

HIV This Week: what scientific journals said

Welcome to the twenty-fourth issue of *HIV This Week!* In this issue we cover **male circumcision** (modelling suggests that reduced sexually transmitted infections did not contribute much to the male circumcision trial results of 48 to 61% efficacy; assessing cost-effectiveness in sub-Saharan Africa), **women's health** (no evidence of increased mortality in breastfeeding mothers in Kenya), **prevention** (a randomised controlled trial documents changes in sexual scripts among women in New York City; need for improved quality in infant feeding counselling in Sao Paulo; prevention strategies among Mexican migrant farm workers; and serostatus discussions among men who have sex with men), **metabolic disease** (people living with HIV actually have lower rates of metabolic disease than the US general population which has high levels of obesity; searching for clues about glucose intolerance), **people who inject drugs** (who attends the supervised injecting facility in Vancouver?), **HIV in the workplace** (you are not going to believe this one - but can porn become an HIV prevention tool in this workplace and beyond?), **prisons** (the impact of condom provision in New South Wales' prisons since 1996), **child health** (confirming positive benefits of cotrimoxazole prophylaxis in HIV-infected children), **young people** (vaginal diaphragm acceptability among young women), **stigma and discrimination** (deconstructing the 2002-2003 World AIDS Day campaign; influence on HIV testing uptake in Nigerian young people), **basic science** (how is it that some exposed infants do not get infected during pregnancy and labour?), **TB/HIV** (a strategy for early detection of prevalent TB in high HIV prevalence settings) and **HIV vaccines** (taking a leaf out of the BCG book).

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1. Male circumcision

Desai K, Boily MC, Garnett GP, Masse BR, Moses S, Bailey RC. The role of sexually transmitted infections in male circumcision effectiveness against HIV - Insights from clinical trial simulation. *Emerg Themes Epidemiol* 2006;3(1):19. <http://www.ete-online.com/content/3/1/19>

A landmark randomised trial of male circumcision in Orange Farm, South Africa recently showed a large and significant reduction in risk of HIV infection, reporting male circumcision effectiveness of 61% (95% CI 34-77%). Additionally, two further randomised trials of male circumcision in Kisumu, Kenya and Rakai, Uganda were recently stopped early reporting 53% and 48% effectiveness, respectively. Since male circumcision may protect against both HIV and certain sexually transmitted infections (STI), which are themselves cofactors of HIV infection, an important question is the extent to which this estimated effectiveness against HIV is mediated by the protective effect of circumcision against STI. The answer lies in the trial data if the appropriate statistical analyses can be identified to estimate the separate efficacies against HIV and STI, which combine to determine overall effectiveness. Focusing on the male circumcision trial in Kisumu, Desai and colleagues used a stochastic prevention trial simulator (1) to determine whether statistical analyses can validly estimate efficacy, (2) to determine whether male circumcision efficacy against STI alone can produce large effectiveness against HIV and (3) to estimate the fraction of all HIV infections prevented that are attributable to efficacy against STI when both efficacies combine. Valid estimation of separate efficacies against HIV and STI as well as male circumcision effectiveness is feasible with available STI and HIV trial data, under Kisumu trial conditions. Under their parameter assumptions, high overall effectiveness of male circumcision against HIV was observed only with a high male circumcision efficacy against HIV and was not possible on the basis of male circumcision efficacy against STI alone. The fraction of all HIV infections prevented which were attributable to male circumcision efficacy against STI was small, except when efficacy of male circumcision specifically against HIV was very low. In the three male circumcision trials which reported between 48% and 61% effectiveness, the fraction of HIV infections prevented in circumcised males which were attributable to STI was unlikely to be more than 10% to 20%. The authors conclude that estimation of the efficacy, attributable fraction and effectiveness leads to improved understanding of trial results, gives trial results greater external validity and is essential to determine the broader public health impact of circumcision to men and women. **Editors' note: Now that these trials have been stopped it will be possible to examine the real data on incident STI and attempt to better tease out the contribution of STI prevention to the reduced incidence of HIV seen in men who underwent circumcision in the trials. WHO/UNAIDS are hosting a global consultation on the policy and programming implications of the three circumcision trial findings for countries in March 2007 which will take a closer look at all available data from the trials.**

Kahn JG, Marseille E, Auvert B. Cost-effectiveness of male circumcision for HIV prevention in a South African setting. *PLoS Med* 2006;3(12):e517. [10.1371/journal.pmed.0030517](https://doi.org/10.1371/journal.pmed.0030517)

