HIV This Week: what scientific journals said

Welcome to the 67th issue of ***HIV This Week!*** In this issue, we cover **nosocomial transmission** (the first review in 15 years presents positive ideas for prevention; lessons from people who inject drugs along the Mexican-US border reveal it's time to make plasma donation a civic duty rather than a money-maker), ***post-exposure prophylaxis*** (a systematic review presents evidence on PEP for non-occupational exposure; limited scenarios in Australia for cost-effective non-occupational PEP), **models of treatment and care** (time for collaboration with practitioners of traditional Indian medicine and homeopathy; Abidjan's mother-to-child transmission-plus programme reaches out to male partners of pregnant women), **surveillance** (implementation ethics and unlinked anonymous surveillance), **dry sex** (only 7% of women in Lusaka who use 'dry sex' traditional medicines do so before sex; vaginal practices, sexual pleasure, and fidelity in KwaZulu-Natal), **basic science** (disconcerting news that HIV has been adapting to our protective immune responses at a population level; making drug-free remission the new goal of HIV therapeutics - the HIV Latency Collaboratory approach; genetic and epidemiological archaeology illuminates 15th century Croatia and CCR5Delta32 selection pressure), **religious beliefs and HIV** (Christianity in Tanzania: stigma or social support for people living with HIV?), **risk compensation** (young men in Kisumu, Kenya with risk compensation beliefs about antiretroviral therapy are more likely to be HIV-positive), **paediatric treatment** (kids reconstitute their immune systems on prolonged antiretroviral therapy but early starters do better), **men who have sex with men** (time for improved surveillance and gay bath HIV prevention programmes in China's Jiangsu province), **epidemiology** (Georgia knows its epidemic and can tailor a response), **treatment: when to start** (dealing with lead-time bias: the ACCORD study reports a 70% increase in mortality for those starting below 350 cells/microl; a thorough review of the evidence suggests there is equipoise for the START trial that is just starting; why we should not have distinct criteria for starting antiretroviral treatment in people in whom we anticipate poor adherence), **male circumcision and manhood** (synergies from joining the worlds of medical circumcision and traditional manhood initiation rituals in the Eastern Cape, South Africa), and **reproductive health and youth** (why fertility intentions are important in HIV prevention programmes for youth in Mozambique; adolescent girls in rural Bangladesh seem to have been on another planet).

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1. Nosocomial transmission

Ganczak M, Barss P. Nosocomial HIV infection: epidemiology and prevention-a global perspective. *AIDS Rev.* 2008;10(1):47-61.

Because, globally, HIV is transmitted mainly by sexual practices and injection drug use and because of a long asymptomatic period, healthcare-associated HIV transmission receives little attention even though an estimated 5.4% of global HIV infections result from contaminated injections alone. It is an important personal issue for healthcare workers, especially those who work with unsafe equipment or have insufficient training. They may acquire HIV occupationally or find themselves before courts, facing severe penalties for causing HIV infections. Prevention of blood-borne nosocomial infections such as HIV differs from traditional infection control measures such as hand washing and isolation and requires a multidisciplinary approach. Since there has not been a review of healthcare-associated HIV contrasting circumstances in poor and rich regions of the world, the aim of this article is to review and compare the epidemiology of HIV in healthcare facilities in such settings, followed by a consideration of general approaches to prevention, specific countermeasures, and a synthesis of approaches used in infection control, injury prevention, and occupational safety. These actions concentrated on identifying research on specific modes of healthcare-associated HIV transmission and on methods of prevention. Searches included studies in English and Russian cited in PubMed and citations in Google Scholar in any language. Medical Subject Headings (MeSH) keywords such as nosocomial, hospital-acquired, iatrogenic, healthcare associated, occupationally acquired infection and HIV were used together with mode of transmission, such as "HIV and haemodialysis". References of relevant articles were also reviewed. The evidence indicates that while occasional incidents of healthcare-related HIV infection in high-income countries continue to be reported, the situation in many low-income countries is alarming, with transmission ranging from frequent to endemic. Viral transmission in health facilities occurs by unexpected and unusual as well as more frequent modes. HIV can be transmitted to patients and to donors of blood products by specific vehicles and vectors during blood transfusion, plasma donation, and artificial insemination, by improperly sterilized sharps, by medical equipment during activities such as dialysis and organ transplantation, and by healthcare workers infected by occupational exposure to hazards such as blood-contaminated sharps. Personal, equipment, and environmental factors predispose to acquisition of nosocomial HIV and all are pertinent for prevention. For infection and injury control, poverty is often an underlying determinant. While sophisticated new tests offer improved HIV detection, increasingly higher marginal costs limit their feasibility in many settings. Modest investment in safer equipment and appropriate integrated training in infection control, injury prevention, and occupational safety should provide greater benefit. **Editors' note: Nosocomial (from the Greek *nosos* [disease] and *komein* [to care for] and later from the Latin for hospital *nosocomium*) infections are those that occur more than 48 to 72 hours after a patient is admitted and were not present or incubating at entry. This exhaustive review, the first in 15 years, is**

essential reading for policy makers, health personnel, and the public alike. The detailed descriptions of modes of health care-associated HIV transmission and of virtually all the documented cases from around the world set the stage for recommended interventions to eliminate/reduce risk for all countries, with special priorities for low-income countries. Arguing that prevention begins when everyone accepts that nosocomial infections are truly avoidable, the authors call for international action to develop and implement appropriate and efficient safety equipment, training, and surveillance that are feasible for even remote areas of low-income countries.

Volkow P, Brouwer KC, Loza O, Ramos R, Lozada R, Garfein RS, Magis-Rodriguez C, Firestone-Cruz M, Strathdee SA. Cross-border paid plasma donation among injection drug users in two Mexico-U.S. border cities. *Int J Drug Policy.* 2009 Feb 18. [Epub ahead of print]

Paid plasma donation has contributed to HIV epidemics in many countries. Eleven million litres of plasma are fractionated annually in the U.S., mainly from paid donors. Deferral of high-risk donors such as injecting drug users is required for paid donations. Volkow and colleagues studied circumstances surrounding paid plasma donation among injecting drug users in two Mexico-U.S. border cities. In 2005, injecting drug users >/=18 years old in Tijuana (N=222) and Cd. Juarez (N=206) who injected in the last month were recruited through respondent-driven sampling. Subjects underwent antibody testing for HIV and HCV and an interviewer-administered survey including questions on donating and selling whole blood and plasma. Of 428 injecting drug users, HIV and HCV prevalence were 3% and 96%, respectively; 75 (17.5%) reported ever having donated/sold their blood or plasma, of whom 28 (37%) had sold their plasma for an average of $16 USD. The majority of injecting drug users selling plasma were residents of Ciudad Juarez (82%); 93% had sold their plasma only in the U.S. The last time they sold their plasma, 65% of injecting drug users had been asked if they injected drugs. Although the median time since last selling plasma was 13 years ago, 3 had done so within the prior 2 years, one within the prior 6 months; of these 3 injecting drug users, 2 were from Cd. Juarez, one from Tijuana; all 3 had only sold their plasma in the U.S. Although selling plasma appears uncommon among injecting drug users in these two Mexican border cities, the majority sold plasma in the U.S. and only one-third were deferred as high-risk donors. Paying donors for plasma should be a matter of public inquiry to encourage strict compliance with regulations. Plasma clinics should defer donors not only on behavioural risks, but should specifically inspect for injection stigmata.

