opens up the possibility that this might be true also for some other protein misfolding diseases as well.”

**Journal Reference:**


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**New research reveals how protein protects cells from HIV infection**

Finding offers potential new drug targets aimed at slowing progression of disease

NEW YORK—A novel discovery by researchers at NYU Langone Medical Center and colleagues reveals a mechanism by which the immune system tries to halt the spread of HIV. Harnessing this mechanism may
open up new paths for therapeutic research aimed at slowing the virus’ progression to AIDS. The study appears online ahead of print today in *Nature Immunology.*

"A lot of research on viruses, especially HIV, is aimed at trying to understand what the body's mechanisms of resistance are and then to understand how the virus has gotten around these mechanisms," said co-lead investigator Nathaniel R. Landau, PhD, a professor of microbiology at the Joan and Joel Smilow Research Center at NYU School of Medicine.

The research focused on a protein called SAMHD1. Recent studies have found that immune cells, called dendritic cells, containing the protein are resistant to infection by HIV. Since the discovery, scientists have sought to understand how SAMHD1 works to protect these cells, with hopes that science might find a way to synthetically apply that protection to other cells.

Dr. Landau and his team are now able to provide an answer:

When a virus, like HIV, infects a cell, it hijacks the cell's molecular material to replicate. That molecular material is in the form of deoxynucleotide triphosphates (dNTPs), which are the building blocks for DNA. Once the virus replicates, the resulting DNA molecule contains all the genes of the virus and instructs the cell to make more virus.

Researchers wanted to understand how cells containing the SAMHD1 protein are protected from such hijacking. They found that SAMHD1 protects the cell from viruses by destroying the pool of dNTPs, leaving the virus without any building blocks to make its genetic information – a process researchers call nucleotide pool depletion. "SAMHD1 essentially starves the virus," Dr. Landau said. "The virus enters the cell and then nothing happens. It has nothing to build and replicate with, so no DNA is made."

As a result, the most common form of HIV does not readily infect these cells. Instead, the virus has evolved to replicate mainly in a different kind of cell, called CD4 T-cells, which do not contain SAMHD1 and therefore have a healthy pool of dNTPs. Dr. Landau explained that the virus has evolved in such a way that it may deliberately avoid trying to infect immune cells with SAMHD1 to avoid alerting the greater immune system to activate a variety of antiviral mechanisms to attack the virus. Viruses that are related to HIV, like HIV-2 and SIV, have developed a protein called viral protein X (VPX) that directly attacks SAMHD1. This allows the virus to infect dendritic cells, an important type of immune cell.

"Viruses are remarkably clever about evading our immune defenses," Dr. Landau said. "They can evolve quickly and have developed ways to get around the systems we naturally have in place to protect us. It's a bit of evolutionary warfare and the viruses, unfortunately, usually win. We want to understand how the enemy fights so that we can outsmart it in the end."

Understanding the mechanism by which SAMHD1 provides protection to cells may provide a new idea about how to stop or slow the virus' ability to spread, Dr. Landau explained. Potential future research efforts, for example, might focus on finding a way to increase the amount of SAMHD1 in cells where it does not exist, or to reduce the amount of dNTPs in cells vulnerable to infection.

"Over the past few years, a number of these natural resistance mechanisms have been identified, specifically in HIV, but some have potential applications to other viruses, as well," he said. "This is a very exciting time in HIV research. Many of the virus' secrets are being revealed through molecular biology, and we're learning a tremendous amount about how our immune system works through the study of HIV."

**Tenofovir associated with increased risk of kidney disease**

Michael Carter
Published: 13 February 2012

Treatment with tenofovir is associated with a modestly increased risk of three key markers of kidney disease, US investigators report in the online edition of *AIDS.*

The large study involved over 10,000 patients who started antiretroviral therapy between 1997 and 2007. Patients treated with tenofovir were significantly more likely to develop proteinuria (high levels of protein in urine), experience a rapid decline in kidney function and have an estimated glomerular filtration rate below 60 ml/min/1.73 m³ (chronic kidney disease, or CKD). The risk of kidney disease also remained elevated for patients who discontinued tenofovir therapy.

“Even after accounting for demographics, HIV-related factors, comorbidities, and other antiretroviral drugs, tenofovir remained associated with an increased risk for each kidney disease outcome," write the investigators.

The authors stress the drug's association with proteinuria and CKD, noting "each is independently associated with cardiovascular disease and death in the setting of HIV infection."
However, they also emphasise the importance of tenofovir in HIV treatment and that the risk of kidney disease associated with the drug should be balanced against its potential benefits. Moreover, the authors do not regard their research as definitive and call for further research.

Patients with HIV have an increased risk of kidney disease. The exact causes are controversial, but appear to include the effects of HIV itself, traditional risk factors such as hypertension and diabetes, co-infection with hepatitis C, and possibly the side-effects of some antiretroviral drugs.

The research exploring the association of tenofovir (Viread, also available in the combination pills Truvada and Atripla) with kidney disease is contradictory. Although some studies found an association between the drug and kidney dysfunction, this was not the case with others.

Differences in patient populations, limited sample sizes and lack of access to the appropriate laboratory data could be the reason for the lack of concordance between studies.

It is important to establish if the drug does increase the risk of kidney disease. Tenofovir is widely used in first-line antiretroviral therapy and also has an important role in pre-exposure prophylaxis (PrEP) regimens. Moreover, kidney dysfunction is a risk factor for cardiovascular disease, which is an increasingly important cause of illness and death in patients with HIV.

Therefore investigators from the US Department of Veterans Affairs designed a study to determine the effects of tenofovir exposure on the risk of kidney disease.

Their study population comprised 10,841 patients who started antiretroviral therapy for the first time over a ten-year period between 1997 and 2007. A total of 4,303 individuals were exposed to tenofovir. There was no difference between the tenofovir-treated patients and the patients treated with alternative antiretroviral drugs in terms of the prevalence of diabetes and hypertension, hepatitis C co-infection, CD4 cell count and viral load. Prevalence of proteinuria at baseline was comparable between the two groups of patients.

The overall mean age was 46 years and 98% of individuals were men.

Mean duration of tenofovir therapy was 1.3 years. The investigators acknowledge that this short period of treatment was a limitation of their study.

The study did not report on the absolute risk of kidney disease. 

In the entire study population there were 3400 proteinuria events in 38,132 person-years of follow-up; 3,078 rapid declines in kidney function during 51,589 person years; and 533 CKD events in 56,416 person years.

In all the investigators’ models, both any use of tenofovir and cumulative exposure to the drug was strongly associated with a significant increase in the risk of all three markers of kidney disease (p = 0.0033 to p < 0.0001).

Therapy with tenofovir was also associated with the presence of both proteinuria and CKD (p = 0.0014), a more stringent measure of kidney disease.

Multivariate analysis which controlled for other variables that could affect the risk of developing kidney disease showed that each year of tenofovir treatment was associated with a 34% increased risk of proteinuria (95% confidence interval 25%–45%, p< 0.0001), 11% increased risk of rapid decline in kidney function (95% CI 3%–18%, p=0.0033) and a 33% increased risk of chronic kidney disease (95% CI 18%–51%, p<0.0001).

Patients who ceased tenofovir therapy continued to have an increased risk of CKD which was of borderline significance (HR = 1.22 per year; 95% CI, 0.99-1.50, p = 0.055).

“The effects of tenofovir on kidney disease risk were not reversible following discontinuation,” comment the authors.

However the presence of other risk factors for kidney disease did not increase the risk of kidney disease while taking tenofovir; indeed, the association between tenofovir treatment and kidney disease was significantly weaker in older people, diabetics and people with cardiovascular disease or hypertension when compared to younger people or those without these conditions.

Tenofovir was the only anti-HIV drug with significant associations for all three measures of kidney disease used in the study. Nevertheless, several other drugs increased the risk of individual measures of renal dysfunction. For instance, ritonavir (Norvir) increased the risk of proteinuria (p < 0.0001). Atazanavir (Reyataz) was associated with a rapid decline in kidney function (p = 0.0035), and abacavir (Ziagen, also in the combination pills Kivexa and Trizivir) had a significant association with CKD (p = 0.0019).

The authors were well aware of the apparent significance of their findings and their potential to cause alarm among patients. They therefore believe it is important to balance the benefits and risks of therapy with the drug.
“Despite tenofovir’s association with progressive kidney disease, it is an important component of effective antiretroviral therapy that may be required in many patients to control viral load,” conclude the investigators. “The balance between its efficacy and probably adverse events requires further study.”

Reference

February 14, 2012, 11:50 AM HKT

Controversy Over China Push to Eliminate Anonymous HIV Tests

Health officials in southern China are proposing new legislation to require real-name registration for HIV testing, a move aimed at lowering infection rates that has sparked controversy over personal privacy. According to a recent report by state-owned Xinhua News Agency, the proposed legislation in China’s Guangxi Zhuang autonomous region, which has one of the highest AIDS rates in the country, would also mandate those who test positive to inform spouses and partners.

Local congress is expected to review the draft regulation for approval, Xinhua said, without specifying a timeframe.

The proposed rules have ignited debate over the privacy of medical patients in China and raised questions about the consequences of requiring people to disclose their identity when testing for the virus. Privacy advocates argue that draft legislation would likely drive away a high-risk population who would otherwise test if their privacy were protected.

Discrimination against China’s estimated 740,000 HIV-positive is highly prevalent in the country. People with AIDS are often barred from jobs in state-owned and private companies and government protection is not guaranteed, despite the existence of anti-discrimination laws.

In 2010, a Chinese court ruled against a man who claimed he was denied a teaching job after the potential employer discovered he was HIV-positive.

Xinhua quoted Li Hu, who runs an HIV support group in China’s northern city of Tianjin, as saying that members of high-risk groups including gay and bisexual men, sex workers and drug users may fear information leaks and dodge HIV testing as a result of the new rules.

HIV testing has dropped sharply in Beijing since similar legislation was passed in the city last year, according to a separate report from state-owned China Daily.

Senior health officials in Beijing are backing the legislation, saying that identity disclosure will boost the speed of test results and early treatment, Xinhua said, citing Wang Yu, director of the Chinese Center for Disease Control and Prevention.

Informing people of their HIV-positive status will also drastically reduce the odds that the virus will be passed to others, Xinhua quoted Mr. Wang as saying: “HIV carriers might spread the virus to others through unprotected sex or other channels. Under such circumstances, should we protect the privacy of the carriers, or control the epidemic and protect public health?” he said.

Xinhua and China Daily both quoted AIDS patients saying that real-name registration was a step in the wrong direction for China’s HIV movement, which has progressed in recent years.

Last year, Li Keqiang, China’s vice premier, announced plans to expand free HIV counseling and testing services in the next five years. In 2010, China lifted its ban against foreign visitors with HIV. Chinese with AIDS have access to free antiretroviral drugs.

SWAZILAND: Reaching out to gays for the first time

MBABANE, 14 February 2012 (PlusNews) — If caught, any Swazi engaged in a same-sex relationship will be arrested and jailed. But public health officials are using Valentine’s Day to urge gays to trust promises of confidentiality and test for HIV.

"February is known as the month of love, when couples express their love for each other through gifts, especially on Valentine’s Day. The purpose of our new campaign, called 'The Love Test', is to encourage couples to undergo HIV testing," said Simon Zwane, Deputy Director of Health.

He acknowledged that in Swazi society gay sex is taboo but said the health ministry was actively extending its reach to include gay couples in HIV counselling and testing.

"Couples need to be consistently aware of their HIV status. This will result in them making joint decisions on risk reduction in their relationships," said Zwane.

Swaziland’s HIV prevalence has remained the world’s highest for years, with about a quarter of all adults living with HIV.
Several NGOs, including the Alliance of Mayors’ Initiative on Coordinated Action against AIDS at the Local Level (AMICAALL) and the family planning company, PSI International, are partners in the nationwide campaign, the first health initiative in the small impoverished country to acknowledge the existence of gays and welcome them to make use of HIV testing and counselling services.

"Just admitting that there are gays in Swaziland is a big step for a government ministry," said Alicia Dlamini, a HIV testing counsellor in Manzini, the country’s industrial hub.

Three months ago the Minister of Justice and Constitutional Affairs, Magwagwa Gamedze, a traditional chief appointed by King Mswati, dismissed a recommendation by a United Nations working group on human rights that Swaziland enact a law to protect gay members of society. Gamedze said so few, if any, gays live in Swaziland that the bother of drafting such a law was not worth the effort.

"It was difficult for government to formulate a policy on homosexuals or enact a law to recognize them because they actually formed a minority if ever they existed. Their numbers do not permit us to start processing a policy," the justice minister said.

Very little information is available on same-sex couples in Swaziland and no gay organizations are involved in "The Love Test" campaign. The Gays and Lesbians Association of Swaziland (GALESWA), formed in the 1990s, has only one known member.

The constitution does not safeguard the rights of homosexuals, and sodomy laws dating from the early 20th century are still on the books. King Mswati has reportedly called same-sex relationships "satanic", and Prime Minister Barnabas Dlamini has called homosexuality "an abnormality and a sickness".

Human rights groups regularly criticize Swaziland for its anti-gay laws, and note that discrimination against gays is routine and acceptable in the conservative society of this small country.

"AIDS is not a 'gay disease' in Swaziland. It is almost entirely spread by heterosexual relationships... No one blames gays for AIDS in Swaziland, they just blame gays for being alive and being gay, so it is hard for a gay person to risk exposure," Alicia Dlamini pointed out.

Dlamini’s fellow HIV counsellor, Thamie Shongwe, feels the health ministry's Valentine's campaign to test couples will fail to attract same-sex couples.

Lucky Gama (not his actual name), 24, a gay auto mechanic, agreed. "A lot of gays are afraid that if they go to get tested they will be found out and disgraced. Maybe the police will be called to arrest you, because this is Swaziland."

There is a high level of mistrust. "I have heard of my gay friends say they are in fear because there is a test they give you without you knowing it that shows if you are gay," Gama said. “I did get an HIV test but it was at school when all the students volunteered to take a test, so the testers were not on the lookout for gays.”

**HIV rate way down thanks to condoms**

KATHARINE CHILD | 14 February, 2012 00:33

The rate at which South Africans contracted HIV fell by 30% between 2000 and 2008, mostly due to increased condom use, according to a new study published in the Royal Society journal Interface last month.

The study was conducted by an actuarial scientist and epidemiologist from the University of Cape Town, an expert from the Human Sciences Research Council and another from the department of infectious disease epidemiology at London’s Imperial College.

One of the study’s authors, Leigh Johnson, of the university’s school of public health, said that the study used mathematical models to work out what is contributing to the significant decrease in HIV infections.

The evidence links condom use to the 30% decrease in the rate of infection and finds that advertising campaigns played a role in encouraging condom use.

The increases in reported condom use coincided with the introduction of HIV education programmes.

Johnson said that the results of the study are important because there has been increasing scepticism about donating money to programmes that encourage condom use and behaviour change—such as being tested or reducing the number of sexual partners.

He said it is often easier to get funding for bio-medical interventions that are measurable, such as medical circumcisions.

Results from the study also showed that "people weren’t using condoms as often as they said they were, or condoms were less than 90% effective".

Researchers believed that people tend to over-report their usage of condoms.
The publication of the study coincides with the third National HIV Communication Survey, which measures the effectiveness of HIV communication campaigns and the role they play in encouraging and maintaining beneficial behaviour change.

The survey was commissioned by NGOs loveLife and Soul City, the Johns Hopkins University health and education research unit in South Africa, and Health and Development Africa, which provides technical assistance in health and development.

The director of the Johns Hopkins unit, Richard Delate, said that previous studies had showed that young men were using condoms far more often.

"Condom use by young men aged 16 to 24 increased from 20% in 1999 to 75% in 2009," he said. However, Delate said, condoms are not always available.

There are huge problems in some areas where there were less than 10 to 15 condoms available per sexually active man over a year.

Figures from the 2008 and 2009 survey show that the City of Johannesburg made about eight condoms available to each sexually active man each year, and the Ekurhuleni municipality on the East Rand provided about six.

Projected Life Expectancy of People with HIV According to Timing of Diagnosis

* AIDS Vol. 26; No. 3: P. 335-343, (01.28.2012) Fumiyo Nakagawa; and others

"Effective antiretroviral therapy has contributed greatly toward survival for people with HIV, yet many remain undiagnosed until very late. Our aims were to estimate the life expectancy of an HIV-infected MSM [man who has sex with men] living in a developed country with extensive access to ART and health care, and to assess the effect of late diagnosis on life expectancy," the researchers wrote.

A stochastic computer simulation model of HIV infection and ART’s effect was used to estimate life expectancy and determine the distribution of potential lifetime outcomes of a 30-year-old MSM who becomes HIV-positive in 2010. The effect of altering the diagnosis rate was investigated.

Projected median age at death (life expectancy) was 75.0 years, assuming a high rate of HIV diagnosis (median CD4 cell count at diagnosis, 432 cells/µl); this implies an average of 7.0 years of life lost due to HIV. Cumulative risks of death by five and 10 years after infection were 2.3 percent and 5.2 percent, respectively. "The 95 percent uncertainty bound for life expectancy was (68.0, 77.3) years. When a low diagnosis rate was assumed (diagnosis only when symptomatic, median CD4 cell count 140 cells/µl), life expectancy was 71.5 years, implying an average 10.5 years of life lost due to HIV," according to the results.

"If low rates of virologic failure observed in treated patients continue, predicted life expectancy is relatively high in people with HIV who can access a wide range of antiretrovirals. The greatest risk of excess mortality is due to delays in HIV diagnosis," concluded the researchers.

Archbishop: Don't Hand Out Condoms


A Roman Catholic archbishop has asked the Philippines Department of Health not to hand out condoms to couples on Valentine's Day, as it did last year. “The Church is against the distribution of condoms ... because we know how the use of contraceptives affects the morality of our people and our society in general,” Jaro Archbishop Angel Lagdameo said Friday. The key to a society without HIV/AIDS, he said, is "abstinence, fidelity to one’s spouse, and obedience to God's will."

Bird Flu Controversy An Opportunity To Set A Higher Tone For Public Debate

In this Huffington Post opinion piece, Leslie Gerwin, associate director of law and public affairs at Princeton University, reflects on the recent controversy over whether to research and publish data about potentially dangerous strains of the H5N1 bird flu virus, writing, "I am disturbed that so much coverage of this dispute—so deserving of sober consideration—is fixated on fear mongering." She notes, "Those opposing research or publication ... predict that publishing results will lead to abuse or misuse by terrorists looking to create a biological weapon. ... Those favoring continuation of the project warn of 'censorship,' a constitutional no-no particularly when involving the 'suppression' of science."

"These are indeed legitimate concerns, but framing the debate in terms of the worst-case scenario does not promote public enlightenment. ..., Scientists and the public health community are losing an opportunity to set a higher tone for public debate in which reasonable people disagree and to make the rest of us smarter and safer as a result," she continues. She concludes, "Rather than simplifications, accusations, and headline grabbing worst-case scenarios, scientists can help the public understand that
sometimes decisions must be made without complete information. ... In short, scientists examining whether to pursue and publish H5N1 and other contagious disease research have an opportunity to provide a model for public policy debates at a time when public discourse is degenerating” (2/10).

**Diagnostics for viruses a step closer to reality**

Scientists have developed a technique which could form the basis of a non-invasive diagnostic for Adenovirus – the virus responsible for a large number of common illnesses.

The biosensor technology developed by researchers at the University of Leeds can not only detect the presence of the virus, it can also identify the individual strain and the number of virus particles present. The study underpinning this research is published today (15 February) in the journal *Biosensors & Bioelectronics*.

Currently, testing for viruses is complicated, time consuming and requires specialist preparation of samples to identify virus DNA. Using this new technique, testing for viruses could be much quicker, simpler and ultimately less costly. For patients, this sort of diagnostic would mean faster treatment.

"This is a significant leap forward in testing for viruses," says Professor Paul Millner of the University’s Faculty of Biological Sciences, who supervised the study. "For the first time we’ve been able to test for the presence of a whole virus, rather than having to seek out its genetic material, and the first time the number of virus particles has been counted using a lab-on-a-chip device. These are both exciting developments."

Adenovirus is a common virus found in vertebrates and causes many illnesses, from the common cold through to gastroenteritis. People with strong immune systems are not badly affected by the virus, but for those with a compromised or immature immune system—such as small children or HIV sufferers—it can have fatal consequences.

The new technique uses antibodies attached to an electrical sensor. By measuring the sensor's electrical changes, researchers were able to identify how many virus particles were present, and determine the type of virus dependent on its response.

"There’s a long way to go before the technology might reach a doctor’s surgery, but we’ve proven the concept," says Rebecca Caygill, the PhD student behind the study. "We now need to increase the sensitivity of the test and optimise the different stages of the process so that we can consider scaling it up for clinical trials."

**New molecule can tangle up DNA for more than 2 weeks**

*Molecule is important step along the path to someday creating drugs that can go after rogue DNA directly*

AUSTIN, Texas — Chemists at The University of Texas at Austin have created a molecule that's so good at tangling itself inside the double helix of a DNA sequence that it can stay there for up to 16 days before the DNA liberates itself, much longer than any other molecule reported.

It's an important step along the path to someday creating drugs that can go after rogue DNA directly. Such drugs would be revolutionary in the treatment of genetic diseases, cancer or retroviruses such as HIV, which incorporate viral DNA directly into the body's DNA.

"If you think of DNA as a spiral staircase," says Brent Iverson, professor of chemistry and chair of the department of chemistry and biochemistry, "imagine sliding something between the steps. That's what our molecule does. It can be visualized as binding to DNA in the same way a snake might climb a ladder. It goes back and forth through the central staircase with sections of it between the steps. Once in, it takes a long time to get loose. Our off-rate under the conditions we used is the slowest we know of by a wide margin."

Iverson says the goal is to be able to directly turn on or off a particular sequence of genes.
"Take HIV, for example," he says. "We want to be able to track it to wherever it is in the chromosome and just sit on it and keep it quiet. Right now we treat HIV at a much later stage with drugs such as the protease inhibitors, but at the end of the day, the HIV DNA is still there. This would be a way to silence that stuff at its source."

Iverson, whose results were published in Nature Chemistry and presented this month at a colloquium at NYU, strongly cautions that there are numerous obstacles to overcome before such treatments could become available.

The hypothetical drug would have to be able to get into cells and hunt down a long and specific DNA sequence in the right region of our genome. It would have to be able to bind to that sequence and stay there long enough to be therapeutically meaningful.

"Those are the big hurdles, but we jumped over two of them," says Iverson. "I'll give presentations in which I begin by asking: Can DNA be a highly specific drug target? When I start, a lot of the scientists in the audience think it's a ridiculous question. By the time I'm done, and I've shown them what we can do, it's not so ridiculous anymore."

In order to synthesize their binding molecule, Iverson and his colleagues begin with the base molecule naphthalenetetra carboxylic diimide (NDI). It's a molecule that Iverson's lab has been studying for more than a decade.

They then piece NDI units together like a chain of tinker toys.
"It's pretty simple for us to make," says Amy Rhoden Smith, a doctoral student in Iverson's lab and co-author on the paper. "We are able to grow the chain of NDIs from special resin beads. We run reactions right on the beads, attach pieces in the proper order and keep growing the molecules until we are ready to cleave them off. It's mostly automated at this point."

Rhoden Smith says that the modular nature of these NDI chains, and the ease of assembly, should help enormously as they work toward developing molecules that bind to longer and more biologically significant DNA sequences.

"The larger molecule is composed of little pieces that bind to short segments of DNA, kind of like the way Legos fit together," she says. "The little pieces can bind different sequences, and we can put them together in different ways. We can put the Legos in a different arrangement. Then we scan for sequences that they'll bind."

SIV infection may lead to increase in immune-suppressive Treg cells
Original research and accompanying editorial highlight mechanism for regulatory T-cell accumulation in lymphoid tissue
February 13, 2012
(SACRAMENTO, Calif.) —
Tissue in monkeys infected with a close relative of HIV can ramp up production of a type of T cell that actually weakens the body's attack against the invading virus. The discovery, in lymph nodes draining the intestinal tract, could help explain how the HIV virus evades the body's immune defenses.

If the same pattern is found in people infected with HIV, the finding could lead to a treatment strategy that slows the production of this restraining type of T cell. This would let the immune soldiers go after the virus more aggressively.

The scientists don't know if the simian virus is directly causing the build-up of the inhibitory T cells, called regulatory T cells, but in any case, reducing regulatory T-cell production could boost the body's resistance to the evasive virus.

The research was a collaboration among scientists at the UC Davis School of Medicine, Cincinnati Children's Hospital and the California National Primate Center.

Regulatory T cells, or Tregs, normally tamp down immune-system attacks, presumably to prevent an over-active assault that can cause harmful inflammation or auto-immune disease. The scientists suspect that the high number of Treg cells in the infected primates might prevent their immune systems from mounting a full-on attack against the virus.

The researchers focused on immune cells called dendritic cells that interact with Tregs in preparation for their policing duty. This occurs in lymph nodes throughout the body's lymphatic system — the part of the circulatory system that also drains many organs of fluids, fatty acids and other substances.

The study found that mature dendritic cells were particularly active in promoting Treg production, and that these promoters were in high concentration in nodes draining the intestine, or mucosa. The
intestinal mucosa is the site of early infection and aggressive transmission for both the primate virus and HIV, making it the first line of defense against the invasion.

"The intestinal mucosa contains highly activated 'helper' T-cells that are prime targets for the HIV virus, so it is important to understand how the body fights HIV in this under-studied tissue," said Barbara Shacklett, associate professor of medical microbiology and immunology at the UC Davis School of Medicine.

"We consider the GI tract as a major 'battlefield' between the immune system and HIV. If we can better understand what happens there, we may finally learn how to eradicate the virus," said Shacklett. Shacklett is a co-author of a paper on the research, entitled "Myeloid dendritic cells isolated from tissues of SIV-infected Rhesus macaques promote the induction of regulatory T cells," published Jan. 28 in the journal AIDS. Julia Shaw, a graduate student in Shacklett's lab, co-led the research with Pietro Presicce of the Cincinnati Children's Hospital Research Foundation.

An editorial in the same issue of AIDS highlights the new research and related studies that are clarifying the interaction between the simian version of HIV and the Treg cells that can control attacks against them.

Shacklett stressed that Tregs usually increase when the immune system is at risk of over-reacting. Their high numbers lead to a reduced immune attack, although the mechanism is not well understood.

But in persistent infections—when a strong immune response is called for—Tregs should decrease in number, taking a "hands-off" approach and freeing the immune army to advance. HIV may sabotage this control by prompting increased Treg production as if the body need not rally its defenses against the virus.

The research draws on earlier research by Shacklett, Shaw and colleagues comparing Treg counts in rectal mucosa of people with high and low HIV viral load. They showed that high viral load was associated with increased frequencies of immunosuppressive Treg in the gastrointestinal mucosa, suggesting these Tregs might be thwarting the body's immune defenses.

**Scientist Works to Detach Protein That HIV Uses as Protective Shield**

ScienceDaily (Feb. 13, 2012) — One of the frustrations for scientists working on HIV/AIDS treatments has been the human immunodeficiency virus' ability to evade the body's immune system. Now an Indiana University researcher has discovered a compound that could help put the immune system back in the hunt.

It's not that the human immune system doesn't recognize HIV. Indeed, an infection causes the body to unleash antibodies that attack the virus, and initially some HIV is destroyed.

But HIV is able to quickly defend itself by co-opting a part of the innate human immune system—the immune system people are born with, called the complement. The complement includes a vital mechanism that prevents immune system cells from attacking the body's own cells. HIV is able to incorporate a key protein in that self-protection mechanism, CD59, and by doing so makes itself appear to be one of the body's normal cells, not an infective agent.

In laboratories at the Indiana University School of Medicine, Andy Qigui Yu, M.D., Ph.D., assistant professor of microbiology and immunology, is testing a promising compound that may counteract HIV's ability to hijack the immune system's protection mechanism.

"HIV is very clever. As it replicates inside cells, it takes on the CD59. The virus is covered with CD59, so the immune system treats the virus like your own normal cells," Dr. Yu said.

In November, the Bill & Melinda Gates Foundation announced it had awarded nine new Grand Challenges Explorations Phase II grants, one of them to Dr. Yu. The Phase II grants were awarded to researchers who had received initial $100,000 awards and had shown promising results.

The new grant will support not only Dr. Yu's research into compounds that may block the ability of HIV to hide behind the CD59 "cloak," but also his work to identify the mechanism the virus uses to incorporate CD59.

"If we find that mechanism, then we can develop something to block that incorporation, and HIV may lose that protection from the immune system," Dr. Yu said.

Researchers have been able in the past to generate antibodies that successfully attacked HIV in the laboratory. But these antibodies have failed in human testing because the virus in the body escapes from immune system attacks, Dr. Yu said.

In an attempt to disrupt HIV's hijacking of CD59, Yu and colleagues at IU and Harvard University crafted a molecule from a bacterial toxin that is known to bind to the CD59 protein. In laboratory tests,
they administered the molecule to blood samples taken from patients with HIV. The bacteria toxin molecule latched on to the CD59 proteins, revealing the viral particles to be invaders and enabling the antibodies to attack the virus.

Reporting their findings in the *Journal of Immunology* in December 2010, the researchers suggested that the molecule could potentially be developed into a new therapy to fight HIV/AIDS.

More recent experiments have indicated that the administration of the molecule enabled the antibody-complement to attack infected cells and not just the virus particles found in the blood samples. The next steps will include more extensive testing of the molecule in a broader range of patient samples, Dr. Yu said.

**Half of all new HIV transmissions in US may originate in undiagnosed individuals**

Michael Carter  
Published: 15 February 2012  
Almost half of all new HIV transmissions in the US originate in individuals who are unaware that they are HIV-positive, a modelling study published in the online edition of *AIDS* estimates.

Only 20% of HIV infections in the US are undiagnosed, but the investigators calculated that they were the source of 49% of all new onward transmissions.

“Decreasing the number of persons unaware of their infection must remain a priority goal of HIV prevention efforts,” comment the authors.

With appropriate treatment and care the prognosis of many HIV-positive patients is now normal. Virologically suppressive antiretroviral therapy also has wider public health benefits, reducing the risk of HIV transmission by 96%.

Late diagnosis is the principal factor underlying much of the HIV-related mortality that continues to be seen in resource-rich countries. Several studies have also suggested that a disproportion amount of new HIV transmissions have their source in undiagnosed individuals.

Testing is therefore a cornerstone of efforts to control HIV. Opt-out HIV testing is now recommended in the US for adolescents and adults aged between 13 and 64 years as part of their routine health care. Screening at least annually is recommended for patients with higher risk of the infection.

Previous research has suggested that HIV transmission rates in the US are 3.5 times higher for undiagnosed individuals compared to patients whose infection has been diagnosed.

Investigators updated the information used to arrive at this estimate, taking into account revised estimates of the proportion of undiagnosed infections and the impact of virologically suppressive HIV therapy on infectiousness.

The model was based on HIV prevalence rates in 2008 and HIV incidence between 2006 and 2009. The proportion of HIV-positive individuals unaware of their infection was 20%, and 39% of patients had a viral load below 400 copies/ml. Other variables included in the model were estimates of the frequency of unprotected sex with HIV-negative partners. The model also took account of the proportion of patients who were successfully linked to HIV care and retained in care.

An estimated 49% of all new transmissions were from individuals who were unaware of their infection status.

If the proportion of diagnosed patients with a viral load below 400 copies/ml increased to 60%, this increased the burden of new transmissions attributed to undiagnosed individuals to almost 60%.

“Increasing the percentage with viral suppression substantially reduced the percentage of transmissions form persons aware of their infection,” comment the authors. “The impact could be even further strengthened with implementation of revised recommendations for antiretroviral treatment for patients with CD4 cell count below 500 cells/mm³, or even higher.”

The transmission rate for patients aware of their infection status varied between 1.8 and 2.7 per 100 persons. It was between three and seven times higher for undiagnosed individuals (9.2 to 12.6 per 100 persons).

In a scenario when 39% of HIV-positive patients had a viral load below 400 copies/ml, then each increase of 100 in the number of diagnosed infections was estimated to avert eight new transmissions.

However, simply reducing the number of undiagnosed infections is not enough in itself to control the HIV epidemic. The authors stress that patients then have to be promptly connected with a specialist clinic, retained in care and achieve virological suppression.

“While current estimates of the percentage of persons diagnosed with HIV who are linked to care are relatively high (69% to 82%), the percentage of persons retained in care is much lower (45% to 59%) and
estimates of the percentage with viral suppression range from 24% to 39% for those who are aware of their infection.”

The authors conclude: “Additional efforts are needed to reduce the number of people unaware of their infection...reduce transmission rates, and improve linkage and retention in care and viral suppression.

Reference
Hall HI et al. HIV transmissions from persons with HIV who are aware and unaware of their infection, United States. AIDS 26, online edition. DOI: 10.1097/QAD013e328351f73f, 2012 (click here for the free abstract).

Hepatitis Central
February 14, 2012

Hepatitis C Survival on Inanimate Objects

We usually think of Hepatitis C as a virus that is passed from person to person. However, most infections occur via an intermediary, inanimate object. Thus, determining the length of time Hepatitis C can survive outside the body is crucial to prevent transmission of this virus.

By Nicole Cutler, L.Ac.

As an increasing number of people are being diagnosed with Hepatitis C, the demand to understand how this virus can be transmitted grows accordingly. Scientists know that the Hepatitis C virus (HCV) is primarily transmitted via blood to blood contact; however, there is usually an intermediary between infected blood and not-yet-infected blood. Depending on several different variables, the inanimate intermediary can keep HCV viable for a surprisingly long time.

Every virus has a different capability for surviving outside the body. According to Mayo Clinic internist James M. Steckelberg, MD, the length of time a virus survives depends partly on where the germ-laden droplets fall. Experiments with specific cold and flu germs have found the following:

• Potential survival times for a virus outside the body range from a few minutes to 48 hours or more.
• Cold and flu germs generally remain active longer on stainless steel, plastic and similar hard surfaces than on fabric and other soft surfaces.
• Demonstrating that all viruses are different, flu viruses seem to live longer than cold viruses do—regardless of the surface.
• Other factors affecting how long germs can survive outside of the body are the temperature of the environment, its humidity and the amount of virus deposited on the surface.

Several of these variables have a direct impact on how long HCV can survive outside the body. Testing blood on exposed surfaces while considering the surface's texture, room temperature, amount of blood exposed, viral load (low/high) and various contaminants in the environment makes the determination of how long Hepatitis C survives outside the body very complex.

Compared to other viruses, HCV is a relatively hardy pathogen. Known to survive outside the body for days in dried blood on surfaces, Hepatitis C can persist for months in a liquid medium under favorable conditions. According to the U.S. Centers for Disease Control and Prevention, HCV can survive on environmental surfaces at room temperature for at least 16 hours but no longer than four days. In contrast, the HIV virus can only live on surfaces for several hours.

• As reported in the June 15, 2010 edition of The Journal of Infectious Diseases, researchers from Germany confirmed that HCV survives longer in liquids than it does when dried on surfaces. They found that in a liquid environment, HCV was detectable for up to five months at lower temperatures.
• As published in a February 2010 edition of Virology Journal, Chinese researchers determined that HCV could survive in a liquid medium for two days at 98°F (body temperature), 16 days at 77 °F and at least six weeks at 40°F (average refrigerator temperature).
• Presented in February 2010 at the 17th Conference on Retroviruses & Opportunistic Infections, American researchers found that under the right circumstances, HCV remained viable in a syringe for up to 63 days. Circumstances that increased HCV infectivity include syringes with detachable needles, lower temperature and larger volume syringes.

HCV’s ability to live for a prolonged period of time outside the body under the right conditions has extraordinary implications for its transmission. Some of the carriers known to transmit the virus include straws used for nasal drug use, needles used for administering drugs, tattooing, sharing personal care equipment like razors or toothbrushes, certain sexual devices and reuse of medical equipment in healthcare settings.

Although we know that it is spread between blood sources, inanimate objects often act as the intermediary to transmit infection. Thus, understanding how long the Hepatitis C virus can survive...
outside the body—in all situations—can help guide us toward failsafe practices for reducing the risk of HCV transmission.

References:

Cost-effectiveness of HAART underestimated
Bohdan Nosyk and Julio Montaner of the British Columbia Centre for Excellence in HIV/AIDS in Vancouver, Canada argue in an Essay published in this week's PLoS Medicine that the cost-effectiveness of HAART roll out has been significantly underestimated, because economic analyses have not yet taken into account the beneficial impact of HAART on prevention of HIV transmission.

The authors comment: "the strategic value of expanded HIV testing and expansion of HAART coverage has dramatically increased. We believe this should open the door for wide-scale implementation of "Seek, Test, Treat and Retain" programs as a means to control HIV and AIDS-related morbidity, mortality, and transmission at once."


Cash payments help cut HIV infection rate in young women, study finds
Research in Malawi finds girls who receive regular payments are able to resist attentions of older men and avoid infection

The randomised controlled trial was carried out in one of the poorest parts of Malawi. Photograph: Martin Godwin

Regular small cash payments to girls and young women can enable them to resist the attentions of older men and avoid HIV infection, according to a new study.

Girls and young women are at the greatest risk of HIV infection in endemic countries. In sub-Saharan Africa, between a quarter and a third have the virus by the time they reach their early 20s.

But educating girls about risks and promoting condom use has had little impact in countries where they are struggling with poor education, low status and poverty, and where older men with money offer one of the few ways out of financial difficulties.

A team of researchers from the World Bank, University of California at San Diego and George Washington University in the US carried out a randomised controlled trial in Malawi to find out whether monthly payments to schoolgirls and their families would help change the girls' behaviour and safeguard their health.

They recruited nearly 1,300 young women, aged from 13 to 22, who were enrolled in school in the Zomba district of southern Malawi – an area of poverty, low school enrolment and high HIV prevalence.

The young women were randomly assigned, according to where they lived, either to receive between $1 and £5 a month, with their families given between $4 and $10 a month, or to get nothing. At the end of 18 months, the girls were tested for HIV and herpes infection.

The study, published online by the Lancet, found that girls who had received money were less than half as likely to have HIV as those who had not been paid – 1.25% (seven out of 490 women) compared with 3% in the control group (17 out of 796).

While the numbers who contracted HIV were relatively small, the researchers believe it shows a significant trend and would make a substantial difference across the population. There was a reduction of three-quarters in the risk of herpes, another sexually-transmitted infection.
Half of those who were given money got it only if they attended school, but there was no difference in the infection rate between those and the others who were paid regardless. Nor did the amount they and their families received make a difference. Girls in the groups receiving payments were more likely to be in school than the others. Condom use did not go up, but the girls were less likely to be having sex frequently and less likely to have a partner over the age of 25.

"The findings suggest that financially empowering school-age girls and their families can have substantial effects on their sexual and reproductive health," write the authors.

In a commentary also published by the journal, Dr Nancy Padian, from the School of Public Health, University of California, Berkeley, and colleagues, say the findings "add to the increasing evidence suggesting that economic development and anti-poverty programmes can alter the context of sexual decision-making and, thus, HIV infection risk".

At a cost per case of HIV averted of $5000-$12,500 (£3,167-£7,918), paying individuals to stay healthy might seem expensive, they say, but it is still probably cost-effective and cheaper than putting people on antiretroviral drugs, which has been shown to reduce the risk of HIV infection.

Femidoms still a taboo
14.02.2012 Siphosethu Stuurman
The female condom, also known as the femidom, provides women with a condom of their own to use for protection against unplanned pregnancies and sexually transmitted diseases, such as HIV and AIDS. However, negative perceptions from the product’s intended users and a perceived low demand for female condoms have considerably slowed its distribution and accessibility.

Twenty-six year-old Lindiwe Zulu from Soweto, shares her experience using the female condom.

“I’ve tried them once and they were not very comfortable. So, I stopped using them then and there. They have these two huge rings that are very scary... I can’t insert that inside of me. Even my boyfriend didn’t like them. So, we use the male condoms”, says Lindiwe Zulu.

Though she had a bad first experience using the femidom, Lindiwe says she would like to give it another try.

“I think, maybe, the problem was that I didn’t know how to use it properly. So, if I get a chance to learn more about them, then I’ll try it again”, she says.

Twenty-one year-old William Mhlanga from Katlehlong also shared his thoughts.