Consistent with observational studies, a randomized controlled intervention trial of adult male circumcision conducted in the general population in Orange Farm (Gauteng Province, South Africa) demonstrated a protective effect against HIV acquisition of 60%. Kahn and colleagues present the first cost-effectiveness analysis of the use of male circumcision as an intervention to reduce the spread of HIV in sub-Saharan Africa. Cost-effectiveness was modelled for 1,000 male circumcisions done within a general adult male population. Intervention costs included performing male circumcision and treatment of adverse events. HIV prevalence was estimated from published estimates and incidence among susceptible subjects calculated assuming a steady-state epidemic. Effectiveness was defined as the number of HIV infections averted, which was estimated by dynamically projecting over 20

years the reduction in HIV incidence observed in the Orange Farm trial, including secondary transmission to women. Net savings were calculated with adjustment for the averted lifetime duration cost of HIV treatment. Sensitivity analyses examined the effects of input uncertainty and programme coverage. All results were discounted to the present at 3% per year. For Gauteng Province, assuming full coverage of the male circumcision intervention, with a 2005 adult male prevalence of 25.6%, 1000 circumcisions would avert an estimated 308 (80% CI 189-428) infections over 20 years. The cost is \$US 181 (80% CI 117-306) per HIV infection averted, and net savings are \$US 2.4 million (80% CI 1.3 million to 3.6 million). Cost-effectiveness is sensitive to the costs of male circumcision and of averted HIV treatment, the protective effect of male circumcision, and HIV prevalence. With an HIV prevalence of 8.4%, the cost per HIV infection averted is \$US 551 (80% CI 344-1071) and net savings are \$US 753,000 (80% CI 0.3 million to 1.2 million). Cost-effectiveness improves by less than 10% when male circumcision intervention coverage is 50% of full coverage. The authors conclude that in settings in sub-Saharan Africa with high or moderate HIV prevalence among the general population, adult male circumcision is likely to be a cost-effective HIV prevention strategy, even when it has a low coverage. Male circumcision generates large net savings after adjustment for averted HIV medical costs. **Editors' note: Cost per case of HIV infection averted will vary widely by setting and by the costs included in the analysis. It is important to include not just the immediate cost of the procedure and care of any adverse events (care provider, costs of equipment and supplies, facility time, etc.) but also in-service training costs, medical/clinical officer/nursing education costs, as well as individual counselling and public education on the benefits and limitations of male circumcision as an HIV prevention measure. The actual service delivery model also has implications for costs. For example, using an 'eye camp' service delivery model will incur quite different costs than a model which contextualises male circumcision within a programme addressing male sexual and reproductive health.**

2. Women's health

Otieno PA, Brown ER, Mbori-Ngacha DA, Nduati RW, Farquhar C, Obimbo EM, Bosire RK, Emery S, Overbaugh J, Richardson BA, John-Stewart GC. HIV-1 disease progression in breast-feeding and formula-feeding mothers: A prospective 2-year comparison of T cell subsets, HIV-1 RNA levels, and mortality. *J Infect Dis* 2007;195:220-29.

There is conflicting evidence regarding the effects of breast-feeding on maternal mortality from HIV-1 infection, and little is known about the effects of breast-feeding on markers of HIV-1 disease progression. Otieno and colleagues enrolled HIV-1-seropositive women during pregnancy and received short-course zidovudine. The authors determined HIV-1 RNA levels and CD4 cell counts at baseline and at months 1, 3, 6, 12, 18, and 24 postpartum and were compared between breast-feeding and formula-feeding mothers. Of 296 women, 98 formula-fed and 198 breast-fed. At baseline, formula-feeding women had a higher education level and prevalence of HIV-1-related illness than did breast-feeding women; however, the groups did not differ with respect to CD4 cell counts and HIV-1 RNA levels. Between months 1 and 24 postpartum, CD4 cell counts decreased 3.9 cells/ μ L/month ($P < 0.001$), HIV-1 RNA levels increased 0.005 log₁₀ copies/mL/month ($P = 0.03$), and body mass index (BMI) decreased 0.03 kg/m²/month ($P < 0.001$). The rate of CD4 cell count decline was higher in breast-feeding mothers (7.2 cells/ μ L/month) than in mothers who never breast-fed (4.0 cells/ μ L/month).

L/month) ($P=.01$). BMI decreased more rapidly in breast-feeding women ($P=.04$), whereas HIV-1 RNA levels and mortality did not differ significantly between breast-feeding and formula-feeding women. The authors conclude that breast-feeding was associated with significant decreases in CD4 cell counts and BMI. HIV-1 RNA levels and mortality were not increased, suggesting a limited adverse impact of breast-feeding in mothers receiving extended care for HIV-1 infection. **Editors' note: This is a very encouraging follow-up publication as concerns evoked by initial reports of possible increased mortality in breastfeeding women in Kenya complicated the discussions of what feeding modalities were feasible and best for infants born to HIV-positive mothers.**

3. Prevention

Dworkin SL, Beckford ST, Ehrhardt AA. Sexual scripts of women: A longitudinal analysis of participants in a gender-specific HIV/STD prevention intervention. *Arch Sex Behav* 2006 Dec 21 [Epub ahead of print].