Editors' note: Selling of blood and plasma was banned in Mexico over two decades ago but, surprisingly, remains legal in some US states such as California and Texas. High-risk donors are screened and deferred and pasteurisation or detergent treatment is used to inactivate potential blood-borne pathogens. Understandably, plasma donors in a paid donation system tend to be over-represented by economically disadvantaged persons who may be at higher risk of HIV exposure. Since deferral and plasma treatment are not fail-safe, all countries should move as quickly as possible to voluntary blood and plasma donations, promoted as part of civic duty rather than for monetary recompense.

2. Post-exposure prophylaxis

Bryant J, Baxter L, Hird S. Non-occupational postexposure prophylaxis for HIV: a systematic review. *Health Technol Assess*. 2009;13(14):1-82.

Bryant and colleagues review the evidence on the clinical effectiveness and cost-effectiveness of non-occupational postexposure prophylaxis (PEP) for HIV. Eleven electronic

databases were searched from inception to December 2007. Selected studies were assessed, subjected to data extraction using a standard template and quality assessment using published criteria. Studies were synthesised using a narrative approach with full tabulation of results from all included studies. One clinical effectiveness study meeting the inclusion criteria was identified, a cohort study of PEP in a high-risk HIV-negative homosexual male cohort in Brazil. The quality of the study was generally weak. Seroincidence in the cohort as a whole (2.9 per 100 person-years) was very similar to that expected in this population (3.1 per 100 person-years, $p > 0.97$), despite the seroconversion to HIV being 1/68 in the PEP group and 10/132 in the group not receiving PEP. High-risk sexual activities declined over time for both PEP and non-PEP users. Four economic evaluations met the inclusion criteria of the review. The methodological quality of the studies was mixed. The studies are constrained by a lack of published data on the clinical effectiveness of PEP after non-occupational exposure, with effectiveness data derived from one study of occupational PEP. Their generalisability to the United Kingdom is not clear. Results suggest that PEP following non-occupational exposure to HIV was cost saving for men who have unprotected receptive anal intercourse with men, whether the source partner is known to be HIV positive or not; heterosexuals after unprotected receptive anal intercourse; and people who inject drugs with contaminated equipment previously used by a known HIV-positive person. PEP following non-occupational exposure to HIV was cost-effective for all male-male intercourse (unprotected receptive and insertive anal intercourse, unprotected receptive oral sex, and 'other') and was possibly cost-effective for people who inject drugs and high-risk women. Four additional studies were identified giving further information about adverse events associated with PEP after non-occupational exposure to HIV. The majority of participants experienced adverse events with the most common being nausea and fatigue. Rates were generally higher in participants receiving triple therapy than in participants receiving dual therapy. Completion of PEP therapy was variable, ranging from 24% to 78% of participants depending on type of therapy. Toxicity was the main reason for discontinuation of treatment. It is not possible to draw conclusions on the clinical effectiveness of non-occupational PEP for HIV because of the limited evidence available. The review of cost-effectiveness suggests that non-occupational PEP may be cost-effective, especially in certain population subgroups; however, the assumptions made and data sources used in the cost-effectiveness studies mean that their results should be used with caution. **Editors' note: Clinical trials of post-exposure prophylaxis (PEP) for occupational exposure are neither ethical nor practical and so, based on animal studies, occupational PEP is standard practice everywhere. For non-occupational exposure, many countries have 5-day PEP starter kits in emergency rooms and other settings for people who may have been exposed to HIV during rape. This review underscores the need for better data collection on the use and outcomes of non-occupational PEP and for counselling about adverse events to improve adherence during the 4-week course of antiretroviral medication. It suggests that PEP for non-occupational exposure could be cost-effective particularly following exposure to blood/body fluids known to contain HIV.**

Guinot D, Ho M, Poynten I, McAllister J, Pierce A, Pell C, Grulich A. Cost-effectiveness of HIV nonoccupational post-exposure prophylaxis in Australia. *HIV Med.* 2009;10(4):199-208

The aim of the study was to determine the cost-effectiveness of HIV non-occupational post-exposure prophylaxis (PEP) in Australia. A retrospective cost analysis of a population-based observational cohort of 1601 participants eligible for non-occupational PEP in Australia

between 1998 and 2004 was carried out. Guinot and colleagues modelled non-occupational PEP treatment costs and combined them with effectiveness outcomes to calculate the cost per seroconversion avoided. They estimated the cost-utility of the programme, and sensitivity and threshold analysis was performed on key variables. The average of non-occupational PEP cost per patient was A$1616, of which A$848 (52%) was for drugs, A$331 (21%) for consultations, A$225 (14%) for pathology and A$212 (13%) for other costs. The cost per seroconversion avoided in the cohort was A$1 647 476 in the base case analysis, and A$512 410 when transmission rates were set at their maximal values. The cost per quality-adjusted life-year (QALY) was between A$40 673 and A$176 772, depending on the risks of HIV transmission assumed. The authors conclude that in their base case, non-occupational PEP was not a cost-effective intervention compared with the widely accepted Australian threshold of A$50 000 per QALY. It was only cost-effective after receptive unprotected anal intercourse exposure to an HIV-positive source. Although non-occupational PEP was a relatively well-targeted intervention in Australia, its cost-effectiveness could be improved by further targeting high-risk exposures.

Editors' note: The cost per HIV infection averted in this Australian non-occupational PEP study was estimated at well over a million dollars, with the result that non-occupational PEP was found cost-effective in Australia only in the context of unprotected anal sex with a known HIV-positive man. Such cost-effectiveness studies are useful for determining the best use of available resources in any setting for non-occupational post-exposure prophylaxis.

3. Models of treatment and care

Fritts M, Crawford CC, Quibell D, Gupta A, Jonas WB, Coulter ID, Andrade A. Traditional Indian medicine and homeopathy for HIV/AIDS: a review of the literature. *AIDS Res Ther.* 2008;5(1):25.

