**Perspectives
Research News in Clinical Context**

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**Published in STI: The effects of condomless vaginal sex and lubricant use on the vaginal metabolome**

The vaginal metabolome plays a key role in urogenital health. This study analysed changes in the vaginal metabolome before and after condomless sex with and without lubricant using self-collected mid- vaginal swabs from 44 reproductive-age women. Condomless vaginal sex and lubricant use did not significantly impact the global vaginal metabolome. However, both independently increased concentrations of metabolites indicative of oxidative stress, epithelial damage (e.g., sarcosine), and host-produced antioxidants. Stress-related metabolites were positively correlated with bacterial vaginosis-associated bacteria and negatively correlated with protective lactobacilli. The findings point to the need for safer lubricant formulations that protect the female reproductive tract.

Borgogna JLC, Grace SG, Holm JB, *et al.* Investigating the impact of condomless vaginal intercourse and lubricant use on the vaginal metabolome: a pre-post observational study. *Sex Transm Infect*. 2023;99:489–96.

**A choice of HIV PrEP for young women in Africa: oral PrEP versus dapivirine ring**

This study compared the safety, adherence, and user preference of two PrEP methods - a monthly dapivirine vaginal ring and daily oral TDF/FTC - in 247 women aged 16-21 years in South Africa, Uganda, and Zimbabwe. Participants were randomly allocated to either PrEP method for 6 months and then switched to the other method for a further 6 months. The randomised phase was followed by a 6-month period when participants chose their preferred method or no PrEP. During the randomised periods, adherence, measured by drug concentration in dried blood spots and returned rings, was 57% for both formulations and did not differ by sequence of initiation. In the third phase, 65% of 238 participants chose the ring, 30% oral PrEP, and 5% no PrEP, with choices remaining stable during six months. Both PrEP formulations were safe. Four incident HIV infections were associated with low or no PrEP use. Offering young women choices in HIV prevention methods may increase adherence and effectiveness.

Nair G, Celum C, Szydlo D, *et al.* Adherence, safety, and choice of the monthly dapivirine vaginal ring or oral emtricitabine plus tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis among African adolescent girls and young women: a randomised, open-label, crossover trial. *Lancet HIV*. 2023;10. doi: 10.1016/S2352-3018(23)00227-8

**Incidence and predictors of anal high-grade squamous intraepithelial lesions (HSIL) in virologically suppressed women with HIV**

This US cohort study determined incidence, cumulative risk, and predictors of anal HSIL among women with HIV and no anal HSIL at study entry; 114 women (63% black, 23% Hispanic, median age 51 years, 99% virologically suppressed) were recruited from a multi-center trial estimating the performance of various screening tests for prevalent HSIL. Over two years, incidence of anal HSIL was 8.5 per 100 person-years, and was significantly associated with detection of anal high-risk HPV and abnormal cytology at baseline. The 2-year cumulative risk was 38%, increasing to 66% with co-detection of anal high-risk HPV and abnormal cytology at baseline. Annual screening with HPV testing or cytology may be needed in women with HIV.

Stier EA, Jain M, Joshi H, *et al.* Two-Year Incidence and Cumulative Risk and Predictors of Anal High- Grade Squamous Intraepithelial Lesions (anal precancer) among Women with HIV. *Clin Infect Dis*.

**Daily oral pitavastatin reduces the incidence of major cardiovascular events in people with HIV**

The global REPRIEVE trial included 7769 adults with treated HIV and low-to-moderate cardiovascular risk (median age 50 years, 31% women, median CD4 count 621cells/mm3, 88% virologically suppressed). Participants were randomly assigned to either pitavastatin (4 mg daily) or placebo. Over a median follow-up of 5.1 years, incidence of 12 major cardiovascular events (per 1000 person-years) was 4.81 in the pitavastatin arm versus 7.32 in the placebo arm (hazard ratio=0.65; 95%CI: 0.48-0.90, indicating a 35% reduction in risk with pitavastatin.) Serious adverse events were rare. Incidence of diabetes mellitus was similar in the two arms, whereas muscle-related symptoms were more common with pitavastatin. The trial was stopped early due to the demonstrated efficacy of pitavastatin, thus informing guidelines on primary prevention for people with HIV.

Grinspoon SK, Fitch K V., Zanni M V., et al. Pitavastatin to Prevent Cardiovascular Disease in HIV Infection. *New England Journal of Medicine*. 2023;389:687–99.

**Metabolomic correlates of *Chlamydia trachomatis* clearance in women**

The metabolic pathways associated with spontaneous clearance of *C. trachomatis* remain unclear, although a depletion of cervicovaginal tryptophan has been hypothesised.1 This study examined metabolic differences in the cervicovaginal environment of 17 women who naturally cleared *C. trachomatis* matched to 17 with persistent infection (>10 days). Untargeted mass-spectrometry of cervicovaginal lavages identified 524 distinct metabolites. Natural clearance was associated with increased levels of oligosaccharides (trehalose, sucrose, melezitose, maltotriose) and decreased levels of indoline and branched-chain amino acids (valine, leucine, isoleucine). Non-tryptophan pathways may impact survival of *C. trachomatis* in vivo, providing new insights into the mechanisms of natural clearance and the role of the cervicovaginal metabolome.

Jordan SJ, Wilson L, Ren J, *et al.* Natural Clearance of Chlamydia trachomatis Infection Is Associated With Distinct Differences in Cervicovaginal Metabolites. *J Infect Dis*. 2023;228:1119–26.

**First-trimester isoniazid exposure may be associated with risk of spontaneous abortion in women with HIV**

A secondary analysis of a randomized tuberculosis prevention trial (2012-2017) examined the risk of adverse pregnancy outcomes associated with exposure to isoniazid during the first trimester among women with HIV from 10 African countries. Among 128 participants (35% on antiretroviral therapy), 39 were exposed to isoniazid (300mg daily) and 89 were unexposed. In unadjusted analyses, exposure was associated with a nearly two-fold increased risk of adverse pregnancy outcomes, primarily spontaneous abortions (relative risk [RR]=1.85; 95%CI 0.99-3.47). The association was attenuated after adjusting for covariates, including antiretroviral therapy use at the time of pregnancy outcome (RR=1.47; 95%CI 0.84- 2.55). There was no association with preterm delivery or low birthweight. High incidence of spontaneous abortion suggests the need for contraceptive counselling among women on isoniazid- containing regimens.

Gupta A, Hughes MD, Cruz JL, *et al.* Adverse Pregnancy Outcomes among HIV-infected Women Taking Isoniazid Preventive Therapy During the First Trimester. *Clin Infect Dis*. Published Online First: 28 September 2023. doi: 10.1093/CID/CIAD583

**References:**

1 Jordan SJ, Olson KM, Barnes S, et al. Lower Levels of Cervicovaginal Tryptophan Are Associated With Natural Clearance of Chlamydia in Women. *J Infect Dis*. 2017;215(12):1888-1892. doi:10.1093/infdis/jix240