Project FIO (The Future Is Ours) was a three arm randomized controlled HIV prevention intervention trial carried out with heterosexually-active women in a high seroprevalence area of New York City. The trial was effective and women in the eight-session intervention arm were significantly more likely to report decreased unsafe sex or no unsafe sex compared to controls at one month and one year post-intervention. Dworkin and colleagues conducted a qualitative analysis of women's sexual scripts at baseline and one year follow-up for a randomly selected sub-sample of participants in Project FIO. The authors examined the domains of sexual initiation, pace setting, sexual decision-making, communication about sexual needs, and the timing of condom introductions in the experimental and control arms at baseline and one year follow-up. At one year follow-up, among both the experimental and control arms, results showed changes away from male-dominated and toward female-dominated sexual initiation and sexual decision-making. Among both the experimental and control arms, results also showed that trial participants shifted from a late condom introduction (right before intercourse) toward much earlier mention of condoms (e.g. during a date). The authors conclude that the fact that shifts in sexual scripts at one year follow-up occurred in both groups is likely reflective of the degree to which a lengthy assessment interview facilitated comfort with discussing and imagining new sexual behaviours, even for control group participants who did not receive the intervention. The value of empirically assessing sexual scripts in HIV prevention and doing so longitudinally is assessed in light of the goals of HIV prevention interventions. **Editors' note: Randomised controlled trials, such as this one, of non-biomedical interventions help determine what works and what does not in HIV prevention – and what should be scaled up for maximum effect.**

Rea MF, Santos RG, Sanchez-Moreno CC. Quality of infant feeding counselling for HIV+ mothers in Brazil: challenges and achievements. *Acta Paediatr* 2007;96:94-99.

Rea and colleagues assessed the information and counselling on infant feeding in HIV+ mothers in a cross-sectional study, based on 118 structured observations of mothers' visits to health professionals (5-8/professional) in 15 purposively selected HIV healthcare units in Sao Paulo, Brazil. The general quality of communication and counselling skills was good: for example, professionals responded to all mothers' questions (98%); kept eye-to-eye contact (82%); and encouraged the mother to talk (77.1%). However, the information provided to

mothers aimed to help their choices concerning infant feeding was of very poor quality. No mother, for example, was informed about alternatives to formula feeding and the danger of mixed feeding. None was offered the option of using banked breast milk. Only around 20% of mothers were informed about the safe preparation of formula feeding. When counselled by a nutritionist (compared with a paediatrician) more mothers were informed about the correct way to prepare bottle-feeds. No mention was made of cup feeding. The authors conclude that although health workers have good communication skills, the information provided to HIV+ mothers is insufficient. Recommending against breast-feeding and providing infant formula may not be enough to achieve safer infant-feeding practices. **Editors' note: This study has important implications for an in-service training focus on the content of counselling on infant feeding and an appropriate division of labour.**

Hovey JD, Booker V, Seligman LD. Using theatrical presentations as a means of disseminating knowledge of HIV/AIDS risk factors to migrant farm workers: An evaluation of the effectiveness of the Informate program. *J Immigr Minor Health* 2006 Dec 21[Epub ahead of print].

Previous research has suggested that Mexican migrant farm workers are at elevated risk for contracting HIV and that they are in need of receiving HIV-related education. Hovey and colleagues evaluated the impact of the Informate adolescent theatre programme on HIV knowledge and attitudes among farm worker audience members of various ages. Audience members from 7 migrant farm worker camps completed a self-administered questionnaire before and after they observed the Informate performance. Paired-samples t-tests and McNemar tests indicated an increase in knowledge in "modes of HIV transmission," "body fluids that can transmit HIV," and items assessing HIV "myths." In addition, a greater percentage of farm workers at post-test reported that they believed that condoms should always be used during sex. The authors conclude that overall findings from this study suggest that theatre can be an effective medium for increasing HIV-related knowledge among migrant farm workers. However, they suggest that, because some farm workers held false beliefs regarding modes of HIV transmission after viewing the theatre programme, theatre used in combination with other prevention activities may provide for a more comprehensive educational experience.