India ranks third in the world in absolute burden of HIV. While increasing numbers of Government-sponsored clinics are providing free antiretroviral therapy, its utility is limited by lack of affordability and acceptability and the requirement for lifelong administration. Allopathic practitioners in India are outnumbered by practitioners of traditional Indian medicine and homeopathy, which is used by two-thirds of its population in rural areas to help meet its primary health care needs. However, little is known about traditional Indian medicine and homeopathy use, safety or efficacy in HIV management. These data suggest that India's community-based, culturally-relevant traditional Indian medicine and homeopathy system, which is one of the largest indigenous medical systems in the world, remains an untapped ally in the fight against its HIV epidemic. The purpose of this review was to assess the quality of peer-reviewed, published literature on traditional Indian medicine and homeopathy for HIV treatment and care. Of 160 original articles reviewed, 19 laboratory studies, 17 clinical studies and six previous reviews of the literature were identified that covered at least one system of traditional Indian medicine and homeopathy, which includes Ayurveda, yoga, naturopathy, Unani medicine, and Siddha medicine and homeopathy. Most studies examined either Ayurvedic or homeopathic treatments. Only four of these studies were randomized controlled trials, and only 10 were published in MEDLINE-indexed journals. Overall, the studies reported positive effects and even cure and reversal of HIV infection, but frequent design flaws call into question their internal and external validity. Common reasons for poor methodological quality included lack of details on products and their standardization, small sample sizes, selection of inappropriate or weak outcome measures,

and incomplete reporting of study results. This review exposes a broad gap between the widespread use of traditional Indian medicine and homeopathy therapies for HIV, and the dearth of high-quality data supporting their effectiveness and safety. In light of the suboptimal effectiveness of vaccines, antiretroviral treatment, barrier methods, and behaviour change strategies for prevention and cure of HIV infection, it is both important and urgent to develop a rigorous research agenda that uses innovative methodologies to investigate, evaluate, and maximize the role of traditional Indian medicine and homeopathy in managing HIV and associated illnesses in India. **Editor's note: This review presents an interesting overview of the history and principles of each system of traditional Indian medicine and homeopathy and highlights the current antiretroviral treatment gap, before summarising the results of *in vitro*, *in vivo*, and clinical studies of the impact of traditional Indian medicine and homeopathy on HIV. While yoga and healthy diet are considered beneficial by most people, the use of herbal preparations and homeopathic treatments for tuberculosis and HIV in the absence of data on effectiveness is concerning. Both the paucity of evidence and the use of these therapies by significant numbers of people living with HIV call for systematic assessment of the potential benefits and potential harms of traditional Indian medicine and homeopathy. Increased cross-training between traditional medicine and allopathic (modern) practitioners and development of a collaborative research agenda for studies using rigorous methodologies hold the promise of improved patient outcomes.**

Tonwe-Gold B, Ekouevi DK, Bosse CA, Toure S, Koné M, Becquet R, Leroy V, Toro P, Dabis F, El Sadr WM, Abrams EJ. Implementing family-focused HIV care and treatment: the first 2 years' experience of the mother-to-child transmission-plus program in Abidjan, Côte d'Ivoire. *Trop Med Int Health.* 2009;14(2):204-12.

Tonwe-Gold and colleagues describe a family-focused approach to HIV care and treatment and report on the first 2 years experience of implementing the mother-to-child transmission (MTCT)-plus program in Abidjan, Côte d'Ivoire. The MTCT-plus initiative aims to enrol HIV-infected pregnant and postpartum women in comprehensive HIV care and treatment for themselves and their families. Between August 2003 and August 2005, 605 HIV-infected pregnant or postpartum women and 582 HIV-exposed infants enrolled. Of their 568 male partners reported alive, 52% were aware of their wife's HIV status and 30% were tested for HIV; 53% of these tested partners were found to be HIV-infected and 78% enrolled into the program. Overall only 10% of the women enrolled together with their infected partner. On the other hand, the program involved half of the seronegative men who came for voluntary counselling and testing in the care of their families. Of 1624 children <15 years reported alive by their mothers (excluding the last newborn infants of the most recent pregnancy systematically screened for HIV), only 10.8% were brought in for HIV testing, of whom 12.3% were found to be HIV-infected. With respect to lessons learned and challenges, the authors conclude that this family-focused model of HIV care pays attention to the needs of families and household members. The program was successful in enrolling HIV women, their partners and infants in continuous follow-up. However engaging partners and family members of newly enrolled women into care involves numerous challenges such as disclosure of HIV status by women to their partners and family members. Further efforts are required to understand barriers for families accessing HIV services as strategies to improve partner involvement and provide access to care for other children in the households are needed in this West African urban setting. **Editors' note: Nondisclosure was the major factor**

limiting this family-centred programme in two poor urban Abidjan slums experiencing multiple unfavourable social and political conditions. The cascade of effort deployed to engage partners resulted in 30% having HIV testing and counselling, however only 69 of the estimated 300 men likely to have HIV infection enrolled in the programme. Testing was also an entry point for seronegative men to participate in adherence support sessions for their family members and attend peer support groups. Recognizing that the immediate environment has a direct impact on an individual's ability to promote his or her own health, the innovative MTCT-plus model of care starts with pregnant women as the entry point to HIV care and services for the whole family.

4. Surveillance

Rennie S, Turner AN, Mupenda B, Behets F. Conducting unlinked anonymous HIV surveillance in developing countries: ethical, epidemiological, and public health concerns. *PLoS Med.* 2009 20;6(1):e4.

Data collected from HIV surveillance are crucial to guide public health interventions, planning, and prevention efforts. The practice of unlinked, anonymous HIV testing, an important form of HIV surveillance, raises ethical, epidemiological, and public health challenges in low-income countries. Some ways of conducting unlinked, anonymous HIV testing in the field violate the spirit and/or the letter of international ethical guidelines. Vulnerable populations, such as sex workers, may be subject to unjust treatment by local health authorities during HIV surveillance initiatives. Conducting unlinked, anonymous HIV testing in ethically and epidemiologically sound ways in low-income countries requires a multifaceted approach including local capacity building, community engagement, and increased access to HIV and testing for sexually transmitted infections. **Editors' note: When Canada began anonymous unlinked HIV studies of leftover dried blood spot specimens in 1988, ethical requirements included public gazetting to raise community awareness and access to free, confidential, voluntary HIV counselling and testing for those who wished to learn their HIV status. The quality of HIV surveillance is not compromised by attention to 'implementation ethics' and can be enhanced through strengthened in-country capacity for the conduct of ethical epidemiological surveillance. Reviews of the methodological and ethical justifications for anonymous unlinked surveillance should be undertaken by key local stakeholders and ethics review boards to ensure that there are no breaches of confidentiality, there is access to HIV testing and counselling, unintended consequences are minimised, and there is a clear understanding among professionals, opinion leaders, and the public about the differences between case finding and public health surveillance.**

5. Dry sex

Mbikusita-Lewanika M, Stephen H, Thomas J. The prevalence of the use of 'dry sex' traditional medicines, among Zambian women, and the profile of the users. *Psychol Health Med.* 2009;14(2):227-38.