“I have never used a female condom with my girlfriend. It’s nasty! Gosh! The size of it... It’s too big. I don’t think it will fit in the vagina”, says William Mhlanga.

Twenty-four year-old Nomonde Bua from Soweto admits that she’s never tried to use the female condom, though she’s known about it since her high-school days.

“Firstly, that thing is huge. I never tried using it because I don’t think it’s that comfortable. It’s such a turn-off. I don’t even know how it’s put on. I don’t think it will work for me. I prefer the male condom”, says Nomonde Bua.

However, she does realise the importance of the female condom as the only female-initiated protective method and that it has the potential to give women the power to practice safer sex.

“I think these condoms [femidoms] will help us as women if they could be introduced to us properly because, sometimes, amadoda [men] don’t want condoms. They will tell you stories, that: ‘I forgot to put on a condom’ or ‘no I didn’t get a chance to buy a condom’. But, if you have your condom, you can say: ‘Okay, here is my condom, let’s use mine’,” she says.

Tian Johnson, a Strategist for the African Alliance for HIV Prevention, says there are a lot of misconceptions around femidoms.

“There is the incorrect perception that there is no demand for the product. And the argument has always been that: How do you demonstrate demand in the absence of product? We still have some areas in this country where women have never seen female condoms”, says Tian Johnson.

Johnson also rubbished the arguments that femidoms are noisy and uncomfortable during sex.

“Who has silent sex? Why are we using the noise of a female condom during sex as a basis to deprive women and men of another tool to prevent HIV? On the issue of discomfort, we have a lot of research that proves that the more you use it, the more comfortable it becomes”, says Tian Johnson.

Currently, 5 million female condoms have been distributed across provinces. But, Johnson says although it’s difficult to gauge the actual demand for female condoms, this number is not nearly enough.
“We have 5 million that have been distributed. But if no more are procured, we foresee a shortage where there will be no stock in provinces”, says Tian Johnson.

Jeanette Hunter, the Chief Executive Officer of the Health Systems Trust, says there needs to be research into the advantages and disadvantages of the use of the female condom.

“We need to do some form of research to find out: Is there consensus around the fact that it's uncomfortable and not conducive to pleasant sexual intercourse? Or are there women who are using it and can actually be advocates for it? I think to just go out on a drive that ignores what may be bonafide complaints against the female condom would not be wise”, says Hunter.

**CDC Warns Untreatable Gonorrhea Is on the Way**


Gonorrhea is increasingly showing resistance to one of the last known effective antibiotic treatments, and researchers say it is time to “sound the alarm” about the potential for untreatable forms of the STD.

“During the past three years, the wily gonococcus has become less susceptible to our last line of antimicrobial defense, threatening our ability to cure gonorrhea,” Dr. Gail Bolan, director of CDC’s STD prevention program, and colleagues wrote in a perspective piece.

Gonorrhea has had a long history of developing resistance to antibiotics, CDC notes, but more effective drugs have usually been available to treat patients. However, today about 1.7 percent of gonorrhea cases are resistant to cephalosporins, the last line of defense against the STD. That is a 17-fold increase in such resistance since 2006, when surveillance data showed the prevalence of resistance was 0.1 percent.

The strains have been appearing most often in western states, where 3.6 percent are showing resistance to cephalosporins, and in men who have sex with men, with nearly 5 percent showing resistance, said Bolan. In the United States, it is estimated there are more than 600,000 incident cases of gonorrhea annually.

It is by using a combination of cephalosporins and other antibiotics that US doctors have been able to prevent gonorrhea infections from being completely untreatable, CDC spokesperson Nikki Mayes wrote in an e-mail. However, “The trends in decreased susceptibility that we’re seeing, coupled with the history of emerging resistance and reported treatment failures in other countries, point to the likelihood of treatment failures on the horizon,” she said.

“As far as gonorrhea goes, I am not aware of any new drugs in the pipeline,” said Nicole Mahoney, senior officer of the antibiotics and innovation project at PEW Charitable Trusts. While a gonorrhea vaccine “remains key to prevention and control,” it is a “distant goal,” Bolan noted.


**One Quarter Of Young Children Worldwide Suffer Effects Of Malnutrition, Save The Children Survey Shows**

"Malnutrition is the root cause of the deaths of 2.6 million children each year, and the bodies and brains of 450 million more will fail to develop properly due to inadequate diet over the next 15 years unless immediate action is taken, according to a survey published Wednesday by" Save the Children, the Guardian reports (Tisdall, 2/14). "A quarter of young children around the world are not getting enough nutrients to grow properly, and 300 die of malnutrition every hour," according to the survey, "A Life Free from Hunger: Tackling Child Malnutrition," the Independent writes (Valley, 2/15).

The survey, conducted in India, Bangladesh, Peru, Pakistan and Nigeria, "found that many families could not afford meat, milk or vegetables," BBC News writes, adding, "A third of parents surveyed said their children complained about not having enough to eat" (2/15). "Soaring food prices are identified as an aggravating factor," the Guardian writes, adding, "But these damaging trends can be halted and reversed using tried and tested solutions if political will exists and public awareness is raised, the report's authors say" (2/14). In a separate article, the Guardian examines child malnutrition in Bangladesh (Tran, 2/15). Al Jazeera provides a video report of child malnutrition in India (Suri, 2/14).

**Seven Sahel Region Nations Declare Emergencies With At Least 12M People Threatened By Hunger**

"Seven out of the eight governments in [Africa's] Sahel ... have taken the unprecedented step of declaring emergencies as at least 12 million people in the region are threatened by hunger," Inter Press Service reports.
Burkina Faso, Chad, Mali, Mauritania, Niger, Cameroon and Nigeria have all called for international assistance to prevent yet another hunger crisis on the continent," the news service writes, noting that Senegal "has refrained from announcing an emergency, largely for political reasons," as it is holding presidential elections later this year (Palitza, 4/15).

The U.N. and international aid agencies are warning more than 20 million people could be affected by drought and food shortages in the region, VOA News reports, adding that the U.N. "notes aid agencies have received only $135 million of the $720 million needed to fund humanitarian operations in six countries of the Sahel" (Schlein, 2/14). On Thursday, Under-Secretary-General for Humanitarian Affairs and Emergency Relief Coordinator Valerie Amos and U.N. Development Programme (UNDP) Administrator Helen Clark will begin a two-day fact-finding trip to Niger, where they will meet with government officials "to highlight the importance of preparations and early action to tackle the food and nutrition crisis," the U.N. News Centre writes (2/14). In a separate article, the U.N. News Centre reports on a new partnership between the U.N. and the African Centre of Meteorological Applications for Development that "will ensure the rapid dissemination of weather updates from African meteorological experts to disaster managers in vulnerable communities" (2/14).

**Contraceptive preferences among young Latinos related to decision-making 2-15-12**

CORVALLIS, Ore. – Half of the young adult Latino men and women responding to a survey in rural Oregon acknowledge not using regular effective contraception – despite expressing a desire to avoid pregnancy, according to a new Oregon State University study.

Researchers say the low rate of contraception among sexually active 18- to 25-year-olds needs to be addressed – and not just among Latino populations. Research has shown many young adults from all backgrounds eschew contraception for many reasons including the mistaken belief that they or their partners cannot get pregnant.

“The National Campaign to Prevent Teen and Unplanned Pregnancy calls this ‘magical thinking,’” said Jocelyn Warren, a public health postdoctoral fellow at OSU. “There is this tendency to believe that if you have unprotected sex once and nothing happens, somehow you are incapable of getting pregnant. It is a widespread issue and certainly not just applicable to our study of rural Latinos.”

Widening the scope of earlier work on the contraceptive practices of rural Latinos, the researchers asked questions about cultural and relationship characteristics whose possible links to contraceptive use had not been previously explored within this population.

The OSU study of 450 sexually active Latino men and women found that more involvement in sexual decision-making was important in contraception use – and increased the likelihood of using male condoms, rather than birth control pills or no method at all. While effective at preventing pregnancy, birth control pills don’t prevent sexually transmitted diseases, the researchers point out.

“People who reported being active decision-makers in their relationship tended to use male condoms, which makes sense because using a condom means that both partners have to agree,” said Warren, lead author on the study. “The importance of including men in delivering contraception services and family planning may strengthen effective use because women do not make these decisions alone.”

Another important finding from the study, which was published in the December issue of Perspectives on Sexual and Reproductive Health, showed that the less acculturated participants were, the more likely they were to use an effective female method rather than no effective method.

Marie Harvey, professor of public health at OSU and one of the study’s co-authors, said this study adds to the growing body of research that points to the need for sexual health research and interventions to be couple-oriented.

“Isolating and targeting women only is not entirely effective,” she said. “Programs and services aimed at preventing unintended pregnancy need to include men because we repeatedly find that women do not make decisions about contraception use on their own, and they do not always have the power in a relationship and this needs to be taken into account.”

**Oncolytic virus extends survival in medulloblastoma model**

- Medulloblastoma is the most common malignant brain tumor in children.
- Disseminated medulloblastoma is particularly lethal and requires extensive radiation therapy to the brain, which can cause brain damage.
- An oncolytic measles virus has shown effectiveness in a new model of disseminated human medulloblastoma.
COLUMBUS, Ohio – A strain of measles virus engineered to kill cancer cells prolongs survival in a model of medulloblastoma that is disseminated in the fluid around the brain, according to a new study by researchers at Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute and the Mayo Clinic. Treatment with the oncolytic virus called MV-GFP extended survival of animals with disseminated human medulloblastoma up to 122 percent, with treated animals surviving 82 days on average versus 37 days for controls. Two of the eight treated animals were left cancer-free.

The findings, published online in the journal *Neuro-Oncology*, could lead to a safer, more effective therapy for medulloblastoma, and particularly for disseminated medulloblastoma, the researchers say. Medulloblastoma accounts for 15 to 20 percent of all childhood brain tumors, with 350 to 400 new cases diagnosed annually in the United States.

Untreated, medulloblastoma is fatal. Current therapy for the disease involves surgery, multidrug chemotherapy and radiation therapy to the entire brain. Five-year survival is about 60 percent, but the extensive radiation therapy often leads to decreased intelligence.

Furthermore, in about 20 percent of newly diagnosed patients and 75 percent of patients with recurrent disease, the tumor has disseminated into the cerebrospinal fluid. Five-year survival for these children is less than 20 percent.

"Patients whose tumor has spread into the fluid around the brain and spinal cord have an especially grim prognosis," says principal investigator Dr. Cory Raffel, professor and vice-chair of neurological surgery.

"Because dissemination of tumor carries a grave prognosis, any treatment that can effectively treat this condition while avoiding radiation therapy could potentially improve survival in these patients and quality of life for survivors."

For this study, Raffel and his collaborators used two human medulloblastoma cell lines that they labeled with firefly luciferase, making the cells bioluminescent and enabling the researchers to track them as they dispersed in the living animal and responded to treatment with the oncolytic virus.

Three or 14 days after the cancer cells were implanted in the brain; the oncolytic virus was injected at the same location in five doses.

In the first medulloblastoma cell line tested, treated animals lived an average of 82 days compared with 37 days for the controls. Two of the eight animals were cured of the disseminated disease, which was determined first according to bioluminescent imaging, then histologically.

In a second experiment using a more virulent human medulloblastoma cell line, treated animals survived 37 days versus 16 days for controls, with one animal left cancer free.

Currently, the investigators are conducting studies to determine optimal dosing of the virus in preparation for a phase I clinical trial in humans.
Diabetes may start in the intestines, research suggests

Scientists at Washington University School of Medicine in St. Louis have made a surprising discovery about the origin of diabetes. Their research suggests that problems controlling blood sugar — the hallmark of diabetes — may begin in the intestines.

The new study, in mice, may upend long-held theories about the causes of the disease. Because insulin is produced in the pancreas and sugar is stored in the liver, many scientists have looked to those organs for the underlying causes of diabetes.

The findings are reported Feb. 16 in the journal *Cell Host & Microbe*.

In the new research, scientists studied mice that are unable to make fatty acid synthase (FAS) in the intestine. FAS, an enzyme crucial for the production of lipids, is regulated by insulin, and people with diabetes have defects in FAS. Mice without the enzyme in the intestines develop chronic inflammation in the gut, a powerful predictor of diabetes.

"Diabetes may indeed start in your gut," says principal investigator Clay F. Semenkovich, MD. "When people become resistant to insulin, as happens when they gain weight, FAS doesn't work properly, which causes inflammation that, in turn, can lead to diabetes."

First author Xiaochao Wei, PhD, and Semenkovich, the Herbert S. Gasser Professor of Medicine, professor of cell biology and physiology and director of the Division of Endocrinology, Metabolism and Lipid Research, collaborated with specialists in gastroenterology and genome sciences to determine what happens in mice that can't make FAS in their intestines.

"The first striking thing we saw was that the mice began losing weight," says Wei, a research instructor in medicine. "They had diarrhea and other gastrointestinal symptoms, and when we looked closely at the tissue in the gut, we found a lot of inflammation."

Initially, the researchers thought that the mice became sick because of changes to the mix of microbes that naturally live in the gut, where they help digest food and synthesize vitamins.

In collaboration with Jeffrey I. Gordon, MD, director of the Center for Genome Sciences and Systems Biology at the School of Medicine, they looked more closely at gut microbes in the mice.

"The mice had substantial changes in their gut microbiome," Semenkovich says. "But it wasn't the composition of microbes in the gut that caused the problems."

Instead, Wei says, the mice got sick because of a defect in fatty acid synthase. The mice without fatty acid synthase had lost the protective lining of mucus in the intestines that separates the microbes from direct exposure to cells. This allowed bacteria to penetrate otherwise healthy cells in the gut, making the mice sick.

In a further collaboration with Nicholas O. Davidson, MD, director of the Division of Gastroenterology, the researchers found gastrointestinal effects resembling some features of inflammatory bowel disease. Other investigators studying humans with ulcerative colitis had previously made the unexplained observation that colon biopsies from these patients have low amounts of fatty acid synthase.

"Fatty acid synthase is required to keep that mucosal layer intact," Wei says. "Without it, bad bacteria invade cells in the colon and the small intestine, creating inflammation, and that, in turn, contributes to insulin resistance and diabetes."

Inflammation and insulin resistance reinforce each other. Inflammatory substances can cause insulin resistance and inhibit the production of insulin, both of which interfere with the regulation of blood sugar. In turn, insulin resistance is known to promote inflammation.

Further study showed that the ability to build the thin, but important, layer of mucosal cells was hindered by faulty FAS.
That the gut is so important to the development of diabetes makes sense because many people with the condition not only have faulty FAS, but they also frequently develop gastrointestinal difficulties, Semenkovich says. "Abdominal pain and diarrhea are some of the most common problems we see in people with diabetes," he says. "We could only connect these 'dots' because other experts at the university could help us link what we observed in these mice to what occurs in patients with diabetes and inflammatory bowel disease," Semenkovich says.

Semenkovich and Wei say much more study is needed, but they say that FAS and a key component of the intestinal mucosa called Muc2 may be potential targets for diabetes therapy. They now plan to study people with diabetes to see whether FAS is altered in a similar way, producing damage to the mucosal layer in the intestines.


Prions Play Powerful Role in the Survival and Evolution of Wild Yeast Strains
ScienceDaily (Feb. 15, 2012) — Prions, the much-maligned proteins most commonly known for causing "mad cow" disease, are commonly used in yeast to produce beneficial traits in the wild. Moreover, such traits can be passed on to subsequent generations and eventually become "hard-wired" into the genome, contributing to evolutionary change.

Prions were first found to produce heritable new traits more than a decade ago in laboratory studies of simple baker’s yeast. The key discovery then was that some proteins could spontaneously switch from a normal shape into a self-perpetuating prion conformation. The switch to the prion state alters protein function, which can result in the appearance of new traits, some helpful, some detrimental. Sophisticated cellular machinery ensures that replicating prion templates are chopped into pieces that can be passed to daughter cells during cell division. Importantly, the rate at which proteins switch into and out of the prion state increases in response to environmental stress, suggesting that they are part of an inherent survival mechanism that helps yeasts adapt to changes in their surroundings.

Yet, as compelling as the case for this protein-based mechanism of inheritance is, its biological significance has been hotly debated for one key reason: prions capable of modifying phenotypes have never been found in nature. Until now.

In a massive undertaking, Whitehead Institute scientists have tested nearly 700 wild yeast strains isolated from diverse environments for the presence of known and unknown prion elements, finding them in one third of all strains. All the prions appear capable of creating diverse new traits, nearly half of which are beneficial. These unexpected findings, reported in this week’s edition of the journal Nature, stand as strong evidence against the common argument that prions are merely yeast "diseases" or rare artifacts of laboratory culture.

"A huge amount of effort has gone into studying this paradigm-shifting mode of inheritance, but with no real understanding of whether it’s genuinely important biologically," says Daniel Jarosz, co-first author of the Nature paper and a postdoctoral researcher in the lab of Whitehead Member Susan Lindquist. "Now it seems clear they do influence the way natural yeasts cope with changing environments and evolve in response to stress."

The hunt for prions in wild yeast strains began in the Lindquist lab when Jarosz and Randal Halfmann, then an MIT graduate student and now a fellow at the University of Texas Southwestern Medical Center, gathered hundreds of wild strains from stock centers all over the world. They then conducted a chemical screen for one well-studied prion, [PSI+], and found it in 10 wild strains. Genetic manipulations confirmed its status as a true prion. They then observed the effects of [PSI+] on biological traits by eliminating the prion conformation in these strains and exposing them to natural stresses, such as high acidity and the presence of antifungal agents. In one strain isolated from Beaujolais wine, for example, the prion resulted in the emergence of traits that could be beneficial or detrimental, depending upon environmental conditions. Another well-known prion, [MOT3+] was found in six wild strains.

To determine whether the wild yeasts might harbor other unknown prion elements, Jarosz and Halfmann exposed sets of cultures of all the wild strains to the same chemical protocol that switched [PSI+] and [MOT3+] out of their prion states. In all, 255 strains demonstrated different phenotypes under varying stressors after this treatment.

"We certainly didn't expect to see this much prion-based phenotypic diversity," Jarosz says. "It's remarkable."
Another surprise was that approximately 40% of the traits produced by the wild prions proved to be beneficial to growth in the dozen different environmental conditions tested. "How frequently beneficial they are suggests that the prions have already been subject to previous, positive selective events," says Lindquist. "We see them as part of a bet-hedging strategy that allows the yeast to alter their biological properties quickly when their environments turn unfavorable."

Convinced of the impact prions have had on yeast evolution, Lindquist speculates that these shape-shifting proteins may be "remnants of early life," from a time when inheritance was predominantly protein-based rather than nucleic-acid based. She also theorizes that prions may play such roles beyond yeast, and her lab intends to take similar approaches in the hunt for prion activity in other organisms.

**Journal Reference:**
Randal Halfmann, Daniel F. Jarosz, Sandra K. Jones, Amelia Chang, Alex K. Lancaster, Susan Lindquist. Prions are a common mechanism for phenotypic inheritance in wild yeasts. *Nature*, 2012; 482 (7385): 363 DOI: [10.1038/nature10875](https://doi.org/10.1038/nature10875)

**Antibodies to Intracellular Cancer Antigens Combined With Chemotherapy Enhance Anti-Cancer Immunity**
ScienceDaily (Feb. 13, 2012) — An international team of scientists in Japan, Switzerland, and the United States has confirmed that combining chemotherapy and immunotherapy in cancer treatment enhances the immune system's ability to find and eliminate cancer cells, even when the cancer-associated proteins targeted by the immune system are hidden behind the cancer cell membrane. In a study published in *Cancer Research* by Noguchi et al., the scientists show that antibodies, which have been successful in treating certain types of cancers, can effectively reach elusive intracellular targets, delaying tumor growth and prolonging survival when combined with chemotherapy.

"The study provides proof-of-principle for a powerful new strategy that may greatly expand the arsenal of potential targets for cancer drug development and that could be broadly applicable to many different cancer types," said Hiroyoshi Nishikawa, M.D., Ph.D., a Cancer Research Institute (CRI)-funded associate professor in the Department of Experimental Immunology at the Immunology Frontier Research Center, Osaka University, and a senior author on the paper.

The introduction of antibodies against cancer represents one of the biggest successes of cancer therapy over the past 20 years. These treatments work by targeting markers on the surface of cancer cells, and include the blockbuster therapies Herceptin, which targets the HER2/neu marker on breast cancer cells, and Rituxan, which targets the CD20 marker on B cell lymphoma.

The majority of markers that can distinguish cancer cells from normal cells, however, are found exclusively inside cancer cells, where antibodies typically cannot access them. "Therapies that can successfully target cancer antigens found within cancer cells may be able to fight cancer without causing unwanted side effects due to collateral damage to healthy cells," said study co-lead author Gerd Ritter, Ph.D., associate director of the New York Branch of the Ludwig Institute for Cancer Research (LICR), and a leading member of the CRI/LICR Cancer Vaccine Collaborative, which also supported the study.

To assess whether antibody treatment against an intracellular antigen might be successful, the researchers used an antibody against the prototypic cancer antigen NY-ESO-1 and tested it in a model of colon cancer engineered to express NY-ESO-1 within its cancer cells. Alone, the antibody had no effect against the cancer. By using chemotherapy to release NY-ESO-1 from the cancer cells prior to the administration of the antibody, however, they were able to significantly delay cancer progression and prolong survival. The researchers then tested the strategy in another cancer model using a different type of chemotherapy and showed similar results, demonstrating that this approach could be applicable to different tumor types using various standard chemotherapies.

By monitoring the immune responses to these treatments, the researchers on the study found that the anti-tumor effect of the combination was dependent on CD8+, or killer, T cells. Rather than working to kill the cancer cells directly, the antibody worked by binding to the NY-ESO-1 antigen and facilitating its presentation to CD8+ T cells, which then exerted the anti-tumor effects. These findings not only have implications for how scientists understand the mechanisms of current antibody treatments for cancer, but they also shed light on a fundamental question in clinical cancer immunology, which asks how people develop spontaneous antibody and/or CD8+ T cell responses against NY-ESO-1.

"These studies are also representative of a growing trend in immunotherapy treatment, namely the use of chemotherapy and other standard therapies to augment anti-tumor immunity," stated Hiroshi Shiku, M.D., chairman and professor in the Department of Medical Oncology and Immunology, Mie University Graduate School of Medicine, Japan, and a lead investigator on the study. Until very recently, it was thought that these treatments served to uniformly dampen the immune system and would therefore
limit the potential efficacy of immunotherapies used in tandem or in sequence. A growing body of literature, however, is suggesting that certain cytotoxic, or "cell-killing," therapies such as chemotherapy and radiation, used in strategic ways, can synergize with immunotherapies to strengthen or expand the anti-tumor immune response.

Based on the success of their preclinical investigations, the study researchers are eager to take the approach into clinical testing. Such a trial would bridge what immunologists refer to as passive immunotherapy and active immunotherapy.

"It's passive because we're using antibodies manufactured outside the body—the body doesn't have to do the work to make these antibodies; but it's also active because these antibodies then mobilize the immune system to actively begin producing potent cells and endogenous molecules like cytokines and complement to attack the tumor. It's a powerful strategy that for the first time capitalizes on the full therapeutic potential of antibodies as mediators of tumor elimination," Ritter said.

**Journal Reference**
Noguchi et al. **Intracellular tumor-associated antigens represent effective targets for passive immunotherapy.** *Cancer Res.*, February 8, 2012

**High prevalence of trauma among HIV-positive women in the US**

Michael Carter
Published: 16 February 2012

Almost a third of HIV-positive women in the US have recent post-traumatic stress disorder and 55% have experienced intimate partner violence, according to the results of a meta-analysis published in *AIDS and Behavior*.

The investigators identified 29 studies examining trauma and post-traumatic stress disorder (PTSD) in women with HIV.

Overall, 33% of women had recent PTSD, some six times the rate seen in the general US population. Almost two-third of women had a lifetime experience of sexual abuse.

"The implications of these findings are highly significant," comment the authors. "These results...support and inform longtime calls for studies of trauma-prevention and trauma-recovery interventions to reduce the high incidence and relatively poor outcomes of HIV among women."

Women now account for 27% of all new HIV diagnoses in the US and 77% of these infections are in Blacks or Latinos. Despite general improvements in the prognosis of HIV-positive patients, HIV/AIDS is now the leading cause of death among Black women aged 25 to 34.

Trauma is increasingly recognised as contributory factor to the increasing prevalence of HIV in US women and their poorer outcomes. However, studies exploring the prevalence of trauma and PTSD among women with HIV have yielded widely varying results, or cannot be generalised to the general population of HIV-positive women.

Investigators therefore undertook meta-analysis to clarify rates of trauma and PTSD in HIV-positive women. Where possible, the observed prevalence was compared to that recorded in the general population of US women.

The authors searched for studies published between 1990 and 2009. To be included, the research had to examine current or past exposure to at least one traumatic stressor.

A total of 29 studies including 5930 women met the investigators’ criteria and were included in the meta-analysis.

The estimated rate of recent PTSD was 30%.

"This estimate is over five times the rate of recent PTSD reported in a national prevalence sample of women," write the authors.

Prevalence of intimate partner violence among women with HIV was an estimated 55%—twice the rate reported in US women as a whole.

Rates of adult sexual and physical abuse were 35% and 54% respectively. Estimated prevalence of childhood sexual abuse and childhood physical abuse were 39% and 42%.

"Both of these samples are approximately twice those documented in a national prevalence sample of women," note the researchers.

They calculated that an estimated 61% of HIV-positive women had a lifetime history of sexual abuse, five times the national US prevalence. The estimated prevalence of lifetime physical abuse was 72%.

"We observed very high rates of all categories of traumatic exposure and PTSD," write the investigators. "The estimates of the various categories of trauma and recent PTSD in HIV-positive women are mostly between two and five-fold higher."
Efforts to address trauma and PTSD should be a priority in HIV prevention and care, argue the authors. “Effectively addressing trauma and PTSD may be an opportunity to make a transformational impact on the HIV epidemic.”

The authors suggest “screening and referrals for recent and past trauma and PTSD should be considered a core component of HIV treatment in this population, along with medication adherence, CD4 cell counts and viral loads.”

Reference

UK guidelines on treatment of HIV in pregnancy give green light to efavirenz
Keith Alcorn
Published: 17 February 2012
New UK draft guidelines on the management of HIV infection in pregnant women recommend that efavirenz-based treatment should no longer be avoided in pregnant women or women who want to have a baby.

Pregnant women were previously recommended to avoid efavirenz treatment, as were women hoping to become pregnant, due to the theoretical risk of birth defects if the foetus was exposed to the drug in the first trimester of pregnancy.

But after rigorous review of the published evidence the British HIV Association guidelines panel concluded: “there are insufficient data to support the former position [of avoiding the drug] and [we] furthermore recommend that efavirenz can be both continued and commenced during pregnancy.”

Women who conceive while taking an efavirenz-containing regimen should continue on it, and women taking any effective HAART regimen should continue on it even if it does not contain AZT (zidovudine), the panel recommends.

World Health Organization guidelines on antiretroviral treatment for the prevention of mother-to-child transmission in resource-constrained settings first recommended the use of efavirenz during pregnancy in 2009, but United States guidelines updated in 2010 recommend avoiding the drug during the first trimester of pregnancy.

The draft guidelines are available for comment until Friday February 24 at the BHIVA website.

Key recommendations from the guidelines
Women who need HAART for their own health
Women requiring HAART for their own health should commence treatment as soon as possible as per the adult treatment guidelines.

In terms of the NRTI backbone there is most evidence and experience in pregnancy with zidovudine plus lamivudine. Tenofovir plus emtricitabine or abacavir plus lamivudine are acceptable alternatives.

In the absence of specific contraindications it is recommended that the third agent in HAART should be nevirapine if the CD4 count is less than 250 or efavirenz or a boosted PI.

No routine dose alterations are recommended for ARVs during pregnancy if used at adult licensed doses but consider third trimester TDM, particularly if combining tenofovir and atazanavir.

For women who do not need HAART for their own health
In the absence of specific contraindications it is recommended that HAART should be boosted-PI-based. The combination of zidovudine, lamivudine and abacavir can be used if the baseline viral load is <100,000 HIV RNA copies/ml plasma.

Zidovudine monotherapy can be used in women planning a caesarean section who have a baseline VL of <10,000 and a CD4 of >350. Women who do not require treatment for themselves should commence temporary HAART at week 14 if the baseline VL is >30K (Consider starting earlier if VL> 100,000). All women should have commenced HAART by 24 weeks.

A woman who presents after 28 weeks should commence HAART without delay. If the viral load is unknown or >100K a 3 or 4 drug regimen that includes raltegravir is suggested.

An untreated woman presenting in labour at term should be given a stat dose of nevirapine and commence fixed-dose zidovudine with lamivudine and raltegravir.

Women presenting in labour/ROM/requiring delivery without a documented HIV result must be recommended to have a HIV diagnostic point of care test (POCT). A reactive POCT result must be acted upon immediately with initiation of the interventions to PMTCT without waiting for formal serological confirmation.
ART can be continued in all women who commenced cART for MTCT with a CD4 count of between 350 and 500 cells during pregnancy.

ART should be discontinued in all women who commenced cART for MTCT with a CD4 count of >500 cells unless there is discordance with her partner (see above) or co-morbidity.

**Mode of delivery**

Vaginal delivery is recommended for women on HAART with an HIV viral load <50 HIV RNA copies/ml at gestational week 36.

Delivery by pre-labour caesarean section (PLCS) is recommended for women taking zidovudine monotherapy irrespective of plasma viral load at the time of delivery and for women with viral load >400 regardless of ART.

Vaginal delivery is recommended for women on HAART with a HIV viral load <50 HIV RNA copies/ml plasma at gestational week 36.

Delivery by PLCS is recommended for women taking zidovudine monotherapy irrespective of plasma viral load at the time of delivery (Grading: 1A) and for women with viral load >400 regardless of ART.

**Infant prophylaxis**

Zidovudine monotherapy is recommended if maternal viral load is <50 HIV RNA copies/ml at 36 weeks gestation/delivery (or mother delivered by PLCS whilst on ZDV monotherapy), irrespective of the mother’s viral resistance pattern or drug history.

Infants <72 hours old, born to untreated HIV-positive mothers, should initiate three drug therapy immediately.

Three drug infant therapy is recommended for all circumstances where maternal viral load at 36 weeks gestation/delivery is not <50 HIV RNA copies/ml.

Three drug infant therapy is recommended for all circumstances where maternal viral load at 36 weeks gestation/delivery is not <50 HIV RNA copies/ml.

Neonatal PEP should be continued for 4 weeks.

**Infant feeding**

All mothers known to be HIV infected, regardless of antiretroviral therapy, and infant PEP, should be advised to exclusively formula feed from birth in the very rare instances where a mother who is on effective HAART with a repeatedly undetectable viral load chooses to breastfeed, this should not constitute grounds for automatic referral to child protection teams. Maternal HAART should be carefully monitored and continued until one week after all breastfeeding has ceased. Breastfeeding, except during the weaning period, should be exclusive and all breastfeeding, including the weaning period, should have been completed by the end of 6 months.

Prolonged infant prophylaxis during the breastfeeding period, as opposed to maternal HAART, is not recommended.

Intensive support and monitoring of the mother and infant are recommended during any breastfeeding period, including monthly measurement of maternal HIV plasma viral load, and monthly testing of the infant for HIV by PCR for HIV cDNA or RNA (viral load).

HIV DNA PCR (or HIV RNA testing) should be performed on the following occasions.

- During the first 48 hours and prior to hospital discharge
- 2 weeks post infant prophylaxis (6 weeks of age)
- 2 months post infant prophylaxis (12 weeks of age)
- On other occasions if additional risk (e.g. breast-feeding)

HIV antibody testing for seroreversion should be done at age 18 months.

**Uganda: Government raid on LGBT-rights workshop**

“This is an outrageous attempt to prevent lawful and peaceful activities of human rights defenders in Uganda,” Salil Shetty, Amnesty International’s Secretary General

A Ugandan cabinet minister on Tuesday raided a workshop run by lesbian, gay, bisexual and transgender (LGBT) activists in Entebbe, prompting Amnesty International to call on the government to end its outrageous harassment of people involved in lawful activities.

The Minister for Ethics and Integrity, Simon Lokodo, who was accompanied by police, announced that the workshop was illegal and ordered the rights activists out of the hotel where it was being held. He told activists that if they did not leave immediately, he would use force against them.

“This is an outrageous attempt to prevent lawful and peaceful activities of human rights defenders in Uganda,” said Salil Shetty, Amnesty International’s Secretary General.
The Minister also attempted to order the arrest of Kasha Jacqueline Nabagasera, a prominent LGBT rights activist and winner of the 2011 Martin Ennals Award for Human Rights Defenders, who was forced to flee from the hotel. The reasons for the attempted arrest were not immediately clear, but were reported to be linked to Kasha Jacqueline’s attempt to challenge the Minister’s actions.

“The Government of Uganda must protect all people against threats, violence and harassment irrespective of their real or perceived sexual orientation or gender identity. The move comes days after the Anti-Homosexuality Bill was re-tabled in the Ugandan Parliament. The Government of Uganda has sought to distance itself from the Bill, stating that the bill did not enjoy government support.

“The Government’s claimed opposition to the Bill needs to be supported through their actions. The Ugandan government must allow legitimate, peaceful gatherings of human rights defenders, including those working on LGBT rights,” said Salil Shetty.

If the Anti-Homosexuality Bill becomes law, it would violate international human rights law and lead to further human rights violations.

Results for viral load on Vacc-4x
Oslo 15.02.2012 – With final review of phase IIb viral load data completed, researchers confirm statistically significant reduction of HIV viral load on Vacc-4x compared to placebo

Bionor’s Clinical Research Program Moves Forward with Three Main Pathways to Market

News Summary

- Final review of phase IIb data confirms statistically significant 64% reduction of viral load “set point” (average of the last two viral load measurements before the end of the study) in patients receiving Vacc-4x compared to those given placebo, indicating a possible new option for patients and doctors.
- The HIV viral load set point in patients given Vacc-4x was 60% lower than pre-ART (level before starting with standard medicine, ART). In the placebo group, no change compared to pre-ART was observed.
- The conclusive data provide a basis for further HIV trials, offering Bionor three main pathways to market:
  - Re-vaccination to reduce the viral set point further—aiming at a ‘functional cure’
  - Immunization in the presence of Revlimid®, targeting patients that fail to regain immune competence (CD4 counts) while on ART
  - Combining Vacc-4x and Vacc-C5, which could potentially revolutionize HIV management

Bionor Pharma announced today that researchers have completed a final review of the Company’s lead therapeutic HIV vaccine, Vacc-4x, and its ability to reduce the amount of HIV circulating in patients (“viral load”). These final conclusions from the phase IIb, placebo-controlled, double-blind, international, multicenter trial, confirm initial findings of a statistically significant difference in viral load set point between Vacc-4x and placebo groups at the end of the study. The full results in addition to the final review of the immunological assessment are being prepared for publication in an international peer reviewed journal.

Vacc-4x is designed to generate immune responses to conserved domains of p24 that are common to all strains of HIV. Sustained immune responses to p24 have previously been shown to delay HIV disease progression.

Researchers from the Ragon Institute, Harvard, and MIT published in 2011 findings confirming the existence of conserved regions on p24 and emphasizing their potential as targets for an HIV vaccine. Bionor identified these domains over a decade earlier, and began developing the vaccine based on these findings. Today Bionor’s Vacc-4x is the most studied immunotherapeutic product targeting p24.

About Vacc-4x phase IIb study and results

136 patients participated in the five country trial, with two-thirds (93) randomized to receive Vacc-4x together with ART, while one-third (43) received a placebo injection and ART. Patients were immunized with Vacc-4x or placebo while on ART over a period of 28 weeks. This was followed by a period without treatment, lasting up to 24 weeks (until week 52).

For patients that successfully completed the study (week 52), the placebo group (n=25) had a viral load set point of 61,900 cmL compared to the Vacc-4x group (n=56) that had a viral load set point of
22,300 cmL. This difference represents a reduction of 64% and is statistically significant (p = 0.04). All values represent median.

A subgroup comparison has been performed with only those patients who had a known viral load measurement before starting ART (pre-A RT). The placebo group (n = 18) had no statistically significant difference between pre-A RT viral load (52,731 cmL) and the viral load set point at the completion of the study (50,400 cmL, p = 0.98). In contrast, the Vacc-4x group (n=45) had pre-A RT viral load of 60,470 cmL, compared to 24,150 cmL at study completion, resulting in a statistically significant reduction of 60% (p= 0.0001).

The previously reported findings showing an association between viral load and HIV-specific immune responses are also confirmed. Patients with immune responses to p24 at study termination had a higher viral load set point in the placebo group (61,900 cmL) compared to the Vacc-4x group (22,925 cmL). HIV-specific immune responses resulted in increased viral load in the placebo subjects, whereas the Vacc-4x group had a significantly better viral control (p=0.048).

“These final results confirm that Vacc-4x lowers viral load in patients with HIV who have remained off ART for at least 6 months,” said Vidar Wendel-Hansen, MD, PhD, Chief Medical Officer, Bionor Pharma, “and suggests a correlation between this effect and the vaccine induced immune responses to p24.”

Several independent further paths to market for Vacc-4x
Based on the conclusive phase IIb data, Bionor is studying several paths to guide the direction towards a Phase III pivotal trial, the final study before regulatory review and market entry:

1. Vacc-4x revaccination of patients from the phase IIb study, to further reduce the viral load set point (study planned 1H 2012). Based on the statistically significant lowering of viral load after vaccination with Vacc-4x compared to before taking ART, Bionor researchers plan to re-vaccinate Vacc-4x patients from the IIb study to see if the viral set point can be reduced even further. Such an approach may eventually form a “functional cure,” meaning that HIV viral load is gradually reduced to lower levels following successive ART-free periods.

2. Vacc-4x in combination with Revlimid® (Lenalidomide), for patients with unmet medical needs (study planned 1H 2012). Based on the confirmed ability for Vacc-4x to lower viral load in HIV patients, Bionor will study the effect of combining Vacc-4x with Revlimid, for patients who are well controlled on ART but fail to regain immune competence (CD4 T-cell counts). By combining Vacc-4x with Revlimid, an immunomodulatory drug, Bionor’s researchers will determine whether patients experience improvement.

3. Vacc-4x in combination with Vacc-C5, to reduce viral load and the spread of infection. Vacc-C5 is designed to induce antibodies to HIV that can reduce HIV associated immune hyperactivation which leads to AIDS. Preclinical studies have shown that Vacc-C5 successfully induced antibodies against HIV in animal models such as rabbits and sheep. Bionor intends to conduct the first clinical study of Vacc-C5 in man in 2Q 2012. Subsequent to the Vacc-C5 phase I/II trial, Bionor intends to combine Vacc-4x with Vacc-C5, a treatment that can potentially revolutionize the management of HIV infections and could form the basis for both a therapeutic and a preventative vaccine.

Bionor is furthermore investigating different options for administration of its vaccines.
An ongoing trial at Oslo University Hospital aims to reveal whether Vacc-4x given by nasal administration can provide equivalent effect compared to delivery by needle injection. Such administration will be important for cost and availability in both Western and especially developing countries. All patients have been successfully included in the trial and the results are expected in first half of 2012.

Partnering process
The successful outcome of the phase IIb clinical trial, together with the Company’s further preclinical and clinical program, makes a partnering process a natural next step for Bionor Pharma.

About Bionor Pharma ASA
Bionor Pharma is a biopharmaceutical, listed company based in Oslo, Norway.

The Company’s lead investigational product, the HIV therapeutic vaccine Vacc-4x, has completed a phase IIb multinational, placebo controlled double-blind trial, which found a statistically significant reduction in viral load in treated subjects.

A second HIV therapeutic vaccine, Vacc-C5 is developed to induce antibodies to HIV that can reduce immune hyperactivation associated with HIV infection, which leads to AIDS. The first clinical trial for Vacc-C5 is planned 2Q 2012. Because researchers have already found that patients with antibodies to the C5 region on HIV have little virus in their blood and slow disease progression, Bionor anticipates that
Vacc-C5 will offer an important weapon towards finding a functional cure for HIV. Vacc-4x in combination with Vacc-C5 can potentially revolutionize the management of HIV infection and could form the basis for a preventative HIV vaccine.