Rietmeijer CA, Lloyd LV, McLean C. Discussing HIV serostatus with prospective sex partners: A potential HIV prevention strategy among high-risk men who have sex with men. *Sex Transm Dis* 2006 Dec 12 [Epub ahead of print].

Rietmeijer and colleagues assessed factors associated with HIV serostatus discussions among men who have sex with men (MSM). The authors conducted a cross-sectional survey among MSM visiting an urban sexually transmitted infection (STI) clinic. MSM were asked about sex partner recruitment, serostatus of partners, condom use, drugs use, and HIV serostatus discussions with sex partners. Among 1,400 MSM reporting occasional sex partners, serostatus discussion with 100% of partners was reported by 509 (36.3%), with 50-99% of partners by 263 (18.8%), and with <50% of partners by 628 (44.9%). Factors associated with serostatus discussion included lower number of sex partners, anal sex with an occasional partner, and sex partner recruitment through the internet. Partner recruitment in bathhouses and having sex with both men and women were negatively associated. The authors conclude that discussion of HIV serostatus was common among MSM studied. Although this strategy has limitations, interventions should address HIV status discussions. Because the internet may facilitate these discussions, web-based interventions

should be evaluated. **Editors' note: Here is yet another study suggesting that prevention activities could use the internet for maximum effect among some men who have sex with men. Challenges include designing effective programmes and convincing internet providers that they have a social responsibility to facilitate their implementation.**

4. Metabolic diseases in HIV

Samaras K, Wand H, Law M, Emery S, Cooper D, Carr A. Prevalence of metabolic syndrome in HIV-infected patients receiving highly active antiretroviral therapy using International Diabetes Foundation and Adult Treatment Panel III Criteria: Associations with insulin resistance, disturbed body fat compartmentalization, elevated C-reactive peptide, and hypoadiponectinemia. *Diabetes Care* 2007;30:113-19.

Metabolic syndrome is a cluster of risk factors for cardiovascular disease and type 2 diabetes. Definitions exist to identify those "at risk." Treatment of HIV infection with highly active antiretroviral therapy can induce severe metabolic complications including lipodystrophy, dyslipidemia, and insulin resistance. Samaras and colleagues report the prevalence of metabolic syndrome in HIV-infected patients and compare insulin resistance and total body, limb, and visceral fat and adipokines in those with and without metabolic syndrome in an international cross-sectional study of a well-characterized cohort of 788 HIV-infected adults recruited at 32 centres. Metabolic syndrome prevalence was examined using International Diabetes Federation (IDF) and U.S. National Cholesterol Education Program Adult Treatment Panel III (ATPIII) criteria, relative to body composition (whole-body dual-energy X-ray absorptiometry and abdominal computed tomography), lipids, glycemic parameters, insulin resistance, leptin, adiponectin, and C-reactive protein (CRP). The prevalence of metabolic syndrome was 14% (n=114; 83 men) by IDF criteria and 18% (n=139; 118 men) by ATPIII criteria; the concordance was significant but only moderate (kappa = 0.46, P<0.0001). Many patients (49%) had at least two features of metabolic syndrome but were not classified as having metabolic syndrome as their waist circumferences or waist-to-hip ratios were in the non-metabolic syndrome range. Metabolic syndrome was more common in those currently receiving protease inhibitors (P=0.04). Type 2 diabetes prevalence was five-to-nine folds higher in those with metabolic syndrome. With IDF criteria, subjects with metabolic syndrome showed disturbances in inflammation and adipokines: they had higher C-reactive protein (P<0.003) and leptin (P<0.0001) and lower adiponectin (P<0.0001) levels. By ATPIII criteria, those with metabolic syndrome had higher leptin (P=0.006) and lower adiponectin (P<0.0001) levels. The authors conclude that metabolic syndrome prevalence in HIV-positive adults was lower than that reported for the general population. Metabolic syndrome was associated with a substantially increased prevalence of type 2 diabetes in this specific cohort. Many subjects without metabolic syndrome had at least two metabolic syndrome components but did not meet waist circumference or waist-to-hip ratio cut-off metabolic syndrome criteria in this group with high rates of body fat partitioning disturbances. **Editors' note: Although the prevalence of metabolic syndrome is not higher among people living with HIV in this general population known for its levels of obesity, it is nonetheless an unwanted side effect of some antiretroviral drugs and a risk factor for diabetes (see next article). A balanced diet and exercise are important prevention measures for everyone, living with HIV or not.**

Hruz PW. Molecular Mechanisms for Altered Glucose Homeostasis in HIV Infection. *Am J Infect Dis* 2006;2:187-192.