Concern has been voiced about the 'dry sex' practice in Southern and Central Africa, and its possible role in HIV transmission. Despite this concern, there has been little information about the practice. Most of the available information has been anecdotal, speculative or inadequate mainly because of cultural reluctance to discuss or investigate personal sexual issues. This article provides information about the prevalence of the practice in Zambia and the profile of its practitioners. A cross-sectional study involving 812 Zambian women was undertaken in Lusaka, the capital city of Zambia. Quantitative and qualitative data was obtained through self-administered questionnaires, interviews, in-depth interviews and focus

group discussions. The quantitative data were analysed using SPSS, and the qualitative data were used to complement and clarify the quantitative data. Awareness of the 'dry sex' practice was almost universal among Zambian women. About two-thirds had used 'dry sex' traditional medicines at some point in their lives, and about half were using them. Those who were most likely to have been using, or to have used 'dry sex' traditional medicines, were those who were older, married, with little or no formal education, mainstream Christians, from the lower socio-economic levels, homemakers, manual workers ($p < 0.001$), originally from the Eastern province of Zambia ($p < 0.002$) and those who had spent most of their formative years in rural areas ($p < 0.006$).The study showed that the knowledge and use of 'dry sex' traditional medicines is widespread among Zambian women, especially among those who were most likely to adhere to traditional views and beliefs about womanhood and marriage, and perhaps those likely to have a poor sense of self-worth or less confidence. In view of the concern about the possible role of 'dry sex' in HIV transmission, these findings would be useful in health education strategies. **Editors' note: This study of 'dry sex practices' or the use of traditional medicines to constrict the vagina or increase body heat, found significant associations with a number of factors but unfortunately the methodology and results of a regression analysis to tease out their interrelationships and identify confounding factors are not presented. However, an important finding was that only 7% of women who practised dry sex did so in anticipation of sexual activity, 16% used the medicines when they felt their bodies needed it, and 76% said they used them regularly anyway. Although qualitative data suggests that this may be related to concepts of womanhood, the possibility cannot be ignored that a vicious circle of chronic inflammation and resultant vaginal discharge induced by this practice may create the motivation for continuing self-medication.**

Scorgie F, Kunene B, Smit JA, Manzini N, Chersich MF, Preston-Whyte EM. In search of sexual pleasure and fidelity: vaginal practices in KwaZulu-Natal, South Africa. *Cult Health Sex.* 2009 Volume 11, Issue 2009,267-283.

Vaginal practices, such as intra-vaginal cleansing, drying and tightening, are suspected of placing women at higher risk of acquiring HIV and sexually transmitted infections. Yet, there is limited understanding of what these practices entail, what motivates women to undertake them and what their socio-cultural and historical meanings are. This paper explores the range of vaginal practices used by women in KwaZulu-Natal, South Africa and locates these within the context of local patterns of migration and understandings of sexual health and pleasure. Study activities took place at an urban and rural site employing qualitative research techniques: semi-structured interviewing and an additional ethnographic component in the rural site. Vaginal practices were believed to be ubiquitous and a wide range of substances and procedures were described. Strong motivations for vaginal practices included women's desire to enhance men's sexual pleasure, ensure men's fidelity and exercise agency and control in their relationships. The common use of traditional medicines in this quest to maintain stable relationships and affect the course of love, suggests a complexity that cannot be captured by simple terms like 'dry sex'. Scorgie and colleagues argue instead that any interventions to change women's reliance on vaginal practices must recognise and attend to the broader social contexts in which they are embedded. **Editors' note: This detailed qualitative study reveals a complex array of motives for potentially harmful vaginal practices among women in Kwa Zulu Natal, a province with very high HIV incidence and prevalence among women. Products used include traditional medicines and a wide range of commercial preparations while procedures include cleansing, topical application,**

insertion, making incisions, and ingestion. Multiple, concurrent sexual partnerships in a context of poverty, labour migration, and unemployment set the stage for women's mutual suspicion, jealousy, and competition over men as sources of income. Promoting notions of vaginal health to change these practices in order to reduce HIV risk will require that local women's groups, advocates, and peer education initiatives address the socioeconomic and gender dynamics that underpin them.

6. Basic Science

Kawashima Y, Pfafferott K, Frater J, Matthews P, Payne R, Addo M, Gatanaga H, Fujiwara M, Hachiya A, Koizumi H, Kuse N, Oka S, Duda A, Prendergast A, Crawford H, Leslie A, Brumme Z, Brumme C, Allen T, Brander C, Kaslow R, Tang J, Hunter E, Allen S, Mulenga J, Branch S, Roach T, John M, Mallal S, Ogwu A, Shapiro R, Prado JG, Fidler S, Weber J, Pybus OG, Klenerman P, Ndung'u T, Phillips R, Heckerman D, Harrigan PR, Walker BD, Takiguchi M, Goulder P. Adaptation of HIV-1 to human leukocyte antigen class I.
***Nature.* 2009. [Epub ahead of print]**

The rapid and extensive spread of the human immunodeficiency virus (HIV) epidemic provides a rare opportunity to witness host-pathogen co-evolution involving humans. A focal point is the interaction between genes encoding human leukocyte antigen (HLA) and those encoding HIV proteins. HLA molecules present fragments (epitopes) of HIV proteins on the surface of infected cells to enable immune recognition and killing by CD8(+) T cells; particular HLA molecules, such as HLA-B*57, HLA-B*27 and HLA-B*51, are more likely to mediate successful control of HIV infection. Mutation within these epitopes can allow viral escape from CD8(+) T-cell recognition. Here Kawashima and colleagues analysed viral sequences and HLA alleles from >2,800 subjects, drawn from 9 distinct study cohorts spanning 5 continents. Initial analysis of the HLA-B*51-restricted epitope, TAFTIPSI (reverse transcriptase residues 128-135), showed a strong correlation between the frequency of the escape mutation I135X and HLA-B*51 prevalence in the 9 study cohorts ($P = 0.0001$). Extending these analyses to incorporate other well-defined CD8(+) T-cell epitopes, including those restricted by HLA-B*57 and HLA-B*27, showed that the frequency of these epitope variants ($n = 14$) was consistently correlated with the prevalence of the restricting HLA allele in the different cohorts (together, $P < 0.0001$), demonstrating strong evidence of HIV adaptation to HLA at a population level. This process of viral adaptation may dismantle the well-established HLA associations with control of HIV infection that are linked to the availability of key epitopes, and highlights the challenge for a vaccine to keep pace with the changing immunological landscape presented by HIV. **Editors' note: The finding that HIV has been evolving at the population level over the past couple of decades to neutralise the slower disease progression advantage conferred by certain protective HLA genetic profiles is disturbing. Escape mutations that do not revert but rather persist stably after HIV transmission appear to accumulate at the population level over time, changing the dynamics of immune control and disease progression. If more effective immune responses now come into play that would be good news but, for now, these findings underscore yet another challenge for vaccine development – keeping up with the moving target of HIV as it worms its way around human immune responses.**

Richman DD, Margolis DM, Delaney M, Greene WC, Hazuda D, Pomerantz RJ. The challenge of finding a cure for HIV infection. *Science.* 2009;323(5919):1304-7.