The Company’s innovative technology platform is also well suited to the development of vaccines for a wide range of other viral diseases, such as Influenza, HCV (Hepatitis C) and HPV (Human Papilloma Virus). Preclinical studies with Vacc-Flu (Universal Influenza vaccine) and Vacc-HCV (Hepatitis C vaccine) are planned to be finalized in second half 2012, preparing for the clinical stage of development and partnering.

Bionor’s vaccines are based on the proprietary technology platform developed following several years of research on peptides. The vaccines are designed to safely activate each person’s immune system to combat viral disease.

Bionor seeks to create positive cash flow at an early stage of development by signing partnering deals with biotechnology and pharmaceutical companies. This includes short-term out-licensing of products with royalty payments or direct funding of clinical trials, such as Bionor’s agreement signed in August 2011 with one of the world’s largest Biotech companies. The collaboration includes a clinical trial on patients/subjects with HIV using a combination of Vacc-4x, and the cancer drug Revlimid.

**HIV warning to women using injectable contraception**

World Health Organisation advises use of condoms for protection against infection

Women who rely on injectable contraception are being strongly advised by the World Health Organisation (WHO) to also use condoms to protect them against the increased risk of HIV infection.

A study in *the Lancet last October found that women living in Aids-hit countries using progestogen-only injections, such as Depo-Provera, were twice as likely to become HIV positive* as other sexually active women.

The findings caused huge consternation, particularly among family planning experts. In sub-Saharan Africa, the centre of the Aids epidemic, the contraceptive most women choose is a long-lasting injection, which they can keep secret from their partner.

The WHO convened an expert group to examine the evidence. It concluded that hormonal contraception – whether the pill or injection – was safe for women at risk of HIV to use if they wanted to prevent pregnancy.

But the guidance says: "It is critically important that women at risk of HIV infection use condoms and, where appropriate, other measures to prevent and reduce their risk of HIV infection and sexually transmitted infections."

Current evidence is not strong enough to prove or disprove an increased risk of HIV from hormonal contraception, according to the experts. They agreed that the use of hormonal contraception should remain unrestricted if a strong clarification was added to the medical advice "which reflected the difficulties the group had with the data, the need for an enhanced message about condom use and other HIV prevention measures and the need for couples to have access to as wide a range of contraceptive methods as possible".

About half of the 34 million people living with HIV are women. In sub-Saharan Africa, nearly 60% of all new infections occur in women. There is an urgent need for women to have better means of protecting themselves against HIV, particularly if their partner refuses to wear a condom.

"Women need safe contraceptive and HIV prevention options that they can own and manage,” said Michel Sidibé, executive director of UNAids. "New investments into research for female controlled HIV prevention options and safe contraceptive methods are essential."

About 25% of the 128 million married or cohabiting women in sub-Saharan Africa aged 15 to 49 want but cannot obtain contraception. UnAids said there was an urgent need for dual solutions to prevent HIV as well as conception.

**ESPN to Show Film on Johnson’s HIV Disclosure**


More than 20 years after basketball great Magic Johnson stunned the world with his announcement that he had contracted HIV, ESPN and the NBA will debut a documentary examining his decision.

Filmmaker and writer Nelson George, also a contributor to the New York Times, said he wanted to show the inside story of Johnson’s personal deliberations but also to “make people aware [HIV/AIDS] hasn’t disappeared.”
“People are still dying of the virus. People are living very tough lives because of it,” George said. “It’s falling off the national agenda, I believe, and this in some way helps us reintroduce it.”

“The Announcement” is slated to run on ESPN March 11. It includes interviews with Johnson friend and confidant Arsenio Hall, longtime fan Chris Rock, Michael Weinstein of the AIDS Healthcare Foundation and Brooklyn-based AIDS activist Andrea Williams, who also is the filmmaker’s sister. But George noted the interviews with Johnson, some of which were conducted at the Forum in Los Angeles where he played as a Laker and disclosed his illness, were “the key to everything.”

According to George, “for a lot of people of a certain age” Johnson’s announcement was the equivalent of “the Kennedy assassination or the King assassination.” “He’s the biggest star in the NBA. He’s one of the biggest stars in professional sports, and he comes up with this disease, which at that time is an immediate killer. So even though he’s walking there and standing in front of everyone giving this press conference, as Karl Malone says, they think they’re seeing a dead man walking.”

**Effect of a Cash Transfer Program for Schooling on Prevalence of HIV and Herpes Simplex Type 2 in Malawi: A Cluster Randomized Trial**

*The Lancet* doi: 10.1016/S0140-6736(11)61709-1, (02.15.2012)  Sarah J. Baird, PhD; Prof. Richard S. Garfein, PhD; Craig T. McIntosh, PhD; Dr. Berk Özler, PhD

“Lack of education and an economic dependence on men are often suggested as important risk factors for HIV infection in women,” wrote the authors, whose current study assessed the efficacy of a cash transfer program to reduce the risk of STIs in young women.

The cluster randomized trial recruited never-married women ages 13-22 from 176 enumeration areas in Malawi’s Zomba district. The women were randomly assigned with computer-generated random numbers by enumeration area (1:1) to receive cash payments (the intervention group) or nothing (the control group). In addition, the intervention enumeration areas were randomly assigned with computer-generated random numbers to conditional (school attendance was required to receive payment) and unconditional (nothing was required to receive payment) groups.

In both intervention groups, participants were assigned by lottery to receive monthly payments ranging from US $1-$5. Their parents were independently assigned with computer-generated random numbers to receive $4-$10. At baseline and at 12 months, behavioral risk assessments were performed. Serology was tested at 18 months. Although the participants were not masked to treatment status, the counselors who performed the serologic testing were. The study’s primary outcomes were prevalence of HIV and herpes simplex virus 2 (HSV-2) at 18 months; these were assessed by intention-to-treat analyses.

Eighty-eight enumeration areas were assigned to the intervention, and 88 to the control condition. Among the 1,289 individuals enrolled in school at baseline with complete interview and biomarker data, weighted HIV prevalence at 18 months was 1.2 percent (seven of 490 participants) in the combined intervention group, compared to 3.0 percent (17 of 799 participants) in the control group (adjusted odds ratio 0.36, 95 percent CI: 0.14-0.91); weighted HSV-2 prevalence was 0.7 percent (five of 488 participants), versus 3.0 percent (27 of 796 participants) (AOR 0.24, 0.09-0.65).

The authors noted no difference between the conditional and unconditional intervention groups for weighted HIV prevalence (3/235 [1 percent] vs. 4/255 [2 percent]) or weighted HSV-2 prevalence (4/233 [1 percent] vs. 1/255 [<1 percent]). Among individuals who had already dropped out of school at baseline, no significant difference was noted between intervention and control groups for weighted HIV prevalence (23/210 [10 percent] vs. 17/207 [8 percent]) or weighted HSV-2 prevalence (17/211 [8 percent] vs. 17/208 [8 percent]).

“Cash transfer programs can reduce HIV and HSV-2 infections in adolescent schoolgirls in low-income settings,” the authors concluded. “Structural interventions that do not directly target sexual behavior change can be important components of HIV prevention strategies.”

**Countdown to the introduction of a norovirus vaccine**

Noroviruses are believed to make up half of all food-borne disease outbreaks in the United States, causing incapacitating (and often violent) stomach flu. These notorious human pathogens are responsible for 90 percent of epidemic nonbacterial outbreaks of gastroenteritis around the world.

On Friday, February 17, 2012 at 10:00 a.m., Charles Arntzen, ASU Regents’ professor, and professor in the Center for Infectious Diseases and Vaccinology at the Biodesign Institute will deliver a lecture entitled Countdown to the Introduction of a Norovirus Vaccine. The talk will take place during the American Association for the Advancement of Science’s annual meeting in Vancouver, BC.
Arntzen’s lecture is part of a special topical seminar: Norovirus—The Modern Scourge of Food and Family.

The seminar title is well chosen—noroviruses are extremely contagious, readily passing from person to person, particularly among those living in the closed quarters of dormitories, nursing homes, child care centers, military bases, and cruise ships. Infections can result from contact with virus particles dispersed in the air or from the ingestion of even tiny quantities of contaminated food. Further, even vigorous hand washing or the use of alcohol wipes or gels may be ineffective in combating norovirus transmission. Noroviruses can persist in a transmissible state for days or weeks even in those who are asymptomatic or are recovering from the disease.

Arntzen will speak about the prospects for a successful vaccine to prevent norovirus infection, based on Virus-Like Particles (VLPs), which are able to mimic actual noroviruses, stimulating a robust immune response, without producing disease symptoms. Due to the frequent mutation of noroviruses, vaccine candidates will need to be adaptable for alternate strains of the pathogen—much the way current vaccines for influenza are modified to keep pace with viral evolution. New strategies for formulating and biomanufacturing such vaccines offer renewed hope for norovirus vaccine development in the near future.

Nasty "Superbug" is Being Studied by UB Researchers
It's virulent, potentially drug-resistant, strikes otherwise healthy, young patients, and Buffalo has already seen one case
Release Date: February 17, 2012
BUFFALO, N.Y. – University at Buffalo researchers are expressing concern about a new, under-recognized, much more potent variant of a common bacterium that has surfaced in the U.S.

"Historically, in Western countries, classical strains of Klebsiella pneumoniae have caused infections mostly in sick, hospitalized patients whose host defense systems are compromised," says Thomas Russo, MD, professor in the Department of Medicine at the UB School of Medicine and Biomedical Sciences and head of its Infectious Disease Division.

"But in the last 10 to 15 years, a new variant of it has begun causing community-acquired infection in young, healthy individuals," he says. "This variant causes serious, life-threatening, invasive infections and is able to spread to other organs from the initial site of infection."

Perhaps most important, says Russo, these hypervirulent strains of Klebsiella pneumoniae have the potential to become highly resistant to antibiotics, similar to Escherichia coli and classical Klebsiella pneumoniae.

"These hypervirulent strains are the next 'superbugs'—in-waiting," he says. "If they become resistant to antibiotics, they will become difficult, if not impossible to treat."

With recent funding from the National Institutes of Health under a program to fund high-risk, high-reward research, Russo and his UB colleagues are studying the microbiology of the new variant of Klebsiella pneumoniae in an effort to identify the genes that make it hypervirulent so they can figure out how to stop it in its tracks.

"Infections due to highly resistant bacteria are becoming increasingly problematic," says Russo. "We are continually threatened by a 'post-antibiotic' era. The combination of a bacterium that is both highly virulent and resistant to antimicrobials is double-trouble."

The researchers' concern stems from the fact that classical Klebsiella pneumoniae is one of the bacterial species that can easily acquire mobile genetic units, called plasmids, that contain multiple genes that confer high levels of antimicrobial resistance.

"That's in part why we're concerned," says Russo. "We know that this bacterium has the potential to acquire these plasmids and it almost certainly will."

He notes that most bacteria that have proven to be resistant to most or all of the drugs currently available do not usually infect healthy members of the community.

"What is alarming about the hypervirulent Klebsiella pneumoniae is that they do possess the potential to infect healthy people," says Russo. "If this hypervirulent bacterium also becomes highly resistant to antimicrobials, we will have a significant problem to manage. We hope that our research and that of others can prevent this possibility."

While the new hypervirulent variant was first seen exclusively in the Pacific Rim, it has now been found in several cities in North America, including Buffalo, and in Europe, Canada, Israel and South Africa as well. The UB researchers characterize it as "under-recognized" both by physicians and microbiology laboratories.
The disease most commonly presents as a liver abscess, which is not typical for otherwise healthy patients.

"This new variant presents with unique and scary features: first is its tendency to infect young, healthy people in the community and the second is its unique propensity for metastatic spread to other parts of the body," says Russo. "It spreads to sites beyond the initial source of the infection, such as the lungs, the central nervous system and the eye, potentially causing loss of vision. If infection spreads to the brain, there can be brain damage as well. Between 10 and 30 percent of cases are fatal."

In Buffalo, this hypervirulent variant of *Klebsiella pneumoniae* was identified in an otherwise healthy, young person several years ago. The patient, who was in his 20s, was hospitalized for several months before making a full recovery. Similar cases are causing concern throughout the international infectious disease community.

At the moment, most cases of hypervirulent *Klebsiella pneumoniae* resolve if treated aggressively with antibiotics and drainage of abscesses; however, some infections, despite optimal treatment, result in a persistent morbidity or death, Russo says.

He notes that the potential for the bug to acquire drug resistance is adding a sense of urgency to the research.

Russo says that microbiology labs should be aware that an important characteristic of these hypervirulent strains (also known as hypermucoviscous strains) is that when bacterial colonies grown on a solid surface in the laboratory are stretched by a common microbiology tool, called an inoculation loop, they form a viscous "string" greater than 5 millimeters in length.

Russo’s team at UB is now beginning to develop a clearer picture of this formidable bacterial opponent.

In November, he and his colleagues published a PLoS ONE paper that showed that hypervirulent *Klebsiella pneumoniae* acquires iron more efficiently than the usual strains of *K. pneumoniae*.

"With the NIH grant, we hope to further elucidate the precise details of the bacterial factors that are responsible for hypervirulent *Klebsiella pneumoniae* acquiring iron so much more efficiently," he says. "The goal of this line of research is that these iron-acquisition factors possessed by hypervirulent *Klebsiella pneumoniae* will then lend themselves as therapeutic or vaccine targets so that we can better treat or prevent infection."

**Light Shed On How Body Fends Off Bacteria**

ScienceDaily (Feb. 16, 2012) — Team develops first 3D look at interaction between immune sensor and protein that helps bacteria move

To invade organisms such as humans, bacteria make use of a protein called flagellin, part of a tail-like appendage that helps the bacteria move about. Now, for the first time, a team led by scientists at The Scripps Research Institute and Sanford-Burnham Medical Research Institute has determined the 3D structure of the interaction between this critical bacterial protein and an immune molecule called TLR5, shedding light on how the body protects itself from such foreign invaders.

The study, published February 17 in *Science*, not only helps decipher the molecular mechanism underlying TLR5 recognition and function, but it also advances knowledge that’s key to the design of new therapeutics.

“The structure of the TLR5-flagellin complex visualizes molecular events that occur on the cell surface to trigger flagellin-induced host immune responses, and provides significant insights into the structural basis for TLR5 recognition and signaling,” said Ian Wilson, D.Sc., Hansen Professor of Structural Biology at Scripps Research who led the study with Andrei Osterman, Ph.D., professor in Sanford-Burnham’s Infectious and Inflammatory Disease Center.

“Gaining knowledge of a molecular interaction and action—as we did in this study—is critically important to the further development of therapeutics based on agonists and antagonists of the TLR5 receptor,” said Osterman.
Flagellin is a component in some vaccines and a derivative of this protein is currently being developed as a medical countermeasure to radiation by Cleveland BioLabs, Inc. (NASDAQ:CBLI), also a contributor to the new study.

**Keeping an eye out for infection**

Some of the body’s first lines of defense against invading bacteria are Toll-like receptors (TLRs), sensors that sit on the surface of many different types of cells. There are roughly a dozen different TLRs, each keeping an eye out for a particular sign of infection.

TLR5, for example, specifically recognizes and binds to flagellin. Like most TLRs, TLR5 does more than just sense bacteria—it also sends signals that call up immune cells to destroy the intruder. But to fully understand how TLR5 works, scientists needed to be able to see its 3D shape and how it binds to flagellin.

The structures of several other TLRs had already been solved, but each of these binds non-protein molecules, such as RNA or lipids. For technical reasons, determining the structure of TLR5—the only TLR that binds a protein—had long been a challenge.

In this study, the Scripps Research team was able to overcome these hurdles using TLR5 found in zebrafish as a proxy for the human protein. The scientists were then able to apply a technique called X-ray crystallography, which uses powerful X-ray beams to produce 3D images of proteins at the atomic level.

At Sanford-Burnham, Osterman and his team used biochemical and protein engineering methods to unravel the mechanistic details of interactions between TLR5 and flagellin and its derivatives.

Scientists at Roswell Park Cancer Institute and Cleveland BioLabs, Inc. in Buffalo, under the leadership of Andrei Gudkov, Ph.D., performed complementary experiments in human cells expressing TLR5 and validated the fish TLR5 as a good surrogate for human TLR5.

**Journal Reference:**


**To Understand Chromosome Reshuffling, Look to the Genome's 3-D Structure**

ScienceDaily (Feb. 16, 2012) — That our chromosomes can break and re_shuffle pieces of themselves is nothing new; scientists have recognized this for decades, especially in cancer cells. The rules for where chromosomes are likely to break and how the broken pieces come together are only just now starting to come into view. Researchers at Children’s Hospital Boston and the Immune Disease Institute (IDI) have helped bring those rules into clearer focus by discovering that where each of the genome's thousands of genes lie within the cell's nucleus—essentially, the genome's three-dimensional organization—holds great influence over where broken chromosome ends rejoin. This knowledge could shed light on fundamental processes related to cancer and normal cellular functions—for example, immunity.

The study team, led by Frederick Alt, PhD, director of the Program in Cellular and Molecular Medicine at Children's Hospital Boston and the IDI; and Job Dekker, PhD, co-director of the Program in Systems Biology at the University of Massachusetts Medical School, reported their results online on February 16 in the journal *Cell*.

In cancer cells, the process of chromosome rearrangement, or translocation—marked by stretches of DNA physically breaking and swapping—often results in the creation of new cancer-promoting "fusion" genes. Similarly, when a naïve B cell starts to produce antibodies for the first time, it establishes its choice of target by breaking and recombining genes for antibody diversity.

"While chromosomal breaks and translocations are fundamental to many cancers, historically we've had no approaches to systematically study how they are generated," said Alt, who is also a Howard Hughes Medical Institute investigator and the Charles A. Janeway Professor of Pediatrics and Professor of Genetics at Harvard Medical School. "About five years ago, our group set out to generate a high-throughput approach to address this important problem in cancer biology."

To accomplish this goal, the Alt lab developed high-throughput genome-wide translocation sequencing (HTGTS, which maps "hot spots" in the genome where chromosome breaks and translocations are more likely to occur) and at a level of resolution not previously thought possible. In early HTGTS studies, they found that broken chromosomes often rearrange within themselves, as opposed to sharing pieces across different chromosomes.

To probe these findings more deeply, his laboratory joined forces with Dekker’s to combine HTGTS with a method called Hi-C. Developed by Dekker's group, Hi-C measures how all the sequences in the genome are organized relative to one another in three dimensions.
The combined data revealed several related but distinct principles of how genomic organization governs chromosome rearrangements. The first is based on the slight differences in how each cell organizes its genome compared to its neighbors (referred to as cellular spatial heterogeneity of genome organization). While the genome is organized in an average fashion that is largely common across all cells of a population, each individual cell harbors small deviations from that average. This latter property allows many genes to be physically close to each other in just a small subset of cells, even if they are not close to each other in the majority of cells.

The second principle involves proximity. If two broken chromosome strands lie in close proximity within the three-dimensional space of a given cell’s nucleus, they are more likely to connect. This finding is of particular importance for translocations involving DNA sequences that do not break frequently, such those involved in translocations found in various non-lymphoid tumors.

The third principle applies the first two to DNA sequences that do break frequently (such as those that drive antibody gene rearrangements during B cell development). Such sequences tend to reshuffle with the same partner sequences in those subsets of cells where the partners lie physically close together, even if the partners do not within most cells. This can fuel recurrent translocations like those seen in many lymphoid tumors.

Together, the principles highlight the relationship between proximity, genomic organization, and break frequency. "Two sequences have to be broken and physically proximal to join," Alt explains. "If two sequences are together in most cells and frequently broken, they will translocate in many cells. If they are frequently together but one of them doesn't break, or if they both break frequently but always lie on opposite sides of the nucleus, the chances that they will translocate are very low or zero. However, if both sequences break very frequently and are close together in a subset of cells, they will very frequently translocate in that subset, contributing to recurrent translocations."

"Our finding that broken chromosome segments are more likely to join with other segments within the same chromosome, rather than other, more physically distant segments from other chromosomes, likely has great relevance to cancer genomes," Alt continued. "For example, cancer treatments that cause breaks may preferentially lead to intra-chromosomal rearrangements. It may also have relevance for 'chromothripsis,' a recently discovered phenomenon in many cancers in which the sequences of one chromosome become scrambled."

The new understanding of the roles of physical spatial proximity and overall three-dimensional genome structure in chromosomal translocations opens up new avenues for deciphering how the way a cell's nucleus is organized affects the genomic disarray found in cancer and other diseases characterized by chromosome reshuffling. The study also shows the power of combining two high-throughput genomic assays—Hi-C and HGTGS—for studying how the organizational plan within the nucleus influences fundamental biological processes.

"We feel that our findings and the application of our approaches will provide a new lens through which to view the genomes of many different types of cancer," Alt concluded.

**Journal Reference:**

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**Severe nevirapine rash linked to slow clearance of drug**
Carole Leach-Lemens
Published: 20 February 2012
The risk of severe rash when taking the antiretroviral drug nevirapine is greater in women who clear the drug from their bloodstream slowly, and clearance of the drug appears to be slower in African women, according to a pharmacokinetic analysis of the relationship between drug levels and severe nevirapine side-effects in a recent large trial of first-line antiretroviral therapy in sub-Saharan Africa.

The findings from the ACTG 5208/OCTANE study are published online in advance of print in the journal AIDS.

This pharmacokinetic (PK) study from the ACTG A5208/OCTANE clinical trial showed that the odds of developing a severe rash were estimated to be 50% higher for every 20% decrease in the rate of nevirapine clearance (p=0.046), and clearance of nevirapine was approximately 40% slower than previously reported in studies carried out in the United States and the Netherlands, suggesting that African women may be genetically predisposed to slower clearance of this drug.
Nevirapine (NVP), a non-nucleoside reverse transcriptase inhibitor (NNRTI), is part of standard first-line ART in resource-poor settings. During the first weeks of ART NVP has been linked to a serious and sometime life-threatening rash and/or liver damage. NVP rash is seen more often in women than in men.

The precise cause of NVP toxicity is unclear. Studies suggest that there is a link between how NVP is absorbed (NVP PK) and an increased risk for toxicity. These findings, however, are from studies with a majority of male subjects. Yet, it appears that women are exposed to the drug for longer since it takes longer to clear. Other factors that may contribute to how the drug is absorbed include: body weight, ethnicity, pre-existing liver disease and pharmacogenetics (how genetic make-up affects the response to medications).

So the authors chose to undertake this study to try and clarify the link of NVP PK with increased risk of rash and/or liver damage among a large cohort of HIV-infected, but not pregnant, women from 10 sites in seven sub-Saharan countries who started NVP-based ART. And secondarily to see if there was a link between these adverse effects and pre-treatment CD4 cell count and weight.

All women enrolled in the trial had a CD4 cell count under 200 cells/mm³ before starting treatment, were ART-naive or had taken zidovudine or single dose nevirapine for PMTCT. They were randomised to get either lopinavir/ritonavir twice a day or NVP twice a day after a 14 day period of once daily NVP each in combination with tenofovir and emtricitabine (Truvada). Those randomised to NVP were included in the PK trial. Single nevirapine blood samples were taken after randomisation at 14 (± 7) days (before dose escalation to twice a day) and at 28 (± 7) days if no NVP doses had been missed in the previous three days. They were followed until the last woman randomised had finished 48 weeks of follow-up.

Toxicity was defined as rash and liver damage that happened during therapy or within seven days of the last dose of nevirapine and before starting another ART regimen.

Population pharmacokinetic analysis modelled NVP pharmacokinetics. The authors note since only a single NVP blood sample was taken at week 2 and week 4 for each subject a simple additive clearance (CL) model was used to capture any additional CL after week 2 (CLweek4=CLweek2+CI additional).

Among the 359 women, included in the analysis, at baseline median age was 33 years (IQR: 28-38); median weight 57 kg (IQR: 52-67); and median CD4 cell count 128 cells/mm³ (IQR: 80-176).

While the screening CD4 count had to be under 200 cells/mm³ there were no restrictions on the baseline CD4 count. 47 women with a CD4 count over 200 cells/mm³ were enrolled with a median of 262 cells/mm³ (IQR: 250-386).

Women weighing less than 50 kg compared to those at or over 50 kg were significantly younger (median 30 compared to 34 years, p=0.012) and had higher viral loads (median 199526 compared to 125893 copies/mL) and more advanced WHO stage 3 or 4 (44% compared to 28%), p=0.013.

54% (194) developed a rash of any grade of which 23% (82) had grade 2+ and 9 (3%) had grade 3+ of which one had grade 3+ liver damage. The link between NVP PK exposure and a significantly increased risk of severe rash was seen at week 4 but not at week 2.

Median clearance at 28 days (week 4) was 1.7L/hr for women with a severe rash (grade 3+) compared to 2.0L/hr for women without severe rash, p=0.046.

Discontinuing nevirapine because of rash and/or liver damage was more frequent among women with CD4 cell counts over 250 cells/mm³ before starting treatment (p=0.003).

The authors note this is the first study to show a link between NVP exposure and grade 3+ rash. While other studies have shown a link between exposure and increased liver enzymes none have shown such a consistent relationship, they add.

The authors note these findings “add to previous data suggesting vigilance and close monitoring for NVP toxicity are required for all African women starting NVP at any CD4 count, but toxicity is more likely in those with CD4 cell counts at or above 250 cells/mm³.”

Limitations include a lack of pharmacogenetic data to link with the pharmacokinetic findings because patient consent was not initially obtained.

The authors suggest caution in interpreting the findings as they are based on the differences between screening and pre-treatment CD4 cell counts of a small number of women and the potential for change within the subject between the two measurements.

Guidelines now recommend starting ART at a higher CD4 cell count leading the authors to stress the importance of further PK and pharmacogenetic studies; in particular in resource-poor settings, notably among African women, to determine the most effective dose of nevirapine to give the best results while minimising toxicity.
White House Holds LGBT Health Conference

The Obama administration rolled out its first campaign-season LGBT conference Thursday in Philadelphia as it seeks to publicize its accomplishments — and court gay support for reelection.

By Andrew Harmon

PHILADELPHIA — The White House rolled out its first campaign-season LGBT conference Thursday, one focused on health care issues facing the community and headlined by Secretary of Health and Human Services Kathleen Sebelius. The conference series was first announced by the White House last month.

Sebelius didn’t break big news on health care initiatives during a morning address at Philadelphia’s Thomas Jefferson University. But the White House’s engagement on the issue, coupled with the HHS secretary’s attendance, brought national visibility to what Sebelius accurately described as a health care system that has been “especially broken for LGBT Americans,” who have lower rates of coverage and have been historically excluded from federal health surveys.

“Given the discrimination that often is faced in the workplace, LGBT Americans often have a harder time getting access to employment-based coverage,” Sebelius said at the conference, also attended by gay White House officials including Gautam Raghavan, the LGBT liaison in the Office of Public Engagement; and John Berry, director of the Office of Personnel Management.

But “all Americans, regardless of where they live, what age, sex, race, sexual orientation, or gender identity, have a basic right to get the health care they need here in the United States, and that’s a principle we are committed to fighting for in this administration,” Sebelius said.

The speech was similar in tone and structure to Sebelius’s address before the National Coalition for LGBT Health in October, where she enumerated the administration’s regulatory accomplishments over the past three years — most famously a hospital visitation mandate for same-sex couples — and touted health care reform as a major step toward improving health care access for the community. The U.S. Supreme Court will hear arguments on the law’s constitutionality in late March.

The lack of marriage rights can be a major barrier to care, as Sebelius discussed with The Advocate in an interview published last month. President Obama has endorsed legislation to repeal the Defense of Marriage Act, which prohibits federal recognition of same-sex marriages, though the White House has not budged in recent months beyond talking points of the president “evolving” on the issue of full marriage rights and opposing “divisive and discriminatory” measures against same-sex couples — this in reference to anti-gay marriage ballot measures in states such as North Carolina and Minnesota.

Another trending topic discussed Thursday was that of cultural competency standards for health care professionals treating LGBT patients. There are no uniform standards for doctors and medical staff on how (and how not) to treat LGBT individuals. Sebelius said in January that she does not necessarily believe codified regulation needs to be implemented, though the Office of Minority Health is working to add sexual orientation and gender identity into the language of its Culturally and Linguistically Appropriate Services in Health Care standards.
Liz Margolies, founder and director of the National LGBT Cancer Network, said mandatory training is essential for creating a health care environment where the specific needs of LGBT patients are thoroughly understood and addressed.

“Offering optional cultural competency is simply preaching to the choir,” said Margolies, who attended Thursday. “The people who don’t get it are the people who probably need it. So the only way to make a difference is to make sure every single person is trained.”

Such training should not be limited to medical school programs, she said: “Think of how many people you see and talk to during an emergency room visit before you are even seen by a doctor.”

Of the conference, Margolies said that face time with White House officials was highly important, though the campaign value of the event for the administration was also clearly evident. “There’s an amazing amount of talent in this room. It’s only with all of us screaming and pushing persistently that we’re going to make any difference.”

On Thursday, Secretary Sebelius also called for reinvigorating domestic HIV/AIDS prevention efforts, remarking that given the continued steady infection rate nationwide, “frankly, what we’ve been doing is not very good.” The president’s 2013 budget, released earlier this week, calls for modest increases in HIV prevention efforts for high-risk groups, including gay men and African-Americans.

“The most frustrating thing is that there’s now very good data about how prevention can work, about how to reduce partner-to-partner transmission, early identification and treatment,” Sebelius said in the January interview. “And yet we have 50,000 new infections popping up. It just doesn’t make any sense. So we’ve got to redouble our efforts on the education front and outreach front to really drill down into the communities most at risk.”

The Obama budget also calls for an additional $75 million for care and treatment through the Ryan White HIV/AIDS program.

Off-the-record sessions for attendees during the Thursday conference focused on aging, LGBT youth, transgender health, cultural competency, and “engagement opportunities with the White House and HHS.”

Dr. Scout, a transgender health advocate with The Fenway Institute in Boston, said the conference "didn't have so much new information," though "its real value is in the fact that it exists."

"We can grumble about how much needs to be done on LGBT health at HHS, and we should, but today the Administration really showed up for us," said Dr. Scout, whose organization received a $250,000 grant last year from the Health Resources and Services Administration to create a national training center for improving LGBT health. "If more healthcare policymakers showed the commitment the people here did, LGBT health disparities could be practically eliminated. Our huge smoking disparity, our access to care problems, our mental health disparities, all of it could be virtually wiped out with smart policies like the ones we heard talked about today."

However, to his disappointment, Dr. Scout said that agencies with substantial power over LGBT health issues, such as the Centers for Disease Control and Prevention and the Agency for Healthcare Research and Quality, didn't have staff in attendance, "which frankly is what I expected considering their lackluster performance in this area. I really do love what was being said today, but we need to start noticing what’s not being said too, and who didn't even show up."

Sebelius, who has been tapped by Obama campaign officials to speak at super-PAC events for the reelection effort, attended a Washington, D.C., fund-raiser last week with the president that drew a who’s who of major LGBT Democratic donors paying $35,800 each for a $1.4 million overall haul. Cohosts of the event included GeoCities founder David Bohnett, Gill Foundation founder Tim Gill, and Laura Ricketts, co-owner of the Chicago Cubs.

1 in 10 children face elevated risk of abuse, future PTSD, due to gender nonconformity
Boston, MA – Children in the U.S. whose activity choices, interests, and pretend play before age 11 fall outside those typically expressed by their biological sex face increased risk of being physically, psychologically, and sexually abused, and of suffering from posttraumatic stress disorder (PTSD) by early adulthood, according to a new study led by researchers at Harvard School of Public Health (HSPH). It is the first study to use a population-based sample to look at gender nonconformity as a risk factor for abuse.

The study was published online February 20, 2012 and will appear in the March 2012 print issue of Pediatrics.
"The abuse we examined was mostly perpetrated by parents or other adults in the home. Parents need to be aware that discrimination against gender nonconformity affects one in ten kids, affects kids at a very young age, and has lasting impacts on health," said lead author Andrea Roberts, a research associate in the Department of Society, Human Development, and Health at HSPH.

PTSD has been linked to risky behavior such as engaging in unprotected sex, and also to physical symptoms such as cardiovascular problems and chronic pain.

The researchers, led by Roberts and senior author S. Bryn Austin, associate professor in the Department of Society, Human Development, and Health at HSPH, and in the Division of Adolescent and Young Adult Medicine at Children's Hospital Boston, examined questionnaire data gathered from nearly 9,000 young adults (average age 23) who enrolled in the longitudinal Growing Up Today study in 1996. Respondents were asked in 2007 to recall their childhood experiences, including favorite toys and games, roles they took while playing, media characters they imitated or admired, and feelings of femininity and masculinity. They also were asked about physical, sexual, or emotional abuse they experienced and were screened for PTSD.

Men who ranked in the top 10th percentile of childhood gender nonconformity reported a higher prevalence of sexual and physical abuse before age 11 and psychological abuse between ages 11 and 17 compared with those below the median of nonconformity. Women in the top 10th percentile reported a higher prevalence of all forms of abuse as children compared with those below the median of nonconformity. Rates of PTSD were almost twice as high among young adults who were gender nonconforming in childhood than among those who were not.

The researchers also found that most children who were gender nonconforming were heterosexual in adulthood (85%), a finding reported for the first time in this study. "Our findings suggest that most of the intolerance toward gender nonconformity in children is targeted toward heterosexuals," said Roberts.

More research is needed to understand why gender nonconforming kids experience greater risk of abuse, and to develop interventions to prevent abuse, the researchers said. They recommend that pediatricians and school health providers consider abuse screening for this vulnerable population.


**Protein That Sends 'Painful Touch' Signals Identified**
ScienceDaily (Feb. 19, 2012) — In two landmark papers in the journal *Nature* this week, scientists at The Scripps Research Institute report that they have identified a class of proteins that detect "painful touch."

Scientists have known that sensory nerves in our skin detect pressure, pain, heat, cold, and other stimuli using specialized "ion channel" proteins in their outer membranes. They have only just begun, however, to identify and characterize the specific proteins involved in each of these sensory pathways. The new work provides evidence that a family of sensory nerve proteins known as piezo proteins are ion channel proteins essential to the sensation of painful touch.

The experiments in the new study were conducted in fruit flies, a model system for the sensory nervous system of mammals, where piezo proteins are also expressed, as well as in certain cell types in the ear, kidney, heart, and other tissues. Future studies will focus on the roles of piezo proteins in sensing sound, blood pressure, and related stimuli that press and/or stretch cell membranes.

"Researchers in this field have been trying for decades to identify pressure-transducing ion channel proteins that exist in mammals, and these piezo proteins are exceptionally strong candidates," said Ardem Patapoutian, a professor in the Department of Cell Biology and the Dorris Neuroscience Center at Scripps Research, and a senior investigator for both papers. "We now have solid clues that we can follow up to learn how the mechanotransduction pathway works and how it is disrupted in diseases."

The two papers appear online in *Nature* on February 19, 2012.

**Following the Path of Clues**
Patapoutian’s laboratory specializes in the study of sensory ion-channel proteins. When hit by a stimulus to which it is sensitive, one of these proteins typically will open its structure to allow charged calcium, sodium, or potassium molecules ("ions") to flow from the fluid outside the cell into the cell's interior. Ion channels that sense mechanical pressure are thought to open when the membrane in which they are embedded is distorted past a certain threshold. The resulting flow of charge can trigger other signals inside the cell, for example a nerve impulse within sensory neurons—and in a human, a sufficient number of these nerve impulses would be interpreted by the brain as a touch- or pressure-related feeling.
In a highly cited paper published in *Science* in late 2010, Patapoutian and his colleagues reported that two mouse proteins of previously unknown function exhibited properties of mechanotransducers. Cells to which these proteins were added drew in positively charged ions when subjected to mechanical pressure. Bertrand Coste, the first author of the paper, named the two closely related proteins piezo1 and piezo2—the prefix "piezo-" being derived from the ancient Greek word for pressure or squeezing.

"Since these proteins bore little resemblance to known ion channel proteins, the next step for us was to confirm that they are indeed ion channel proteins," Patapoutian said. The new studies take this step and more.

In the first of the new studies, lead authors Bertrand Coste, Bailong Xiao, and their colleagues confirmed that piezo proteins are indeed ion channel proteins, and very large ones. "It assembles into a 'tetramer' complex of four piezo proteins, which appears to be the biggest plasma membrane ion channel yet discovered," said Coste, a research associate in the Patapoutian lab. The protein sequences within piezo also suggest that its ion channel structure weaves through the cell membrane more than 100 times.

Collaborating researchers in the laboratory of Mauricio Montal, a Distinguished Professor of Neurobiology at the University of California, San Diego, found that even in the absence of other proteins, piezo proteins could self-assemble into this tetramer complex, forming ion channels in artificial membranes known as lipid bilayers.

The second of the new studies involved experiments with the fruit fly *Drosophila*. Sung Eun Kim, first author of the study, genetically engineered a line of *Drosophila* that does not express the *Drosophila* piezo (*dpiezo*) gene. "We found that their larvae showed a severe loss of responsiveness to mechanical stimuli that would be expected to generate pain-related signals, though they responded normally to other kinds of stimuli such as heat and mild pressure," she said. Kim is a graduate student who divides her time between the Patapoutian lab and the lab of Scripps Research Assistant Professor Boaz Cook, who was co-principal investigator of this study.

Kim also used genetic "knockdown" techniques in *Drosophila* to show that interrupting *dpiezo* expression in certain sensory neurons could reproduce this loss of sensitivity. Finally, when she artificially reinstated *dpiezo* expression in larvae that had been born without the gene, they displayed normal sensitivity to strong pressure. "It's the first demonstration of a specific physiological function of a piezo family protein," said Cook.

The Patapoutian lab now is now conducting detailed follow-up studies of piezo and other possible mechanotransduction proteins. "In the next several years, we'll be trying to determine all the biological processes and diseases in which these pressure-sensing proteins play a role," he said.

**Journal References:**
**Traitorous Immune Cells Promote Sudden Ovarian Cancer Progression**

ScienceDaily (Feb. 20, 2012) — Aggressive ovarian tumors begin as malignant cells kept in check by the immune system until, suddenly and unpredictably, they explode into metastatic cancer. New findings from scientists at The Wistar Institute demonstrate that ovarian tumors don’t necessarily break "free" of the immune system, rather dendritic cells of the immune system seem to actively support the tumor's escape. The researchers show that it might be possible to restore the immune system by targeting a patient’s own dendritic cells.

"Our model shows where the cancer is kept in check for relatively long periods, but once they become noticeable, tumors grow exponentially," said José R. Conejo-Garcia, M.D., Ph.D., an associate professor at Wistar and leader of the Tumor Microenvironment and Metastasis Program of Wistar’s Cancer Center. "More importantly, we show that by depleting these dendritic cells of the immune system, we can reverse the effect, once again allowing our immune system to recognize the ovarian tumors."

Their findings, presented in the March issue of the *Journal of Experimental Medicine*, available online now, represent the first successful attempt to model the tumor microenvironment of human ovarian cancer in a mouse model of the disease. In essence, the model replicates the inflammatory surroundings that ovarian tumors experience in humans. The more accurate model provides a better tool for researchers to understand, prevent, and treat tumors.

"Our system uses oncogene-driven tumors that are spontaneously antigenic, thus avoiding the use of artificial foreign antigens that do not accurately replicate what drives anti-tumor immune responses in humans," Conejo-Garcia said.

Ovarian cancer remains one of the most deadly forms of cancer in women. According to the National Cancer Institute, 21,990 women will be diagnosed with ovarian cancer, and 15,460 women will die of the disease this year. Because early-stage ovarian cancer does not often exhibit noticeable symptoms, many women are not diagnosed until the cancer is at a later stage, when it is most difficult to treat.

"While we have seen an increase in survival rates for most cancers over the last 40 years, ovarian cancer survival has only improved slightly since the 1970s," Conejo-Garcia said. "We created our ovarian cancer model to get a better understanding of how these tumors acquire such aggressive characteristics and evade the immune system."

According to Conejo-Garcia, their model demonstrates how a localized ovarian tumor flares into an aggressive metastatic disease.

"You can see where, if one ovary is cancerous, it is almost unrecognizable until an instantaneous moment, when it explodes into exponential growth," Conejo-Garcia said. "The key to this moment, our evidence suggests, is in the phenotypic changes taking place in the dendritic cells that are part of the tumor microenvironment."