<http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=17186064>

A complete understanding of the molecular mechanisms leading to HIV-associated insulin resistance remains elusive. Complex interrelationships between genetic predisposition, disease-related body changes and multi-drug therapy all contribute to alterations in glucose homeostasis. These abnormalities can be differentiated between acute and reversible changes directly induced by ART and more chronic and less reversible changes due to the development of lipodystrophy and hyperlipidaemia. Implicated pathways include changes in adipokine secretion, insulin signalling, lipid homeostasis and disease-related increases in inflammatory mediators. The insulin responsive facilitative glucose transporter GLUT4 is the first molecule to have been identified as a direct target of HIV protease inhibitors. Efforts to elucidate the mechanisms directly responsible for the evolution of insulin resistance during HIV infection and therapy will be greatly assisted by the further identification and characterization of direct molecular targets amenable to pharmacologic therapy and/or the development of newer antiretroviral agents that do not adversely affect these target proteins.

5. People who inject drugs

Tyndall MW, Wood E, Zhang R, Lai C, Montaner JS, Kerr T. HIV seroprevalence among participants at a medically supervised injection facility in Vancouver, Canada: Implications for prevention, care and treatment. *Harm Reduct J* 2006;3:36.

<http://www.harmreductionjournal.com/content/3/1/36>

North America's first government sanctioned medically supervised injection facility was opened during September 2003 in Vancouver, Canada. This was in response to a large open public drug scene, high rates of HIV and hepatitis C transmission, fatal drug overdoses, and poor health outcomes among the city's injection drug users. Between December 2003 and April 2005, a representative sample of 1,035 supervised injection facility participants were enrolled in a prospective cohort that required completing an interviewer-administered questionnaire and providing a blood sample for HIV testing. HIV infection was detected in 170/1007 (17%) participants and was associated with Aboriginal ethnicity (OR 2.70, 95% CI 1.84-3.97), a history of borrowing used needles/syringes (OR 2.0, 95% CI 1.37-2.93), previous incarceration (OR 1.87, 95% CI 1.11-3.14), and daily injection cocaine use (OR 1.42, 95% CI 1.00-2.03). The supervised injection facility has attracted a large number of marginalized injection drug users and presents an excellent opportunity to enhance HIV prevention through education, the provision of sterile injecting equipment, and a supervised environment to self-inject. In addition, the supervised injection facility is an important point of contact for HIV positive individuals who may not be participating in HIV care and treatment. **Editors' note: This supervised injecting facility is attracting a clientele which often has poor contact with health and social services. Increased safer injecting, lowered morbidity and mortality and lower HIV incidence are the end results to be achieved and documented, as they have in been in Switzerland.**

6. HIV in the workplace

Taylor MM, Rotblatt H, Brooks JT, Montoya J, Aynalem G, Smith L, Kenney K, Laubacher L, Bustamante T, Kim-Farley R, Fielding J, Bernard B, Daar E, Kerndt PR. Epidemiologic

investigation of a cluster of workplace HIV infections in the adult film industry: Los Angeles, California, 2004. *Clin Infect Dis* 2007;44:301-5.

Adult film production is a legal, multibillion dollar industry in California. In response to reports of HIV transmission by an adult film worker, Taylor and colleagues sought to determine the extent of HIV infection among exposed workers and to identify means of improving worker safety. The Los Angeles County Department of Health Services initiated an outbreak investigation that included interviews of infected workers to elicit information about recent sex partners, review of the testing agency's medical records and laboratory results, molecular analysis of HIV isolates from the 4 infected workers, and a risk assessment of HIV transmission in the adult film industry. Many adult film workers participate in a monthly program of screening for HIV infection by means of polymerase chain reaction-based technology to detect HIV DNA in blood. A male performer tested negative for HIV on 12 February 2004 and 17 March 2004, then tested positive for HIV on 9 April 2004. During the period between the negative test results, he experienced a flulike illness after performing unprotected vaginal and anal intercourse for an adult film produced outside the United States by a US company. After returning to California, he performed unprotected sex acts for adult films with 13 female partners who had all tested negative for HIV in the preceding 30 days; 3 subsequently tested positive for HIV (a 23% attack rate). Contact tracing identified no reasonable sources of infection other than the male index patient. The authors conclude that although current testing methods may shorten the window period to diagnosis of new HIV infection, they fail to prevent occupational acquisition of HIV in this setting. A California Occupational Safety and Health Administration-approved written health and safety programme that emphasizes primary prevention is needed for this industry. **Editors' note: Given these findings, why can't this legal, multibillion dollar industry move away from sole reliance on regular HIV testing and introduce safer sex techniques in all their movies - what a message that would send!**