Although combination therapy for HIV infection represents a triumph for modern medicine, chronic suppressive therapy is required to contain persistent infection in reservoirs such as

latently infected CD4+ lymphocytes and cells of the macrophage-monocyte lineage. Despite its success, chronic suppressive therapy is limited by its cost, the requirement of lifelong adherence, and the unknown effects of long-term treatment. This review discusses current understanding of suppressive antiretroviral therapy, the latent viral reservoir, and the needs for and challenges of attacking this reservoir to achieve a cure. **Editors' note: Ongoing viraemia detected at the level of 1 to 50 copies/ml in the majority of patients is thought to result from episodic production of HIV by long-lived cells rather than ongoing rounds of replication. Exploring how the mechanisms that drive this latency can be therapeutically exploited, this review paper argues that drug-free remission should now be the new goal of HIV therapeutics. It proposes a public-private joint research venture, called the HIV Latency Collaboratory, which would see government contributing funding, regulatory oversight, and coordination; industry contributing funding, drug discovery, technology, and expertise; and academia contributing ideas and investigative capacity.**

Biloglav Z, Zgaga L, Smoljanovic M, Hayward C, Polasek O, Kolcic I, Vitart V, Zemunik T, Boraska V, Torlak V, Mulic R, Ropac D, Grkovic I, Rudan D, Ristic S, Barbalic M, Campbell H, Wright AF, Rudan I. Historic, Demographic, and Genetic Evidence for Increased Population Frequencies of CCR5Delta32 Mutation in Croatian Island Isolates after Lethal 15th Century Epidemics. ***Croat Med J. 2009;*****50(1):34-42.**

Biloglav and colleagues assessed the frequency of 32 base pair deletion in CCR5 (CCR5Delta32), which has been shown to confer resistance to HIV infection in a homozygous form, in 10 isolated island communities of Dalmatia, Croatia, with different histories of exposure to epidemics during and since the medieval period. In 2002, DNA analysis of 100 randomly selected individuals from each of the 10 isolated communities of 5 Croatian islands (Susak, Rab, Vis, Lastovo, and Mljet) showed high levels of 3-generational endogamy, indicating limited gene flow. Five of the communities were decimated by epidemics of unknown cause between 1449-1456, while the other 5 villages remained unaffected. Genotyping of the CCR5 gene was performed using the polymerase chain reaction method with primers flanking the region containing 32-bp deletion. The frequency of CCR5Delta32 in the 5 villages affected by the epidemic was 6.1-10.0%, and 1.0-3.8% in the 5 unaffected villages. The Delta32 mutation was found in 71 of 916 alleles among the individuals from the affected villages (7.5%), and in 24 of 968 alleles in unaffected villages (2.5%, chi(2)=27.3, P<10-6). A previous study in 303 random Croatian blood donors showed the frequency of the CCR5 Delta32 of 7.1% in the general population. The difference remained significant after correcting for population structure using both STRAT and STRUCTURE software and the genomic control test, to ensure results do not arise from the background genetic differences. The authors concluded that their results and historical evidence, suggest that the mid-15th century epidemic could have acted as a selection pressure for the CCR5Delta32 mutation. **Editors' note: This fascinating article enters the ongoing debate on the genetic and epidemiological 'archaeology' of the CCR5Delta32 mutation which provides almost complete resistance to HIV in homozygous form (both gene alleles) and partial resistance/slower progression to AIDS in heterozygous form. The average frequency of this mutation in European populations is 10% but it is almost absent in African, American Indian, and East Asian populations. Based on this analysis of historical and genetic information obtained for 10 isolated communities in Croatia, this research programme (entitled '10,001 Dalmations') concludes that two exceedingly lethal viral epidemics characterised by peak incidence in the summer months, a long incubation**

period (about 1 month), 70% cumulative mortality, and person-to-person transmission, were most likely a hemorrhagic fever rather than bubonic plague or smallpox. The disease, thought to have arrived from northern Europe through the 'route of Amber' to Venice, caused the fall of Croatian Benedictine monasteries where the ill sought treatment. These epidemics could have created selection pressure upon an already widespread but rare CCR5Delta32 mutation resulting in the unusually high frequencies now observed across Europe today.

7. Religious beliefs and HIV

Zou J, Yamanaka Y, John M, Watt M, Ostermann J, Thielman N. Religion and HIV in Tanzania: influence of religious beliefs on HIV stigma, disclosure, and treatment attitudes. *BMC Public Health.* 2009;9(1):75. [Epub ahead of print]

Religion shapes everyday beliefs and activities, but few studies have examined its associations with attitudes about HIV. This exploratory study in Tanzania probed associations between religious beliefs and HIV stigma, disclosure, and attitudes toward antiretroviral treatment. A self-administered survey was distributed to a convenience sample of parishioners (n=438) attending Catholic, Lutheran, and Pentecostal churches in both urban and rural areas. The survey included questions about religious beliefs, opinions about HIV, and knowledge and attitudes about antiretroviral treatment. Multivariate logistic regression analysis was performed to assess how religion was associated with perceptions about HIV, HIV treatment, and people living with HIV. Results indicate that shame-related HIV stigma is strongly associated with religious beliefs such as the belief that HIV is a punishment from God ($p<0.01$) or that people living with HIV have not followed the Word of God ($p<0.001$). Most participants (84.2%) said that they would disclose their HIV status to their pastor or congregation if they became infected. Although the majority of respondents (80.8%) believed that prayer could cure HIV, almost all (93.7%) said that they would begin antiretroviral treatment if they became HIV-infected. The multivariate analysis found that respondents' hypothetical willingness to begin antiretroviral treatment was not significantly associated with the belief that prayer could cure HIV or with other religious factors. Refusal of antiretroviral treatment was instead correlated with lack of secondary schooling and lack of knowledge about antiretroviral treatment. The decision to start antiretroviral treatment hinged primarily on education-level and knowledge about antiretroviral treatment rather than on religious factors. Research results highlight the influence of religious beliefs on HIV-related stigma and willingness to disclose, and should help to inform HIV-education outreach for religious groups. **Editors' note: Christians make up about 30% of the population in Tanzania, with churches being influential social networks with the power to support or stigmatize people living with HIV, promote or impede HIV education, and endorse or reject HIV medical treatment. Only 42.7% of respondents had been tested for HIV and, interestingly, Catholics were least likely (42.7%) and Pentecostals were most likely (69.7%) to report never having used condoms. Despite the study's limitations, including data collection in the presence of pastors after church services, the findings are relevant for the design of outreach campaigns and theological discussions in faith-based communities to reduce shame-related stigma, enhance disclosure, and contribute to improved social support for people living with HIV.**

8. Risk compensation

Cohen CR, Montandon M, Carrico AW, Shiboski S, Bostrom A, Obure A, Kwena Z, Bailey RC, Nguti R, Bukusi EA. Association of attitudes and beliefs towards antiretroviral therapy with HIV-seroprevalence in the general population of Kisumu, Kenya. *PLoS ONE.* 2009;4(3):e4573.