In healthy tissue, dendritic cells function as sort of alarm system to alert the adaptive part of the immune system to potential threats. They work as antigen-presenting cells, offering foreign or disease-causing molecules (called antigen) to the white blood cells that can then respond to an infection or, in this case, tumorous growths. Amid the ovarian cancer microenvironment, dendritic cells also induce the immune system to attack tumor cells and inhibit their growth.

Until, that is, dendritic cells seem to switch sides.

"We see a change in the dendritic cells themselves, which allows tumors to progress to terminal disease in a very short time," Conejo-Garcia said. "Interestingly, the tumors themselves are still immunogenic—they could still otherwise elicit an immune response—it is just that the dendritic cells are actively suppressing the involvement of other anti-tumor immune cells; primarily T cells."

Conejo-Garcia and his colleagues believe that their findings offer a twist on the emerging theory of "cancer immunoediting." The immunoediting hypothesis suggests that the immune system actively "edits" tumor cells to eliminate antigens that are recognized by immune cells, keeping the cancer at bay before it becomes symptomatic. All symptomatic tumors, therefore, represent a failure of the immune system,
where tumors lose their immunogenicity— their ability to trigger and be recognized by our immune system.

The researchers found that depleting dendritic cells early on accelerating tumor expansion, while removing dendritic cells later on actually delayed the tumor's progression. According to Conejo-Garcia, their findings suggest it is a change in the immune system itself, specifically the dendritic cells, and not primarily any loss of immunogenicity on the part of the tumor.

"It is almost as if anti-tumor T cells become exhausted, they can no longer keep up the effort," Conejo-Garcia said. "Still, our findings suggest that the enduring activity of these T cells would allow us to control metastatic ovarian cancer by targeting the dendritic cells that actively prevent their anti-tumor functions."

In fact, Conejo-Garcia and his colleagues have already developed a strategy to reprogram traitorous dendritic cells. In an upcoming edition of the journal Cancer Research, available online now, the researchers demonstrate how synthetic RNA molecules can be used to win back the allegiance of dendritic cells and restore their ability to stimulate tumor suppression.

**Journal Reference:**

**Live from the Thymus: T-Cells On the Move**

ScienceDaily (Feb. 17, 2012) — For the first time, scientists have followed the development of individual immune cells in a living zebrafish embryo.

T-cells are the immune system's security force. They seek out pathogens and rogue cells in the body and put them out of action. Their precursors are formed in the bone marrow and migrate from there into the thymus. Here, they mature and differentiate to perform a variety of tasks. Scientists at the Max Planck Institute of Immunobiology and Epigenetics in Freiburg have now succeeded for the first time in observing the maturation of immune cells in live zebrafish embryos. During their development, the immune cells migrate into and out of the thymus more than once. The zebrafish is thus an ideal animal model for studying the dynamic processes of immune cell development.

The thymus is a small, inconspicuous organ, but it is also vital for a functional immune system. This is because it is the development site of the T-lymphocytes (T-cells), which play a central role in the body's immune defences. Their precursors come from the bone marrow and are lured into the thymus by chemical attractants called chemokines. Once in the thymus, they develop into different T-cell types, which are eventually deployed into the rest of the body.

A research team at the Max Planck Institute of Immunobiology and Epigenetics in Freiburg has now succeeded for the first time in observing these processes live. They have tracked the real-time development of T-cells in living zebrafish embryos, starting with the formation of the thymic anlage (the cluster of embryo cells from which the thymus develops), via the cells' migration into the organ from the bone marrow, right up to the stage when the fully formed T-cells are released from the thymus.

As the researchers discovered, this is a highly dynamic process: the precursor cells do not take a direct migration route into the thymus. Instead, they seem "undecided" and leave the organ several times before they finally settle there. "So far, we have no idea why this happens," says Thomas Boehm, Director at the Freiburg-based Max Planck Institute, who leads the study. The cells also migrate within the thymus. "This dynamic behaviour was previously unknown, as we were not able to observe the cells for any length of
time," explains the scientist. These observations also show that the migration from bone marrow into the thymus is driven by the chemokines alone and is largely independent of the blood circulation. For their study, the investigators used genetically modified zebrafish embryos. They are particularly well suited for this type of research, as the thymus is embedded in translucent tissue and the embryos can be observed live under the microscope. T-cell development in the zebrafish is comparable to that of mammals. The researchers used a fluorescent dye to make the thymus tissue visible. They labelled the immune cells with a different fluorescent protein, which changes colour from green to red when it is exposed to light. By illuminating the thymus, they were then able to watch the green cells migrate into the thymus, while the red cells migrated back out again. "This change in colour clearly shows that the same cells were involved," says Thomas Boehm. The technique also made the cell movements within the thymus visible: if the scientists briefly exposed only a small area of the thymus to the light source, they could then observe green and red cells gradually mingling back together again. Zebrafish mutants without a beating heart provided the researchers with proof that the precursor cells do not simply follow the blood flow when they migrate into the thymus, but that they are instead attracted there by the chemokines. The researchers in Freiburg have thus succeeded in tracking the development of immune cells in a vertebrate for the first time. "It turns out that the zebrafish is well suited for this kind of experiment," says Thomas Boehm. "For example, we can now carry out direct tests to determine what effect certain substances have on the formation and maturation of the T-cells and the thymus tissue." Therefore, the study not only contributes towards a better understanding of the way the immune system works, the method could also help with the development of drugs to treat malfunctions of the thymus.

**Journal Reference:**

**Which Anti-HIV Drug Combinations Work Best and Why?**
ScienceDaily (Feb. 19, 2012) — Using a mathematical formula that carefully measures the degree to which HIV infection of immune system cells is stalled by antiretroviral therapy, AIDS experts at Johns Hopkins have calculated precisely how well dozens of such anti-HIV drugs work, alone or in any of 857 likely combinations, in suppressing the virus. Results of the team's latest research reveal how some combinations work better than others at impeding viral replication, and keeping the disease in check.

"Our study results should help researchers and clinicians develop simpler treatments, using either existing or new drugs, for people who are just starting therapy or people who have already tried and developed resistance to another combination," says senior study investigator and infectious disease specialist Robert Siliciano, M.D., Ph.D.

Siliciano, a professor at the Johns Hopkins University School of Medicine and a Howard Hughes Medical Institute investigator, and colleagues constructed the measurement tool, called the instantaneous inhibitory potential, or IIP, in the laboratory several years ago by analyzing the shape of drug dose-response curves in human immune system cells infected with HIV. They found that the curves' steepness reflects the extent to which small increases in the amount of drugs can further suppress attempts by the virus to bounce back, reproduce and spread.

Researchers say their latest study findings, to be published in the journal *Nature Medicine* online Feb. 19, along with other recent studies, provide valuable information to physicians about the potential strength of different combination drug therapies, and can help in streamlining and tailoring so-called highly active antiretroviral therapy, or HAART, to as few possible drugs as needed. Several hundred thousand of the more than 1 million Americans living with HIV disease are currently using HAART to fight the disease.

Among the latest study's key findings was that the most potent drug combos included the drugs efavirenz (a non-nucleoside reverse transcriptase inhibitor) and darunavir (a protease inhibitor.) According to the Hopkins team's calculations, the drug mix suppressed viral replication by more than a trillion times, enough to prevent infection of every single lymphocyte, or immune system cell, of which there are a trillion in the body.

The least-powerful drug was found to be one of the oldest anti-HIV medications, d4T, or stavudine (a nucleoside analogue reverse transcriptase inhibitor), which had the power to suppress viral replication by less than 10 times if used on its own (although, Siliciano points out, it works much better when taken in combination with other drugs.)
Siliciano says the most widely used combination, a single pill known as Atripla, consisting of tenofovir disoproxil fumarate (a nucleotide analogue reverse transcriptase inhibitor), emtricitabine (a nucleoside analogue reverse transcriptase inhibitor), and efavirenz, was able to reduce viral replication to as few as one in a billion.

Siliciano points out, however, that any drug combination which suppresses viral replication to the degree that out of every 100,000 lymphocytes exposed to the drugs, only one lymphocyte is likely to be infected (for five tenfold reductions)—is sufficient to keep the disease in check, so long as people take their medication as prescribed.

"This means that overall access to anti-HIV medications could also improve as we develop simpler combinations of fewer drugs to achieve near total suppression," says Siliciano. Less than 7 million of the 34 million people worldwide infected with HIV are taking antiretroviral therapy, he notes.

The Johns Hopkins team based its new calculations on five years of analyzing just how antiretroviral drugs hinder key steps in HIV’s life cycle, preventing it from replicating and infecting other immune system cells.

Scientists have for decades focused on multiple drugs targeting different enzymes that are key to the viral life cycle, thinking that multiple barriers along the chain could best halt replication.

Although the strategy worked, scientists had, until now, no theory to explain why some drug combinations worked well and others did not. Indeed, they point out, one of the newest classes of anti-HIV medications, so-called integrase inhibitors, did not work well as single drug treatments in laboratory experiments, but were highly effective in people when combined with other drugs.

Siliciano says that as a result of the Hopkins team’s latest research and another of their recent findings, published in Science Translational Medicine in July, experts can finally demonstrate how different drug combinations disrupt and halt viral replication.

Researchers found that the steepest curves occurred when the drug targeted a stage in HIV’s life cycle, in which many copies of viral enzymes, were needed. Citing protease inhibitors as an example, Siliciano says several copies of protease enzyme are needed to cleave the virus into hundreds of working parts before HIV can infect a new immune system cell. He goes on to say that "a level of inter-enzyme cooperation" is happening, specific to each stage of HIV replication.

"Our research shows that drugs like protease inhibitors really work like an on-off switch," says Siliciano. "Above a certain concentration, these drugs completely turn off viral replication. When you have only one copy of a viral enzyme needed in any key part of HIV’s life cycle, a little more drug won't give you a lot more suppression; but, when you have more than one copy of enzyme needed for viral replication, then the dose-response curve for the drug will be a lot steeper, and a little more drug will completely shut off viral replication, which is what we want.

"It’s gratifying to finally have a consistent metric for evaluating HAART medications that offers reliable information on how well they work in stopping HIV replication, and which also gives us a baseline target for suppression at less than one in 100,000 immune cells becoming infected in the presence of any drug combination," he adds.

The Johns Hopkins inhibition index was first developed to compare the level of viral inhibition from different drugs in different classes and to show how they could be graded.

Having measured the different potencies of many drugs, Siliciano conducted his next set of lab experiments to focus on the explanation behind different strengths of viral inhibition. The scientists measured the changes in the dose-response curves, plotting the results on graphs and comparing the sloping curves for each drug or combination of drugs.

Currently, there are more than 34 million people in the world living with HIV, including an estimated 1,178,000 in the United States.

Journal Reference:
Benjamin L Jilek, Melissa Zarr, Maame E Sampah, S Alireza Rabi, Cynthia K Bullen, Jun Lai, Lin Shen, Robert F Siliciano. A quantitative basis for antiretroviral therapy for HIV-1 infection. Nature Medicine, 2012; DOI:

Anthrax-Killing Foam Proves Effective in Meth Lab Cleanup, Study Suggests
ScienceDaily (Feb. 16, 2012) — Sandia’s decontamination foam, developed more than a decade ago and used to decontaminate federal office buildings and mailrooms during the 2001 anthrax attacks, is now being used to decontaminate illegal methamphetamine labs.

Mark Tucker, a chemical engineer in Sandia’s Chemical & Biological Systems Dept. and co-creator of the original decontamination foam, said it renders all types of typical chemical and biological agents harmless.
"For structures contaminated with meth, owners have two choices: demolish it or reclaim it," said Kevin Irvine, vice president and general manager at EFT Holdings, which licenses the Sandia formulation and sells it under two names, EasyDecon® DF200, certified against chemical and biological agents, and Crystal Clean, intended for meth cleanup.

The meth cleanup problem is a big one. The U.S. Drug Enforcement Administration's (DEA) Clandestine Meth Lab registry lists thousands of locations in the U.S. where law enforcement agencies have found chemicals or paraphernalia indicating the presence of either clandestine drug laboratories or dumpsites.

In 2007, EFT released Crystal Clean, a chemically identical formula to EasyDecon DF200, but packaged and marketed specifically for meth cleanup. Sites contaminated with meth are considered crime scenes, but the contamination is chemical rather than biological.

The approximately 700 remediation companies that clean up meth lab contamination also do other types of crime scene cleanup because they are accustomed to the sampling and documentation process.

**Holding the bag**

"Property owners are often liable for expensive cleanup costs since most insurance companies won't pay for cleanup related to methamphetamine, viewing damage resulting from meth labs as arising from a criminal act," Irvine said. "That means that property owners and landlords are often left holding the bag for the cost of remediating a residence or business contaminated as a result of meth cooking."

According to the Department of Justice, the chemicals used to cook meth and the byproducts from its manufacture, produce toxic fumes, vapors and residues. The report said anyone exposed to these byproducts, especially children, could suffer short- and long-term health problems. Prolonged exposure to meth byproducts may cause cancer; damage the brain, liver, kidney, spleen and immunologic system; and result in birth defects.

Tucker said many cleaning methods don't remove methamphetamine and the chemicals used to produce it. Incompletely or improperly cleaned surfaces, such as floors, countertops and drywall, can remain contaminated for months or even years, even after many cleanups.

Sandia's decontamination formulation includes a collection of mild, nontoxic and noncorrosive chemicals found in common household products, such as hair conditioner and toothpaste. It contains both surfactants, which lift agents off a surface, and mild oxidizers, which break down the agent's molecules into nontoxic pieces that can be washed down a household drain like detergent or dish soap.

**Formulation left meth nondetectable**

In experiments from a few years ago, John Martyny, associate professor and industrial hygienist at the National Jewish Medical and Research Center's Division of Environmental and Occupational Health Sciences and a national expert on the effects of meth exposure on children, compared the effectiveness of common cleaners, such as detergent and bleach, on methamphetamine cleanup. Martyny included Sandia's decontamination formula in the testing. His experiments showed that, after cleaning with EasyDecon, the methamphetamine present on tested surfaces was likely oxidized to another compound and was nondetectable.

Irvine said even if a meth site is known, it doesn't always mean it gets cleaned up, due to the expense. Some states don't have cleanup guidelines and don't require homeowners to disclose whether a structure is contaminated with meth. Some families have discovered they were living in a house contaminated with meth only after family members were hospitalized for respiratory problems characteristic of chronic meth exposure.

In the 22 states that have guidelines, structures contaminated with meth are seized by police and the structure is quarantined by a local or state agency (depending on the state) until the structure is proven cleared of methamphetamine to a certain level. During structure remediation with Crystal Clean, a remediation crew removes everything from the structure, including carpets and drapes, until the house is stripped bare except for the fixtures.

The crew mixes the Crystal Clean solution on site and sprays the foam on walls, ceilings and floors. The foam expands to about 15 times its liquid volume through a special nozzle that draws air into the spray, allowing it to reach contamination in crevices and in the air. In an hour, it collapses back to a liquid. Using only fresh water, rags and sponges, the crew then removes the benign residue from all surfaces.

After the site is cleaned, an independent industrial hygienist tapes off a sample area in the cleaned structure and takes a number of swipe samples appropriate for the location size. The samples are treated as evidence, a formal chain of custody is established and they are taken to an independent lab. The lab runs the samples through a mass spectrometer to determine the level of contamination.
Foam deployed as a preventive measure

In most instances, Crystal Clean reduces the levels to .02 μg/100 square cm (microgram/sq. cm) or less, which is considered nondetectable.

Irvine said the Crystal Clean formula is more expensive than other cleaners, but it saves greatly on labor costs and lab costs because other cleaning solutions usually require more than one cleaning, with a larger crew doing the cleaning and with costly sampling taking place in between cleanings. Another advantage of this cleanup method, Irvine said, is that some other methods are destructive or use more corrosive substances and the resulting chemical residues are themselves toxic. Crystal Clean is rendered nonhazardous and nontoxic, requiring only a surface wipe when finished.

Sandia’s decontamination formula was developed with funding provided by the DOE and NNSA Chemical and Biological National Security Program (CBNP).

Hepatitis C surpasses HIV as a cause of death in the US

Michael Carter
Published: 21 February 2012

Deaths in the US due to hepatitis C now exceed those caused by HIV, according to research published in the Annals of Internal Medicine. The study showed that there is a downward trend in HIV-related mortality, but incidence of deaths due to hepatitis C is increasing.

“This analysis shows the rapidly increasing number of deaths among HCV [hepatitis C virus]-infected persons, which now surpass deaths among HIV-related persons,” write the authors.

Mortality was concentrated in the “baby boomer” generation, individuals aged between 45 to 64 years. The investigators believe this pattern “portends a large and ever-increasing health care burden.”

The majority of hepatitis C infections in the US are undiagnosed and a separate study published in the same journal shows that targeted hepatitis C screening of individuals in this age group would be cost-effective and could avert up to 121,000 deaths compared to current risk-based screening.

Infection with hepatitis B and hepatitis C are leading causes of chronic liver disease and liver cancer in the US. In 2007, they were listed among the 15 leading causes of death.

Investigators used information recorded on death certificates to plot trends in mortality due to hepatitis B and hepatitis C between 1999 and 2007. These trends were compared to the incidence of HIV-related deaths over the same period. Analysis was also undertaken to determine the factors associated with hepatitis-related deaths in 2007.

Approximately 21.8 million death certificates were included in the investigators’ analysis.

There was a non-significant decrease in hepatitis B-related mortality of 0.02 deaths per 100,000 person years. However, the incidence of hepatitis C-related deaths increased by a significant 0.18 per 100,000 person years (p = 0.002). This compared to a reduction in HIV-related mortality of 0.21 per 100,000 person years (p = 0.001). Indeed, in 2007 mortality associated with hepatitis C infection surpassed that from HIV infection.

Hepatitis B was documented as the underlying cause of 724 deaths (0.03%) and as the single underlying or contributing cause in 1815 deaths (0.07%; adjusted mortality rate, 0.56 deaths per 100,000 person years).

Infection with hepatitis C virus was documented as the underlying cause of 6605 deaths (0.27%) and as the underlying or contributing cause of 15,106 deaths (0.62%; adjusted mortality rate, 4.58 deaths per 100,000 person years).

This hepatitis C-related mortality exceeded that attributed to HIV. Infection with HIV was listed as the underlying cause of death on 11,332 death certificates (0.47%), and the underlying or contributory cause in 12,734 deaths (0.52%; adjusted mortality rate, 4.16 deaths per 100,000 person years).

The investigators believe that these data grossly underestimate the true burden of hepatitis C-related mortality. “HCV infection and HCV-related chronic liver disease have remained consistently poorly ascertained and, thus, under-reported on death certificates.”

A number of co-morbid conditions were strongly related to death attributed to hepatitis B. These included chronic liver disease (AOR = 34.4; 95% CI, 31.0-38.1), co-infection with hepatitis C (AOR = 31.5; 95% CI, 28.0-35.4), HIV infection (AOR = 4.0; 95% CI, 3.2-5.1) and alcohol-related illness (AOR = 3.7; 95% CI, 3.2-4.2).

Co-morbid conditions related to hepatitis C mortality were chronic liver disease (AOR = 32.1; 95% CI, 31.0-33.3), co-infection with hepatitis B (AOR = 29.9; 95% CI, 26.5-33.6), alcohol-related illness (AOR = 4.6; 95% CI, 4.4-4.8) and HIV co-infection (AOR = 1.8; 95% CI, 1.6-2.0).
Deaths attributable to viral hepatitis infection were clustered in the “baby boomer” generation, individuals born between 1945 and 1964. In all, 59% of hepatitis B-related deaths were involved persons aged between 45 and 64 years as did 73% of deaths attributed to hepatitis C.

“Few diseases of such morbidity and mortality in the United States have received so little public attention and funding as chronic viral hepatitis,” comment the authors.

Current screening strategies are risk-based, targeting individuals with a history of injecting drug use. The investigators suggest this has been “notably unsuccessful, as few have been screened for risk and are still only tested when they have symptoms...few physicians ask about the major risk factor for HCV, injecting drug use, and few interviewees wish to admit this behavior.”

Because almost 75% of hepatitis C-related deaths involved individuals aged between 45 and 64 the researchers suggest “screening efforts that target middle-aged persons may be profitable.”

A second study published in the same edition of the Annals showed that such a strategy could be cost-effective and save tens of thousands of lives.

Researchers wanted to ascertain the effectiveness, benefits and cost of three approaches to hepatitis C screening and treatment. These were:

- Model 1: Risk-based screening, and hepatitis C therapy including pegylated interferon and ribavirin.
- Model 2: Age-based screening (45 to 64 years) in routine care, with hepatitis C treatment with pegylated interferon and ribavirin.
- Model 3: Age-based testing, and hepatitis C triple hepatitis C therapy including a protease inhibitor, pegylated interferon and ribavirin.

The authors calculated that 2.4 million hepatitis C-infected individuals had a primary care consultation in 2006 and that 50% of these infections were undiagnosed.

Risk-based screening would lead to 135,000 patients receiving hepatitis C therapy, which would be successful for 53,000 patients. A total of 592,000 patients would die of liver-related causes.

Screening based on age would identify 1,070,840 infections. An estimated 552,000 patients would receive treatment with pegylated interferon and ribavirin and 229,000 would be cured of their infection. Compared to the risk-based strategy, 82,000 deaths would be averted compared to risk-based testing. The cost of this age-based screening with standard two-drug treatment was $15,700 per QALY compared with risk-based screening.

The addition of a protease inhibitor would increase the number of patients achieving a cure to 311,000, avertig 121,000 deaths compared to screening based on risk. The estimated cost was $35,700 per QALY gained. The cost of this strategy was equivalent “to cervical cancer or cholesterol screening.”

The authors therefore conclude, “birth-cohort screening seems to be a reasonable strategy to identify asymptomatic cases of HCV.”

Reference

Sexual Compulsivity, Co-Occurring Psychosocial Health Problems and HIV Risk Among Gay and Bisexual Men: Further Evidence of a Syndemic
American Journal of Public Health Vol. 102; No. 1; P. 156-162, (01..2012) Jeffrey T. Parsons, PhD; Christian Grov, PhD, MPH; Sarit A. Golub, PhD, MPH

The authors set out to evaluate whether sexual compulsivity fits into a syndemic framework, in which it is “one of a number of co-occurring psychosocial health problems that increase HIV risk among men who have sex with men (MSM).”

In New York City from 2003-04, the team conducted an anonymous survey of 669 MSM; the men were approached at gay, lesbian and bisexual community events. Bivariate and multivariate logistic regression were used to analyze the data.

“We found strong positive interrelationships among syndemic factors including sexual compulsivity, depression, childhood sexual abuse, intimate partner violence and polydrug use,” the authors reported.

Bivariate analyses showed all syndemic health problems except childhood sexual abuse were positively related to HIV seropositivity and high-risk sexual behavior. The multivariate models showed “an array of interrelationships among psychosocial health problems. We found amplified effects of these
problems on HIV seropositivity and on the likelihood of engaging in high-risk sexual behavior," the authors wrote.

“Our findings support the conclusion that sexual compulsivity is a component of a syndemic framework for HIV risk among MSM,” the team concluded. “HIV prevention interventions should consider the overlapping and compounding effects of psychosocial problems, including sexual compulsivity.”

**Russian Government’s Censorship Of Websites With Harm Reduction Methods For Drug Users Helps Fuel HIV Epidemic, IPS Reports**

"A recent government crackdown on Russian media, particularly online information portals specializing in health tips and harm reduction methods for drug users, has sparked widespread public opposition, with critics claiming that the ‘draconian silencing’ of public health advocates could worsen an already perilous health situation in the country,” Inter Press Service reports. "Given that Russia currently has one of the largest populations of injecting drug users in the world as well as one of the fastest growing HIV epidemics, the dissemination of such information is essential to keep the spread of the virus under control," IPS writes. "The fact that the United Nations listed universal treatment for people living with HIV/AIDS as one of its most urgent millennium development goals (MDGs)—with a deadline of achieving universal treatment by 2015—human rights and health advocates contend that Russia's failure to allow information or services helpful to drug users breaches international human rights and public health laws," according to the news service (Klomegah, 2/17).

**India Still Faces Challenges In Efforts To Eradicate Polio**

The PBS NewsHour examines polio eradication efforts in India, which has gone an entire year without reporting a polio case. "For India, the challenge is to remain vigilant and polio free for two more years to officially fall off the list of endemic countries," according to the news service (De Sam Lazaro, 2/20). "The success in India has been achieved through a partnership between the Indian government, with support from the World Health Organization (WHO), Rotary, UNICEF and with major contributions from the Bill & Melinda Gates Foundation," BBC News reports in an analysis of India’s success. "The global effort to eradicate polio is the biggest public health initiative in history. It has cost billions and has already stopped a huge amount of disability and many deaths," but the disease remains endemic in three countries—Afghanistan, Nigeria and Pakistan, the news service notes (Walsh, 2/19).

**Evolution of staph 'superbug' traced between humans and food animals**

FLAGSTAFF, Ariz.—A strain of the potentially deadly antibiotic-resistant bacterium known as MRSA has jumped from food animals to humans, according to a new study involving two Northern Arizona University researchers.

Paul Keim, Regents’ professor and director of NAU’s Center for Microbial Genetics and Genomics, and Lance Price, NAU faculty member and director of the Center for Food Microbiology and Environmental Health at the Translational Genomics Research Institute, collaborated with scientists at 20 institutions around the world on the study published today in the online journal mBio.

The TGen-led research utilized whole genome sequencing to study 89 genomes from humans and animals — including turkeys, chickens and pigs — with samples from 19 countries on four continents.

The research focused on methicillin-resistant Staphylococcus aureus CC398, also known as pig MRSA or livestock-associated MRSA because it most often infects people with direct exposure to swine or other food animals. It is likely that MRSA CC398 started as an antibiotic-susceptible strain in humans before it jumped to food animals.

After transferring to food animals, MRSA CC398 became resistant to two important antibiotics, tetracycline and methicillin, which are used for treating staph infections. The resistance likely is a result of the routine antibiotic use that characterizes modern food-animal production. The animals commonly are given antibiotics to prevent infection and promote growth.

Keim, who also serves as director of TGen’s Pathogenic Genomics Division, said the study describes evolution in action. "The most powerful force in evolution is selection. And in this case, humans have supplied a strong force through the excessive use of antibiotic drugs in farm animal production. It is that inappropriate use of antibiotics that is now coming back to haunt us."
Price, the study’s lead author, said the research was “like watching the birth of a superbug—it is simultaneously fascinating and disconcerting.” He said that while this strain of MRSA was discovered less than a decade ago it appears to be spreading very quickly.

“Our findings underscore the potential public health risks of widespread antibiotic use in food animal production,” Price said. “Staph thrives in crowded and unsanitary conditions. Add antibiotics to that environment and you’re going to create a public health problem.”

**Influenza vaccination of pregnant women helps their babies**
**Randomized controlled trial**

Vaccinating pregnant women against the influenza virus appears to have a significant positive effect on birth weight in babies, according to a study published in CMAJ (Canadian Medical Association Journal).

The study, a randomized controlled trial involving 340 healthy pregnant women in Bangladesh in the third trimester, looked at the effect of immunization with the influenza vaccine on babies born to vaccinated mothers. It was part of the Mother’sGift project looking at the safety and efficacy of pneumococcal and influenza vaccines in pregnant women in Bangladesh. The participants were divided into two groups, one with 170 women who received the influenza vaccine, and the second who received the pneumococcal vaccine as a control. Researchers compared the weight of babies born in two periods, one in which there was circulation of an influenza virus and one with limited circulation.

Babies that are small for their gestational age are at increased risk of health and other issues over their lives.

The researchers found that there were fewer babies who were small for their gestational age born to mothers in the influenza vaccine group when the virus was circulating, with 25.9% who were small compared with 44.8% in the control group. When the virus was dormant, the proportion of small-for-gestational-age births was similar in both groups. During the period with circulating influenza virus, the mean birth weight was 3178 g in the influenza vaccine group and 7% higher than 2978 g in the control group. The rate of premature births was lower in the influenza vaccine group as well.

“We found that immunization against influenza during pregnancy had a substantial effect on mean birth weight and the proportion of infants who were small for gestational age,” writes Dr. Mark Steinhoff, Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, with coauthors. “Our data suggest that the prevention of infection with seasonal influenza in pregnant women by vaccination can influence fetal growth,” state the authors.

The researchers calculate that 10 maternal influenza vaccinations given year-round prevented one small-for-gestational-age birth, dropping to 6 vaccinations during the period in which the influenza virus was circulating.

The authors suggest that if further research supports their findings, adding an influenza vaccine to routine vaccination programs during pregnancy could help children have a better start in life.

**Substantial number of HIV infections in UK-born patients acquired abroad**

Michael Carter
Published: 22 February 2012

A substantial number of HIV infections in UK-born individuals were acquired abroad, investigators report in HIV Medicine. Overall, 15% of HIV infections in UK nationals were probably acquired abroad, and “sex tourism” was a risk factor.

“We provide evidence of a substantial number of UK-born adults over the past decade acquiring HIV infection in countries with generalised epidemics, and in common holiday destinations,” write the authors. “Thailand…has become synonymous with ‘sex tourism’, [and] was by far the country most commonly reported. Of particular concern was the high proportion of men infected in Thailand who reported sex with a commercial sex worker.”

There is no sign that the UK’s HIV epidemic is abating. Between 2002 and 2010 a total of 15997 UK-born individuals were diagnosed with the infection in England and Wales. Investigators from the Health Protection Agency wished to determine how many of these infections were acquired abroad and the characteristics of these patients.

Information on the country of infection was available for 13891 individuals, of whom 15% (2066 people) probably acquired their infection outside the UK.

Compared with UK-born adults who were probably infected with HIV in the UK, the patients who were infected abroad were more likely to be female (19% vs. 15%), non-white (16% vs. 10%), and acquired
HIV heterosexually (70% vs. 22%) (all p < 0.001). Individuals infected abroad were also older (median 42 v. 36 years) and had lower CD4 cell counts at the time of diagnosis (median 340 vs. 390 cells/mm³). A significantly higher proportion of individuals infected abroad were diagnosed late (CD4 cell count below 350 cells/mm³, 52% vs. 45%).

The characteristics of UK-born men and women infected abroad differed somewhat.

The majority of men infected abroad were white (90%) and heterosexual (64%; 33% gay and other men who have sex with men). The most commonly reported countries where HIV infection was probably acquired were Thailand (31%), USA (6%), and South Africa (5%).

Among the men acquiring HIV heterosexually, 41% of infections occurred in Thailand, 5% in Nigeria and 5% in South Africa. For gay men, the most commonly reported countries were the USA (16%), Thailand (11%) and Spain (10%).

Almost all the women infected abroad reported heterosexual sex as their risk factor. Over half (58%) were white, 21% were black African and 12% black Caribbean.

The most commonly reported countries were Zimbabwe (16%), Nigeria (9%) and Jamaica (9%). The findings suggest that infection abroad is often linked to travel for reasons of family ties—99% of black African women acquired HIV in an African country.

Overall, 5% of UK-born adults infected abroad reported sex with a commercial sex worker compared to 1% of UK-born adults infected in the UK. Contact with a commercial sex worker was most frequently reported by men infected in Thailand (11%).

The investigators believe their findings have important implications for the design of HIV prevention initiatives.

“Limited funds for HIV prevention and testing have largely been focused on groups most at risk of acquiring HIV infection in the UK. Our findings call for the extension of these efforts to reduce HIV transmission and promote earlier diagnosis...among travellers abroad.

The authors conclude, “safer sex messages should include an awareness of the detrimental health and social impacts of the sex industry.”

Reference

Norwegian HIV vaccine—Very modest results seen in recent clinical trial
21 February 2012

Although HIV infection can be treated with combination therapy (commonly called ART or HAART), such therapy has at least the following drawbacks:

- ART must be taken at least once a day for the rest of one’s life
- ART has side effects
- ART does not cure HIV infection
- ART does not fully restore the immune system
- ART is expensive

Therefore, some scientists are undertaking the very difficult and long-term research that is needed to attempt to cure HIV infection. Not hedging their bets—it may not be possible to cure HIV infection—other scientists are working on vaccines for HIV. Such vaccines fall into two categories, as follows:

- a vaccine that can be given to HIV-negative people to protect them from infection
- a vaccine that can be given to HIV-positive people to help train their immune systems to fight HIV

These latter types of vaccines are called therapeutic vaccines.

The Norwegian biotechnology company Bionor Pharma ASA recently issued a press release about the results of its candidate therapeutic vaccine called Vacc-4x. The placebo-controlled study was conducted to assess safety and preliminary efficacy in HIV-positive people. Researchers had hoped that this vaccine would allow participants to have a prolonged interruption of ART with very low levels of virus in their blood. This did not happen. However, the vaccine is safe and does stimulate the immune system.

How does it work?

The vaccine is made from four small molecules taken from an inner, or core, protein of HIV called p24. These molecules or peptides used in the candidate vaccine cannot cause HIV. In some other studies, researchers have found that HIV-positive people who naturally produce high levels of antibodies against p24 seem to have a reduced pace of damage to their immune system as a result of HIV infection.
Researchers first gave participants a small dose of the bone marrow stimulant GM-CSF (granulocyte-macrophage-colony-stimulating factor; Leukine, sargramostim), as this can temporarily stimulate the formation of several types of cells, including dendritic cells (DCs). The vaccine is then injected into the skin—the body’s largest organ—where it is taken up by DCs. These cells serve to capture invading germs and alert the rest of the immune system about them. Also, DCs can help amplify the subsequent reaction by the immune system to invading germs.

When vaccinated with the peptides in Vacc-4x, DCs capture the peptides and take them to lymph nodes and lymph tissues. There, DCs show other cells of the immune system the peptides and encourage them to attack p24 and, therefore, HIV and HIV-infected cells. Ultimately, researchers hoped that the vaccine would coax the immune system into destroying HIV-infected cells and reduce the burden of HIV in the body.

**Study details**

As we received word about the study via press release from Bionor Pharma ASA, we cannot provide our readers with the details that we normally provide.

HIV-positive participants on ART were recruited from the following countries:

- Germany
- Italy
- Spain
- UK
- United States

Participants were randomly assigned to receive one of the following interventions in a 2:1 ratio:

- Vacc-4x – 93 participants
- placebo (fake vaccine) – 43 participants

For the first six months of the study, participants took ART. For the second half of the one-year study, participants stopped taking ART and were monitored. If the amount of HIV in their blood during this second part of the study was very low, they were allowed to remain free from therapy for up to 24 consecutive weeks.

**Results**

The corporation’s latest press release suggests that 25 people who received placebo and 56 who received Vacc-4x completed the study. The trial failed to fulfill its primary purpose: finding a significant difference between vaccine and placebo in the time that participants were able to stay off ART. Details about this were absent from the press release.

When participants stopped taking ART, levels of HIV in the blood appeared to stabilize as follows:

- Vacc-4x – 23,000 copies/ml
- placebo – 62,000 copies/ml

This difference was statistically significant; that is, not likely due to chance alone.

This difference, while hinting that Vacc-4x may indeed have helped the immune system, needs to be understood in the context of HIV treatment. Whatever impact Vacc-4x had on viral load, it did not allow recipients to remain off therapy longer than people on placebo.

These results are interesting but do not mean that Vacc-4x is suitable for approval by regulatory authorities in any high-income country because the clinical benefit (time off therapy) was not significant.

In general, interrupting ART is fraught with risk. Without the suppression provided by drugs, production of HIV increases and the spread of the virus resumes throughout the body. HIV also causes inflammation that damages many organs, including the following:

- brain
- heart
- kidneys
- liver
- lungs

The press release did not mention any changes in assessments of inflammation during the study.

**Vaccine + lenalidomide**

The corporation is considering an additional study of Vacc-4x together with the drug Revlimid (lenalidomide). This drug is chemically related to thalidomide. Drugs such as lenalidomide and thalidomide appear to suppress inflammation and some immune responses. In theory, such suppression may be useful in cases where there is excessive inflammation or inappropriate immune responses, such as...
occur in cancers and HIV infection. However, these drugs carry the potential of weakening the immune system. Several clinical trials in HIV-negative people have found an increased risk for developing other cancers in people who received lenalidomide. Therefore, this drug needs to be used cautiously. Additionally, lenalidomide and thalidomide can cause fetal deformities and so their use is not suitable in women who wish to become pregnant or in men who are trying to help women conceive, as researchers do not know if these drugs are ejaculated.

The American Food and Drug Administration (FDA) is currently reviewing data on lenalidomide and will issue a statement once it has completed its review.

**Are two vaccines better than one?**
Bionor has another HIV vaccine candidate called Vacc-C5. By giving HIV-positive people both Vacc-4x and Vacc-C5, the corporation hopes that immune responses to HIV will be better. This will require a well-designed clinical trial.

**The long road to an HIV vaccine**
In 1983, Françoise Barré-Sinoussi, PhD, isolated HIV from the lymph node of an infected patient. Shortly after that time researchers hoped that an effective vaccine against HIV would be quickly created. However, in the 30 years since the discovery of HIV, researchers have struggled to create an effective vaccine. In part, this is because HIV appears to be unique among viruses, infecting the immune system—the system that serves the purpose of protecting the body from infection. Shortly after it penetrates the wet tissues of the anus and vagina and begins to infect cells, HIV quickly spreads to the lymph nodes and every organ, destroying critical immune system cells and embedding itself so that it becomes very difficult to remove. Moreover, it causes continuing dysfunction within the immune system, hampering its ability to clear this virus. Also, researchers are continually amazed by the never-ending complexity of the immune system. Until they have a better understanding of how the immune system works, particularly its interaction with HIV, they cannot create an effective vaccine.

**Looking to the future**
HIV vaccine research is inherently time consuming, complex and intellectually challenging. Although the results of Vacc-4x are disappointing, Bionor should be praised for attempting such a difficult research program. If anything, the Bionor results should stimulate other research teams to continue their work so that a better understanding of HIV’s interaction with the immune system can lead to drugs and therapeutic vaccines that can help HIV-positive people and to an effective vaccine to protect HIV-negative people.

If we are to see a world free from the threat of AIDS, then we need to be conscious of the general complexity of vaccine research and be patient with the efforts of immunologists and virologists who toil away in laboratories in Canada and around the world. Major funding agencies such as Canada’s CIHR (Canadian Institutes of Health Research), the American NIH (National Institutes of Health) and France’s ANRS (Agence nationale de recherches sur le sida et les hépatites virales) also need to demonstrate patience and give scientists the long-term support they need for equipment and personnel so that they can learn more about how the immune system works.

In the future there will be news about other HIV vaccines and, in the short-term, likely very modest results. We should not be surprised about that. However, such results can be used to improve future vaccines. We will one day have a world free from AIDS, but that day is not yet here.

**Sean R. Hosein**

**References:**
France: Untested gay man found criminally liable for two previous partners' HIV acquisition

A 39-year-old gay man who was so in denial of the possibility that he might have been HIV-positive that he refused to take an HIV test until 2007 has been found criminally liable for infecting two former partners in 2003 and 2005.

He was sentenced last Thursday by the criminal court of Draguignan to two years in prison, one year of which was suspended, with a further three years’ probation. Having already served his sentence whilst on remand, he was freed after the hearing but will have to wear an electronic bracelet for a year.

The man, a special education teacher named only as Christophe in the most detailed French language report (his accuser’s first names were also published which is why I am using his first name) was found guilty of "administering noxious substances leading to mutilation or permanent infirmity". He will also have pay between 30,000 and 50,000 euros to each of the two men.

The case dates back to May 2003 and September 2005 when on two separate occasions Christophe had unprotected sex with each of the two complainants, Pierre-Yves and Julien. Both testified that Christophe had reassured them he was he was "clean" and that unprotected sex "would be OK."

Although it’s not clear how they both discovered that Christophe may have been the common source of their infection, the two men complained to the police in May 2006 after discovering their HIV-positive status.

A police investigation subsequently found that both were HIV-negative prior to their meeting with Christophe (although how they found this is not explained). The police also found all (!) the sexual partners the men had had before and after Christophe. The news reports do not state how they were certain that Christophe was, in fact, the source of both men’s HIV, and there is no mention of the use of phylogenetic analysis.

Regardless, the most worrying part of the case is that Christophe did not himself test HIV-positive until 2007. However, according to one of the news reports

The police investigation revealed that although he "knew" he had been infected by a former partner he refused to be tested until 2007. According to the psychiatrist, he was in "denial about the reality of his illness." To his lawyer Michel Roubaud, who pleaded for his release, "the element of intent is impossible to characterize."

