

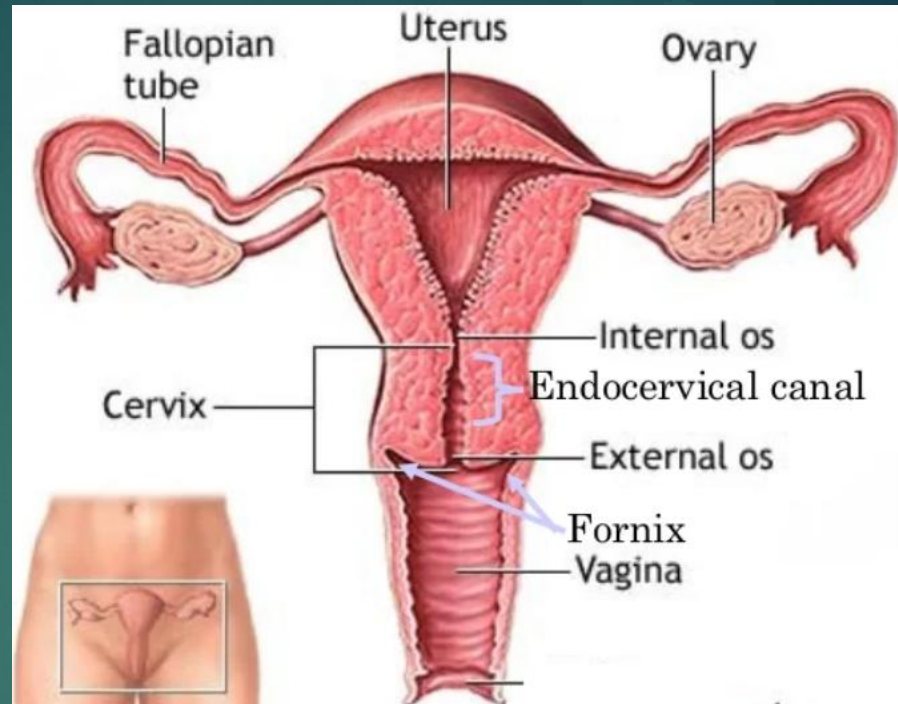
Genital microbiome environment on STI: Benefit or harm?

NATIONAL POLICE HOSPITAL
DEPARTMENT OF UROLOGY
IN-CHANG CHO

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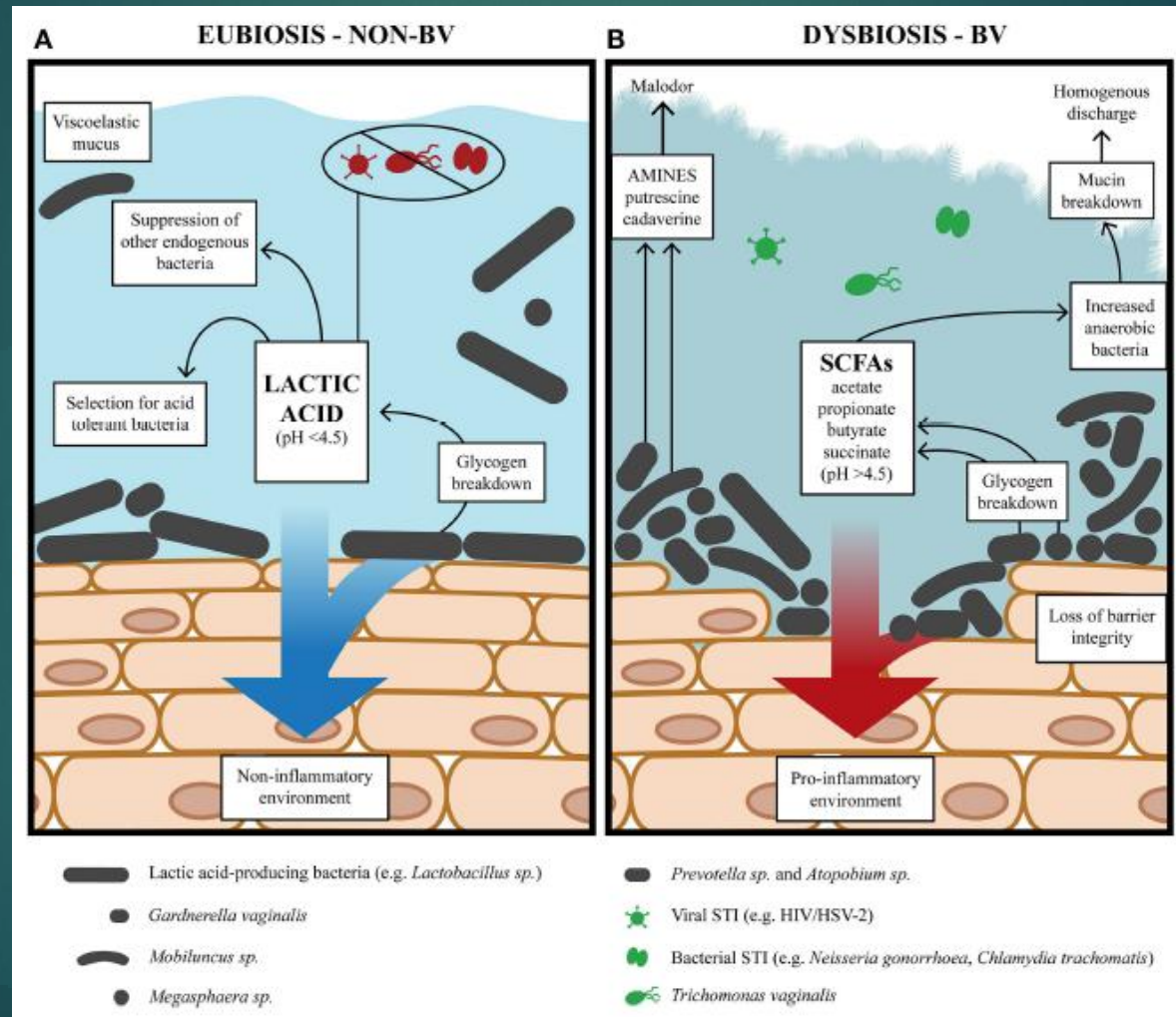
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Female