Since antiretroviral therapy became available in the developed world, the prevalence of unprotected sex and the incidence of sexually transmitted infections (STIs) and HIV have increased. Cohen and colleagues hypothesized that a similar phenomenon may be occurring in sub-Saharan Africa concomitant with the scale-up of HIV treatment. They conducted a general population-based survey in Kisumu, Kenya. Participants completed an interview that included demographics as well as antiretroviral therapy-related attitudes and beliefs and then underwent HIV serological testing. Exploratory and confirmatory factor analyses of attitudes and beliefs about antiretroviral therapy indicated two factors: 1) antiretroviral therapy-related risk compensation (increased sexual risk taking now that antiretroviral therapy is available); and 2) a perception that HIV is more controllable now that antiretroviral therapy is available. Logistic regression was used to determine associations of these factors with HIV-seroprevalence after controlling for age. 1,655 (90%) of 1,844 people aged 15-49 contacted, including 749 men and 906 women, consented to participate in the study. Most participants (n = 1164; 71%) had heard of antiretroviral therapy. Of those who had heard of antiretroviral therapy, 23% believed antiretroviral therapy was a cure for HIV. Antiretroviral therapy-related risk compensation (Adjusted (A)OR = 1.45, 95% CI 1.16-1.81), and a belief that antiretroviral therapy cures HIV (AOR = 2.14, 95% CI 1.22-3.76) were associated with an increased HIV seroprevalence in men but not women after controlling for age. In particular, antiretroviral therapy-related risk compensation was associated with an increased HIV-seroprevalence in young (aged 15-24 years) men (OR = 1.56; 95% CI 1.12-2.19). Antiretroviral therapy-related risk compensation and a belief that antiretroviral therapy cures HIV were associated with an increased HIV seroprevalence among men but not women. HIV prevention programs in sub-Saharan Africa that target the general population should include educational messages about antiretroviral therapy and address the changing beliefs about HIV in the era of greater antiretroviral therapy availability. **Editors' note: This general population household survey is the first to examine attitudes and beliefs about antiretroviral treatment and their relationship with HIV seroprevalence. The numerous studies to date in the US and Europe that have identified an upward trend in risky sexual behaviours since the introduction of antiretroviral treatment in 1996 have all been conducted in key populations at higher risk of HIV exposure, particularly men who have sex with men. This study in Kisumu, where 28% of those in need of antiretroviral treatment were receiving it at the start of 2007, found that young men with treatment-related risk compensation beliefs were more likely to be HIV-positive than young men without such beliefs. The relationship may reflect personality traits related to risk-taking rather than being causal. Nonetheless, the implications are evident for integrated HIV prevention and treatment programming in Kisumu and widespread dissemination of accurate information about antiretroviral treatment and the need for changes in social norms to reduce sexual risk-taking as treatment rollout continues.**

9. Paediatric treatment

Weinberg A, Dickover R, Britto P, Hu C, Patterson-Bartlett J, Kraimer J, Gutzman H, Shearer WT, Rathore M, McKinney R; PACTG 1021 team. Continuous improvement in the immune system of HIV-infected children on prolonged antiretroviral therapy. *AIDS.* 2008;22(17):2267-77.

The goal of antiretroviral treatment is to promote reconstitution of CD4+ T cells and other immune responses. Weinberg and colleagues evaluated the extent and the kinetics of immune reconstitution in HIV-infected children over 144 weeks of successful antiretroviral treatment. Thirty-seven children receiving their first antiretroviral treatment regimen had

plasma HIV RNA; T cells and subpopulations; T-cell rearrangement excision circles (TREC) DNA; candida, HIVCD4 and HIVCD8 enzyme-linked immunospot measured at regular intervals. Plasma HIV RNA became undetectable in 81% of patients at 24 weeks and remained undetectable in 77% at 144 weeks. In contrast, CD4+% continuously increased. Distribution of T-cell subpopulations changed rapidly during the first 48 weeks of antiretroviral treatment and more slowly thereafter. At 144 weeks, total, naive and activated CD4+% and naive CD8+% of HIV-infected children were not significantly different from those of healthy age-matched controls, whereas total and activated CD8+% remained elevated. CD4 and CD8 TREC content increased only during the first 48 weeks of antiretroviral treatment. They positively correlated with each other and with total CD4+%, naive CD4+% and naive CD8+%. Candida and HIVCD4 enzyme-linked immunospot increased over time reaching peak values at 48 weeks and 144 weeks, respectively. HIVCD8 enzyme-linked immunospot decreased in magnitude over 144 weeks of antiretroviral treatment but retained its breadth. Baseline CD4+% positively correlated with CD4+% and with functional immune reconstitution at week 144, whereas baseline TREC correlated with TREC at week 144. The authors concluded that HIV-infected children acquired normal distribution of CD4 T cells and other subpopulations and recovered CD4-mediated HIV immunity after 144 weeks of antiretroviral treatment. **Editors' note: This study is the first to demonstrate complete normalisation of T-cell subpopulations in children on antiretroviral treatment for 3 years, with the exception of elevated activated CD8+ percentage, which possibly may be due to low-level viral replication. CD4+ percentage was used as the main parameter in these analyses because it does not vary with the age of children whereas CD4 cell counts do. Given that both higher baseline CD4+ percentage and TREC levels indicating higher thymus function at treatment initiation predicted more robust immune reconstitution, it is clear that earlier HIV diagnosis and earlier antiretroviral treatment initiation in infants, combined with attention to adherence and monitoring of side effects, improve paediatric prognosis.**

10. Men who have sex with men

Guo H, Wei JF, Yang H, Huan X, Tsui SK, Zhang C. Rapidly Increasing Prevalence of HIV and Syphilis and HIV-1 Subtype Characterization Among Men Who Have Sex With Men in Jiangsu, China. *Sex Transm Dis.* 2009;36(2):120-5

Guo and colleagues investigated the prevalence of HIV, hepatitis B (HBV), hepatitis C (HCV), and syphilis among men who have sex with men in 2 cities of Jiangsu, China, and to characterize the HIV-1 subtypes prevalent among this population. During September 2006 and July 2007, 296 and 173 men who have sex with men were recruited from Nanjing and Yangzhou, respectively. Sera samples were collected and tested for HIV, HBV, HCV, and syphilis infections. The nucleotide sequences of p17 and C2V3 regions were determined by reverse transcriptase-nested-PCR and sequencing. HIV-1 subtypes were characterized by phylogenetic analysis. The prevalence of HIV, HBV, HCV, and syphilis infections among men who have sex with men was 5.8%, 11.1%, 0.7%, and 27.7%, respectively. The prevalence of HIV and syphilis was significantly higher in 2006-2007 than in 2003 (P </=0.0013) in Jiangsu than in other regions of China (P </=0.003). In contrast, there was no significant difference in HBV and HCV prevalence between present and 2003 studies (P >0.05). The phylogenetic tree of p17 showed that HIV-1 subtypes B, CRF01_AE, and CRF07_BC accounted for 35.7%, 35.7%, and 28.6%, respectively. The result of C2V3 showed that 45.5%, 36.4%, and 18.2% sequences belonged to HIV-1 subtype B, CRF01_AE, and BC recombinants, respectively. The subtype characterization in Jiangsu was significantly different from those in Beijing (P

<0.05). Furthermore, Jiangsu HIV-1 B strains were different from majority of China B' strains and originated from Beijing. The rapidly increasing prevalence and complex subtypes of HIV-1 suggest that effective prevention and intervention strategies are urgently needed for men who have sex with men in Jiangsu. **Editors' note: In China, gay bars, saunas, and baths are major venues for men who have sex with men to meet. This study used convenience sampling to recruit 433 men in gay baths in 2 cities of Jiangsu province which is located at the Yangtze River Delta, one of the most developed economic areas of China. Although the HIV prevalence for the Nanjing bath subjects (4.7%) was not different from that found in a previous similar study (4.73%), the high (26.7%) and rapidly increasing prevalence of syphilis suggests significant levels of unprotected anal sex. There is an urgent need to work with this community to design and implement effective HIV prevention programmes in the places where men meet and to better document trends in HIV incidence and viral subtype characterisation.**

11. Epidemiology

Chokoshvili O, Abutidze A, Tsintsadze M, Gatserelia L, Badridze N. Overview of HIV epidemiological situation in Georgia. *Georgian Med News*. 2008;(165):87-94.