How does someone "know" they are HIV-positive without having an HIV antibody test? Certainly, one can suspect this, but that’s not the same as "knowing". This is characterised in law as "wilful ignorance" but then the law does not take into account the stigma of HIV and that stigma can lead to denial.

As far as I am aware there have only been two previous cases where a court has found someone criminally liable for another’s HIV infection despite not having had a confirmed HIV-positive diagnosis.

The first took place in England in 2004, where a man pleaded guilty to 'reckless' HIV transmission despite not having had an HIV-positive diagnosis but rather he "had been warned he was a potential carrier of the virus."

The second took place in Switzerland in 2008. Here, Switzerland’s highest court—the Federal Court in Lausanne—ruled that a man who was unaware of his infection when he had unprotected sex that transmitted HIV was still criminally liable for his partner’s HIV-positive diagnosis because he did not disclose his sexual history which included a former partner who was living with HIV.

Update (Tues 21st, 8.30pm): I’m also now aware of a case similar to this French one (untested gay man that claimed he was HIV-negative when he apparently ‘should have been aware he might have been HIV-positive because of a risky past’) that took place in Rastatt, Germany in 2010. In this case he was found guilty of reckless grievous bodily harm and received a 2 1/2 year prison sentence.

In this current case, several things appear to have gone against Christophe. First, after one of the men accused him of infecting them, he apparently emailed him a falsified HIV-negative test (although this is not the same as showing a falsified test in order to obtain unprotected sex under false pretences.)

Second, both men testified as to the negative impact of having HIV on their health and career.

Today, Julian is on triple therapy. He had to give up being a nurse in pediatrics and settle for an administrative job in a Swiss hospital. Pierre-Yves, too, had to give up his career as a caregiver, he now works as a car salesman.

What seems incredible about this case is that two gay men would consider themselves victims under such circumstances. Until recently most prosecutions in France were of heterosexual men. It seems the concept of shared responsibility for HIV prevention for gay men has now well and truly disappeared.
Finally, the shorter article on this case, in Le Point, also states that another man has also recently been found criminally liable for HIV transmission (although I imagine this man was diagnosed HIV-positive before having sex with the complainants). It states that on February 14, a 38 year-old bus driver was sentenced to six years in prison for infecting two partners (gender not specified), one of whom subsequently committed suicide.

**Oslo Declaration**

1. A growing body of evidence suggests that the criminalisation of HIV non-disclosure, potential exposure and non-intentional transmission is doing more harm than good in terms of its impact on public health and human rights.[1]
2. A better alternative to the use of the criminal law are measures that create an environment that enables people to seek testing, support and timely treatment, and to safely disclose their HIV status.[2]
3. Although there may be a limited role for criminal law in rare cases in which people transmit HIV with malicious intent, we prefer to see people living with HIV supported and empowered from the moment of diagnosis, so that even these rare cases may be prevented. This requires a non-punitive, non-criminal HIV prevention approach centred within communities, where expertise about, and understanding of, HIV issues is best found.[3]
4. Existing HIV-specific criminal laws should be repealed, in accordance with UNAIDS recommendations.[4] If, following a thorough evidence-informed national review, HIV-related prosecutions are still deemed to be necessary they should be based on principles of proportionality, foreseeability, intent, causality and non-discrimination; informed by the most-up-to-date HIV-related science and medical information; harm-based, rather than risk-of-harm based; and be consistent with both public health goals and international human rights obligations.[5]
5. Where the general law can be, or is being, used for HIV-related prosecutions, the exact nature of the rights and responsibilities of people living with HIV under the law should be clarified, ideally through prosecutorial and police guidelines, produced in consultation with all key stakeholders, to ensure that police investigations are appropriate and to ensure that people with HIV have adequate access to justice.
6. We respectfully ask Ministries of Health and Justice and other relevant policymakers and criminal justice system actors to also take into account the following in any consideration about whether or not to use criminal law in HIV-related cases:
7. HIV epidemics are driven by undiagnosed HIV infections, not by people who know their HIV-positive status.[6] Unprotected sex includes risking many possible eventualities – positive and negative – including the risk of acquiring sexually transmitted infections such as HIV. Due to the high number of undiagnosed infections, relying on disclosure to protect oneself – and prosecuting people for non-disclosure – can and does lead to a false sense of security.
8. HIV is just one of many sexually transmitted or communicable diseases that can cause long-term harm.[7] Singling out HIV with specific laws or prosecutions further stigmatises people living with and affected by HIV. HIV-related stigma is the greatest barrier to testing, treatment uptake, disclosure and a country’s success in “getting to zero new infections, AIDS-related deaths and zero discrimination”.[8]
9. Criminal laws do not change behaviour rooted in complex social issues, especially behaviour that is based on desire and impacted by HIV-related stigma.[9] Such behaviour is changed by counselling and support for people living with HIV that aims to achieve health, dignity and empowerment.[10]
10. Neither the criminal justice system nor the media are currently well-equipped to deal with HIV-related criminal cases.[11] Relevant authorities should ensure adequate HIV-related training for police, prosecutors, defence lawyers, judges, juries and the media.
11. Once a person’s HIV status has been involuntarily disclosed in the media, it will always be available through an internet search. People accused of HIV-related ‘crimes’ for which they are not (or should not be found) guilty have a right to privacy. There is no public health benefit in identifying such individuals in the media; if previous partners need to be informed for public health purposes, ethical and confidential partner notification protocols should be followed.[12]

**References**

d, director of CDC's Division of

- is a lot to ask," Ward said. DWB provides antiretroviral drugs to n

funding more than half of all HIV treatment being provided to 43,000 patients, said Peter Paul de Groote, surg. TB is a leading cause of death for the country's HIV patients. About 18,000 people die from people in Myanmar and treated another 10,000 patients stricken with drug donations, DWB said. The expected Global Fund grants could have supplied HIV medicine to 46,500 Fund to Fight AIDS, TB and Malaria recently suspended new gra

Without Borders reported Wednesday. Myanmar's situation could grow even worse, since the Global

Report: Myanmar Desperate for HIV and TB Drugs

Lack of funding is causing some 85,000 people with HIV in Myanmar to go without treatment, Doctors Without Borders reported Wednesday. Myanmar's situation could grow even worse, since the Global Fund to Fight AIDS, TB and Malaria recently suspended new grant-making activities due to a shortfall in donations, DWB said. The expected Global Fund grants could have supplied HIV medicine to 46,500 people in Myanmar and treated another 10,000 patients stricken with drug-resistant TB.

Myanmar's tuberculosis rate is nearly triple the global rate, and drug-resistant strains continue to surge. TB is a leading cause of death for the country's HIV patients. About 18,000 people die from HIV/AIDS annually in Myanmar, the UN estimates.

DWB provides antiretroviral drugs to nearly 23,000 people at 23 clinics throughout Myanmar, funding more than half of all HIV treatment being provided to 43,000 patients, said Peter Paul de Groote, leader of DWB's Myanmar operation.

Hepatitis C Deaths Up, Baby Boomers Most at Risk


Two-thirds of Americans with hepatitis C virus were born between 1945 and 1965, and federal health officials are considering whether to recommend one-time HCV testing for this group. “One of every 33 baby boomers are living with hepatitis C infection,” said Dr. John Ward, director of CDC's Division of Viral Hepatitis. “Most people will be surprised, because it’s a silent epidemic.”

Recorded deaths from HCV have surpassed those from HIV, a new CDC study of mortality data between 1999 and 2007 found. Deaths from HCV had increased significantly to 15,106 in 2007, while HIV deaths fell to 12,734. Three-fourths of hepatitis deaths occurred in people ages 45-64.

An estimated 3.2 million Americans have chronic HCV, but at least half may not know it. Before 1992, when widespread HCV testing of the blood supply began, the virus commonly was spread through blood transfusions. A one-time experiment with drugs, even if it was decades ago, also could have led to an infection. “Asking someone about a risk that happened 20 to 30 years ago is a lot to ask,” Ward said.

Current CDC guidelines recommend testing those known to be at high risk, but federal health officials are considering whether anyone born between 1945 and 1965 should get a one-time HCV blood test. A second CDC-funded study analyzing that option concluded it had the potential to save 82,000 lives.

“Mortality will continue to grow for the next 10 to 15 years at least, unless we do something different” to find and treat silent HCV infections, Ward said.

Research suggests that adding to standard HCV treatment one of two new drugs could boost cure rates as high as 75 percent, with some patients able to complete therapy in just six months. A third study from Stanford University found the new triple HCV therapy would be cost-effective for people with advanced disease, and genetic testing could be used to help identify those with mild disease needing such treatment.


Report: Myanmar Desperate for HIV and TB Drugs

Associated Press. (02.22.2012)

Lack of funding is causing some 85,000 people with HIV in Myanmar to go without treatment, Doctors Without Borders reported Wednesday. Myanmar’s situation could grow even worse, since the Global Fund to Fight AIDS, TB and Malaria recently suspended new grant-making activities due to a shortfall in donations, DWB said. The expected Global Fund grants could have supplied HIV medicine to 46,500 people in Myanmar and treated another 10,000 patients stricken with drug-resistant TB.

Myanmar’s tuberculosis rate is nearly triple the global rate, and drug-resistant strains continue to surge. TB is a leading cause of death for the country’s HIV patients. About 18,000 people die from HIV/AIDS annually in Myanmar, the UN estimates.

DWB provides antiretroviral drugs to nearly 23,000 people at 23 clinics throughout Myanmar, funding more than half of all HIV treatment being provided to 43,000 patients, said Peter Paul de Groote, leader of DWB’s Myanmar operation.
Although a civilian government assumed office last year, international assistance to Myanmar has remained minimal due to its previous rule by a reclusive military government. “Regardless of what is happening in the country, the people that are in need of treatment need treatment,” said de Groote. “Of course, we all hope that the developments as they seem to be going in that direction will lead to more money into the country, but, in general, I think this money should be coming in regardless of what the situation is.”

**Instant Infant HIV Diagnosis to Be Rolled Out in Rural Areas**
*Inter Press Service (Johannesburg)*, (02.20.2012) Isaiah Esipisu

Last year, students at Kenya’s Strathmore University began software development on a database system to help speed up the delivery of HIV test results for infants in remote areas. Diagnosis within six weeks of birth ensures the timely initiation of antiretroviral therapy.

With the system already implemented in 75 of Kenya’s most remote health centers, blood samples are logged into one of the four central Kenya Medical Research Institute (KEMRI) CDC laboratories. A text message is sent to the rural health center confirming the sample’s receipt. Upon diagnosis, another text confirmation is generated to the rural center, which notifies parents the results are ready.

“As a policy, all positive results on the [polymerase chain reaction] equipment have to be re-run for confirmation in order to avoid false positives that might be due to contamination,” said Oscar Mulondanome, a lab technologist at the Alupe Center testing laboratory.

Use of the system is cutting down the time spent waiting for a diagnosis, delays that can span up to 18 weeks. An additional 50 facilities will be connected to the testing sites in trial phases, said Silvia Kadima, a researcher with KEMRI. By April, the software will be further customized and officially rolled out by the government, Kadima said.

**Purdue Study Links Abstinence Programs, Academic Success**
*Indianapolis Star*, (02.08.2012)

A study of Indiana high schools similar in enrollment, community size and racial demographics finds those that offered a specific abstinence education program demonstrated better overall academic achievement.

Purdue University Sociology Professor Kenneth Ferraro analyzed 42 high schools, one-half of which offered the Peers Educating and Encouraging Relationship Skills (PEERS) Project, an abstinence-based curriculum that uses peer educators to discuss risky behaviors. Under the program, high school students are recruited to talk to pupils in grades six through eight in science or health and wellness classes.

“We were interested in whether abstinence education programs were good, bad or benign for academic performance,” said Ferraro. “We found that school corporations with a specific abstinence education program had a higher percentage of their high school sophomores pass the math portion of the ISTEP+ Graduation Qualifying Exam in 2008-09 than was the case for matched controls.”

The longer the schools used PEERS, the better the results, said Ferraro. “We saw greater gains in the percent passing the math exam when the program was sustained for several years,” he said. However, there was no association between PEERS and attendance rates at the schools.

PEERS Executive Director Eve Jackson said the program benefits both younger and older students. High school students who serve as mentors tend to grow more confident in their own positive values as they promote them to younger students, she said. “When exemplary role models explain why it is important to set future goals and make healthy choices as well as abstain from all risky behavior, including sexual activity, middle school students pay attention,” she noted. Overall, “Students abstaining from risky behavior do better in school,” she added.

The study, “Do Abstinence Education Programs Influence High School Academic Performance?” was published in the American Journal of Health Studies (2011;26(4)).

**South Asia Makes Little Progress In Meeting Maternal, Child Mortality MDGs, U.N. Report Says**

“South Asian nations are making the least progress in the Asia-Pacific region on meeting key development goals, which they pledged to achieve by 2015,” Bindu Lohani, vice president for sustainable development at the Asian Development Bank (ADB), said on Friday at the launch of a U.N. progress report on the Millennium Development Goals (MDGs), Reuters reports (Bhalla, 2/19). The Asia-Pacific region already
has reached the MDG of halving the incidence of poverty, "but still has high levels of hunger as well as child and maternal mortality," the report said, according to Asian Scientist (2/21).

"At the present rate of progress, the region as a whole is unlikely to meet MDGs related to eradicating hunger, reducing child mortality and improving maternal health, among others, the report warns," the U.N. News Centre writes. "The report notes that many countries can speed up progress with just a little effort" and "outlines an eight-point agenda to fast-track progress towards the health MDGs that includes establishing an equitable, accessible, responsive and integrated primary health care system as well as ensuring preventive and curative mother and child health services," the news service notes (2/17).

Cholera Epidemic Spreads In DRC; Efforts To Combat Disease Remain Underfunded, U.N. Reports
"A cholera epidemic has spread to nine out of 11 provinces in the Democratic Republic of the Congo, the United Nations said on Tuesday," SAPA/News24 reports (Gold, 2/21). "Health authorities in the Republic of Congo have recorded 340 cases of cholera, nine of them fatal, since June 2011, in the northern district of Likouala, and have warned that the disease continues to spread and that some health centers lack sufficient treatment," IRIN reports (2/21).

Efforts to combat the spread of cholera in the country "remain underfunded, the United Nations humanitarian office reported [Tuesday], saying the lack of access to potable water is the single most important cause of recurring outbreaks of the disease in the country," the U.N. News Centre reports, adding, "Over the past six months, the U.N.-managed Central Emergency Response Fund (CERF) has allocated more than $13 million to support the fight against cholera, according to Elisabeth Byrs, spokesperson for the U.N. Office for the Coordination of Humanitarian Affairs (OCHA) in Geneva" (2/21).

Scientific American Examines Gates Foundation Toilet-Design Initiative
"Advocates for universal access to and use of basic personal sanitation hope their efforts will get a big boost in August, when the Bill & Melinda Gates Foundation present several hygienic innovations developed through its Reinventing the Toilet Challenge," Scientific American reports in a feature article. "The foundation's involvement could do for sanitation what it has accomplished in the battle to eradicate malaria—raise the visibility of a fundamental health care crisis and encourage new efforts to end it," the magazine writes.

The magazine describes some of the proposed prototypes and notes, "Frank Rijsberman, director of the Gates Foundation's Water, Sanitation and Hygiene Initiative, says he is hoping for something that goes beyond the minimum criteria to become the 'iPad of sanitation,'" adding, "He says, 'There must be an aspirational element' to toilets or even latrines if they are going to become the norm. People have to want to be seen owning one." The magazine concludes, "The hope is that efforts such as sanitation marketing and the Gates Foundation's challenge will have an impact on sanitation problems worldwide, but the reality of what they face is daunting" (Nash, 2/21).

Uncovered: Genetic cause of complex disease seen in Irish Traveller community
Two independent groups of researchers — one led by Adrian Clark, at Queen Mary University of London, United Kingdom; and the other led by Jean-Laurent Casanova, at The Rockefeller University, New York — have now identified the disease-causing gene in patients with a complex inherited syndrome most commonly observed in the Irish Traveller community. As noted by Jordan Orange, at the University of Pennsylvania School of Medicine, Philadelphia, in an accompanying commentary, the new data provide deep mechanistic insight into a complex human condition and expand our understanding of the human immune and endocrine systems, both of which are disrupted in patients.

Within the Irish Traveller community, several families have been found to suffer from an inherited condition characterized by failure of the adrenal glands to produce adequate amounts of steroid hormones, abnormal development (in particular, retarded growth), and a deficiency in immune cells known as NK cells. Both groups of researchers found that mutations in the MCM4 gene are responsible for this complex inherited condition. The MCM4 gene is responsible for templating a protein that is required for DNA to replicate itself, something that happens every time a cell divides. Consistent with this, both groups of researchers found that the MCM4 mutations associated with disease caused genomic instability, something that they suggest might possibly put affected individuals at increased risk for cancer.
Theory of the 'rotting' Y chromosome dealt a fatal blow

CAMBRIDGE, Mass. (February 22, 2012) – If you were to discover that a fundamental component of human biology has survived virtually intact for the past 25 million years, you’d be quite confident in saying that it is here to stay.

Such is the case for a team of Whitehead Institute scientists, whose latest research on the evolution of the human Y chromosome confirms that the Y—despite arguments to the contrary—has a long, healthy future ahead of it.

Proponents of the so-called rotting Y theory have been predicting the eventual extinction of the Y chromosome since it was first discovered that the Y has lost hundreds of genes over the past 300 million years. The rotting Y theorists have assumed this trend is ongoing, concluding that inevitably, the Y will one day be utterly devoid of its genetic content.

Over the past decade, Whitehead Institute Director David Page and his lab have steadily been churning out research that should have permanently debunked the rotting Y theory, but to no avail.

"For the past 10 years, the one dominant storyline in public discourse about the Y is that it is disappearing," says Page. "Putting aside the question of whether this ever had a sound scientific basis, the story went viral—fast—and has stayed viral. I can't give a talk without being asked about the disappearing Y. This idea has been so pervasive that it has kept us from moving on to address the really important questions about the Y."

To Page, this latest research represents checkmate in the chess match he's been drawn into against the "rotting Y" theorists. Members of his lab have dealt their fatal blow by sequencing the Y chromosome of the rhesus macaque—an Old World monkey whose evolutionary path diverged from that of humans some 25 million years ago—and comparing it with the sequences of the human and chimpanzee Y chromosomes. The comparison, published this week in the online edition of the journal *Nature*, reveals remarkable genetic stability on the rhesus and human Ys in the years since their evolutionary split.

Grasping the full impact of this finding requires a bit of historical context. Before they became specialized sex chromosomes, the X and Y were once an ordinary, identical pair of autosomes like the other 22 pairs of chromosomes humans carry. To maintain genetic diversity and eliminate potentially harmful mutations, autosome pairs swap genes with each other in a process referred to as "crossing over." Roughly 300 million years ago, a segment of the X stopped crossing over with the Y, causing rapid genetic decay on the Y. Over the next hundreds of millions of years, four more segments, or strata, of the X ceased crossing over with the Y. The resulting gene loss on the Y was so extensive that today, the human Y retains only 19 of the more than 600 genes it once shared with its ancestral autosomal partner.

"The Y was in free fall early on, and genes were lost at an incredibly rapid rate," says Page. "But then it leveled off, and it's been doing just fine since."

How fine? Well, the sequence of the rhesus Y, which was completed with the help of collaborators at the sequencing centers at Washington University School of Medicine and Baylor College of Medicine, shows the chromosome hasn’t lost a single ancestral gene in the past 25 million years. By comparison, the human Y has lost just one ancestral gene in that period, and that loss occurred in a segment that comprises just 3% of the entire chromosome. The finding allows researchers to describe the Y's evolution as one marked by periods of swift decay followed by strict conservation.

"We've been carefully developing this clearcut way of demystifying the evolution of the Y chromosome," says Page lab researcher Jennifer Hughes, whose earlier work comparing the human and chimpanzee Ys revealed a stable human Y for at least six million years. "Now our empirical data fly in the face of the other theories out there. With no loss of genes on the rhesus Y and one gene lost on the human Y, it's clear the Y isn't going anywhere."

"This paper simply destroys the idea of the disappearing Y chromosome," adds Page. "I challenge anyone to argue when confronted with this data."

In food form, some probiotics have a better chance to promote health

New model to evaluate probiotic survival in the gut described in the Journal of Dairy Science

Amsterdam, February 22, 2012 – Functional foods containing bacteria with beneficial health effects, or probiotics, have long been consumed in Northern Europe and are becoming increasingly popular elsewhere. To be of benefit, however, the bacteria have to survive in the very hostile environment of the gut.
digestive tract. A group of scientists from the Norwegian University of Life Sciences in Ås, Norway have developed a "model gastric system" for evaluating the survival of bacteria strains in the human digestive system, and determined that some bacteria strains survive better when consumed as fermented milks. Their results are published in the February issue of the Journal of Dairy Science.

"Most of the bacterial strains we tested have interesting functional properties related to food products. We wanted to evaluate whether these strains could contribute with beneficial health functions, or even have the potential as probiotics for human consumption," explains lead investigator Professor Siv Skeie of the Department of Chemistry, Biotechnology, and Food Sciences.

Researchers tested 5 Lactococcus bacteria strains, including 4 Lc. lactis ssp. cremoris strains, which are found in ropy milks, traditional Nordic fermented milk products reported to have beneficial effects on consumer health, as well as 3 Lactobacillus strains, and one strain of Enterococcus hirae. The study tested whether the strains could survive exposure to acidic conditions and bile salts, the traditional method of evaluating the potential of probiotic bacteria. The bacteria were also subjected to a process that mimicked the human digestive system, incubating the bacteria in human gastric and duodenal juices at body temperature. The bacterial strains were tested both as pure cells from cultured media and in the form of fermented milk.

The initial in vitro testing in acid and bile salts found that Lactobacillus strains had a significantly higher acid tolerance than the lactococci strains and E. hirae. The model digestion experiments allowed researchers to simulate with more precision the multiple stress factors that might ultimately affect the survival and subsequent performance of bacteria in the gut. The lactobacilli strains showed the highest survival rate in the model digestive system, whereas the cocci, with some exceptions, performed similarly in both systems. Interestingly, while none of the lactococcal stains and the E. hirae strain survived in significant numbers after exposure to the gastric juices, their numbers increased in the subsequent duodenal phase.

"This could mean that lactococci and enterococci are able to resurrect their viability if they are exposed to more suitable conditions like those in the small intestine. This is very interesting because it is in the intestine that functional or probiotic bacteria confer their health benefit to the host," suggests Dr. Skeie.

In testing whether fermented milk gave protection to the bacteria through the digestive tract, the results were mixed. The Lactococcus strains Af-1 and ML-8 and Lb. paracasei INF448 showed lower numbers of viable cells compared with the digestion of pure bacterial cells. The other strains showed higher numbers of viable cells in comparison. In particular, the fermented milk improved the viability of the Lactococcus strains Ar-1, Bf-2, the active bacteria in ropy milk, and E. hirae INF E1 during incubation under gastric conditions.

"These results seem to confirm that foods, such as fermented milks, could be a protective matrix enhancing survival of some bacteria," Dr. Skeie concludes.


New way to tap largest remaining treasure trove of potential new antibiotics

Scientists are reporting use of a new technology for sifting through the world’s largest remaining pool of potential antibiotics to discover two new antibiotics that work against deadly resistant microbes, including the “super bugs” known as MRSA. Their report appears in the Journal of the American Chemical Society.

Sean Brady and colleagues explain that an urgent need exists for new medications to cope with microbes that shrug off the most powerful traditional antibiotics. Methicillin-resistant Staphylococcus aureus (MRSA) infections, for instance, are resistant to most known antibiotics. MRSA strikes at least 280,000 people in the U.S. alone every year, and almost 20,000 of those patients die. The typical way of discovering new antibiotics involves identifying and growing new bacteria from soil and other environmental samples in culture dishes in the laboratory. That environmental treasure-trove is the largest remaining potential source of new antibiotics. Researchers then analyze the bacteria to see if they make substances that could be used as antibiotics to kill other microbes. But most bacteria found in nature can’t grow in the laboratory. That’s why Brady and colleagues took a new approach to this problem.

The researchers removed DNA from soil bacteria that wouldn’t grow in the lab. Then, they put this DNA into different bacteria that do grow well in culture dishes, and these bacteria acted like incubators for the new DNA. The approach enabled Brady’s team to study the substances made by the soil bacteria’s
DNA in the lab. With this "metagenomics" method, they identified two new possible antibiotics called fasamycin A and fasamycin B that killed MRSA and vancomycin-resistant Enterococcus faecalis, which also is becoming more resistant to known antibiotics. They also determined how the new antibiotics work. "Metagenomics has the potential to access large numbers of previously inaccessible natural antibiotics," say the researchers.

**How Cancer Cells Change Once They Spread to Distant Organs**

ScienceDaily (Feb. 22, 2012) — Oncologists have known that in order for cancer cells to spread, they must transform themselves so they can detach from a tumor and spread to a distant organ. Now, scientists at Weill Cornell Medical College have revealed critical steps in what happens next—how these cells reverse the process, morphing back into classical cancer that can now grow into a new tumor.

Their findings, now published online and in a upcoming issue of Cancer Research and funded through a National Cancer Institute grant to the Cornell Center on the Microenvironment and Metastasis and the Neuberger Berman Foundation, show that a single protein, versican, is key to this process in breast cancer, the tumor they studied. When researchers stopped versican from functioning in mice, breast cancer could not "seed" themselves into the lungs and form secondary tumors.

"Our findings both help us understand how breast cancer metastasizes to the lungs and ways to possibly prevent that deadly spread," says the study's senior investigator, Dr. Vivek Mittal, an associate professor of cell and developmental biology in cardiothoracic surgery and director of the Neuberger Berman Lung Cancer Laboratory at Weill Cornell Medical College.

"These are exciting insights into a poorly investigated area," Dr. Mittal says. "There are no clinically approved drugs now that can effectively target metastatic lesions, which is why more than 90 percent of human cancer-related deaths come from spread of the disease from a primary tumor."

"The results of this study are a critical step in deconstructing the process of metastases—which is critical to curing our patients," says co-author Dr. Linda T. Vahdat, professor of medicine, chief of the Solid Tumor Service and director of the Breast Cancer Research Program at Weill Cornell. "As a direct result of this study, we are working on ways to interrupt the process by which tumors co-opt the infrastructure in our bodies to grow and spread."

This important study starts to unravel the mechanistic basis of cancer metastases, not only in breast cancer but possibly in other types of cancer, says Dr. Nasser Altorki, the David B. Skinner Professor of Thoracic Surgery at Weill Cornell Medical College and director of the division of thoracic surgery at NewYork-Presbyterian/Weill Cornell. "The need for a prepared and receptive soil may be required for cancer cell seeding regardless of the primary cancer's site of origin."

The Seed and the Soil Cancer researchers have believed that for a cancer to spread, its "seed" must find the right "soil" in a distant organ in order to thrive. And they have hypothesized that this seed is formed through a process known as epithelial-mesenchymal transition (EMT), in which cancer cells lose their sticky grip to other cells in a primary tumor and become more mobile, able to travel through the blood to a distant organ.

But what happens next is conjecture. Scientists have speculated that the cells undergo a reverse process, called mesenchymal-epithelial transition (MET), in which the cancer seeds morph back into epithelial cells that can make contact with tissue and integrate in the new organ. Little is known about MET compared to EMT.

In this study, Dr. Mittal, along with his colleagues at Weill Cornell, studied mouse models of spontaneous breast cancer development. They first discovered that primary breast tumors send a signal that forces bone-marrow-derived hematopoietic cells to move into the lungs of the mice. "This appears to be the soil the cancer seeds need," says Dr. Mittal. The next question was obvious: What is it about the soil that helps the seed?

The team found that a subtype of these bone marrow cells expressed versican, which allowed the cancer cells, once they traveled to the lungs, to morph back into epithelial cells. "The primary tumor sets up the lung microenvironment to promote metastasis," he says. "MET resulted not from properties within the cancer cell itself, but due to a unique crosstalk between the microenvironment and tumor cells in the lung."

In their next experiment, the researchers blocked versican production by injecting small interfering RNAs (siRNAs) in the bone marrow that silenced the versican gene, which prevented MET and blocked tumor outgrowth in the lung.
Human Tumors Express Versican Next, they investigated human breast metastases to the lung, utilizing lung samples obtained from breast cancer patients contributed by researchers at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University. "We found versican was highly expressed in those lung tumors, which matched what we found in our mice," Dr. Mittal says. "This all made sense to us, because versican has been linked to cancer progression, although no one knew why.

"This is the first study demonstrating the significance of MET in the formation of macrometastases in distant organs," Dr. Mittal says. "Given the findings, we now have a potential strategy to stop cancer spread before it starts, or to shut it down if it has already occurred."

Journal Reference:

The scientist who discovered Hepatitis C says he’s now discovered the vaccine
In a poetic turn of virology, the scientist who discovered hepatitis C in 1989 has now also discovered a vaccine that will hopefully cure the now-incurable disease.

Not only is it poetic, it’s an accomplishment that many thought was impossible. Because hepatitis C is more virulent than HIV, no one was confident a vaccine against all the various strains around the world could be developed. But Michael Houghton, the University of Alberta researcher who announced his work today at the Canada Excellence Research Chairs Summit in Vancouver, says his vaccine works against every known strain of the virus...

It could still be up to seven years before the vaccine goes through the necessary phases of clinical trials and receives FDA approval, but it’s amazing news for people who thought they’d be living with hepatitis C for the rest of their lives. It also remains to be seen how much impact the vaccine will have in people who already have the disease—it will be most effective as a preventive against acquiring the disease. Hundreds of thousands of people get hepatitis C every year, and 20 to 30 per cent of them develop liver disease.

Researchers at Oxford have also made progress towards a vaccine. With news out earlier today that hepatitis C now kills more Americans than HIV, a vaccine can’t come soon enough.

Getting Tough on Criminalisation
“Nothing short of barbaric.” This was the comment of a BBC presenter, confronted with the number and sheer arbitrary injustice of criminal convictions of people accused of transmitting HIV or exposing other people to it. In some cases, people have been jailed for failing to disclose HIV in situations where they couldn’t possibly have transmitted it.

And yet, says Edwin J Bernard, there have been some encouraging international policy developments in the fight against the unjust persecution of people with HIV. Worldwide, arrests, prosecutions and their associated media reports continue to have a devastating impact on the people accused of exposing or transmitting HIV, as well as adding further to the stigma of living with HIV.

Yet since HTU last covered the issue of HIV and the criminal law (HTU 199, September 2010), there have been some remarkably encouraging national and international policy developments. "Nothing short of barbaric"
For the past 18 months, the Global Commission on HIV and the Law, led by the United Nations Development Programme (UNDP) on behalf of the Joint United Nations Programme on HIV/AIDS (UNAIDS), has been gathering evidence from all over the world about the impact of the law on HIV. The Commission has been examining issues much broader than the criminalisation of HIV non-disclosure, exposure and transmission. These include the criminalisation of sex between men, sex work and drug use; the impact of the law on women and children; and the impact of intellectual property law and trade agreements on the availability of generic antiretrovirals.

However, some of the world’s leading experts on the criminalisation of HIV non-disclosure, exposure and transmission are part of the Commission’s Technical Advisory Group, including the UK’s Professor Matthew Weait. And the Commission’s report (due soon) is expected to censure countries that continue to treat people with HIV as potential – and actual – criminals and where HIV-related stigma is trumping evidence-informed laws and policies.1

At the Commissions’ High Income Countries Dialogue held in Oakland, California, in September 2011, the issue of criminal prosecutions for HIV non-disclosure, exposure or transmission was very much at the
heart of the meeting. The often emotional testimony was skillfully moderated by BBC presenter Nisha Pillai, herself moved to tears by the end of the meeting, overwhelmed by the stories of legal injustices perpetrated against people with HIV.

"The Western world's treatment of many people with HIV is nothing short of barbaric," Pillai wrote in a blog entry a few days later. "The distressing testimony I witnessed from people living in the world's richest countries – the US, Canada, the UK, Denmark, Germany, and elsewhere in Europe – left me profoundly shocked... The reason is simple – criminalisation... In some states of America you can kill someone in a car accident and get a lighter sentence than if you fail to pass on HIV to a sexual partner. Passing on herpes or hepatitis C isn't prosecuted, but not passing on HIV is. The injustice is staggering. Seldom in my many years as a BBC journalist, and now as an international moderator, have I felt so outraged."2

The meeting was hosted by the sole US member of the Commission, Oakland Congresswoman Barbara Lee. Congresswoman Lee recently unveiled the Repeal HIV Discrimination Act which creates financial incentives and support for states to review and reform HIV-specific laws that are not consistent with good public health or HIV science.3

The Western world's treatment of many people with HIV is nothing short of barbaric. The distressing testimony I witnessed...left me profoundly shocked. Nisha Pillai, international moderator

"Laws that place an additional burden on HIV-positive individuals because of their HIV status lag far behind the medical advances and scientific discoveries in the fight against the epidemic," said Congresswoman Lee. "Instead of progress against the disease and protection for people living with HIV/AIDS, criminalisation laws breed fear, discrimination, distrust, and hatred. Although our country has made notable advances in the global fight against HIV/AIDS, we have a long way to go. The decriminalisation of HIV/AIDS is one way we can reduce stigma in our communities, while fighting the epidemic in a rational, holistic, and truly rights-based fashion."4

Although it is unknown whether the bill will pass when introduced to the US House of Representatives, at the very least it will create awareness and debate amongst US lawmakers about the issue.

Since 2008, when they produced their policy brief on the issue,5 UNAIDS and UNDP have been actively trying to persuade governments and policymakers to repeal HIV-specific criminal laws and to limit the application of general criminal law to actual cases of intentional transmission, where a person:

- knows his or her HIV-positive status;
- acts with the intention to transmit HIV;
- and does in fact transmit it.

At the heart of this position is the need to establish a threshold for criminal liability that would serve justice in truly blameworthy cases – where the intention to harm can be clearly established – while avoiding overly broad application of the criminal law which risks jeopardising public health objectives and fundamental human rights.

**Basing legal decisions on good science**

Three years before the 'Swiss statement'6 on the impact of antiretroviral therapy on infectiousness, the Netherlands' highest court decided that one act of insertive unprotected anal sex when the accused was on treatment was not significant enough to be considered a risk of serious harm. The result is that, consistent with UNAIDS' recommendations, only maliciously intentional exposure or transmission remains a criminal offence.7 The impact of the Swiss statement was not only felt in Geneva, where HIV exposure charges were dropped because the risks were considered to be purely "hypothetical",8 but also in Austria,9 Canada10 and the US military.11

In August 2011, UNAIDS convened an expert meeting in Geneva on the scientific, medical, legal and human rights aspects of the criminalisation of HIV non-disclosure, exposure and transmission. This was the first part a project funded by the Government of Norway to expand on its 2008 policy brief in order to provide more detailed guidance and inform law and policy internationally.12

Criminalisation laws breed fear, discrimination, distrust and hatred. Congresswoman Barbara Lee

The meeting presented a unique opportunity to explore the latest developments in HIV science – such as the impact of treatment on transmission risk and life expectancy. It was also a chance to provide the UNAIDS Secretariat and other stakeholders with recommendations that would promote an application of criminal law to HIV non-disclosure, exposure and transmission, if any, that serves justice, without jeopardising public health objectives and fundamental human rights. The meeting reached expert
consensus on issues such as HIV-related risk and harm; clarifying criminal intent and acceptable
defences; and highlighting limitations of scientific evidence in proving transmission.\textsuperscript{33}

The second part of the project – a high level policy consultation – will take place in February 2012 in
Oslo. It is hoped that the Oslo meeting will lead to a greater understanding of the current issues around
HIV non-disclosure, exposure and transmission and assist countries to reform their HIV-related criminal
laws, policies and practices.

\textbf{The problem with HIV-specific laws}

However, for every sign of progress – such as the February 2011 suspension of Denmark's HIV-specific
criminal law\textsuperscript{41} or Guyana's rejection of a new HIV-specific criminal law in September 2011\textsuperscript{15} – there have
been at least as many problematic developments, such as Romania's new HIV-specific criminal statute,
implemented in October 2011,\textsuperscript{16} or South Africa's opposition leader Helen Zille's recent speech calling for
men who don't use condoms to be prosecuted for attempted murder.\textsuperscript{17}

In addition, many jurisdictions, notably high-income countries in Australasia, western Europe and
North America, continue to prosecute people living with HIV inappropriately for non-disclosure, alleged
exposure and non-intentional transmission.\textsuperscript{18} Last year also saw prosecutions in Belgium\textsuperscript{19} and in the
Congo\textsuperscript{20} for the first time, both using anti-poisoning laws. The vast majority do not meet criteria for
"deliberate" transmission, despite the frequent use of this word in the media.

HIV-specific laws are found all over the world — notably in Africa, central Asia, eastern Europe and
Latin America.\textsuperscript{21} At least 32 states of the United States also have such laws, and in the US there are arrests
on an almost daily basis.\textsuperscript{22}

Rather than criminalising HIV transmission, most US laws criminalise behaviour that may or may not
(and in some cases \textit{definitely does not}) risk HIV transmission. Some outlaw practices that are not
significantly risky or harmful (for example, sharing sex toys, spitting, performing oral sex); and others
criminalise non-disclosure of known HIV-positive status, regardless of whether or not a condom or other
risk-reduction methods is relied upon.\textsuperscript{23} Consequently, states with HIV-specific laws that make disclosure
compulsory, that do not require proof of intent and/or that do not require proof of significant harm or
transmission have generally had much higher prosecution rates than those without.\textsuperscript{24}

For example, Louisiana's HIV-specific criminal law, first enacted in 1987 and revised in 1993,\textsuperscript{25}
specifies that it is "unlawful for any person to intentionally expose another to HIV through sexual contact
or through any means or contact (including spitting, biting, stabbing with an HIV contaminated object, or
throwing of blood or other bodily substances) without the knowing and lawful consent of the victim." The
maximum prison sentence is ten years. A 1993 appeal\textsuperscript{26} found that the statute was neither too vague nor
too broad and it has not been challenged since.

In recent years, several people with HIV in Louisiana have been arrested for behaviour that carries a
very low risk of HIV transmission, including a man for having oral sex with his wife;\textsuperscript{27} a male sex worker
for suggesting to an undercover policeman, but not actually having, unprotected sex;\textsuperscript{28} and an injured
man receiving medical attention for throwing a "blood-covered identification card into the face" of, and
"trying to spit" on, a healthcare worker.\textsuperscript{29} The outcome of these cases is unknown.

\textbf{Criminalisation confusion}

In the rest of the world, most prosecutions are taking place under general criminal laws, such as physical
or sexual assault statutes. Their relevance to HIV non-disclosure, exposure or transmission is often based
on legal precedents informed by one or more cases taken to appeal early in the HIV epidemic that were
commonly informed by HIV-related stigma and/or incomplete understanding of HIV science. In an
attempt to fit non-disclosure, exposure or transmission into a wide variety of legal definitions, many
jurisdictions appear to have inappropriately characterised the risks and/or harms of these acts. When the
law is unclear – as it often is when it evolves based on case law – this also creates uncertainty over what
behaviour is criminal and what is not, leading to conflicting standards of HIV-related risk and the
conflation of non-disclosure with a malicious intent to deceive or harm.