7. Prisons

Yap L, Butler T, Richters J, Kirkwood K, Grant L, Saxby M, Ropp F, Donovan B. Do condoms cause rape and mayhem? The long-term effects of condoms in New South Wales' prisons. *Sex Transm Infect*. 2006 Dec 19; [Epub ahead of print]

Concerns raised by opponents to condom provision in prisons have not been objectively examined and the issue continues to be debated. Yap and colleagues examined the long-term effects of the introduction of condoms and dental dams into New South Wales prisons in 1996, focusing on particular concerns raised by politicians, prison officers, prison nurses, and prisoners. These groups were worried that: (a) condoms would encourage prisoners to have sex, (b) condoms would lead to an increase in sexual assaults in prisons, (c) prisoners would use condoms to hide and store drugs and other contraband, and (d) prisoners would use condoms as weapons. Data sources included the New South Wales Inmate Health Surveys in 1996 and 2001 and official reports from the New South Wales Department of Corrective Services. The 1996 IHS involved 657 men and 132 women randomly selected from all prisons with a 90% response rate. The 2001 survey involved 747 men and 167 women inmates with an 85% response rate. There was a decrease in reports of both consensual male-to-male sex and male sexual assaults 5 years after the introduction of condoms into prisons in 1996. Condoms were often used for concealing contraband items and other purposes but this was not associated with an increase in drug injecting in prison. Only three incidents of a condom

being used in assaults on prison officers were recorded between 1996 and 2005; none were serious. The authors conclude that they found no evidence of serious adverse consequences of distributing condoms and dental dams to prisoners in New South Wales. Condoms are an important public health measure in the fight against HIV and sexually transmitted diseases; they should be made freely available to prisoners as they are to other high- risk groups in the community. **Editors' note: Condoms have been available in Canadian penitentiaries since 1994 and in prisons in New South Wales since 1996 but the vast majority of prisons worldwide do not make condoms available to inmates with dire results. Results such as these can be used to influence correctional system leadership, particularly when national laws invest them with responsibility for detainee health on their watch.**

8. Child health

Mulenga V, Ford D, Walker AS, Mwenya D, Mwansa J, Sinyinza F, Lishimpi K, Nunn A, Gillespie S, Zumla A, Chintu C, Gibb DM; the CHAP Trial Team. Effect of cotrimoxazole on causes of death, hospital admissions and antibiotic use in HIV-infected children. *AIDS* 2007;21:77-84.

Cotrimoxazole prophylaxis reduces morbidity and mortality in HIV-1-infected children, but mechanisms for these benefits are unclear. CHAP was a randomized trial comparing cotrimoxazole prophylaxis with placebo in HIV-infected children in Zambia where background bacterial resistance to cotrimoxazole is high. Mulenga and colleagues compared causes of mortality and hospital admissions, and antibiotic use between randomized groups. Of 534 children (median age, 4.4 years; 32% 1-2 years), 186 died and 166 had one or more hospital admissions not ending in death. Cotrimoxazole prophylaxis was associated with lower mortality, both outside hospital (P=0.01) and following hospital admission (P=0.005). The largest excess of hospital deaths in the placebo group was from respiratory infections [22/56 (39%) placebo versus 10/35 (29%) cotrimoxazole]. By 2 years, the cumulative probability of dying in hospital from a serious bacterial infection (predominantly pneumonia) was 7% on cotrimoxazole and 12% on placebo (P=0.08). There was a trend towards lower admission rates for serious bacterial infections in the cotrimoxazole group (19.1 per 100 child-years at risk versus 28.5 in the placebo group, P=0.09). Despite less total follow-up due to higher mortality, more antibiotics (particularly penicillin) were prescribed in the placebo group in year one [6083 compared to 4972 days in the cotrimoxazole group (P=0.05)]. The authors conclude that cotrimoxazole prophylaxis appears to mainly reduce death and hospital admissions from respiratory infections, supported further by lower rates of antibiotic prescribing. As such infections occur at high CD4 cell counts and are common in Africa, the role of continuing cotrimoxazole prophylaxis after starting antiretroviral therapy requires investigation. **Editors note: The positive benefits of cotrimoxazole prophylaxis in HIV-infected children are confirmed, not only by reduced respiratory infection hospital admissions and deaths but also in terms of antibiotic usage.**

9. Young people

Thorburn S, Harvey SM, Tipton J. Diaphragm acceptability among young women at risk for HIV. *Women Health* 2006;44:21-39.