Georgia still belongs to the low HIV epidemic countries and by December 1st, 2008 there were 1825 HIV cases registered at the Institute of Drug Addiction (IDACIRC) with an estimated number of 3500-4000 (estimated prevalence 0.09%). Majority of HIV patients are male (75%). Four hundred and sixty one patients were receiving antiretroviral treatment, including 23 children. Despite low HIV prevalence, Georgia is considered to be at risk for imminent epidemic spread of HIV mainly due to widespread drug use with high risk practices (needle-reuse), high levels of sexually transmitted infections, and migration to Russia, Ukraine, and other countries, and vice versa. The major route of HIV transmission is associated with drug injecting. At the moment approximately 60% of all reported HIV cases are due to drug injection. However, the heterosexual route of transmission has been gaining in importance, and increased from 29.1% to 36.1% for last five years. The first significant increases of HIV incidence were observed from 1999 to 2000 (2.24 times) and 2003 to 2004. From 2004 incidence has been relatively stable at 6.5-7/100,000. Most HIV positive patients are diagnosed at the age from 25 to 45. The highest HIV prevalence rates are found in Western Georgia, particularly Black Sea coast regions - Megrelia and Adjara (with prevalence of 131.11 and 132.03 among adult HIV cases per 100 000 adult population). Expanding educational activities and prevention interventions, including harm reduction and access to condoms, better financing of HIV programs, and improvement of capacity building will help the country to keep its HIV epidemic at a low prevalence and give it the possibility of achieving "Universal Access to HIV Prevention, Treatment, Care and Support" for 2010 year. **Editor's note: Georgia began responding to HIV in 1994 and introduced universal access to antiretroviral treatment and care in 2004. No case of mother-to-child HIV transmission has been detected since the prevention of mother-to-child transmission programme was introduced in 2005. Its big challenge will be to reduce HIV transmission due to contaminated injecting equipment as the numbers of people who inject drugs continues to increase in seaside and border locations. Effective harm reduction programmes will be crucial to Georgia's success in achieving universal access.**

12. Treatment: when to start

Kitahata MM, Gange SJ, Abraham AG, Merriman B, Saag MS, Justice AC, Hogg RS, Deeks SG, Eron JJ, Brooks JT, Rourke SB, Gill MJ, Bosch RJ, Martin JN, Klein MB, Jacobson LP, Rodriguez B, Sterling TR, Kirk GD, Napravnik S, Rachlis AR, Calzavara LM, Horberg MA,

Silverberg MJ, Gebo KA, Goedert JJ, Benson CA, Collier AC, Van Rompaey SE, Crane HM, McKaig RG, Lau B, Freeman AM, Moore RD, for the NA-ACCORD Investigators*. Effect of Early versus Deferred Antiretroviral Therapy for HIV on Survival. N Engl J Med 2009;360. [Epub ahead of print]

The optimal time for the initiation of antiretroviral therapy for asymptomatic patients with human immunodeficiency virus (HIV) infection is uncertain. Kitahata and colleagues conducted two parallel analyses involving 17,517 asymptomatic patients with HIV infection in the United States and Canada who received medical care during the period from 1996 through 2005. None of the patients had undergone previous antiretroviral therapy. In each group, the authors stratified the patients according to the CD4+ count (351 to 500 cells per cubic millimetre or >500 cells per cubic millimetre) at the initiation of antiretroviral therapy. In each group, they compared the relative risk of death for patients who initiated therapy when the CD4+ count was above each of the two thresholds of interest (early-therapy group) with that of patients who deferred therapy until the CD4+ count fell below these thresholds (deferred-therapy group). The results of the first analysis, which involved 8362 patients, 2084 (25%) initiated therapy at a CD4+ count of 351 to 500 cells per cubic millimetre, and 6278 (75%) deferred therapy. After adjustment for calendar year, cohort of patients, and demographic and clinical characteristics, among patients in the deferred-therapy group there was an increase in the risk of death of 69%, as compared with that in the early-therapy group (relative risk in the deferred-therapy group, 1.69; 95% confidence interval [CI], 1.26 to 2.26; P<0.001). In the second analysis involving 9155 patients, 2220 (24%) initiated therapy at a CD4+ count of more than 500 cells per cubic millimetre and 6935 (76%) deferred therapy. Among patients in the deferred-therapy group, there was an increase in the risk of death of 94% (relative risk, 1.94; 95% CI, 1.37 to 2.79; P<0.001). The authors concluded that the early initiation of antiretroviral therapy before the CD4+ count fell below two prespecified thresholds significantly improved survival, as compared with deferred therapy. **Editor's note: Most observational studies do not take account of the lead-time bias that is introduced by unobserved person-time among individuals who do not present for care until their CD4+ cell count drops below the threshold of interest (e.g. 200 cells/ul). These individuals have survived without clinical progression until the time of their diagnosis. This analysis, which used methods to take account of lead-time bias, suggests an approximate 70% increase in survival when antiretroviral treatment is initiated in the 350-500 CD4+/µl count range rather than at lower CD4+ counts.**

Sabin CA, Phillips AN. Should HIV therapy be started at a CD4 cell count above 350 cells/microl in asymptomatic HIV-1-infected patients? *Curr Opin Infect Dis*. 2009;22(2):191-7.

The aim was to review the available data that contribute to the debate on the optimal time to initiate highly active antiretroviral therapy in HIV-infected individuals with a CD4 cell count more than 350 cells/microl. Although few randomized data exist that can contribute to this debate, a number of findings from observational studies generally support earlier initiation of highly active antiretroviral therapy. In particular, the findings that death rates remain higher in HIV-infected individuals than in uninfected individuals, even when successfully treated, and that both AIDS and several serious non-AIDS events are more common in those with a lower CD4 cell count (even when this count is above 350 cells/microl), suggest that earlier initiation of highly active antiretroviral therapy may prevent much of the excess morbidity and mortality that remains in this patient group. Currently, the data would generally support initiation of highly active antiretroviral therapy in patients with CD4 cell counts more than 350 cells/microl. However, given the strong potential for confounding

in observational studies and the lack of adjustment for lead-time bias in many analyses, it is not possible to rule out possible long-term detrimental effects of earlier use of highly active antiretroviral therapy until the results from fully powered randomized trials that directly address this issue become available. **Editors' note: Current discussions of when to initiate antiretroviral treatment focus on issues such as the inequity of two-tiered start criteria (CD4+ counts less than 200/µl in most resource-constrained settings and CD4+ less than 350 in most high-income countries), the logistical and other challenges experienced now in reaching toward universal access with current CD4+ count less than 200 criteria, the need to focus resources first to encourage earlier HIV testing in many countries, the concerns about long-term known and unknown toxicities of antiretroviral drugs, and the belief that the lifelong high adherence requirements of antiretroviral treatment may be too demanding for patients who then risk developing resistance, exhausting their future drug options. Although this review of available data on the impact of earlier antiretroviral treatment initiation suggests positive benefits for individuals, there is equipoise for a randomised controlled trial. The START (Strategic Timing of AntiRetroviral Treatment) trial now beginning enrolment will assess whether treatment initiation in patients with CD4+ counts greater than 500 cells/ul is superior than delaying treatment initiation until CD4+ cell counts fall below 350.**

Braithwaite RS, Roberts MS, Goetz MB, Gibert CL, Rodriguez-Barradas MC, Nucifora K, Justice AC. Do benefits of earlier antiretroviral treatment initiation outweigh harms for individuals at risk for poor adherence? *Clin Infect Dis.* 2009;48(6):822-6.