This is the case in Canada, the country with the second highest number of prosecutions – at least
130\textsuperscript{30} – after the United States. That's about one prosecution for every 550 people with HIV –
considerably higher \textit{per capita} than in the US where there have been well over 300 prosecutions but
whose larger HIV-positive population means that about one person per 3300 has been prosecuted.
Prosecutions intensified following a 1998 Supreme Court ruling which established that a person who
knows they are living with HIV has a duty to disclose their HIV status before engaging in conduct that
poses a "significant risk" of exposing another person to the virus. Non-disclosure (regardless of whether it
is active deceit or as a result of not discussing HIV risk) is treated as fraud that invalidates consent to sex
and which results in this sexual contact being classified as an assault.
The problem is that "significant risk" has not been clearly or consistently defined and prosecutions for non-disclosure prior to oral sex\textsuperscript{31} and sex with condoms\textsuperscript{32} have taken place. As a result, substantial confusion amongst people living with HIV, healthcare workers and legal practitioners exists regarding when the duty to disclose arises.\textsuperscript{33}

Next month, in a case that will have far-reaching implications for people living with HIV in Canada, its Supreme Court will revisit two cases, allowing a re-examining of the 1998 ruling in the light of inconsistent lower court decisions. In particular, it will examine what constitutes a "significant risk" of HIV transmission in the context of recent scientific developments. Although both sides agree that the "significant risk" test is unfair and should be reassessed, the representatives of the Crown are arguing that the only way to make the law work fairly is to obligate disclosure (and, therefore, criminalise non-disclosure) before any kind of sexual activity, regardless of the risk involved. Advocates working to assist the defence are hoping that the Court will recognise advances in HIV science and rule that when a person with HIV uses a condom and/or has an undetectable viral load due to effective antiretroviral therapy the criminal law will not apply.\textsuperscript{34}

**When disclosure is no defence**

Although the current situation in Canada seems harsh, some countries in Europe have an even more draconian approach. In Austria, Finland, Norway, Switzerland and Sweden, people with HIV can be prosecuted for having consensual unprotected sex even when there was prior disclosure of HIV-positive status and agreement of the risk by the HIV-negative partner.\textsuperscript{35}

Fortunately, most of these countries are in the process of examining such laws and policies. Norway has set up a special committee to examine whether its current law should be rewritten or abolished: its recommendations are due in May.\textsuperscript{36} Switzerland is currently revising its *Law on Epidemics*, to be enacted later this year, and the latest version appears to be mostly consistent with UNAIDS’ recommendations.\textsuperscript{37}

And a recent conference attended by police, prosecutors and politicians that highlighted the many human rights concerns over its current laws and policies, may result in a review of the Swedish *Communicable Diseases Act*, as well as a change in the application of legislation and regulations for people with HIV in Sweden by the end of the year.\textsuperscript{38}

**England and Wales: a 'best practice' example...**

The expert meeting heard how a partnership between the HIV sector and the criminal justice system in England and Wales led to the creation of prosecutorial\textsuperscript{39} and police guidelines,\textsuperscript{40} which have helped to clarify the circumstances regarding when prosecutions might be warranted and reduced the flow of cases reaching court. Attempts to replicate this pragmatic response are now going on in Scotland,\textsuperscript{41} the Canadian provinces of Ontario and Quebec, on a federal level in Canada\textsuperscript{42} and in the Australian state of Victoria.\textsuperscript{43}

The Crown Prosecution Service prosecutorial guidelines were recently updated to highlight how tests for recent infection are unreliable for legal purposes,\textsuperscript{44} and to clarify that the reduced transmission risks of having an undetectable viral load on treatment could be seen as an "appropriate safeguard" alongside condoms and thus be used as an affirmative defence in 'reckless' transmission cases.\textsuperscript{45}

...but guidelines aren't always followed

However, there continue to be inappropriate investigations, arrests and prosecutions with remarkably different outcomes often solely depending on whether the accused obtained timely access to good legal advice. "What's weighing on my mind," Lisa Power, policy director at Terrence Higgins Trust (THT) tells *HTU*, "probably because of these latest cases, is how often the police are still not following their own guidelines and what a huge difference it makes if someone gets a decent, experienced lawyer early on. It's important to remember that so far not one person has been found guilty in England and Wales [who] pleaded not guilty from the start and got decent representation."

Not one person has been found guilty in England and Wales [who] pleaded not guilty from the start and got decent representation. Lisa Power, policy director, Terrence Higgins Trust

This suggests that not only should anyone living with HIV contact THT Direct for referral to a lawyer and/or other support the moment they are involved in a criminal case – as a defendant or a complainant – but also that any healthcare worker should do the same, mindful, of course, of patient confidentiality issues. The benefit of the latter is that THT is then aware of an ongoing case and the healthcare worker may receive some good advice about how to best support the prospective complainant or defendant.

"I think a healthcare worker should ring THT Direct if they have doubts as to their own practice," Yusef Azad, NAT's director of policy and campaigns tells *HTU*, "and also, when it is published, look to the [updated] BHIVA/BASHH guidance [on the management of the sexual and reproductive health of people
living with HIV]—but they, of course, should not disclose any identifiers of a patient without that patient’s consent.”

**For more information**

For NAM’s book on HIV and the criminal law and the latest news on the subject, visit:

www.aidsmap.com/law

For information if you are personally affected, see: www.myhiv.org.uk/Telling-people/Law. If you are being investigated, or you think that someone may make a complaint against you, it’s important you get good advice from an HIV organisation and find an experienced lawyer prior to making any statement. THT Direct, can help you find both these; you can speak to them in confidence on 0808 802 1221. You may also want to speak to THT Direct if you are thinking of making a complaint. You can find HIV organisations near where you are using NAM’s online e-atlas at www.aidsmap.com/e-atlas. Edwin’s own blog, which gathers together news and developments on the subject from around the world, is at http://criminalhivtransmission.blogspot.com and you can follow him on Twitter @edwinjbernard. POZ magazine founder Sean Strub has made a trailer for what he hopes will be a full-length documentary featuring people unjustly criminalised for HIV non-disclosure, exposure or non-intentional transmission. See www.youtube.com/watch?v=1B-6blJbJjc.

**References**

1. The report will be available at the Global Commission on HIV and the Law’s website, www.hivlawcommission.org
3. Available at: www.hivlawandpolicy.org/resources/download/650
6. See www.aidsmap.com/page/1922904
7. See http://aidsmap.com/law-country/Western-Europe/page/1444983--item1444987
12. UNAIDS *Expert meeting reviews scientific, medical, legal and human rights issues related to the criminalisation of HIV exposure and transmission*, 7 September 2011.
13. Comprehensive background papers and the meeting report will be available soon at www.unaids.org.
15. Isles K *Guyana hailed for not criminalising HIV transmission*. Demarara Waves, 8 September 2011.
17. Fokazi S *Zille targets men who don’t use condoms*. Cape Argus, 9 November 2011.
18. Global Network of People Living with HIV (GNP+) ‘The Global Criminalisation Scan Report’, Amsterdam, 2010. For more up-to-date information, see the author’s blog, criminalhivtransmission.blogspot.com.
31. See *R v. Aziga*, (4 April 2009), Hamilton CR-08-1735 (convicting on aggravated sexual assault charge based on unprotected oral sex).
Abstinence and Birth Control in Sex Education Class?

**Chicago Daily Herald**, (02.19.2012) Larissa Chinwah

A bill recently proposed in the Illinois General Assembly would require sex education courses in grades six through 12 to include instruction on both abstinence and contraceptive methods for preventing STDs and unwanted pregnancy. Currently, sex education must be abstinence-based, and districts can decide whether or not to include instruction on contraception. HB 3027, Senate Amendment 1, also would define what materials and curricula are acceptable.

Supporters say the measure would ensure students are learning all methods for preventing STDs and unwanted pregnancy. However, critics say it would weaken the message of abstinence. The Senate passed the bill in a 30-28 vote, and it has been placed on the House calendar for possible consideration this spring.

Schools that choose to offer sex education, which is not a state-mandated course, can select a curriculum that suits their community's needs, so long as it is supported by recognized research and age-appropriate, said Rep. Camille Lilly (D-Chicago), the bill's sponsor.

"We want to make it clear to those who are providing information that it needs to be medically accurate, age-appropriate, and complete," Lilly said. For instance, some students are given false statistics on the efficacy of contraceptive methods, she said.

"What one community thinks is age-appropriate, another may not," said Sen. Matt Murphy (R-Palatine). "That's a decision that is best left up to local school boards, rather than a one-size-fits-all mandate handed down from Springfield."

A 2008 survey found two-thirds of Illinois public schools provided comprehensive sex education, and 93 percent offered some form of sex education.

Teachers Urged to Address Porn Factor

**The Age (Melbourne)**, (02.13.2012) Denise Ryan

A team of Australian researchers is updating sex education resources to address the widespread availability of online pornography and teens' exposure to it. The materials being developed are for universities that train sex education teachers and for schools.

Teachers must have the skills to address pornography, said Dr. Debbie Ollis, a sex education expert at Deakin University in Victoria. The idea of school lessons on the topic might sound controversial, but youths need to learn to think critically about pornographic representations of gender, sex, expectations, and consent, and to distinguish between what is depicted and reality, said Maree Crabbe of Brophy Family Youth Services, who is involved in the project.

A 2006 Australian study of youths ages 13-16 found 92 percent of boys and 61 percent of girls have been exposed to online porn. A 2003 survey found 84 percent of boys and 60 percent of girls have been accidentally exposed to such sites.

"Pornography is now our most prominent sex educator," said Crabbe. Under the “Reality and Risk” project, she and researcher Dr. David Corlett recorded 140 interviews with youths, academics, and porn industry workers that collectively suggest pornography both is widely accessed by teens and becoming more violent.

The interviews will provide footage for a documentary film, which is being funded by philanthropists and will be completed in a few months. Video clips also will be used for audio-visual resources for
classrooms. The researchers are developing updated teaching materials for the popular “Catching On” curriculum, in which students will be presented with diverse scenarios to discuss.

**Sexual Risk Behaviors Among African-American and Hispanic Women in Five Counties in the Southeastern United States: 2008-2009**

*Women's Health Issues Vol. 22; No. 1: P. e9-e18, (01..2012)  Eleanor McLellan-Lemal; and others*

In this study, the authors examined sexual risk behaviors and unrecognized HIV infection among heterosexually active African-American and Hispanic women. Multiple methods were used to recruit women not previously diagnosed with HIV infection in rural counties in North Carolina (African-American) and Alabama (African-American), and an urban county in southern Florida (Hispanic). The participants completed a computer-assisted questionnaire and underwent HIV testing.

A total of 1,527 women (1,013 African-American; 514 Hispanic) were enrolled between October 2008 and September 2009. The women ranged in age from 18 to 59 (median age=35). Thirty-three percent were married or living as married. Fifty percent reported an annual household income of $12,000 or less; 56 percent were employed full- or part-time.

Two of the women (0.13 percent) tested HIV-positive. In the preceding 12 months, 19 percent had been diagnosed with an STD (other than HIV); 87 percent had engaged in unprotected vaginal intercourse (UVI); and 26 percent had had unprotected anal intercourse (UAI).

Multivariate analysis showed UAI was significantly (p<.05) more likely among the women who reported ever being pregnant, binge drinking in the previous 30 days, ever exchanging sex for things they needed or wanted, engaging in UVI or being of Hispanic ethnicity. As opposed to casual partners, UAI was more likely with partners with whom the participants had a current or past relationship.

“A high percentage of our sample of heterosexually active women of color had recently engaged in sexual risk behaviors, particularly UAI,” the authors concluded. “More research is needed to elucidate the interpersonal dynamics that may promote this high-risk behavior. Educational messages that explicitly address the risks of heterosexual anal intercourse need to be developed for heterosexually active women and their male partners.”

**WHO Urging Afghans To Vaccinate Children For Measles Following Outbreak In Western Region**

The WHO "is calling on all Afghans to vaccinate their children after a recent measles outbreak that has been made worse by severe weather that hampers access to immediate treatment as well as low immunization coverage," the U.N. News Centre reports. At least "20 children have died due to measles and pneumonia in the western provinces of Ghor and Baghdis," the news service notes (2/22). "As the outbreak has grown more serious, Afghan authorities and the WHO set up five temporary clinics and vaccinated more than 3,600 children in the outbreak zone, while treating more than 6,000 patients, health officials said," according to the Los Angeles Times' "World Now" blog (2/21).

**Researchers Begin Clinical Trial Of First Visceral Leishmaniasis Vaccine**

"Researchers say they've developed the first vaccine for visceral leishmaniasis (VL)—a disease that affects 500,000 people each year and has been called the 'parasitic version of HIV,'" although the diseases are unrelated, U.S. News reports. "The vaccine took researchers more than two decades to develop and entered Phase I trials in recent weeks, according to Steve Reed, founder of the Infectious Disease Research Institute (IDRI), the vaccine's developer," the news service writes (Koebler, 2/22).

IDRI is launching Phase 1 trials of the vaccine, the Puget Sound Business Journal notes, adding that "research will include dual clinical trials for VL in Washington State at IDRI and with a partner in Pune, India." According to the journal, "The Bill & Melinda Gates Foundation has supported this research with a $32 million grant awarded in 2006 to further trial phases 1, 2 and 3" (Bauman, 2/22). "Subsequent clinical trials will involve larger numbers of people who are at high risk of developing VL during their daily lives," an IDRI press release states, adding, "Only such large trials, conducted in real-life situations of disease exposure, will determine the full effectiveness of the LEISH-F3 + GLA-SE vaccine" (2/22).
**Disarming the botulinum neurotoxin**  
**Sanford-Burnham researchers determine the first 3-D structure of the botulinum neurotoxin, together with the protein bodyguard that guides it through the body—revealing weak spots that could be exploited to develop new counterterrorism measures**

LA JOLLA, Calif., February 23, 2012 – Researchers at Sanford-Burnham Medical Research Institute (Sanford-Burnham) and the Medical School of Hannover in Germany recently discovered how the botulinum neurotoxin, a potential bioterrorism agent, survives the hostile environment in the stomach on its journey through the human body. Their study, published February 24 in *Science*, reveals the first 3D structure of a neurotoxin together with its bodyguard, a protein made simultaneously in the same bacterium. The bodyguard keeps the toxin safe through the gut, then lets go as the toxin enters the bloodstream. This new information also reveals the toxin’s weak spot—a point in the process that can be targeted with new therapeutics.

"Now that we better understand the structure of the bacterial machinery that was designed for highly efficient toxin protection and delivery, we can see more clearly how to break it,” said Rongsheng Jin, Ph.D., assistant professor in Sanford-Burnham's Del E. Webb Neuroscience, Aging and Stem Cell Research Center and senior author of the study.

**The Janus-faced toxin**

The botulinum neurotoxin is two-faced. On one side, it's the most poisonous substance known to man, causing botulism. Accidental botulinum neurotoxin poisoning is usually food-borne, but it’s also considered a potential bioterrorism agent. On the other side, botulinum neurotoxin is also used as an effective therapy and popular cosmetic, such as in BOTOX.

The neurotoxin accomplishes both the good and the bad using the same trick—paralyzing muscle cells by disrupting their connections with the nerves that tell them how and when to move. But before the neurotoxin can gain access to muscles and the neurons that control them, it must make a remarkable journey through the body—surviving the digestive enzymes and extreme acidic environment in the stomach, penetrating the small intestine, and entering the bloodstream.

**Sneaking a peek at the neurotoxin and its bodyguard**

This latest study on the botulinum neurotoxin was the result of a close collaboration between the Jin group and a research group at the Institute of Toxicology at the Medical School of Hannover, led by Andreas Rummel, Ph.D., an expert on clostridial neurotoxins. They used a technique called X-ray crystallography, which uses powerful X-ray beams to produce 3D images of proteins at the atomic level, to study a genetically inactivated, nontoxic version of the botulinum neurotoxin.

These experiments helped the team visualize the atomic structure of all three parts of the toxin: 1) the region that recognizes neurons, 2) the enzyme that acts like a pair of scissors to cut human neural proteins and cause paralysis, and 3) the needle that punches holes to help deliver the enzyme to the nerve terminal. What's more, the researchers also captured the toxin's interaction with a second bacterial protein, called nontoxic nonhemagglutinin (NTNHA).

"We were surprised to see that NTNHA, which is not toxic, turned out to be remarkably similar to botulinum neurotoxin. It’s composed of three parts, just like a copy of the toxin itself. These two proteins hug each other and interlock with what looks like a handshake,” said Jin.

As the toxin moves through the body, NTNHA acts as its bodyguard, keeping it from being degraded when times are tough in the acidic stomach. However, as this study revealed, the toxin has a weak spot: when the toxin/NTNHA complex punches its way out of the small intestine, it’s the change in pH that triggers a conformational change, breaks up the duo, and releases only the unprotected toxin into the bloodstream.

**Towards prevention and therapy**

According to Jin, this new knowledge about how the botulinum neurotoxin and NTNHA balance the need for strong binding and a timely release could be exploited to outsmart them.

"We now hope we might be able to fool the toxin and its bodyguard using a small molecule that sends the wrong signal—mimicking pH change, prematurely breaking up their protective embrace, and leaving the stomach's digestive enzymes and acid to do their job,” he said. "We envision this type of therapy—either alone or in
combination with other therapies currently in development—could be given preventively at a time when botulinum neurotoxin contamination becomes a public health concern."

Moreover, this type of therapy could be designed for oral delivery, rather than injection, making it easier to treat large numbers of people during an outbreak. A similar strategy could be used to deliver other protein-based drugs that usually need to be injected. "Here, protein drugs could be linked to a botulinum neurotoxin fragment and protected with NTNHA. Then we could possibly take them by mouth," Jin said.

Slamming the brakes on the malaria life cycle

Scientists have discovered a new target in their fight against the devastating global disease 'malaria' thanks to the discovery of a new protein involved in the parasite's life cycle.

The research has uncovered a vital player in the sexual phase of the malaria parasite's reproduction which could prove an effective target for new treatments to stop the disease in its tracks.

The scientists from The University of Nottingham’s School of Biology, with collaborators from the Universities of Leicester, Oxford, Imperial College London and Leiden in the Netherlands, have just published the results of their work in the journal *PLoS Pathogens*.

Biting back

Malaria is a devastating global disease with several hundred million clinical cases and just under a million people die from it every year. The disease is caused by an infection of the red blood cells with a tiny parasite called a *Plasmodium*, of which there are four important species. These organisms are carried from person to person by the *Anopheles* mosquito. When it bites an infected person, the mosquito sucks up blood containing the parasite, which may then be passed on to the mosquito’s next victim.

Dr David Guttery, lead scientist of the paper and part of Dr Tewari’s group from the University of Nottingham's Centre for Genetics and Genomics in the School of Biology said:

"The malaria parasite is a complex organism and to understand how it multiplies is crucial to stopping its transmission. Our study has identified a cell-division cycle gene in the malaria parasite and its role in the development of male sex cells and is hence a good candidate for putting the brakes on its development. We have shown that by deleting this gene, male gametes cannot form and burst out of their host cell (a process called exflagellation). Blocking the formation of these cells can be an important strategy in the prevention of malaria transmission from mosquito to mammalian hosts".

New Target

The protein that has been identified is called CDC20 and plays a part in the cell division cycle of the malaria parasite *Plasmodium berghei* which infects mice and rats. This gene has been shown to have an important role in cell division in many organisms, but up to now nothing has been known about its function in the malaria parasite. The new study provides the first description of the role of CDC20 in *Plasmodium* cell division and in the development of the malaria parasite's male sex cells (microgametes), which are essential for parasite transmission between humans and the mosquito carrier. The scientists have discovered that the absence of this gene stops the male sex cell from bursting out of its host cell and fertilising a female cell as they are arrested in their cell division.

The sexual stage of the malaria parasite's life-cycle occurs within the mosquito after it has fed on malaria-infected blood. This activates the parasite's sexual phase and during this period, the male sex cell precursor (microgametocyte) rapidly replicates its DNA and produces 8 male sex cells (gametes). These gametes then burst out of the microgametocyte in a process called exflagellation and seek out a female sex cell to fertilise. By blocking the process of exflagellation, the team have identified a way of slamming the brakes on malaria transmission.

The team of researchers were from the Centre of Genetics and Genomics at The University of Nottingham, the University of Oxford, Imperial College London, Leiden University, the University of Leicester and the MRC National Institute for Medical Research funded by the MRC, Wellcome Trust, and EviMalar.

The group at Nottingham has previously uncovered other major players in the life cycle of the malaria parasite. More details on these can be found in earlier media releases 'Stopping the spread of malaria' and 'Malaria research begins to bite'.
**Protein scouts for dangerous bacteria**

**How the immune system detects listeria and other bad bacteria**

CHICAGO — Millions of "good" bacteria exist harmoniously on the skin and in the intestines of healthy people. When harmful bacteria attack, the immune system fights back by sending out white blood cells to destroy the disease-causing interlopers. But how do white blood cells know which bacteria are good and which are harmful?

Northwestern University Feinberg School of Medicine researchers studied one type of white blood cell known as a macrophage, which is among the immune system's first to detect and eliminate harmful bacteria. The research team, led by Christian Stehlik, John P. Gallagher Research Professor of Rheumatology at Feinberg, discovered that the protein NLRP7 serves as a "scout" in macrophage cells, identifying bacterial cell wall components in harmful gram-positive bacteria such as *Staphylococcus aureus* and *Listeria monocytogenes*.

The findings will be published in the February 23 issue of the journal *Immunity*.

"NLRP7 is a novel intracellular pattern recognition receptor that specifically recognizes bacterial cell wall components, known as lipopeptides, in harmful bacteria," says Stehlik, who worked closely with collaborators Andrea Dorfleutner, research assistant professor of medicine at Feinberg, and Yon Rojanasakul, Robert C. Byrd Distinguished Professor and Benedum Distinguished Professor at West Virginia University. "We show that activation of NLRP7 is necessary for eradicating bacterial infections through the formation of protein complexes called inflammasomes, which enable the production of defense factors in immune cells."

Identifying the molecule was complicated, says Sonal Khare, postdoctoral fellow at Feinberg and first author on the research paper, because the family of proteins within macrophages is quite large. "There were 22 likely candidates. To determine which one of these proteins is able to recognize bacteria in macrophages, we had to remove each one of them," she says. Through process of elimination, the team identified NLRP7 as the required protein.

Stehlik says the finding is significant because it contributes to a better understanding of how bacteria such as *Listeria* and *Staphylococcus* are recognized by the immune system. *Listeria* is found in uncooked meats, vegetables, and fruits such as cantaloupes. In 2011, listeria was the cause of the deadliest food contamination outbreak in the U.S. in more than a decade. *S. aureus* infections are most commonly contracted in hospitals, and 500,000 patients acquire *Staphylococcus* infections annually in the U.S. Methicillin-resistant *S. aureus*, or MRSA, strains are highly resistant to commonly-used antibiotics.

Understanding how the immune system recognizes these deadly intruders could one day lead to novel treatment strategies to combat these infections.

"The next phase of research related to NLRP7 and inflammasomes is progressing," says Stehlik. "We are continuing the research to explore mechanisms behind how this NLRP7 inflammasome is formed. We want to know whether we can manipulate this process to make the response stronger. We also will be exploring the use of mouse models in this pathway to study this response in vivo."

The article, "An NLRP7-Containing Inflammasome Mediates Recognition of Microbial Lipopeptides in Human Macrophages" will be available for download on the journal *Immunity*'s web site.

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**Opinion: H5N1 flu is just as dangerous as feared, now requires action**

WASHINGTON, DC—February 22, 2012—The debate about the potential severity of an outbreak of airborne H5N1 influenza in humans needs to move on from speculation and focus instead on how we can safely continue H5N1 research and share the results among researchers, according to a commentary to be published in *mBio®,* the online open-access journal of the American Society for Microbiology, on Friday, February 24.

H5N1 influenza has been at the center of heated discussions in science and policy circles since the U.S. National Science Advisory Board for Biosecurity (NSABB) asked the authors of two recent H5N1 investigations and the scientific journals that planned to publish the studies to withhold crucial details of the research in the interest of biosecurity.

In the *mBio®* commentary, Michael Osterholm* and Nicholas Kelley, of the Center for Infectious Disease Research and Policy at the University of Minnesota, present their case that H5N1 is a very dangerous virus, based on their analysis of published studies of the seroepidemiology of H5N1 in humans. H5N1 flu infections have exceedingly high mortality, they say, and current vaccines and antiviral drugs will not pull us out of a global H5N1 pandemic. "We believe that the assertion that the case-fatality rate of H5N1 influenza in humans may be overestimated is based on a flawed data analysis," Osterholm said.
Analysis of reports of H5N1 seroprevalence that include data from the 1997 Hong Kong outbreak as well as data from 2004 to date will give a misleading impression because the 1997 outbreak was a very different “biologic event” that is recognized as such by the WHO, because the 1997 H5N1 virus has a significantly different genotype from that of later H5N1 viruses. This is why the WHO does not include the Hong Kong H5N1 virus data in any analysis of H5N1 transmission, and the 1997 Hong Kong virus is not recommended for inclusion in H5N1 vaccines, Osterholm explained.

Seroepidemiologic studies that have examined the exposure of various groups of people to H5N1 viruses only from 2004 onward indicate that only a small segment of the population has ever been exposed to H5N1, and that among those that have been exposed, many become seriously ill or die.

"The available seroepidemiologic data for human H5N1 infection support the current WHO reported case-fatality rates of 30% to 80%," Osterholm says. In the event of an H5N1 pandemic, they point out, if the virus is even one tenth or one twentieth as virulent as has been documented in these smaller outbreaks, the resulting fatality rate would be worse than in the 1918 pandemic, in which 2% of infected individuals died.

Vaccines will not head off an H5N1 pandemic either, the authors say, since the time required to develop and manufacture an influenza vaccine specific to new outbreak strain has resulted in “too little, too late” vaccine responses for the 1957, 1968, and 2009 influenza pandemics, and not much in the process has changed since 2009.

"The technology behind our current influenza vaccines is simply not sufficient to address the complex challenges associated with an influenza pandemic in the 21st century," Osterholm and Kelley say.

This is the heart of the matter, they say: there has been enough discussion about how severe an H5N1 pandemic might be. Moving forward, the current controversy has provided a valuable opportunity for scientists and public policy experts to discuss influenza research and preparedness and create "a roadmap for the future." The discussion among scientists and policy makers needs to move on from whether H5N1 poses a serious international threat—as it clearly does—and begin discussing how we can prevent these viruses from escaping labs and how scientists can share their flu-related results with those who have a need to know.

There are critical questions that need to be answered, the authors say. For instance, how can scientists conduct virus-transmission studies in mammals safely and how can scientists share research methods and results with those who have a need to know? We also need to come to agreement on how to ensure that strains of H5N1 viruses created in the lab don’t escape those controlled environments, the authors say. And new, more effective vaccine technologies are needed that can enable substantially faster production. Resolving these issues could allow H5N1 research and preparedness to serve as a springboard for solving similar problems with existing or emerging pathogens.

**New strategies for treatment of infectious diseases**

**Article in journal Science proposes new look on killer diseases**

The immune system protects from infections by detecting and eliminating invading pathogens. These two strategies form the basis of conventional clinical approaches in the fight against infectious diseases. In the latest issue of the journal *Science*, Miguel Soares from the Instituto Gulbenkian de Ciência (Portugal) together with Ruslan Medzhitov from Yale University School of Medicine and David Schneider from Stanford University propose that a third strategy needs to be considered: tolerance to infection, whereby the infected host protects itself from infection by reducing tissue damage and other negative effects caused by the pathogen or the immune response against the invader. The authors argue that identifying the mechanisms underlying this largely overlooked phenomenon may pave the way to new strategies to treat many human infectious diseases.

Upon invasion by pathogens (bacteria, viruses or parasites), the immune system kicks into action, by detecting, destroying and ultimately eliminating the pathogen. This so-called "resistance to infection" is crucial in protecting the host from infection, but is often accompanied by collateral damage to some of the host's vital tissues.
(liver, kidney, heart, brain). If uncontrolled tissue damage may have lethal consequences, as often happens, for example, in severe malaria, severe sepsis and possibly other infectious diseases. Tolerance reduces the harmful impact of infection and of the ensuing immune response on the host.

Although a well-studied phenomenon in plant immunity, tolerance to infection has been largely overlooked in mammals, including humans. While there is still much to be learnt about how and under which circumstances tolerance to infection is employed by the host, most of what is currently known about the molecular mechanisms underlying this host defense strategy comes from work carried out at the Instituto Gulbenkian de Ciência by the group led by Miguel Soares. The team is particularly interested in identifying disease-specific tolerance mechanisms, on the one hand, and also general strategies of tolerance, that may, possibly, be employed protectively, to precondition the host to future infections.

Because resistance is, generally, the only mechanism considered in animal and human studies, when the host capitulates to infection it is often attributed to failure of the immune system. The authors argue that this is not always the case, and underscore the importance of distinguishing between failed resistance and failed tolerance as the cause for morbidity and mortality by infectious diseases. This distinction will dictate the choice of therapeutic approaches. When the primary problem is failed tolerance, then boosting the immune system, or administering antibiotics, may be ineffective. In this case, enhancing tolerance would possibly be much more effective in fighting infectious, inflammatory and auto-immune diseases.

**Fat accumulation linked to cognitive impairment in patients with HIV**

Michael Carter  
Published: 24 February 2012

Central fat accumulation is associated with an increased risk of neurocognitive impairment for HIV-positive patients, according to a study published in the February edition of *Neurology*. Overall 40% of patients in the study were diagnosed with impairment and increased waist circumference was a significant risk factor. Diabetes was also a factor, but only for patients aged 55 and over.

“Waist circumference, a measure of central obesity and a risk factor for insulin resistance and atherosclerosis contributed to neurocognitive impairment,” comment the authors. They note that their findings accord with research conducted in the general population which “identified...effects on cognition by central obesity as measured by waist circumference or hip-to-waist ratio.”

Antiretroviral therapy can significantly prolong the life expectancy of patients with HIV. However, this treatment can cause a number of side-effects, including metabolic abnormalities. Disturbances in the way the body stores and processes fat are now well-recognised complications of some antiretroviral regimens. There is concern that long-term use of anti-HIV drugs could increase the risk of diabetes and cardiovascular disease.

Rates of neurocognitive impairment among HIV-positive patients are also high. The exact prevalence is controversial. So too are the causes, but these could include metabolic disturbances and diabetes, recognised risk-factors for neurocognitive impairment in the general population.

Investigators from the US CHARTER (CNS HIV Anti-Retroviral Therapy Research) group wanted to clarify the relationship between metabolic disturbances and neurocognitive impairment in patients with HIV.

They therefore designed a cross-sectional study involving 130 patients who received care between 2006 and 2007. These patients completed a standard test to assess their cognitive function. The results were adjusted to take account of age, education, gender and race. Fasting blood samples were obtained to determine levels of total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides and the prevalence of insulin resistance. Waist circumference was measured and body mass index (BMI) assessed.

Information on HIV-related factors including duration of infection, use of HIV therapy, CD4 cell count and viral load was also obtained.

The patients had a mean age of 46 years, 57% were white and 87% were men.  
Overall, 40% of patients had some form of cognitive impairment.

The first analysis revealed a number of risk factors for this condition. These included older age (48 vs. 44 years, p = 0.02), longer duration of infection with HIV (15 vs. 12 years, p = 0.03) and increased waist circumference (99 vs. 88 cm, p = 0.0005). Patients with impairment were also significantly more likely to have been diagnosed with diabetes (15% vs. 3%, p = 0.007).

A total of ten patients were diabetic and eight (80%) had neurocognitive impairment. This compared to a prevalence rate of 37% among non-diabetic patients.
The investigators explored the apparent association between diabetes and impairment in a larger population totalling over 1300 individuals. They found some evidence of a relationship between diabetes and neurocognitive impairment, but only among patients aged 55 and above.

"Thus, if diabetes contributes to neurocognitive impairment, it may do so only in older patients," write the authors.

Multivariate analysis was then undertaken to see which metabolic and HIV-related factors increased the risk of impairment.

The first analysis included the 90 patients with a restricted dataset. BMI rather than waist circumference was used as a marker of body composition. The results showed that age (p = 0.027) and BMI (p = 0.039) were both predictors of impairment.

A second model included the 55 patients for whom information on waist circumference was available. BMI (p = 0.038) and waist circumference (p = 0.001) both predicted impairment, as did an AIDS diagnosis (p = 0.027).

The investigators believe that BMI was only significant because “it is a marker of waist circumference.” They add, “central, rather than generalised obesity conveys increased risk...for neurocognitive impairment.” The authors believe this finding has implications for the use of HIV therapy. “These findings suggest that the selection of combination antiretroviral therapy that induces less central obesity might reduce the risk of HIV-associated brain damage and cognitive impairment.”

A possible mechanism whereby central fat accumulation is contributing to neurocognitive impairment was suggested by the investigators. “Systemic inflammation...or adipose derived hormones may mediate generalised or focal cerebral degeneration that leads to cognitive dysfunction.”

Reference

HIV Epidemic Feared on Ontario Reserves
Ottawa Citizen, (02.23.2012) Heather Yundt
A rise in injection drug use on reserves in northern Ontario could fuel an HIV epidemic, health officials are warning.

In January, the remote community of Cat Lake declared a state of emergency over IV drug use there. Up to 70 percent of Cat Lake residents are addicted to prescription drugs such as OxyContin, according to Nishnawbe Aski Nation, a political group representing 49 First Nations in northern Ontario. In 2009, NAN declared a similar state of emergency over its entire territory.

The situation parallels that in Saskatchewan, where a spike in injection drug use has led to an HIV outbreak in the province during the last eight years. Injecting drugs became popular around 2004, said Saskatchewan Chief Medical Health Officer Dr. Moira McKinnon. A rise in HIV rates soon followed, and the province currently has an HIV rate more than two times the national average.

Provinces like Saskatchewan are "illustrative of what we might anticipate, especially if some of the efforts to try and reduce and, hopefully, even prevent new cases of HIV in the area in this context of injection drug use aren't recognized, and if we don't take advantage of those strategies now," said Dr. Kathy Pouteau, a family doctor for Kasabonika Lake First Nation in northern Ontario.

Saskatchewan’s needle-exchange programs distribute about 3 million needles annually for a population of roughly 1 million.

Of the 172 new HIV cases in Saskatchewan in 2010, 77 percent were aboriginal people. Nearly two-thirds of all new HIV cases in aboriginals result from injecting drugs.

Two New Analyses Raise Questions About Fatality Rate Of Bird Flu
In an analysis (.pdf) published Thursday in the online edition of the journal Science, a team led by virologist Peter Palese of Mount Sinai School of Medicine in New York raises questions about the WHO's estimated fatality rate from H5N1 bird flu, saying the rate of 59 percent is based on "an estimate of human bird flu cases that is simply too low," Reuters reports. The WHO has recorded 586 cases of people infected by bird flu, and of those, 346 have died, the news agency notes (Begley, 2/23). Palese and colleagues say "it is not possible to determine an accurate fatality rate for H5N1 infections based on" available data, but "if one assumes a one to two percent infection rate in exposed populations, this would likely translate into millions of people who have been infected, worldwide" (Wang et al., 2/24). And in a paper published Friday in mBio, the journal of the American Society for Microbiology, Michael Osterholm of the
University of Minnesota and a member of the U.S. National Science Advisory Board for Biosecurity (NSABB) and a colleague conclude that "[t]he available seroepidemiologic data for human H5N1 infection support the current WHO-reported case-fatality rates of 30% to 80%" (Osterholm/Kelley, 2/24).

The studies "add[d] fuel to the heated controversy over publication of bird flu research" in the journals Science and Nature describing how two teams created H5N1 strains that are easily transmissible among ferrets, which are used as lab models for humans, Reuters writes (2/23). Fears that terrorists possibly could use the information prompted the U.S. National Science Advisory Board for Biosecurity in December to request the scientists redact some information prior to publishing their study results and investigators in January to institute a 60-day moratorium on bird flu research, USA Today's "Your Life" notes. "A WHO summit that ended this week called for full publication of the two studies and for an extended halt to such research until stronger safety measures were assured in labs," the blog writes (Vergano, 2/23).

**South Sudan's Army Calls For Concerted Efforts To Fight HIV/AIDS**
"South Sudan's army on Wednesday appealed for concerted efforts to fight against HIV/AIDS, stressing that the war against the sexually transmitted disease cannot be fought by one institution or group of some officials tasked by the government," the Sudan Tribune reports. "Speaking in an interview with Sudan Tribune on Wednesday, Lieutenant Colonel John Woja, the HIV/AIDS Secretariat Program Manager of the military, warned that prevalence of disease poses a big threat to the military" and "called on media to complement the efforts of his directorate in sensitizing civilians and the army," the newspaper writes.

"The senior military official said the prevalence rate of the disease within the army is over four percent," and he added the military is working toward a goal of no new infections among soldiers by 2015, the newspaper notes. "South Sudan had a relatively low rate of HIV/AIDS up until 2005 when a peace deal opened up the region to immigration and returnees from neighboring countries with higher rates, such as Kenya and Uganda," it adds (2/22).

**Eradication Of River Blindness In Africa Is Feasible**
In this AlertNet opinion piece, Simon Bush, director of neglected tropical diseases (NTDs) at Sightsavers, an international NGO helping people with visual impairments in developing countries, examines efforts to rid Africa of onchocerciasis—a blinding NTD. "In 1947 when Sightsavers' founder, Sir John Wilson, coined the phrase river blindness to describe the almost unpronounceable disease, ... there was little choice for those living in areas where we now call a neglected tropical disease was endemic," he writes, adding, "Today, although the World Health Organization estimates that 120 million people are at risk of river blindness, there is hope."

"For the last 25 years, drug distribution programs to treat river blindness have been established across most endemic countries, and community-based distribution systems are used to ensure people receive an annual dose" of the drug ivermectin, he writes. He continues, "However the real hope comes through evidence from the African Program for Onchocerciasis Control (APOC)," which "shows that elimination of the disease as a public health threat by the end of 2012 in regions in Uganda, Nigeria and Mali should be feasible." Bush describes Sightsavers' 10-year plan to target areas for disease elimination and praises the U.K. government for increasing its support for NTDs. Bush concludes, "Helping rid Africa of this parasitic disease would not just eliminate one of the NTDs but it would alleviate the impact of blindness in Africa by reducing those needlessly blinded by this disease, removing a serious obstacle to socio-economic development across the continent" (1/16).

**Natural method for clearing cellular debris provides new targets for lupus treatment**
Augusta, Ga. – Cells that die naturally generate a lot of internal debris that can trigger the immune system to attack the body, leading to diseases such as lupus.

Now Georgia Health Sciences University researchers report that an enzyme known to help keep a woman’s immune system from attacking a fetus also helps block development of these autoimmune diseases that target healthy tissues, such as DNA or joints.

The findings point toward new treatment strategies for autoimmune diseases, which are on the rise in light of a germ-conscious society that regularly destroys many of the previously pervasive microbes that made the immune system more tolerant.
"The basic premise of lupus is you have lost normal tolerance to yourself, your own proteins and DNA," said Dr. Tracy L. McGaha, GHSU immunologist and corresponding author of the study published in Proceedings of the National Academy of Sciences.

They found that IDO, or indoleomine 2,3-dioxygenase, helps promote tolerance to debris generated by natural cell death and that when IDO is removed from the mix, the debris spurs an immune response that can trigger autoimmune disease. In mice genetically programmed to develop lupus, blocking IDO resulted in earlier, more aggressive disease.

"This connects IDO and macrophages. It's a newly described role for IDO in regulation of tolerance toward self," McGaha said. Consequently, increasing IDO production or its downstream effects might be a way to regain lost tolerance, he said.

They studied activity in the spleen, a hard-working immune organ, that constantly filters blood. In a perfectly orchestrated defense, the entrance to the spleen is surrounded by immune cells that scour blood for viruses, bacteria, even fat and cholesterol floating by.

A nearby subset of macrophages, which are essentially scavengers, then capture and consume the undesirables, McGaha said. Interestingly, a lot of what macrophages consume is dead immune cells.

Macrophages also appear to help keep the peace by preventing the immune system from joining the fray. McGaha earlier found that if he destroyed macrophages, then fed the spleen dead cells, there was inflammation instead of calm. "That tells us there is something inherent in this subset of macrophages that is important for the suppressive process," McGaha said referencing the paper published in 2011 in the journal Blood.

The new paper shows IDO is part of that "something." Efficient elimination of cell debris while keeping nearby immune cells quiet is important because some debris is known to grab the attention of the immune system, McGaha said. He noted that it's normal – and healthy – for damaged cells to become targets.

"We are really interested in this process of normal cell debris removal because in lupus, it's thought to be one of the main drivers of inflammation," he said.

The immune system has points of expansion and regulation where it decides whether or not to act. Knowing key points, such as IDO's regulatory role, provides treatment targets that can interrupt a destructive cascade of immune activity, McGaha said. Previous studies have shown evidence of self-attack is present many years before disease symptoms appear, he said.

Environmental assaults, such as a bad sunburn, can be the initial trigger of the abnormal immune response in diseases like lupus. In healthy individuals, the immune system rises to the occasion of an infection then goes back to baseline. In autoimmune disease, patients tend not to return to normal levels.