Thorburn and colleagues assessed the acceptability of the diaphragm among young women at risk for HIV and other sexually transmitted infections (STIs) in the U.S. A total of 140 young (aged 18-25 years) women who had never used the diaphragm and who were at risk for

HIV and other STIs completed questionnaires that included questions about the diaphragm and other sexual and reproductive health topics. These women were participants in a focus group study. The majority of participants perceived that the diaphragm had several characteristics (e.g., is a method they can control, is effective in preventing pregnancy, will not cause side effects, does not decrease sexual pleasure) considered important when selecting a birth control method. However, most were not confident in various aspects of diaphragm use, including their ability to use the method correctly, without breaking the mood, or when sexually excited. In multivariate analyses, intention to use the diaphragm was significantly higher among participants who were less motivated to avoid pregnancy and those with greater perceived self-efficacy to use a diaphragm in different contexts (e.g., when sexually excited). The authors conclude that the diaphragm has characteristics that some women consider desirable, suggesting that it could be an acceptable HIV prevention method for some at-risk women. **Editors' note: Trial results from the MIRA trial (Methods for Improving Reproductive Health in Africa) in Zimbabwe and South Africa, which is assessing the efficacy of the vaginal diaphragm plus gel for HIV prevention, are expected in 2007. They will show whether efficacy can combine with acceptability to increase the HIV prevention choices available to women worldwide.**

10. Stigma and discrimination

Johnny L, Mitchell C. "Live and let live": An analysis of HIV/AIDS-related stigma and discrimination in international campaign posters. *J Health Commun* 2006;11:755-67.

As a corollary to The Declaration of Commitment adopted by the United Nations General Assembly Special Session on HIV/AIDS in June 2001, UNAIDS developed a World AIDS Campaign that sought to eradicate HIV-related stigma and discrimination. The campaign incorporated several educational strategies, including a poster campaign that advocated the just and equal treatment of people living with HIV. In an effort to develop an understanding of these educational efforts, Johnny and Mitchell deconstruct the 2002-2003 World AIDS Campaign posters. While the overall results suggest that the campaign has been successful in redefining images of HIV and AIDS, they also show that certain aspects of these posters may actually serve to reinforce stigma and discrimination. Using a visual studies approach to textual analysis, the authors explore the underlying ideological and cultural assumptions that exist within the posters and provide a method for evaluating such materials.

Babalola S. Readiness for HIV testing among young people in northern Nigeria: The roles of social norm and perceived stigma. *AIDS Behav* 2006 Dec 27; [Epub ahead of print].

Babalola examined the predictors of readiness for HIV testing among young people in northern Nigeria, paying special attention to the role of stigma. Stigma was measured at two levels: individual and community (social norm). There are commonalities and differences in the correlates of readiness for HIV testing among men and women. For men and women, knowledge about HIV prevention, knowledge about a source for VCT, discussion about condom use for HIV prevention and perceived risk are strong predictors. Knowledge that an apparently healthy person can be HIV-infected is only significant for women. Perceived stigma is a significant predictor for both men and women although the specific dimension of note differs between the sexes. Social norm is strongly and directly associated with readiness among men but has no apparent influence among women. For both sexes, social norm appears to have strong mediating influence on the relationship between personal

perceived stigma and readiness. The author concludes that the results strongly suggest that to eliminate HIV-related stigma, it is not enough to target individual cognitive processes; strategic efforts should target social structures in order to change negative social norms. **Editors' notes: Here is yet another study highlighting the importance of well designed social change communication strategies to create enabling environments for behavioural change and maintenance - in this case, the decision to take an HIV test.**

11. Basic science

Legrand FA, Nixon DF, Loo CP, Ono E, Chapman JM, Miyamoto M, Diaz RS, Santos AM, Succi RC, Abadi J, Rosenberg MG, de Moraes-Pinto MI, Kallas EG. Strong HIV-1-Specific T cell responses in HIV-1-exposed uninfected infants and neonates revealed after regulatory T cell removal. *PLoS ONE* 2006;1:e102.