Clinicians may defer antiretroviral treatment for patients with suboptimal adherence. Braithwaite and colleagues used a validated computer simulation of HIV disease progression to compare alternative treatment thresholds for patients with suboptimal adherence. Earlier treatment increased life expectancy across a wide adherence range (50%-100% of doses taken). Delaying treatment for patients with suboptimal adherence may not always be appropriate. **Editors' note: Improving adherence substantially increases life expectancy and quality adjusted life years (QALYs). This modelling work shows that, in all adherence strata, the immunological benefit of early antiretroviral treatment initiation outweighs the harms of greater resistance mutation accumulation and reduced future drug options. It suggests that patients with anticipated suboptimal adherence do not warrant distinct criteria for starting antiretroviral treatment. They are likely to benefit substantially from surveillance to detect poor adherence and strategies to improve it, such as treating hazardous levels of alcohol consumption and prompting prescription refills.**

13. Male circumcision and manhood

Peltzer K, Kanta X. Medical circumcision and manhood initiation rituals in the Eastern Cape, South Africa: a post intervention evaluation. *Cult Health Sex.* 2009;11(1):83-97.

The objectives of this study were first, to report the adverse events reported following male circumcision performed by medical professionals after a one-day training workshop; second, to report on the attitudes towards, beliefs surrounding and experiences regarding circumcision and initiation; and third, to assess the HIV-risk behaviour of young men attending initiation schools post medical circumcision. Initiates who had been medically circumcised by trained healthcare providers were examined and interviewed on the seventh day after circumcision and, in addition, focus-group discussions were conducted with initiates. Results indicate that of the 78 initiates physically examined on the seventh day

after circumcision by a trained clinical nurse, seven (9%) adverse events (complications) were found. Initiates reported mixed attitudes towards combining medical circumcision with traditional initiation. The majority of the initiates (70%) felt that they could be stigmatized as a result of choosing medical rather than traditional circumcision and 20% thought that the relationship between medical and traditionally circumcised men was hostile. Prior to circumcision, most initiates (92%) had been sexually active and had engaged in HIV-risk behaviour. Focus-group discussions revealed that sexually active initiates, when asked about sex after circumcision, indicated they wished to abstain for a short period before resuming sexual activities with intended condom use being high. Findings are promising for efforts to up-scale integrated medical circumcision alongside traditional initiation into manhood. **Editors' note: As discussions with traditional leaders in some settings are showing, traditions are not static and synergies can be constructed between traditional and clinic-based systems for male circumcision. Traditional circumcision teaching can be adapted to include reproductive health and life skills. These would be added to the traditional community mobilisation and emotional, social, and philosophical aspects of the preparation for circumcision and for relations with women. Community discussions can highlight the improved safety of clinic-based circumcision and pre-screening for sexually transmitted infections (30% of the study participants had a sexually transmitted disease diagnosed in the previous 12 months) while exploring the extent to which participant perceptions of possible stigma would actually reflect current and evolving realities in traditionally circumcising communities.**

14. Reproductive health and youth

Speizer IS, White JS. The unintended consequences of intended pregnancies: youth, condom use, and HIV transmission in Mozambique. *AIDS Educ Prev.* 2008;20(6):531-46.

Although unwanted pregnancies can cause social and economic problems for sub-Saharan African youth, the consequences of intended adolescent pregnancies have gone unnoticed. Rarely do studies recognize that youth who desire a pregnancy are less likely to practice safe sex and, therefore, are at greater risk of contracting sexually transmitted infections (STIs), including HIV. This study uses data from the 2003 Mozambique Demographic and Health Survey to explore youth fertility desires and condom use. In multivariate analyses, controlling for other factors associated with condom use, female youth who want to get pregnant soon are significantly less likely (odds ratio: 0.35; 95% confidence interval: 0.22-0.55) to use condoms with non-marital partners than youth who want to delay childbearing. Programs for sexually active youth should recognize the importance of fertility desires as a potential moderator of condom use, even if the woman is at risk of HIV or STI. Recommendations are provided for HIV prevention counselling for youth who want to get pregnant and youth who are ambivalent about a future pregnancy.

Editor's note: A common reality in many settings in sub-Saharan Africa is that, in the transition to adulthood, pregnancy (or childbirth) is often a precursor to union formation and marriage/cohabitation. HIV prevention programmes should determine which youth have an unmet need for family planning and condoms to prevent unintended pregnancy and sexually transmitted disease and which youth want to get pregnant in the near future. Strategies that the latter group of young women can use to reduce HIV risks include having sex only in the fertile period, discussing HIV risks with a partner, and undertaking HIV testing and counselling with this partner. This broader HIV prevention

programme focus, considering the fertility desires of youth, can help reduce their HIV and unintended pregnancy risks.

Uddin MJ, Choudhury AM. Reproductive health awareness among adolescent girls in rural Bangladesh. *Asia Pac J Public Health.* 2008;20(2):117-28.

This article presents the status of rural Bangladeshi adolescent girls' awareness about reproductive health. Analysis of data revealed that a sizable proportion of adolescent girls had incorrect knowledge or misconceptions about the fertile period, reproduction, sexually transmitted diseases, and HIV. Age, education either of adolescents or their mothers, residence, and exposure to mass media were the significant predictors of adolescent girls' knowledge about reproductive health. Strong efforts are needed to improve awareness and to clarify misconceptions about reproductive health. Improved access to mass media and education could improve rural Bangladeshi adolescent girls' awareness about reproductive health. **Editor's note: Only 7% of the 920 rural adolescent girls, aged 10 to 19 years, participating in this study had correct knowledge about the fertile period and 18 of 20 married adolescents who had given birth in the previous 6 months did not understand why they became pregnant. Only 20% of the girls had heard about sexually transmitted disease and of the 40% who had heard about AIDS, only 22% had correct knowledge about the routes of HIV transmission. These findings underscore the evident need to enhance behaviour change communication with culturally appropriate messages on reproductive health and strengthen access for adolescent girls in Bangladesh to sexual and reproductive health information and services through multiple entry points (school, work, sports, social activities) and settings (home, community, workplace, school or clinic).**

That was ***HIV this week***, signing off.

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