GHSU's Drs. Andrew Mellor and David Munn reported in 1998 in the journal Science that the fetus expresses IDO to help avoid rejection by the mother's immune system. Subsequent studies have shown tumors also use it and that it could help transplanted organs escape rejection. They suggested that McGaha look at IDO as a regulatory mechanism used by macrophages.

In the Genes, but Which Ones? Studies That Linked Specific Genes to Intelligence Were Largely Wrong, Experts Say
ScienceDaily (Feb. 24, 2012) — For decades, scientists have understood that there is a genetic component to intelligence, but a new Harvard study has found both that most of the genes thought to be linked to the trait are probably not in fact related to it, and identifying intelligence's specific genetic roots may still be a long way off.

Led by David I. Laibson '88, the Robert I. Goldman Professor of Economics, and Christopher F. Chabris '88, Ph.D. '99, assistant professor of psychology at Union College in Schenectady, N.Y., a team of researchers examined a dozen genes using large data sets that included both intelligence testing and genetic data. As reported in a forthcoming article in the journal Psychological Science, they found that in nearly every case, the hypothesized genetic pathway failed to replicate. In other words, intelligence could not be linked to the specific genes that were tested.

"It is only in the past 10 or 15 years that we have had the technology for people to do studies that involved picking a particular genetic variant and investigating whether people who score higher on intelligence tests tend to have that genetic variant," said Chabris. "In all of our tests we only found one gene that appeared to be associated with intelligence, and it was a very small effect. This does not mean intelligence does not have a genetic component, it means it's a lot harder to find the particular genes, or the particular genetic variants, that influence the differences in intelligence."
To get at the question of how genes influence intelligence, researchers first needed data, and plenty of it.

Though it had long been understood, based on studies of twins, that intelligence was a heritable trait, it wasn’t until relatively recently that the technology emerged to allow scientists to directly probe DNA in a search for genes that affected intelligence.

The problem, Chabris said, was that early technology for assaying genes was very expensive, meaning that such studies were typically limited to, at most, several hundred subjects, who would take IQ tests and provide DNA samples for testing.

As part of their study, Chabris and his colleagues relied on several pre-existing data sets—a massive study of Wisconsin high school graduates that began in the 1950s, the Framingham Heart Study, and an ongoing survey of all twins born in Sweden—to expand that subject pool from a few hundred to many thousands.

"What we want to emphasize is that we are not saying the people who did earlier research in this area were foolish or wrong," Chabris said. "They were using the best technology they had available. At the time it was believed that individual genes would have a much larger effect—they were expecting to find genes that might each account for several IQ points."

To identify genes that might play a role in intelligence, previous researchers used the "candidate gene approach," which requires identifying a gene that is already linked with a known biological function—such as Alzheimer's disease or the production of a specific neurotransmitter. If people who scored high on intelligence tests shared a particular variant of that gene, it was believed, that demonstrated the gene's role in intelligence.

"These were reasonable hypotheses," said study co-author Daniel J. Benjamin ’99, Ph.D. ’06, assistant professor of economics at Cornell University. "But in retrospect, either the findings were false positives or the effects of the genes are much, much smaller than anyone had anticipated."

Chabris, however, emphasized that the results don't point to the idea that the dozen genes examined in the study play no role in intelligence, but rather suggest that intelligence may be tied to many genes and the ways in which they interact.

"As is the case with other traits, like height, there are probably thousands of genes and their variants that are associated with intelligence," he said. "And there may be other genetic effects beyond the single gene effects—there could be interactions between genes, there could be interactions between genes and the environment. What our results show is that the way researchers have been looking for genes that may be related to intelligence—the candidate gene method—is fairly likely to result in false positives, so other methods should be used."

**Alzheimer's, Parkinson's, Certain Cancers: Correct Protein Folding Illuminated**

Berkeley Lab researchers at the Advanced Light Source have discovered a nucleotide-sensing loop that synchronizes conformational changes in the three domains of group II.
chaperonin for the proper folding of other proteins. (Credit: Image courtesy of DOE/Lawrence Berkeley National Laboratory)

ScienceDaily (Feb. 24, 2012) — The gold standard for nanotechnology is nature’s own proteins. These biomolecular nanomachines—macromolecules forged from peptide chains of amino acids—are able to fold themselves into a dazzling multitude of shapes and forms that enable them to carry out an equally dazzling multitude of functions fundamental to life. As important as protein folding is to virtually all biological systems, the mechanisms behind this process have remained a mystery. The fog, however, is being lifted.

A team of researchers with the U.S. Department of Energy (DOE)'s Lawrence Berkeley National Laboratory (Berkeley Lab), using the exceptionally bright and powerful x-ray beams of the Advanced Light Source, have determined the crystal structure of a critical control element within chaperonin, the protein complex responsible for the correct folding of other proteins. The incorrect or “misfolding” of proteins has been linked to many diseases, including Alzheimer’s, Parkinson’s and some forms of cancer.

“We identified, for the first time, a region within group II chaperonins we call the nucleotide-sensing loop, which detects the presence of the ATP molecules that fuel the chaperonin folding motion,” says Paul Adams, a bioengineer with Berkeley Lab’s Physical Biosciences Division and leading authority on x-ray crystallography who led this work. “We knew that ATP hydrolysis is important for promoting protein folding, but we did not know how ATP activity was sensed and communicated.”

Adams is the corresponding author of a paper in The EMBO Journal that describes this study, which was performed in collaboration with colleagues at MIT and Stanford. The paper is titled “Mechanism of nucleotide sensing in group II Chaperonins.” Co-authoring this paper were Jose Pereira, Corie Ralston, Nicholai Douglas, Ramya Kumar, Tom Lopez, Ryan McAndrew, Kelly Knee, Jonathan King and Judith Frydman.

Chaperonins promote the proper folding of newly translated proteins and proteins that have been stress-denatured—meaning they’ve lost their structure—by encapsulating them inside a protective chamber formed from two rings of molecular complexes stacked back-to-back. There are two classes of chaperonins, group I found in prokaryotes; and group II found in eukaryotes. Much of the basic architecture has been evolutionarily preserved across these two classes but they do differ in how the protective chamber is opened to accept proteins and closed to fold them. Whereas group I chaperonins require a detachable ring-shaped molecular lid to open and close the chamber, group II chaperonins have a built-in lid.

“We obtained crystal structures at sufficient resolution to allow us to examine, in detail, the effects that changes in nucleotides states have on ATP binding and hydrolysis in group II chaperonins,” Adams says. “From these structures we see that the nucleotide-sensing loop monitors ATP binding sites for changes and communicates this information throughout the chaperonin. Functional analysis further suggests that the nucleotide-sensing loop region uses this information to control the rate of ATP binding and hydrolysis, which in turn controls the timing of the protein folding reaction.”

The double-ring chaperonin complex features multiple subunits that are grouped into three domains—apical, intermediate and equatorial. For group II chaperonins, the closing of the lid for protein-folding causes all three domains to rotate as a single rigid body, resulting in conformational changes to the chamber that enable the proteins within to be folded. The synchronized rotation of the chaperonin domains is dependent upon the communication to all the subunits that is provided by the nucleotide-sensing loop. In identifying the nucleotide-sensing loop and its controlling role in group II chaperonin protein-folding, Adams and his colleagues may have opened a new avenue by which modified protein-folding activities could engineered.

“The strong relationship between incorrectly folded proteins and pathological states is well documented,” Adams says. “Since ATP hydrolysis is required for protein folding, it could be possible to engineer a nucleotide-sensing loop that promotes slower or faster protein folding activity in a given chaperonin. This could, for example, be used to increase the protein folding activity of human chaperonin, or perhaps reduce the cellular accumulation of misfolded proteins that can cause disease and other problems.”

A key factor that enabled Adams and his colleagues to solve the three-dimensional crystal structure of the nucleotide sensing loop and determine its pivotal role in the protein folding of group II chaperonins was the unique protein crystallography capabilities of the Berkeley Center for Structural Biology. The BCSB operates five protein crystallography beamlines for Berkeley Lab’s Advanced Light Source (ALS), a DOE Office of Science national user facility for synchrotron radiation, and the first of the world’s third generation light sources. For this particular study, Adams and his colleagues used ALS beamlines 8.2.1
and 8.2.2, which are powered by a superconducting bending magnetic to yield higher energy x-rays that are optimized for the study of single crystals of biological molecules.

In this study, Adams and his colleagues studied an archaeon chaperonin. In their followup research, they will apply what they have learned to study the chaperonin known as TRiC, which is the human chaperonin.

"We believe that chaperonins have evolved to work on specific substrates and that the rates of protein folding may vary greatly between chaperonins in different organisms," Adams says. "The structural and biochemical identification of the changes related to ATP hydrolysis provides important insights into the complex puzzle of protein folding for each type of chaperonin."

**Journal Reference:**

**Stronger Intestinal Barrier May Prevent Cancer in the Rest of the Body, New Study Suggests**

ScienceDaily (Feb. 21, 2012) — A leaky gut may be the root of some cancers forming in the rest of the body, a new study published online Feb. 21 in *PLoS ONE* by Thomas Jefferson University researchers suggests.

It appears that the hormone receptor guanylyl cyclase C (GC-C)—a previously identified tumor suppressor that exists in the intestinal tract—plays a key role in strengthening the body’s intestinal barrier, which helps separate the gut world from the rest of the body, and possibly keeps cancer at bay. Without the receptor, that barrier weakens.

A team led by Scott Waldman, M.D., Ph.D., chair of the Department of Pharmacology and Experimental Therapeutics at Jefferson and director of the Gastrointestinal Cancer Program at Jefferson’s Kimmel Cancer Center, discovered in a pre-clinical study that silencing GC-C in mice compromised the integrity of the intestinal barrier. It allowed inflammation to occur and cancer-causing agents to seep out into the body, damaging DNA and forming cancer outside the intestine, including in the liver, lung and lymph nodes.

Conversely, stimulating GC-C in intestines in mice strengthened the intestinal barrier opposing these pathological changes.

A weakened intestinal barrier has been linked to many diseases, like inflammatory bowel disease, asthma and food allergies, but this study provides fresh evidence that GC-C plays a role in the integrity of the intestine. Strengthening it, the team says, could potentially protect people against inflammation and cancer in the rest of the body.

"If the intestinal barrier breaks down, it becomes a portal for stuff in the outside world to leak into the inside world," said Dr. Waldman. "When these worlds collide, it can cause many diseases, like inflammation and cancer."

The role of GC-C outside the gut has remained largely elusive. Dr. Waldman and his team have previously shown its role as a tumor suppressor and biomarker that reveals occult metastases in lymph nodes. They’ve used to it better predict cancer risk, and have even shown a possible correlation with obesity.

Reporting in the *Journal of Clinical Investigation*, Dr. Waldman colleagues found that silencing GC-C affected appetite in mice, disrupting satiation and inducing obesity. Conversely, mice who expressed the hormone receptor knew when to call it quits at mealtime.

However, its role in intestinal barrier integrity, inflammation, and cancer outside the intestine is new territory in the field.

A new drug containing GC-C is now on the verge of hitting the market, but its intended prescribed purpose is to treat constipation.

This study helps lay the groundwork, Dr. Waldman said, for future pre-clinical and clinical studies investigating GC-C’s abilities beyond those treatments in humans, including prevention and treatment of inflammatory bowel disease and cancer.

"We’ve shown that when you pull away GC-C in animals, you disrupt the intestinal barrier, putting them at risk for getting inflammatory bowel disease and cancer. And when you treat them with hormones that activate GC-C it helps strengthen the integrity of the intestinal barrier," Dr. Waldman said. "Now, if you want to prevent inflammation or cancer in humans, then we need to start thinking about feeding people hormones that activate GC-C to tighten up the barrier."
Journal References:


Cell Energy Sensor Mechanism Discovered
ScienceDaily (Feb. 21, 2012) — Johns Hopkins and National Taiwan University researchers have discovered more details about how an energy sensing "thermostat" protein determines whether cells will store or use their energy reserves.

In a report in the Feb. 9 edition of Nature, the researchers showed that a chemical modification on the thermostat protein changes how it's controlled. Without the modification, cells use stored energy, and with it, they default to stockpiling resources. When cells don't properly allocate their energy supply, they can die off or become cancerous. The Johns Hopkins team focused especially on enzymes that add or remove so-called acetyl groups from protein molecules.

"Understanding how cells are affected by adding acetyl groups to proteins, particularly those involved in energy use, is important because there is increasing use of drugs that block acetyl-removing enzymes for treatment of cancer and neurodegenerative diseases," says Jef Boeke, Ph.D., professor of molecular biology, genetics and oncology, and director of the High Throughput Biology Center at the Johns Hopkins University School of Medicine. "Blocking acetyl-removing enzymes turns on anticancer genes that help fight cancer; however, it is not known what other genes and cellular processes may also be affected by these treatments."

To determine which enzymes remove acetyl chemical groups from which proteins, the researchers engineered human cells with reduced levels of each of 12 enzymes known to remove acetyl chemical groups. In each of these cell lines, they then turned down each of about 20,000 genes and used a DNA "chip" to identify which genes were affected by reduced levels of the acetyl-removing enzymes. The DNA chip highlighted a specific interaction between the thermostat protein, AMP-activated protein kinase (AMPK), and one of the acetyl-removing enzymes, HDAC1.

With less HDAC, AMPK was turned "off," presumably because it retains its acetyl group, the researchers concluded. AMPK acts like an energy thermostat because when energy levels are low in the cell, AMPK kick-starts processes that use the cell's energy reserves and cuts off reactions that store energy. On the other hand, when the cell has plenty of energy, AMPK turns off, causing energy in the form of sugar and fats being stored for later use.

Because the HDAC1 protein turned on AMPK, the researchers presumed there would be a corresponding acetyl-adding enzyme to specifically turn off AMPK. To find this enzyme, they extracted AMPK protein from eight different cell lines, each with reduced levels of a type of acetyl-adding enzyme. They found that AMPK in cells with reduced levels of this acetyl-adding enzyme, called p300, was less acetylated than in cells containing normal amounts of p300.

To confirm the idea that adding or removing acetyl groups directly affects how AMPK controls the way the cell uses energy, they measured the cell's energy stores with the help of a dye that accumulates in the fat globules of a cell. The dye let them estimate the size of fat globules that store energy. The cells unable to add acetyl to AMPK contained less of the dye and therefore smaller fat globules compared to normal human cells. Conversely, the cells unable to remove acetyl groups from AMPK contained more of the dye, indicating bigger fat globules. The research team concluded that when AMPK contains acetyl groups the cell uses less of its energy reserves than when AMPK does not contain acetyl groups.

Boeke says the work on human cells followed similar studies on yeast energy proteins done earlier in his laboratory.

**Journal Reference:** Yu-yi Lin, Samara Kiihl, Yasir Suhail, Shang-Yun Liu, Yi-hsuan Chou, Zheng Kuang, Jin-ying Lu, Chin Ni Khor, Chi-Long Lin, Joel S. Bader, Rafael Irizarry, Jef D. Boeke. **Functional dissection of lysine deacetylases reveals that HDAC1 and p300 regulate AMPK.** Nature, 2012; 482 (7384): 251 DOI: 10.1038/nature10804
RNA Chases Its Tail
New research suggests that circular RNA transcripts are not as rare as previously thought.
By Sabrina Richards | February 2, 2012
Although previous work identified isolated examples of circular forms of RNA, a new study in *PLoS ONE* shows that the molecule assumes this shape much more than previously thought. By surveying the full RNA complement of several human cell types for alternative splice variants, researchers at Stanford University identified a significant portion of these are not linear, but circular.

“It’s the global approach” that’s so novel, said Jørgen Kjems, an RNA biochemist at Aarhus University in Denmark, who was not involved in the study. Kjems’s own work on RNA identified a circular antisense RNA transcript of a neuronal gene, targeted by microRNAs and involved in protein suppression.

Rather than examine splice variants for specific genes, the Stanford researchers were using RNA to scan the genome for “scrambled” exons—where nucleic acid sequences in RNA transcripts were out of order compared to their sequence on the chromosome. The idea arose from previous work investigating chromosomal rearrangements in cancer, which can lead to unexpected RNA transcripts, said co-author Julia Salzman, a biostatistician at Stanford.

To do this, the researchers removed ribosomal RNA from tumor cells, then fragmented the remaining RNA before creating a cDNA library to scan. This created a huge array of sequences, a jigsaw puzzle of RNA, that Salzman and her colleagues reassembled by comparing them to databases of known transcripts. Thus the scientists could identify exons that were joined out of sequence, said Salzman.

Instead of discovering a few translocations, the team identified hundreds of scrambled sequences, explained co-author and Stanford University pediatric oncologist Charles Gawad, which suggested that they were finding alternatively spliced RNA. As Gawad and Salzman tried to reassemble the library of sequence fragments, they found that many sequences didn’t seem to fit, unless the scientists modeled the sequences as circles.

Thinking that they’d hit upon a characteristic of cancerous cells, Salzman and Gawad performed the same experiments on normal human cells—and found a similarly high percentage of scrambled transcripts that seemed to be circular. To confirm this, the researchers subjected the RNA to RNase R treatment, which only digests linear transcripts. Most of the predicted circular transcripts resisted RNase R digestion.

One of the reasons the Stanford researchers were able to identify so many circular RNAs when others had not was their unbiased approach, said bioinformatics expert Alexei Fedorov of Ohio University, who did not participate in the research. Rather than pulling out and examining poly-adenylated RNA, which is generally linear, their method retained RNAs without poly-A tails, which most circular RNAs lack.

“It’s an important finding, but the significance is not proven,” said Alberto Kornblitt, a molecular biologist at the University of Buenos Aires and the National Research Council (CONICET) of Argentina. Kornblitt, who studies alternative RNA splicing but was not involved in the research, points out that although there are examples of functional circular RNA, “enzymatic reactions are not perfect,” and it remains to be seen how many of the circular transcripts are functional, and how many are “evolutionary noise.”

Salzman agreed that it’s too soon to predict how functionally relevant circular RNA is, but she said she’s cautiously optimistic, noting that circular RNAs have been identified in a variety of species.

Gawad pointed to the location of the circular RNAs in the cytoplasm as a hint that some may perform some function. One might expect non-functional splicing byproducts to remain in the nucleus, or to be quickly degraded.

For now, the researchers are investigating how circular RNAs form, hoping to gain insight into the required factors. Later, they might try knocking down the circular form of a specific RNA, to see whether any function can be inferred. The function “is the big question, and really challenging,” said Fedorov. “It will take many years and many labs.”

Long Live the Y
Despite suggestions to the contrary, the Y chromosome is not necessarily rotting away.
By Megan Scudellari | February 22, 2012
About 300 million years ago, early mammalian X and Y chromosomes were identical. But in the intervening time, the Y chromosome lost hundreds of genes, decaying into a shell of its former self. This has led some scientists to propose the “rotting Y” theory, which suggests that the human Y chromosome
will continue to decay until it totally disappears in about 5 to 10 million years. New research, however, suggests that the Y chromosome has a long, healthy life ahead of it and is in no danger of disappearing. The study, reported this week in *Nature*, compared the newly sequenced Y of the rhesus monkey to human and chimpanzee Y chromosomes, and found that the primate Y has been remarkably genetically stable for the past 25 million years.

“This and other evidence suggest that some of these genes are important and have been retained in primate lineages,” said Mark Jobling, who studies the sex chromosome at the University of Leicester in the United Kingdom and was not involved in the research. The Y chromosome does not appear to be decaying away, he said.

But not everyone agrees. “I don’t think this means we can relax about the human Y chromosome,” said Jennifer Graves of La Trobe University in Melbourne, Australia, who was also not involved in the study. Graves has been an outspoken advocate of the rotting Y theory, and, in a 2006 review of the subject, predicted that the Y chromosome will decay in an uneven, jerky process. The new data support that prediction, she argued. “One can’t predict [the degradation of the Y], because it’s a very stochastic process,” she said.

Roughly 300 million years ago, during early mammalian evolution, a segment of the X chromosome stopped crossing over with the Y, causing rapid genetic decay on the Y. This occurred another 4 times throughout the history of mammals, and each time the Y chromosome experienced gene loss. The events were so extensive that today the human Y retains only 3 percent of the more than 600 genes it once shared with the X chromosome.

Prior to the present study, only the human and chimpanzee Y chromosomes had been sequenced, though numerous organisms, from fish to insects to plants, have independently evolved Y chromosomes. Jennifer Hughes, David Page, and colleagues at the Whitehead Institute for Biomedical Science in Cambridge, Massachusetts, sequenced the Y of the rhesus monkey and compared it to the other two sequences. Chimpanzees diverged from humans only 6 million years ago, but rhesus monkeys diverged 25 million years ago, so the new information provides a look at how the primate Y chromosome has changed over a much longer period of time. Genetically speaking, it hasn’t changed much.

The rhesus monkey hasn’t lost a single ancestral gene on its Y chromosome in the past 25 million years, and the human Y has lost just one gene in that period. The Y chromosome’s evolution, therefore, is marked by periods of swift decay followed by strict conservation, said Hughes. And that should put the “rotting Y” theory to rest, she added. “We finally have this very strong empirical evidence that there’s been essentially no change in gene content for 25 million years,” she said. “I’m pretty sure it’s going to be hard to argue with that.”

Yet the study also revealed that the rhesus Y does not have large sections of repeated DNA sequences, called palindromes, that the human and chimpanzee Y chromosomes both have, Graves pointed out. “This means human and chimpanzee Y chromosomes have been around for a long time, and that suggests they must actually be doing something useful,” said Jobling. Unfortunately, scientists don’t know what that is. “The Y chromosome has been neglected,” he said. Beyond sex determination, “we really have very little idea” what most of the genes on the chromosome do.

Whether the Y continues to degrade or not, the fact that a core set of genes has stuck around, despite major loss events, suggests that these genes were selected for by natural selection. “The genes that are still on the human Y chromosome have been around for a long time, and that suggests they must actually be doing something useful,” said Jobling. Unfortunately, scientists don’t know what that is. “The Y chromosome has been neglected,” he said. Beyond sex determination, “we really have very little idea” what most of the genes on the chromosome do.

“But we’d love to know,” added Hughes, who plans to follow up the research with functional studies of the conserved genes. The team also plans to sequence Y chromosomes from other animals, including the rat, mouse, and opossum. “They have interesting positions in the mammalian tree and are model organisms,” Hughes said.

**New Kind of Cellular Suicide**

Researchers identify a gene that drives a type of cellular suicide that differs from the more commonly observed apoptosis phenomenon.

By Jef Akst | February 23, 2012

Apoptosis isn’t the only way to kill a cell, according to new research published today (February 23) in *Science*, in which researchers identified a gene underlying a new cell death pathway.

Cell death is an important part of life. It is critical for shaping developing organs and eliminating infected or dying cells, among other functions. The most well studied mechanism of cell death is apoptosis, which can be found in widespread organisms and tissue systems. But mice have been known to survive without key apoptosis genes, and certain cells of *Caenorhabditis elegans* worms undergo a death process that doesn’t require the caspases and other known apoptosis genes, suggesting some other cell death process is at work.

Taking a closer look at the linker cells of *C. elegans*, whose death is an important part of the development of the male reproductive system, Elyse Blum of The Rockefeller University and colleagues found a clue towards the answer. A genome-wide RNA interference screen revealing genes whose inactivation prevents linker cell death identified the pqn-41 gene, which is expressed early on in linker-cell death. Identifying this gene and factors involved in regulating its expression will help researchers work out further details regarding how the process differs from apoptosis.

The researchers further noted that this linker-cell death pathway is morphologically similar to the neuronal death seen in certain neurodegenerative diseases. “Our results may therefore provide molecular inroads to understanding nonapoptotic cell death in metazoan development and disease,” the authors wrote.

**Antimicrobial Cross-Resistance Risk**

Bacteria that evolve resistance to antimicrobial therapies may be able to evade natural immune peptides.

By Sabrina Richards | January 24, 2012

The struggle to surmount antibiotic-resistant bacteria seems to grow daily. One line of research aims to develop a new class of antimicrobial therapy—antimicrobial peptides (AMP), based on small molecules of the innate immune system that exhibit microbicidal and immuno-modulatory activity. But like antibiotics, bacteria can evolve resistance to AMPs, risking the possibility that bacteria will also be able to resist the first arm of the human immune system.

In new research published in *Biology Letters*, scientists demonstrate for the first time that forcing bacteria to evolve resistance to one AMP can confer some cross-resistance to a natural host-defense peptide.

The study is an “important proof of principle,” said Gabriel Perron, an evolutionary microbiologist at Harvard University, who did not participate in the research, by email. Though previous studies have shown emergence of cross-resistance to AMPs before, explained Perron, this is the first demonstration that “evolution of resistance to a synthetic AMP, designed purely for therapeutic usage, can lead to cross-resistance with human AMPs.”

“It’s [a] pretty important [study],” agreed Angus Buckling, an evolutionary biologist at the University of Exeter, who was not involved in the research. It emphasizes the danger that use of “a potential therapeutic peptide can result in cross resistance to a human defensin.”

Antimicrobial peptides are small, positively charged proteins produced as part of the innate immune system of organisms as disparate as amphibians, insects, and humans. Widely varying in their sequence and structure, AMPs act on bacteria by disrupting the cell membrane or slipping inside and affecting internal processes. AMPs can also indirectly facilitate microbial defense by recruiting phagocytes to the site of infection and boosting the immune cells’ killing activity. AMPs’ wide distribution and the apparent lack of resistance in bacterial populations have made AMPs attractive potential therapeutics.
However, bacteria can evolve resistance to AMPs under strong selective pressure in vitro. In 2003, Graham Bell at McGill University and Pierre-Henri Gouyon at Université Paris-Sud published an article voicing another concern—that when cross-resistance evolved, as it surely would, bacteria might become resistant not only to AMPs adopted for therapeutic use, but also to endogenous human peptides.

To test this possibility, Michelle Habets and Michael Brockhurst at the University of Liverpool cultured *Staphylococcus aureus* with increasing concentrations of pexiganan, an AMP derived from frogs. Sure enough, after 14 passages to plates containing higher pexiganan, the bacteria not only evolved resistance to the therapeutic AMP, but two of the five strains also showed cross-resistance to human neutrophil defensin-1 (HNP-1).

Not everyone is concerned, however. Though Robert Hancock of the University of British Columbia acknowledges that microbial resistance to AMPs must be addressed during therapeutic development, and that cross-resistance is a possibility, he pointed out that the cross-resistance seen in this study is slight. HNP-1 is found at orders-of-magnitude higher concentrations in neutrophils than the researchers used to test the pexiganan-resistant isolates of *S. aureus*, he explained. Furthermore, pexiganan has been tested on more than 800 people in a large-scale clinical trial for treatment of diabetic foot ulcers, and while it failed to emerge as an effective antimicrobial therapy, clinicians saw no signs of pexiganan-resistant bacteria. Until such resistance to human AMPs is reproduced in an in vivo model, Hancock is not convinced that worries about cross-resistance are well-founded.

“We really need drugs, badly,” said Hancock, who sees this focus on theoretical concerns about cross-resistance as tangential to the “bigger concern” of antibiotic resistance.

But Brockhurst and others feel that such investigations are needed now to forestall a repeat of the endless battle against antibiotic resistance. Brockhurst also points to another worrying aspect of the data: even once pexiganan was removed from the culture media, the bacteria retained resistance to the AMP for 100 bacterial generations, suggesting that cross-resistance to endogenous AMPs may be difficult to get rid of once bacteria acquire it.

For now, Brockhurst acknowledges that this is just the first step, and longer-term studies are needed to better address the level of cross-resistance that could evolve in bacteria. But even these preliminary data highlight the importance of “evolutionary thinking in public health,” said Perron. “This fundamental issue will tell a great deal whether AMPs are likely to stay efficient for a while or whether they will follow the same fate as classic antibiotics.”


**Immune Heat**

*Editor’s choice in immunology*

*By Edyta Zielinska | February 1, 2012*

![Image of macrophage](https://example.com/macrophage.png)

**THAT'S SO HOT:** The macrophage, an immune cell known for engulfing infected cells or pathogens, may also play a role in temperature regulation. Photo Researchers, David M. Phillips

**The paper**

The finding
Maintenance of body temperature in response to cold was thought to be the purview of the sympathetic nervous system. But now, Ajay Chawla at the University of California, San Francisco, and colleagues have demonstrated that the immune system—specifically macrophages—plays a critical role in turning fat stores into energy and heat.

The search
The researchers found that brown fat—the heat-producing fatty tissue found mostly in babies and hibernators—contained higher numbers of macrophages than other tissue. So Chawla exposed mice to cold temperatures to see if the numbers of macrophages changed. Although there was no difference in number, the macrophages in the brown and white fat of the chilled mice were more active than in other tissue.

The surprise
The fat-tissue macrophages were not activated via the normal inflammatory pathway, but by an alternative route. The macrophages also appeared to be producing the neurotransmitter norepinephrine, which activates the release of stored fat into free fatty acids and was previously thought to only be produced by neuronal cells. When Chawla inhibited the alternative activation, the mice produced 75-80 percent fewer free fatty acids than control mice.

The future
Now Chawla wants to know whether and how the nerves that detect low temperature activate the alternative pathway in macrophages. “There has to be cross-talk higher up,” says Chawla. Also, the results could be used to develop therapies for obesity, says Shaun Morrison at Oregon Health & Science University.

C. diff Infection Source Unclear
Only a quarter of Clostridium difficile infections in one hospital system were traced to contact with a symptomatic patient.
By Sabrina Richards | February 7, 2012
Only 25 percent of hospital-associated Clostridium difficile infections can be traced to contact with a symptomatic patient in one particular hospital system, according to new research. Surveying recent diarrhea cases in one county in England, the study, published in PLoS Medicine today (February 7), throws the effectiveness of costly prevention strategies typically employed by hospitals into doubt.

The study is “ambitious and far-reaching in its conclusions,” said Kent Sepkowitz, a clinical epidemiologist at Sloan Kettering Memorial Hospital in New York who was not involved in the research. “It shakes the foundation of what we understood” about hospital-associated C. diff infections.

C. difficile is a spore-forming bacterial species associated with severe, sometimes fatal, diarrhea. It’s unclear how many healthy, asymptomatic adults carry C. diff in their colons, but in times of ill health, and especially after broad-spectrum antibiotic treatment, it can overgrow and cause disease. C. diff produces several types of toxins—A, B and CDT. Most strains produce only one, but the hypervirulent Ö27 strain, which caused epidemics of C. diff infection during the early 2000s, can produce all three. C. diff can remain viable in the environment for long periods of time after generating spores that are resistant to heat, alcohol-based disinfectants, and routine surface cleaning. C. diff outbreaks are recurrent problems in hospitals and elderly care facilities, but can also be “community-acquired”—meaning infections occur outside of hospitals.

In the United Kingdom, where C. diff reporting has been mandatory since 2007, its prevalence is an indicator of hospital quality, and hospitals with high rates of C. diff are fined, said study co-author Tim Peto of the University of Oxford. The study results suggest that preventive steps, like hand washing and isolation of infected patients, may only address about a quarter of C. diff infections in some hospitals.
In order to trace the connections between infected hospital patients, the researchers focused on Oxfordshire, a county with a population of about 600,000 in the UK, where almost all health care is provided by one hospital system, which relies on one lab to run diagnostic tests for C. difficile. Over the course of two and half years, samples from all patients with diarrhea, and most patients over 65, were sent to this central facility. Hospitals as well as general practitioners sent samples. The researchers also had access to data on patient locations and movements. Stool samples were screened for C. diff toxins, positive samples were cultured, and the isolates genotyped based on several loci.

Genotyping allowed Peto and his colleagues to trace the path of specific strains, and the hospital ward data gave insight into possible instances of contact between patients. Although rates of infection varied by specialty (oncology vs. general surgery, for example), only a quarter of cases could be traced back to a known infected patient.

Peto said he suspects that instead of encountering C. diff upon entering the hospital, most patients who fell ill carried it in with them. Then, poor health and antibiotic treatment combined to encourage C. diff to overrun the intestines and cause disease. “You blame the hospital,” Peto explained, “but that’s were you go when you’re ill.”

It’s the inability to ascertain the relative impact of asymptomatic carriers that worries Louis Valiquette, an epidemiologist at Université de Sherbrooke in Quebec who did not participate in the study. In healthy adults, only about 3-5 percent will have C. diff in their stool, Valiquette explained, but that rate jumps to more than 40 percent in people who have contact with hospital environments. Though he agreed that the study’s scope and felt the results were impressive, Valiquette said that the data is limited by the standard of preventive practices used in the surveyed hospitals. It’s unclear, Valiquette said, whether the results could be replicated in hospitals with different practices.

Even if only 25 percent of C. diff infections are acquired inside the hospital, it’s a worrisome rate, and doesn’t argue against stringent control measures, added Valiquette.

In contrast, Sepkowitz sees in the results a recommendation for restraint. Most C. diff cases are associated with antibiotic treatment, meaning that regardless of the route of acquisition, disease might be avoided with more judicious use of the drugs.

Peto’s team is now performing whole genome sequencing of C. diff strains and focusing on community acquired C. difficile infection.

Much about C. diff infection and epidemiology is unknown, said Peto. The hypervirulent strain, O27, which was most prevalent at the study’s inception, almost never pops up anymore, Peto said. Whether C. diff mutated away from virulence, or new, less-virulent strains replaced O27, is unclear. Whole genome sequencing will also help researchers hoping to identify virulence-conferring mutations. Sepkowitz hopes that future research brings a deeper understanding of C. diff biology, its incubation time and the “magic moment” when spores become viable.


Cellular Workout

Autophagy, the cell’s recycling system, may be responsible for the health benefits of exercise.

By Megan Scudellari | January 18, 2012

It’s indisputable—exercise is good for you. But on a molecular level, scientists don’t really know why. Published online today in Nature, researchers show for the first time that a cellular housekeeping mechanism, called autophagy, could be the source of the beneficial effects of exercise, including protection against diabetes. Targeting the pathway could mimic the health effects of exercise—all the perks with none of the sweat—and help treat type II diabetes, the authors suggest.

“It’s really a new idea,” said Marc Francaux, who studies the biochemistry of exercise at the Université catholique de Louvain and was not involved in the research. “They use three different transgenic mouse models. It’s really convincing.”

“It provides a fresh look into how exercise produces its benefits,” said Gökhan Hotamisligil, who studies metabolic regulatory pathways at the Harvard School of Public Health and also did not participate in the study. “It’s an important and convincing article.”

Autophagy is an internal recycling system that degrades damaged or unwanted organelles and proteins in a cell and produces energy. In animal models, this process has been shown to protect against cancer, neurodegenerative disorders, infections, diabetes, and more. “Exercise is known to protect against...
all these same diseases,” said Beth Levine, a biologist at the University of Texas Southwestern Medical Center, “so it made sense to us that exercise might induce autophagy.”

Levine’s team first analyzed transgenic mice that form green fluorescent protein dots in their cells during autophagy. They found that after running on a treadmill for at least 30 minutes, the mice’s cells exhibited higher levels of autophagy, demonstrating that exercise stimulates the digestive process in vivo.

Next, the researchers created mice with a mutation in Bcl2, an important autophagy regulator. These mutant mice were still capable of performing basic, low-level autophagy but were unable to ramp up autophagy during exercise. When exercised on a treadmill, the mice could not run as long and did not metabolize glucose as well as control mice. The team confirmed their findings in two other mouse models with mutations at different steps of the autophagy pathway.

Finally, Levine and her team assessed the protective effects of exercise in mice fed a high fat diet to induce diabetes. Normally during exercise, blood glucose levels decrease and the animal becomes more sensitive to insulin, so that low or normal levels of insulin are sufficient to maintain healthy blood glucose levels and prevent diabetes. “We postulated that autophagy is necessary for these protective effects of exercise,” said Levine. When placed on the high fat diet, both the normal and mutant mice gained weight and showed impaired insulin sensitivity, a hallmark of type II diabetes. Running on a treadmill improved these symptoms in animals capable of exercise-induced autophagy. The mutant mice, on the other hand, lost some weight but did not enjoy the diabetes-reversing effects of exercise.

The findings raise the possibility that upregulating autophagy could be a potential new method to mimic the effects of exercise and possibly treat diabetes, said Levine. Her team next plans to investigate the role of autophagy in other diseases in which exercise has beneficial effects, such as cancer and Alzheimer’s.

Another surprising result from the study was the evidence that autophagy is activated during exercise in the liver and pancreas—tissues other than skeletal and cardiac muscle. “The entire field has been focused on benefits of exercise coming from things that happen in muscle,” said Hotamisligil. “This suggests that certain pathways engaged by exercise extend beyond muscle tissue and influence other metabolically critical sites.”


**Forced Feeding**

*Editor’s choice in drug development*

By Edyta Zielinska | February 1, 2012

HUNGRY FOR PROTEIN: Colored scanning electron micrograph (SEM) of a group of *Legionella pneumophila* bacteria. CDC Public Health Image Library

**The paper**

The finding
When University of Louisville’s Yousef Abu Kwaik and colleagues stumbled upon a eukaryotic protein in Legionella bacteria, he suspected the prokaryotes had stolen the gene from its host to help it co-opt their eukaryotic prey—either an amoeba or a human cell. Their investigations revealed that the protein, called AnkB, forces the host cell to degrade its own proteins into amino acids to provide sufficient quantities of nourishment for the parasitic bacterium.

The digest
The protein AnkB was known to tag perfectly healthy proteins with ubiquitin—an address label that marks misfolded proteins for proteasomal degradation—but it was unclear how this process benefited the bacterium. And, although bacteria are known to be able to steal nutrients, “such strategies vary a lot with the pathogen being studied, and we still do not know much about most of them,” writes Rui Appelberg from University of Porto, Portugal, in an e-mail.

The food factory
“This bacterium really lives on an Atkins diet,” says Abu Kwaik, consuming only proteins in the form of free amino acids. When researchers blocked the host cell’s protein degradation machinery, replication of the Legionella ceased, only to be restarted if pure amino acids—in particular cysteine or serine—were added to the culture medium.

The application
Infection with Legionella can only occur by exposure to contaminated water. In theory, these water sources could be treated with currently available proteasome inhibitors to starve the bacteria to death, says Abu Kwaik.

Repeal of HPV Immunization Mandate Is Killed
Washington Post, (02.28.2012) Anita Kumar
A contentious measure that would have repealed a five-year-old requirement that sixth-grade girls in Virginia be vaccinated against human papillomavirus (HPV) died in the state Senate Monday.

The HPV bill passed the House earlier this year, and supporters of the measure figured they had a better chance of repeal in the GOP-controlled Senate. But Republican Sens. John Watkins (Chesterfield) and Frank Wagner (Virginia Beach) joined all Democrats in voting 22-17 to table the matter until 2013.

Supporters said parents, not the state, should decide whether girls should be vaccinated against the STD. But dissenters like Sen. John Edwards (D-Roanoke) maintain “the source of this threat is not sex. It is a virus.” “Whatever we do in this body, we should do based on reason and not based on rigid ideology,” he noted.

Virginia was the first and only state to adopt an HPV vaccine mandate after a federal advisory panel recommended routine vaccination for girls ages 11-12 as a way to prevent cervical cancer; the District of Columbia also passed a mandate. Virginia’s HPV vaccination rates are above the national average: 54 percent of girls ages 13-17 in the state had received at least one dose of the vaccine, compared with 49 percent nationwide, a 2010 CDC survey found.

Many African Men Fail to Get HIV Treatment
Sub-Saharan African men do not obtain HIV/AIDS treatment as often as women, and they die prematurely because of it, researchers say.

“There are a lot of men at the testing centers, but yet, you don’t see them at the clinics for antiretroviral care,” said Edward Mills, associate professor and Canada Research Chair of Health Sciences at the University of Ottawa. “Somewhere in between the time of testing and the time of accessing clinical care we’re missing out on these men.”

Mills supervised HIV/AIDS treatment programs in Africa for several years and questioned this gender disparity. For some men, being HIV-positive carries a stigma of wrongdoing connected to having pre-marital sex, visiting sex workers, or having a relationship outside of their marriage, he said. Disease-related shame drives these men to defer treatment and seek ineffective alternatives.

“Men initially try to treat the HIV themselves,” said Mills. “They maybe go to pharmacies and they buy some aspirin or some Tylenol and they don’t want to accept that they’ve got HIV.” Men need more education about HIV and the importance of early treatment, he said.
Male circumcision campaigns could be used as an opportunity to encourage testing and counseling, but broader efforts may be needed to address men who are resistant to accessing health care, as well as women in discordant couples, Mills said.