<http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=17183635>

In utero transmission of HIV-1 occurs on average in only 3-15% of HIV-1-exposed neonates born to mothers not on antiretroviral drug therapy. Thus, despite potential exposure, the majority of infants remain uninfected. Weak HIV-1-specific T-cell responses have been detected in children exposed to HIV-1, and potentially contribute to protection against infection. It was recently shown that the removal of CD4(+)CD25(+) T-regulatory (Treg) cells can reveal strong HIV-1 specific T-cell responses in some HIV-1 infected adults. Legrand and colleagues assessed whether T-regulatory cells could suppress HIV-1-specific immune responses in young children. The authors studied two cohorts of children. The first group included HIV-1-exposed-uninfected as well as unexposed neonates. The second group comprised HIV-1-infected and HIV-1-exposed-uninfected children. They quantified the frequency of T-regulatory cells, T-cell activation, and cell-mediated immune responses. The authors detected high levels of CD4(+)CD25(+)CD127(-) T-regulatory cells and low levels of CD4(+) and CD8(+) T cell activation in the cord blood of the HIV-1-exposed-uninfected neonates. They observed HIV-1-specific T cell immune responses in all of the children exposed to the virus. These T-cell responses were not seen in the cord blood of control HIV-1 unexposed neonates. Moreover, the depletion of CD4(+)CD25(+) T-regulatory cells from the cord blood of HIV-1-exposed-uninfected newborns strikingly augmented both CD4(+) and CD8(+) HIV-1-specific immune responses. The authors conclude that they provide new evidence that HIV-1-exposed-uninfected infants can mount strong HIV-1-specific T cell responses, and that in utero CD4(+)CD25(+) T-regulatory cells may be contributing to the lack of vertical transmission by reducing T cell activation. **Editors' note: Understanding how and why some exposed infants do not get infected during pregnancy and labour is critical to the development of neonatal vaccines.**

12. TB/HIV

Corbett EL, Bandason T, Cheung YB, Munyati S, Godfrey-Faussett P, Hayes R, Churchyard G, Butterworth A, Mason P. Epidemiology of tuberculosis in a high HIV prevalence population provided with enhanced diagnosis of symptomatic disease. *PLoS Med* 2006;4(1):e22. [10.1371/journal.pmed.0040022](http://dx.doi.org/10.1371/journal.pmed.0040022)

Directly observed treatment short course (DOTS), the global control strategy aimed at controlling tuberculosis transmission through prompt diagnosis of symptomatic smear-positive disease, has failed to prevent rising tuberculosis incidence rates in Africa brought

about by the HIV epidemic. However, rising incidence does not necessarily imply failure to control tuberculosis transmission, which is primarily driven by prevalent infectious disease. Corbett and colleagues investigated the epidemiology of prevalent and incident tuberculosis in a high HIV prevalence population provided with enhanced primary health care. Twenty-two businesses in Harare, Zimbabwe, were provided with free smear- and culture-based investigation of tuberculosis symptoms through occupational clinics. Anonymous HIV tests were requested from all employees. After two years of follow-up for incident tuberculosis, a culture-based survey for undiagnosed prevalent tuberculosis was conducted. A total of 6440 of 7478 eligible employees participated. HIV prevalence was 19%. For HIV-positive and -negative participants, the incidence of culture-positive tuberculosis was 25.3 and 1.3 per 1,000 person-years, respectively (RR 18.8, 95% CI 10.3-34.5: population attributable fraction = 78%), and point prevalence after 2 years was 5.7 and 2.6 per 1,000 population (OR 1.7; 95% CI 0.5-6.8: population attributable fraction = 14%). Most patients with prevalent culture-positive tuberculosis had sub-clinical disease when first detected. The authors conclude that strategies based on prompt investigation of tuberculosis symptoms, such as DOTS, may be an effective way of controlling prevalent tuberculosis in high HIV prevalence populations. This may translate into effective control of tuberculosis transmission despite high tuberculosis incidence rates and a period of sub-clinical infectiousness in some patients.

13. HIV vaccines

Joseph J, Saubi N, Pezzat E, Gatell JM. Progress towards an HIV vaccine based on recombinant *Bacillus Calmette-Guerin*: failures and challenges. *Expert Rev Vaccines* 2006;5:827-38.

The need for an affordable, safe and effective HIV vaccine has never been greater. As the immunogenicity of all the vaccine vectors being evaluated currently in human populations is limited, novel vaccine strategies are needed to stimulate the innate immune system, to generate high levels of neutralizing antibodies and to induce strong cell-mediated and mucosal immunity. There is strong evidence for a role for cytotoxic T lymphocytes in the containment of HIV replication. Several vaccine approaches have been tested to elicit anti-HIV cytotoxic T-lymphocyte responses. One promising approach is *Bacillus Calmette-Guerin* (BCG) as a bacterial live recombinant vaccine vehicle. BCG has a long record of safety in humans and is able to induce long-lasting immunity. Joseph and colleagues described the limitations and challenges of developing a recombinant BCG-based HIV vaccine. The authors also emphasize possible approaches for overcoming the plasmid instability in vivo and the low levels of gene expression and immunogenicity induction. Today, projects all over the world are focused on the development of an AIDS vaccine. The authors conclude that overcoming the remaining scientific, logistical and financial hurdles to the development of an effective HIV vaccine will require real imagination and firm commitment from all stakeholders.

That was *HIV This Week*, signing off.

Editors' notes on journal access

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