“In any discordant relationship you would expect the person who is HIV-positive to be the male,” said Mills. “But when you look at the evidence, actually about 50 percent of the time it’s the male and 50 percent of the time it’s the female. So, there are several different interpretations of this, but the best one is it appears that both genders go outside of their marriage.”

HIV Testing, Gay Community Involvement and Internet USE: Social and Behavioral Correlates of HIV Testing Among Australian Men Who Have Sex with Men

AIDS and Behavior Vol. 16; No. 1: P. 13-22, (01..2012)  M. Holt; P. Rawstorne; J. Wilkinson; H. Worth; M. Bittman; S. Kippax

Among MSM in Australia, “a significant minority” have never undergone HIV testing, while many others do not test as often as recommended. The researchers used data from 1,770 HIV-negative and untested MSM collected in a national online survey to compare men who had never tested for HIV with those who tested more than 12 months ago, and men who had tested more than 12 months ago with those who had tested in the past year. Two multivariate logistic regression models were constructed.

Compared with men who tested more than 12 months ago, the results showed the untested men were younger; less educated; less likely to have unprotected anal intercourse with a regular male partner; and less likely to have sought the advice of a doctor, nurse or community organization. They also were more likely to expect HIV-negative disclosure, and they had fewer gay friends and spent more time on social networking websites.

Compared with men who had tested more than 12 months ago, the men who had tested in the past year were younger; more likely to expect HIV-negative disclosure and to disclose to casual partners; more likely to have sought the advice of a doctor or nurse; and had attended gay beaches, gyms or pools. They also had more gay friends and more male sex partners.

“Our findings suggest that the Internet and sex education in schools are important ways to promote HIV testing to untested MSM,” the authors concluded. “Testing reinforcement messages delivered through gay community outreach and primary care will reach previously tested MSM.”

The Burden of HIV-Associated Neurocognitive Impairment in Australia and Its Estimates for the Future

Sexual Health Vol. 8; No. 4: P. 541-550, (11..2011)  Lucette A. Cysique; Margaret P. Bain; Bruce J. Brew; John M. Murray

“The growing number of older individuals with HIV in Australia implies that the prevalence of dementia and additional HIV-associated neurocognitive disorders will increase,” wrote the authors, who commented on the lack of estimates “of the future burden of neurocognitive disease in this population.”

Using data from the HIV/AIDS Registry, the team estimated the number and age profile of people living with HIV to the end of 2009, then extrapolated these estimates to 2030. The future burden of HIV-associated dementia was estimated based on the prevalence of HAD from 2005 to 2010 in a large Sydney hospital, and cost estimates from the AIDS Dementia and HIV Psychiatry Service were used to estimate future costs.

The authors’ calculations suggest that the number of Australians with HIV will increase from 16,228 men and 1,797 women in 2009 to 26,963 men and 5,224 women in 2030. The numbers of these individuals age 60 and older are expected to increase from 1,140 men and 78 women to 5,442 men (a 377 percent increase) and 721 women (an 825 percent increase).

“Based on a 7.8 percent (157/2,004) HAD prevalence obtained from hospital data, individuals with HAD will increase in number from 1,314 men and 143 women in 2009 to 2,204 men and 421 women in 2030,” the authors reported. The estimated 22 men and two women with non-HIV dementia in 2009 is predicted to increase to 104 men and 12 women by 2030. Annual cost of care is forecast to rise from approximately $29 million (US $31 million) in 2009 to $53 million (US $56.7 million) in 2030, chiefly for full-time residential care.

“Neurocognitive disorders will place an increasing burden on resources, especially as those living with HIV age,” the authors concluded. “Because it is unclear if HAD is an increased risk factor for non-HIV dementia, our calculations may be conservative.”
Florida’s AIDS Drug Program Has the Longest Waiting List in the United States

*Florida Independent*, (02.27.2012)  Marcos Restrepo

Advocates are pressing Florida lawmakers to secure additional funding for the state AIDS Drug Assistance Program. As of Feb. 23, Florida’s ADAP had 1,085 people on its waiting list, the most for any state ADAP in the nation, according to the National Alliance of State & Territorial AIDS Directors. “The Florida Senate’s budget proposes an increase for Florida’s ADAP program, but currently there are no recommendations for similar increases from the Florida House of Representatives,” noted the Florida HIV/AIDS Advocacy Network. In response, the network is seeking “to gain support among House members to join the Florida Senate and work together to eliminate the waiting list for Florida ADAP.” Of those on the waiting list in mid-February, almost half resided in Broward and Miami-Dade counties, according to the state Bureau of HIV/AIDS. While Gov. Rick Scott did not propose additional ADAP funding for 2012-13, his office said “he is looking at the whole program with the goal of reducing unnecessary administrative costs and making it operate more efficiently so that more people can be served with the funds we already have.”

U.N. Helps Kick Off Polio Immunization Campaigns In Angola, Central African Republic

U.N. Secretary-General Ban Ki-moon on Monday "launched a national polio vaccination campaign in Angola, where the crippling disease has returned despite being eradicated in 2001, and praised the government for its leadership on the issue," the *U.N. News Centre* reports. "Angola provides a large majority of the funding needed to vaccinate the country’s children," the news service writes. Ban said the return of polio to Angola within four years after it was eradicated in 2001 illustrated the importance of immunization against polio and other vaccine-preventable diseases, as well as responding to any new polio cases, according to the news service (2/27).

Meanwhile in the Central African Republic, UNICEF, WHO, and government officials are "launching a vaccination campaign that seeks to reach children in hard-to-reach populations as well as those living in conflict and post-conflict zones where there is limited access to health services," the *U.N. News Centre* reports in a separate article. The country had gone two years without detecting any polio cases, until it recorded four imported cases last year, according to the news service. The campaign also will provide vitamin A supplements and de-worming treatments to children under five years old, the news service notes (2/27).

Novartis Defends Challenge To Indian Medicines Patent Law

Pharmaceutical company Novartis "has spoken out following criticism about its challenge to India's patent laws, insisting that access to life-saving drugs is not under peril by the move," *Pharma Times World News* reports. The case, which the Indian Supreme Court is scheduled to hear next month, challenges "Indian patent law, notably Section 3(d), which states that a modification of a known chemical composition is non-patentable," the news service writes.

According to Novartis, currently available generic medicines, including HIV/AIDS medications, made in India prior to 2005, when the country began granting patents, "will continue to be available under a grandfather clause [whereby an old rule continues to apply] in the Indian patent law regardless of the legal outcome of our case," Pharma Times writes. The international aid agency Medecins Sans Frontieres, along with several other groups, is urging Novartis to drop its challenge to the law, the news service notes (Grogan, 2/27).

IRIN Examines Potential Strategies To Fight Sleeping Sickness In Tanzania's Rural Communities

"Tackling land-use conflicts around game parks must form part of the national strategy to stop the spread of [Trypanosomiasis, or sleeping sickness], warn doctors fighting the disease in Tanzania," *IRIN* reports. According to the news service, "Tanzania's booming tourism industry has been driven largely by its wildlife parks, which contribute almost $1.8 billion a year to the economy," but "[a] growing number of communities find their villages 'squeezed' between wildlife areas, putting them at risk from tsetse flies that spread ... sleeping sickness, a debilitating and often fatal disease."

"Furaha Mramba, director of [the Tsetse & Trypanosomiasis Research Institute (TTRI)], said efforts to stamp out the disease faced numerous challenges in Tanzania—from scarce resources to the laborious process needed to develop traps and targets and poaching, which disturbs animal populations and
transfers the fly larvae outside the parks,” IRIN writes. “One of the biggest challenges Tanzanian health authorities face is the sheer scale of the areas they need to cover,” the news service adds, and discusses the use of ”Nze traps, which use blue targets treated with insecticide that attract flies,” buffer zones surrounding parks, aerial insecticides, and SIT, an insect birth control, as potential strategies to address the problem (2/27).

Do parasites evolve to exploit gender differences in hosts?
Some disease-causing parasites are known to favor one sex over the other in their host species, and such differences between the sexes have generally been attributed to differences in immune responses or behavior. But in a new article, published February 28 in the magazine section of the online, open-access journal *PLoS Biology*, David Duneau from Cornell University and Dieter Ebert from the University of Basel now propose that all sorts of characteristics that differ between the sexes of the host species can influence a parasite's adaptation.

These characteristics, such as morphology, physiology, behavior, diet and life history traits can, in fact, pose very different challenges and opportunities to the parasites, and may result in the parasite adapting more to one host sex than the other. Sex-specific adaptations in parasites may also occur when parasites routinely encounter one host sex more frequently than another. Parasites that adapt to male or female hosts may help explain why we find differences in parasite prevalence and disease expression in the different sexes.

"Our ideas may help explain the widespread phenomenon of host sex-biased parasitism and disease expression," said Duneau. "We suggest a new perspective on host-parasite interactions, taking parasite evolution into account."

The paper outlines different scenarios in parasite evolution that might lead to sex-specific disease. These include 'sex-specific adaptations,' with subpopulations of the parasites having fixed but distinct adaptations to females or males; or 'single sex specialization,' where the parasite is specifically adapted to only one host sex; and finally 'plastic sex-specific disease expression,' where the parasite can vary its response depending on whether it finds itself in a male or female host.

However, there are very few documented examples of parasite adaptation to host sex and, to the authors' knowledge, there is no example of a host sex-specific dimorphism. There are only a few examples of parasites being adapted to only one sex, such as a mite that infects only females of its host species—the bat Myotis daubentoni.

The authors argue that more research is now required to study how sex differences affect the evolution of parasites and the diseases they carry. Host sex is a key factor in studies in medicine and disease control, and if parasites adapt differently to the sexes then there is a strong argument, for example, that both sexes need to be included equally in clinical trials—currently an important concern in medicine.

In humans, there are well documented host-sex differences in parasite prevalence and infection symptoms, as well as prevention and treatment of infection. Further research in a range of organisms may reveal why the effects of vaccines can be sex-specific; how parasites are distributed among hosts and why parasites can be locally adapted to certain host sexes.


Scientists discover new 'off switch' in immune response
Discovery provides new insights into inner workings of our immune system
Scientists from Trinity College Dublin have discovered a new 'off switch' in our immune response which could be boosted in diseases caused by over-activation of our immune system, or blocked to improve vaccines. The findings are published this week in the journal *Nature Communications*. The research was funded by Health Research Board, Ireland and Science Foundation Ireland.

The research team, led by Dr Anne McGettrick and Professor Luke O'Neill, at the Trinity Biomedical Sciences Institute, have discovered that a protein, called TMED7, can shut down part of our immune system once an infection has been eliminated. "Without stop signals like TMED7 our immune system would continue to rage out of control long after the infection has been cleared, leading to diseases such as septic shock," says Dr Anne McGettrick. Manipulating these stop signals could help dampen down our immune system to prevent it attacking our own bodies.

In certain cases, removing stop signals and boosting our immune system can be advantageous. Several diseases such as Malaria and HIV are lacking good vaccines and research laboratories and drug
companies around the world are looking to solve this problem. One major issue facing vaccine development is the fact that our immune systems do not mount a strong enough immune response to the vaccine, causing the vaccine to be ineffective. TMED7 limits a key process needed for vaccines to work involving a protein called TLR4. "Removing TMED7 from our cells could help boost our immune response to vaccines thus making the vaccines much more effective," says Dr Sarah Doyle, lead author on the publication.

TMED7 is part of a family of proteins and it is the first member of this family to be implicated in regulating our immune system. Interestingly, it is conserved through evolution and a version in fruit flies called logjam acts similarly to TMED7, limiting antibacterial responses. Further research will reveal if other members of this family play key roles in immunity, and this could lead to exciting new prospects for understanding our immune system. The research was carried out in collaboration with the Norwegian University of Science and Technology, Trondheim, Norway.

Women decrease condom use during freshman year of college, study finds

**Miriam Hospital researchers uncover predictors of changes in condom use during college years**

PROVIDENCE, R.I. – Women gradually use condoms less frequently during their first year of college, according to a new study by researchers from The Miriam Hospital's Centers for Behavioral and Preventive Medicine. This was particularly true for women who binge drink, have lower grade point averages or come from lower socioeconomic backgrounds.

The findings, published online in the *Journal of Sex Research*, offer some of the first clues to how condom use changes during the college years – a time when young people are sexually active and use condoms inconsistently.

"We know unprotected sex puts women at greater risk for unplanned pregnancies and sexually transmitted diseases, yet there has been a gap in research specifically focusing on changes in condom use during women's college years," said lead author Jennifer Walsh, Ph.D., a researcher with The Miriam Hospital's Centers for Behavioral and Preventive Medicine. "Identifying the demographic and behavioral changes associated with decreases in condom use can eventually lead to more targeted educational and intervention efforts."

The study included 279 first-year female college students who provided monthly reports on condom use. Predictors of condom use were assessed at the beginning of the academic year and included questions about participants’ high school GPA, religious beliefs, parents’ education levels and whether the had smoked marijuana or engaged in binge drinking during the month prior to college entry (August). Nearly three-quarters of participants were Caucasian.

Using a statistical technique known as latent growth modeling, researchers observed a gradual decline in condom use over the course of the students’ first year of college, as predicted. This included condom use with all partners and with romantic partners specifically.

However, the study revealed several unexpected predictors of initial condom use. African American women, women who did not smoke marijuana, women who said they are less likely to practice safe sex after drinking and women with more previous sexual partners were less likely to use condoms at the start of the study.

Changes in condom use during the course of the year were predicted by women’s socioeconomic status, high school GPA and substance use.

"College women often engage in serial monogamy, resulting in multiple partners during the college years, and they are often unaware of their partners' risk. This makes continued condom use important for women's health," said Walsh.

**Significant State-By-State Differences in Black, White Life Expectancy**

ScienceDaily (Feb. 24, 2012) — A UCLA-led group of researchers tracing disparities in life expectancy between blacks and whites in the U.S. has found that white males live about seven years longer on average than African American men and that white women live more than five years longer than their black counterparts.

But when comparing life expectancy on a state-by-state basis, the researchers made a surprising discovery: In those states in which the disparities were smallest, the differences often were not the result of African Americans living longer but of whites dying younger than the national average. And,
Interestingly, the area with the largest disparities wasn’t a state at all but the nation’s capital, Washington D.C.

The findings are published in the February issue of the peer-reviewed journal Health Services Research.

"In health-disparities research, there is an assumption that large disparities are bad because vulnerable populations are not doing as well as they should, while areas with small disparities are doing a better job at health equity," said Dr. Nazleen Bharmal, the study's lead researcher and a clinical instructor in the division of general internal medicine and health services research at the David Geffen School of Medicine at UCLA. "In our study, we show that the reason there are small disparities in life expectancy is because white populations are doing as poorly as black populations, and the goal in these states should be to raise health equity for all groups."

The data on which the researchers relied included both health-related and non-health-related deaths, such as murder and accidents. The findings, however, still highlight the need to improve the health of the nation’s African Americans, the researchers said.

The research team studied death-certificate data from the U.S. Multiple Cause of Death for the years 1997-2004. The data covered 17,834,236 individuals in all 50 states and the District of Columbia. The researchers noted race/ethnicity, sex, the age at death and the state where each subject was born, lived and died.

Overall, the national life expectancy was 74.79 years for white men and 67.66 years for black men. Among women, the average life span was 79.84 years for whites and 74.64 for blacks. In every state, gaps were narrower between women than men.

New Mexico had the smallest disparities between blacks and whites (3.76 years for men and 2.45 years for women), while the District of Columbia had the largest (13.77 years for men and 8.55 years for women).

States with the largest disparities
In addition to Washington, D.C., the states with the largest disparities between white and black men were New Jersey, Nebraska, Wisconsin, Michigan, Pennsylvania and Illinois; in these states, the gap was greater than eight years because African American men's lives were shorter than the national average for black men and white men's life spans were equal to or greater than the national average.

For women, the states with the largest disparities in longevity were Illinois, Rhode Island, Kansas, Michigan, New Jersey, Wisconsin, Minnesota, Iowa, Florida and Nebraska, where the difference between black and white women was more than six years. White women in these states lived longer than average, while black women had average or lower life expectancy.

States with the smallest disparities
In addition to New Mexico, which had the smallest disparities, eight other states had black-white disparities of less than six years among men: Kentucky, West Virginia, Nevada, Oklahoma, Washington, Colorado, New York and Arizona.

In four of these states—Kentucky, West Virginia, Nevada and Oklahoma—the smaller disparities were due to a combination of African American men living longer than the national average and whites having shorter lives. But in New Mexico, Washington, Colorado, New York and Arizona, both black and white men lived longer than average, with black men having life spans that were particularly longer than the national average.

Among women, the states with the smallest differences were New Mexico, New York, West Virginia, Kentucky and Alabama—each with disparities of less than four years. These smaller disparities were the result of black women being longer-lived than average and whites being shorter-lived.

Fifty-eight percent of African Americans live in 10 states: New York, California, Texas, Florida, Georgia, Illinois, North Carolina, Maryland, Missouri and Louisiana. Eliminating the disparities in just these states, the researchers said, would bring the national disparity down substantially. For instance, eliminating the disparity in Florida alone would reduce the national disparity from 7.13 years to 6.63 years for men and from 5.20 years to 4.74 years for women.

Because disease prevention and health promotion efforts identify and monitor magnitudes in disparities, these findings could point to new ways that government agencies can track and measure differences in health outcomes, the authors write. Also, the researchers feel that these differences in life expectancy should be considered when funding health programs at local and national levels. Finally, they write, state governments should consider these differences in black-white longevity in formulating health policy, given that coverage through health programs such as Medicaid varies widely among states.
There are some limitations to the study. Among them, the researchers did not account for population changes during the years covered in their analysis, though, they said, it is doubtful such changes would alter the overall findings. Also, they did not consider the tendency of people to move from place to place, which could influence health. They also could not use data from 11 states, but those areas had such small numbers of African Americans that the estimates would not have been reliable.

Also, the study covered all causes of mortality, including murder and accidental deaths. Going forward, the researchers plan to investigate disparities in life expectancy by cause of death.

Journal Reference:

Blood Mystery Solved: Two New Blood Types Identified
ScienceDaily (Feb. 23, 2012) — You probably know your blood type: A, B, AB or O. You may even know if you're Rhesus positive or negative. But how about the Langereis blood type? Or the Junior blood type? Positive or negative? Most people have never even heard of these.

Yet this knowledge could be "a matter of life and death," says University of Vermont biologist Bryan Ballif.

While blood transfusion problems due to Langereis and Junior blood types are rare worldwide, several ethnic populations are at risk, Ballif notes. "More than 50,000 Japanese are thought to be Junior negative and may encounter blood transfusion problems or mother-fetus incompatibility," he writes.

But the molecular basis of these two blood types has remained a mystery—until now.

In the February issue of Nature Genetics, Ballif and his colleagues report on their discovery of two proteins on red blood cells responsible for these lesser-known blood types.

Ballif identified the two molecules as specialized transport proteins named ABCB6 and ABCG2.

"Only 30 proteins have previously been identified as responsible for a basic blood type," Ballif notes, "but the count now reaches 32."

The last new blood group proteins to be discovered were nearly a decade ago, Ballif says, "so it's pretty remarkable to have two identified this year."

Both of the newly identified proteins are also associated with anticancer drug resistance, so the findings may also have implications for improved treatment of breast and other cancers.

As part of the international effort, Ballif, assistant professor in the biology department, used a mass spectrometer at UVM funded by the Vermont Genetics Network. With this machine, he analyzed proteins purified by his longtime collaborator, Lionel Arnaud at the French National Institute for Blood Transfusion in Paris, France.

Ballif and Arnaud, in turn, relied on antibodies to Langereis and Junior blood antigens developed by Yoshihiko Tani at the Japanese Red Cross Osaka Blood Center and Toru Miyasaki at the Japanese Red Cross Hokkaido Blood Center.

After the protein identification in Vermont, the work returned to France. There Arnaud and his team conducted cellular and genetic tests confirming that these proteins were responsible for the Langereis and Junior blood types. "He was able to test the gene sequence," Ballif says, "and, sure enough, we found mutations in this particular gene for all the people in our sample who have these problems."

Transfusion troubles
Beyond the ABO blood type and the Rhesus (Rh) blood type, the International Blood Transfusion Society recognizes twenty-eight additional blood types with names like Duffy, Kidd, Diego, and Lutheran. But Langereis and Junior have not been on this list. Although the antigens for the Junior and Langereis (or Lan) blood types were identified decades ago in pregnant women having difficulties carrying babies with incompatible blood types, the genetic basis of these antigens has been unknown until now.

Therefore, "very few people learn if they are Langereis or Junior positive or negative," Ballif says.

"Transfusion support of individuals with an anti-Lan antibody is highly challenging," the research team wrote in Nature Genetics, "partly because of the scarcity of compatible blood donors but mainly because of the lack of reliable reagents for blood screening." And Junior-negative blood donors are extremely rare too. That may soon change.

With the findings from this new research, health care professionals will now be able to more rapidly and confidently screen for these novel blood group proteins, Ballif wrote in a recent news article. "This
will leave them better prepared to have blood ready when blood transfusions or other tissue donations are required," he notes.

"Now that we know these proteins, it will become a routine test," he says.

A better match
This science may be especially important to organ transplant patients. "As we get better and better at transplants, we do everything we can to make a good match," Ballif says. But sometimes a tissue or organ transplant, that looked like a good match, doesn't work—and the donated tissue is rejected, which can lead to many problems or death.

"We don't always know why there is rejection," Ballif says, "but it may have to do with these proteins."

The rejection of donated tissue or blood is caused by the way the immune system distinguishes self from not-self. "If our own blood cells don't have these proteins, they're not familiar to our immune system," Ballif says, so the new blood doesn't "look like self" to the complex cellular defenses of the immune system. "They'll develop antibodies against it," Ballif says, and try to kill off the perceived invaders. In short, the body starts to attack itself.

"Then you may be out of luck," says Ballif, who notes that in addition to certain Japanese populations, European Gypsies are also at higher risk for not carrying the Langereis and Junior blood type proteins.

"There are people in the United States who have these challenges too," he says, "but it's more rare."

Other proteins
Ballif and his international colleagues are not done with their search. "We're following up on more unknown blood types," he says. "There are probably on the order of 10 to 15 more of these unknown blood type systems—where we know there is a problem but we don't know what the protein is that is causing the problem."

Although these other blood systems are very rare, "if you're that one individual, and you need a transfusion," Ballif says, "there's nothing more important for you to know."

Journal Reference:
Virginie Helias, Carole Saison, Bryan A Ballif, Thierry Peyrard, Junko Takahashi, Hideo Takahashi, Mitsunobu Tanaka, Jean-Charles Deybach, Hervé Puy, Maude Le Gall, Camille Sureau, Bach-Nga Pham, Pierre-Yves Le Pennec, Yoshiihiko Tani, Jean-Pierre Cartron, Lionel Arnaud. **ABCB6 is dispensable for erythropoiesis and specifies the new blood group system Langereis.** Nature Genetics, 2012; 44 (2): 170 DOI: 10.1038/ng.1069

Gay Sex Legal, Says India Government
Posted: 02/28/2012 6:09 am
NEW DELHI (AP) — The Indian government Tuesday clarified to the Supreme Court that it accepts a recent ruling legalizing gay sex in the country.

A lawyer told the Supreme Court that the government would not challenge a 2009 order by the Delhi High Court striking down a colonial-era law that made gay sex a crime.

The order was appealed by conservative groups and the Supreme Court is now hearing opinions from those groups as well as gay rights activists.

The latest statement comes days after another government lawyer told the court that gay sex was "highly immoral" and should be banned. The government quickly denied that lawyer's statement, prompting confusion about its stance on the law.

On Tuesday, a Supreme Court justice asked the government’s lawyers to file an affidavit to reconcile the two divergent positions heard in court. Neither lawyer explained Thursday's confusion.

The 2009 high court order had said that treating consensual gay sex between adults as a crime was a violation of fundamental rights protected by India's constitution.

Sex between people of the same gender had been illegal in India since the 1860s, when a British colonial law classified it as "against the order of nature."

Prosecutions were rare, but the law was used frequently to harass people.

Over the last decade, homosexuals have slowly gained a degree of acceptance in some parts of India, especially its big cities. The last two years have also seen large gay pride parades in New Delhi and other big cities, including Mumbai and Kolkata.

Still, being gay remains deeply taboo in most of the country, and many gays and lesbians hide their sexual orientation from friends and relatives.
China (Reuters) — China hopes to cap the number of people living with HIV/AIDS at 1.2 million by 2015, up from around 780,000 at present, partly by promoting increased condom use, the government said in an action plan released on Wednesday.

While praising achievements made over the past few years, including improved life expectancy for AIDS patients, the State Council, or cabinet, said China still faced a difficult task to prevent the spread of the disease.

"The present spread of AIDS is still severe, there is widespread discrimination in society, the virus is a serious (problem) in some areas and amongst high-risk groups," it said in a statement on the central government's website (www.gov.cn).

Sexually transmitted diseases are also on the rise, it added, a particular concern as AIDS is now mostly spread in China through sexual intercourse.

"The situation is becoming more complex and prevention work is extremely difficult," the statement added.

China hopes to tackle these issues partly through a large increase in condom use, the government said.

By 2015, condoms or condom vending machines should be available in 95 percent of hotels and other, unspecified, public areas, and 90 percent of high-risk groups should be using condoms, the action plan states.

It did not provide comparative figures for current usage. The term "high risk groups" usually refers to gay men, intravenous drug users and others.

"By the end 2015, bring under basic control the rapid rise of the AIDS virus in main areas and among main groups of people, and reduce by 25 percent compared with 2010 the number of new infections," the government said in its plan.

To deal with ignorance among local officials about the disease, their knowledge of AIDS and ability to promote public education will become part of annual performance reviews, the government said.

The government was slow to acknowledge the problem of HIV/AIDS in the 1990s and had sought to cover it up when hundreds of thousands of impoverished farmers in rural Henan province became infected through botched blood-selling schemes.

Beijing has since stepped up the fight, spending more on prevention programs, launching schemes to give universal access to anti-retroviral drugs to contain the disease, and introducing policies to curb discrimination.

But in a country where taboos surrounding sex remain strong and discussion of the topic is largely limited, people with HIV/AIDS say they are often stigmatized.

Maurice Tomlinson’s Countdown to Tolerance: The Cultural War Against Homosexuals is Heating Up

By Maurice Tomlinson

I am loath to return to a topic more than once, but in this case I must make an exception. You see, the cultural war being waged against recognizing the human rights of homosexuals is heating up on the African continent, and the losers will inevitably be Africans themselves.

Since my last post on this subject, Uganda’s Minister of Ethics—ironically, acting unethically and illegally—broke up a private conference of LGBT activists just a week after the parliament saw the reintroduction of the bill that provides for the state-sanctioned murder of gays. After driving nearly 20 miles to personally trample on the constitutional rights of fellow Ugandans, the Minister admitted to the media that he had no legal right to deny the group their right to assemble. However, he justified his arbitrary abuse of power by claiming that Ugandans don’t want gays even associating in private. Adding insult to injury, in the very same week, Uganda’s President Museveni made the astonishing statement, during a BBC HARDtalk interview, that gays are “not persecuted or discriminated” against in his country. Such willful and transparent denialism by a world leader beggars belief.

Meanwhile in West Africa, a “kill the gays” bill similar to the one before the Uganda parliament was introduced into the Liberian Senate by Senator Jewel Howard Taylor, the former first lady whose ex-husband is currently on trial for his role in the savage atrocities committed during the Liberian Civil War. Apparently, Mrs. Taylor learned well the art of inflicting misery on innocent civilians from her ex-husband. It is remarkable that the President of this former US protectorate (and reputed US dual citizen),
Nobel Peace Prize winner Ellen Johnson Sirleaf, has been silent on this proposed bill, which would strengthen the already draconian laws against homosexuals in her country.

In the same week, a meeting of gays to discuss safer sex techniques was broken up by a mob led by Muslim imams in Mpato, Kenya. Kenyan news coverage of the event showed the group of homosexuals fleeing in chaos as the enraged rabble descended. Thankfully, no one was hurt in this latest violation of the human rights of Kenyan gays.

The supreme irony in these stories is that those responsible for these human rights violations actually believe their actions are in some way preserving African culture and, ostensibly, preventing the spread of HIV and AIDS. Such misguided logic is a function of centuries of western indoctrination in the art of divide-and-conquer which was used to keep Africa underdeveloped. Africans are once again being taught that resolving their differences (this time on the sensitive issue of sexual rights) should be done through the adoption of the most extreme measures, instead of relying on the spirit of tolerance for diversity which once saw advanced civilizations appearing on the continent while Europeans still lived in caves. Bankrupt African governments are also seeking to deflect attention from their poor performing economies by making scapegoats of gays.

Those who think trying to suppress homosexuality will somehow cause it to disappear must not have been paying attention during biology/bible class. Same-sex attraction is a fact of human sexuality. Pyramid paintings in Egypt show the first record of a homosexual couple in history, Khnumhotep and Niankhkhnum, who lived around 2400 BCE. Homosexuality is therefore clearly not un-African. Instead, it is homophobia that was imported into the continent, usually by western fundamentalist evangelical Christian missionaries. Trying to suppress same-sex attraction is futile; it can also be deadly. Male homosexuals are biologically more vulnerable to HIV, and unless they are allowed access to effective HIV prevention, treatment, care and support interventions, they will become infected with this still incurable virus. Professor Chris Beyrer of Johns Hopkins University has produced research that demonstrates that the median access to HIV prevention, treatment, care and support interventions is much lower in contexts that criminalize male same-sex intimacy. And if these men have to take female partners as a “cover” for their sexuality, the result is that the virus becomes entrenched in the general population.

Africa already has the highest HIV and AIDS burden. Efforts by those engaged in the cultural war against homosexuals on the continent are ensuring it stays that way.

**Mugabe admits losing cabinet to HIV and AIDS**

While launching the Zimbabwe Parliamentarians against HIV (ZIPAH) in Harare Mugabe who is 88 and has been in power since 1980 said that over the past three decades his comrades have fallen to the condition.

“Apart from what I have said that the pandemic took lives of my family members, but in my political family, comrades I have worked with, a lot of cabinet ministers perished, we did not announce it though but I can tell you a number of them died of AIDS, not all of them but quite a number of them,” President Mugabe said.

In September last year Mugabe said he was ashamed of some HIV positive senior officials in his government who continue to be promiscuous spreading the HIV virus at a time the country was working towards an HIV free generation.

The usual statement that has been expressed in the past years when senior government officials die has been “a short illness’ but on Thursday Mugabe confirmed the long suspected belief that it is HIV that is depleting his cabinet.

Mugabe challenged legislators to reveal their status after getting tested something that is sure to raffle feathers among MPs who have never declared their status even though after having been tested.

“You must walk the talk and for you to be good advisors to the public and even to intellectuals like cabinet Ministers. We know that you policy makers including cabinet ministers have small houses, tisu zvivevenga zvacho (We are the very culprits).We should not allow ourselves to be the epitome of the immorality that we condemn. That’s where the problem lies.

Zimbabwe is one of the few countries which have done well in the management of HIV and AIDS. The country has reduced its HIV prevalence from over 26% in 1997 to 13, 7% to date this despite challenges in funding AIDS programmes.

However, the cancellation of round 11 of Global Fund and indications by international that there are about to withdraw AIDS funding is likely to reverse gains that the country has achieved over the years.
Zimbabwe Parliamentarians against HIV and AIDS is a network of individual legislators committed to increasing their role in the response to HIV. It contributes to collective efforts to reduce the impact of HIV in Zimbabwe communities.

New indicator diseases reveal hidden HIV
Today, heterosexuals in Europe are at particular risk of carrying HIV for so long that they remain undiagnosed until their immune system starts to fail and they become ill. An international study under the leadership of the HIV in Europe initiative has now revealed that a number of diseases, including herpes zoster and certain forms of cancer, should be on the list of indicators for having HIV—and thus serve to prompt health care professionals to suggest an HIV-test to their patients. The new results and guidelines are to be debated at a major international HIV conference in Copenhagen on 19th-20th March.

"At the HIV in Europe conference we will be discussing how to disseminate knowledge of the new HIV indicator diseases to non-HIV doctors and health care professionals across Europe," says Jens Lundgren, Co-chair of the HIV in Europe initiative.

He's also a Professor of Viral Diseases at Rigshospitalet and the Faculty of Health and Medical Sciences at the University of Copenhagen, where he heads the Copenhagen HIV Programme, one of the leading HIV/AIDS centres in the world.

Too many HIV-infected individuals are remain undiagnosed
Half of all people living with HIV are diagnosed very late in the course of their chronic HIV infection. People infected through heterosexual transmission now comprise 42 per cent of these late presenters, as a study of 90,000 Europeans tested HIV positive since 2,000 shows.

UNAIDS has estimated that 2.5 million Europeans carry an HIV infection, and as many as 900,000 of these, are still unaware of this. Inside EU the numbers are 800,000 infected with 250,000 undiagnosed.

Ton Coenen, co-chair of the HIV in Europe initiative, Director of Aids Funds and Soa AIDS Nederland suggests that since the HIV/AIDS issue is no longer high on the agenda in many European countries, and since people have to actively choose to be HIV-tested, many perhaps no longer consider going for a test if they have had unsafe sex.

However, the sooner HIV-infected individuals receive a diagnosis and start therapy, the greater are their chances of survival and their quality of life. And new research also shows therapy lowers the risk of passing the infection on to someone else.

"The currently situation shows that we need more effective testing strategies and guidelines," Ton Coenen continues. "More than 300 doctors, health care professionals, NGOs and health politicians from 40 European countries will be discussing this need at the conference on 19th and 20th of March, so we have the ideal forum for it."

Eight new HIV-defining diseases should warrant and HIV-test
"We already have a list of Aids defining diseases, the vast majority of which indicate a weak immune system. This is a symptom of HIV and should lead to an immediate HIV test," Professor Lundgren explains. "We need to find people living with HIV sooner than is currently the case, but to do so requires that doctors and other health care professionals offer tests to people presenting with diseases indicative of a hidden and undiagnosed HIV infection earlier in the course of the disease."

The HIV in Europe initiative took up this challenge in 2009 and started the HIDES study (HIV Indicator Diseases Across Europe), which investigated eight new diseases and how often they proved to be signs of an undiagnosed HIV infection among the 3588 patients in the study.

"We could see that if an adult had a sexually transmitted infection, malignant lymphoma, cervical or anal cancer/dysplasia, herpes zoster, hepatitis B or C, ongoing mononucleosis-like illness, inexplicable, persistent decline in the number of circulating white blood cells, or seborrheic dermatitis/exanthema, the risk of HIV infection was so high that it would be cost-effectiveness for society to routinely offer them a test," Professor Lundgren says. He also emphasises that the new indicator diseases do not necessarily mean that the patient has HIV.

"But the incidence of HIV is greater for these eight indicator diseases and they should encourage health care professionals to offer the patient an HIV test. Draft guidelines on how to ensure this throughout Europe are one of the topics we need to debate and decide on, before they can be implemented."
Utah House Passes Bill to Allow Schools to Skip Sex Education
*Salt Lake Tribune*, (02.23.2012) Lisa Schencker

The Utah House of Representatives on Feb. 22 passed a bill that would let school districts drop sex education classes. It also would bar instruction on contraceptives in those that elect to keep the courses.

HB 363 passed by a 45-28 late-afternoon vote, following attempts by various lawmakers to modify the bill. The final version would permit districts to forgo teaching about sex altogether and prohibit those that do from instructing students in “the use of contraceptive methods or devices.” An earlier version of HB 363 would have banned “instruction in the advocacy or encouragement of the use of contraceptive methods or devices.”

The measure represents a significant shift from current law, which requires high schools to teach sex education and prohibits only the advocacy of contraceptive use. Districts choose whether to simply emphasize abstinence or teach abstinence-only.

Lawmakers also amended HB 363 on the floor to reinforce the role of parents in the development and recommendation of abstinence-only materials and to require that those materials include components to help parents address the topic. The measure now advances to the Senate.

Censorship and Dirty Needles Fuel HIV/AIDS Epidemic
*Inter Press Service*, (02.17.2012) Kester Kenn Klomegah

Russian health advocates are alarmed over the “draconian silencing” of online information about harm-reduction approaches to injection drug use. Russia has one of the world’s largest populations of IDUs.

On Feb. 3, the Federal Drug Control Service of the Moscow Department—citing the need to prevent the “placement of materials that propagandize the use of drugs, information about distribution and purchasing of drugs and inciting the use of drugs”—ordered the shutdown of a website run by the Andrey Rylkov Foundation (ARF).

But ARF President Anya Sarang said the media crackdown is “over methadone, plain and simple.” The foundation has been a vocal critic of the government ban on methadone, which global health experts consider an essential tool in preventing HIV transmission and treating opioid addiction. Its website often linked to research demonstrating methadone’s public health benefits.

“We are very concerned about the closure of the website, which is one of very few Russian-language websites with accurate information about drug treatment, particularly drug treatment using methadone,” said Diederik Lohman of Human Rights Watch. The senior researcher said the Russian government routinely misinforms the public about methadone, claiming it to be dangerous and ineffective.

The result has been a growing HIV/AIDS epidemic, said Lohman. Thousands of disease-related deaths during recent years could have been prevented if the government supported proper IDU treatment and prevention programs, he said.

Russia has roughly 980,000 HIV/AIDS cases, a number that may reach 1.65 million by 2015 if current trends continue.

Do Asian-American Women Who Were Maltreated as Children Have a Higher Likelihood for HIV Risk Behaviors and Adverse Mental Health Outcomes?
*Women's Health Issues Vol. 22; No. 1: P. e35-e43*, (01..2012) Hyeouk Chris Hahm; Eric Kolaczyk; Yookyong Lee; Jisun Jang; Lisa Ng

The authors reported that the current study “is the first to systematically investigate whether multiple child maltreatment is associated with HIV risk behaviors and adverse mental health outcomes among Asian-American women.” Using computer-assisted survey interviews, they conducted a cross-sectional study of 400 unmarried Chinese, Korean, and Vietnamese women, ages 18-35, identified as children of immigrants.

Having experienced maltreatment as a child was reported by about seven in 10 women, while 6.8 percent reported any type of sexual abuse. Having sex at age 16 or younger was reported by 15 percent of respondents. Almost 60 percent had ever engaged with potentially risky sexual partners.

“Contrary to the findings from previous studies of white and black women, sexual abuse plus other maltreatment was not associated with HIV risk behaviors among Asian-American women,” the team wrote. It was, however, found to be associated with “a marked increase in depression, lifetime suicidal ideation, and suicide attempts.” Increased odds of HIV risk behaviors, including ever having had anal sex and ever having potentially risky sex partners, were associated with a higher education level.
“There was no evidence indicating that multiple child maltreatment was linked with HIV risk behaviors, but it exhibited a robust association with poor mental health outcomes,” the authors concluded. “These empirical patterns of internalizing trauma, suffering alone, and staying silent are in accord with Asian-cultural norms of saving face and maintaining family harmony. The prevention of multiple child maltreatment may reduce high levels of depression and suicidal behaviors in this population. It is urgent to identify victims of multiple child maltreatment and provide culturally appropriate interventions.”

**Exposed Persons Tested in Emory TB Case**

*Atlanta Journal-Constitution*, (02.29.2012)  David Ibata

Hundreds of people have been tested for TB at Emory University in Atlanta after officials recently confirmed a worker there had an active case of the disease, local WSB-TV reported. The custodian, now deceased, was apparently unaware he had the disease, university officials said. The DeKalb County Medical Examiner’s Office determined on Feb. 17 that the man had had active TB.

The employee reportedly cleaned buildings on the Druid Hills campus, none of them dormitories, and had minimal contact with students. However, some students, faculty, and staff may have been exposed. In more than 43,000 e-mails sent to the campus community, Emory said any potential exposure may have been between Aug. 1 and Feb. 2. Emory said it is working with university departments and state and local health officials to determine who may need to undergo testing.

“The notification and testing of those persons on campus who were substantially exposed to our employee have already begun,” Emory said in the e-mail.

TB skin tests have been given to about 400 people. Anyone testing positive would receive a chest X-ray and, if necessary, treatment.