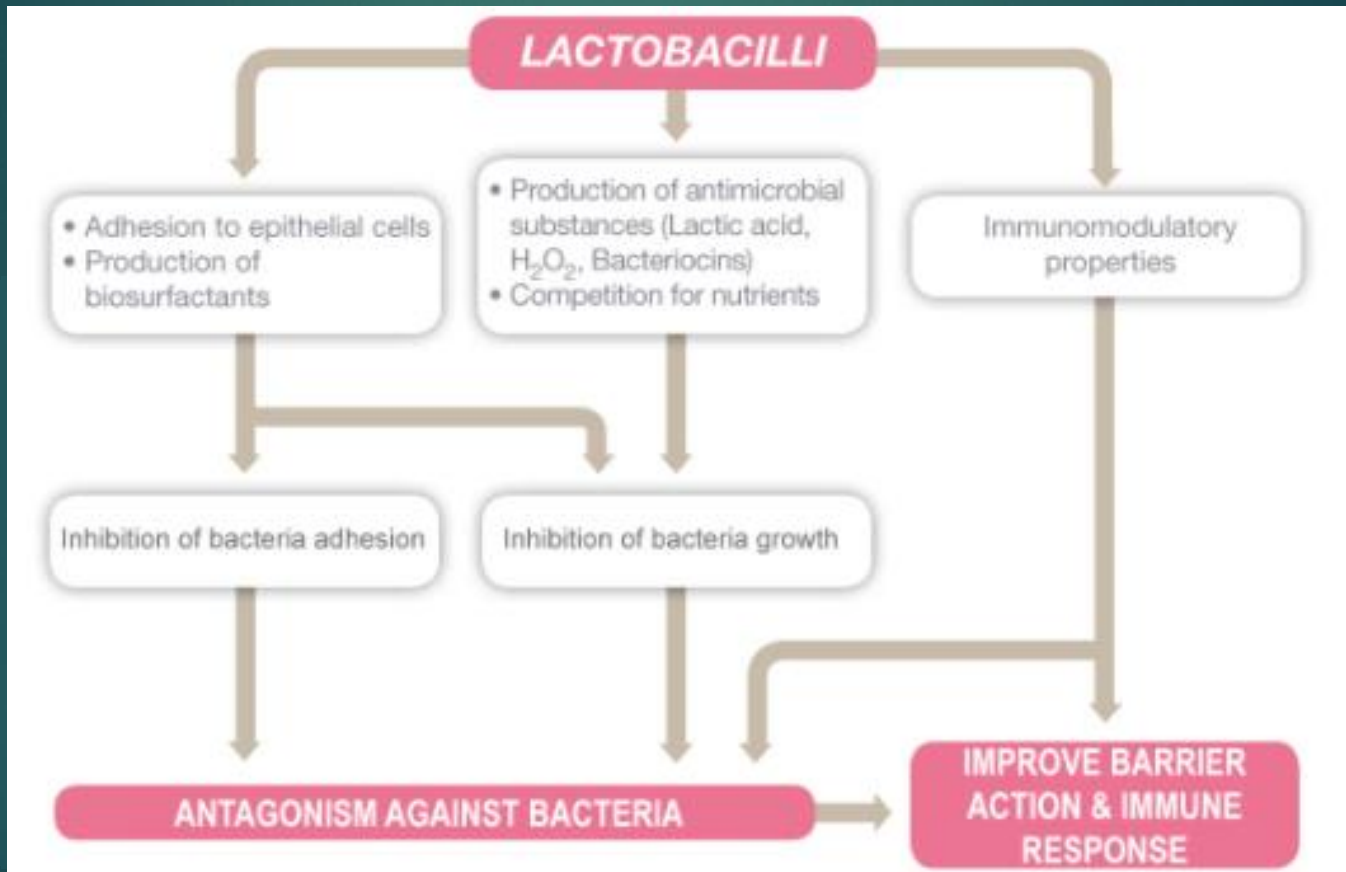


- ▶ Cervix, fornices, vaginal canal
- ▶ Surface area of the cervicovaginal mucosa is considerably larger than that of the penis and foreskin, resulting in greater potential exposure to STI pathogens
- ▶ Semen may remain within the female genital tract for up to 3 days postcoitus, prolonging exposure to STIs, including HIV
- ▶ Women have increased mucosal expression of the HIV coreceptor CCR5 (HIV target cell) in the genital tract as compared to men

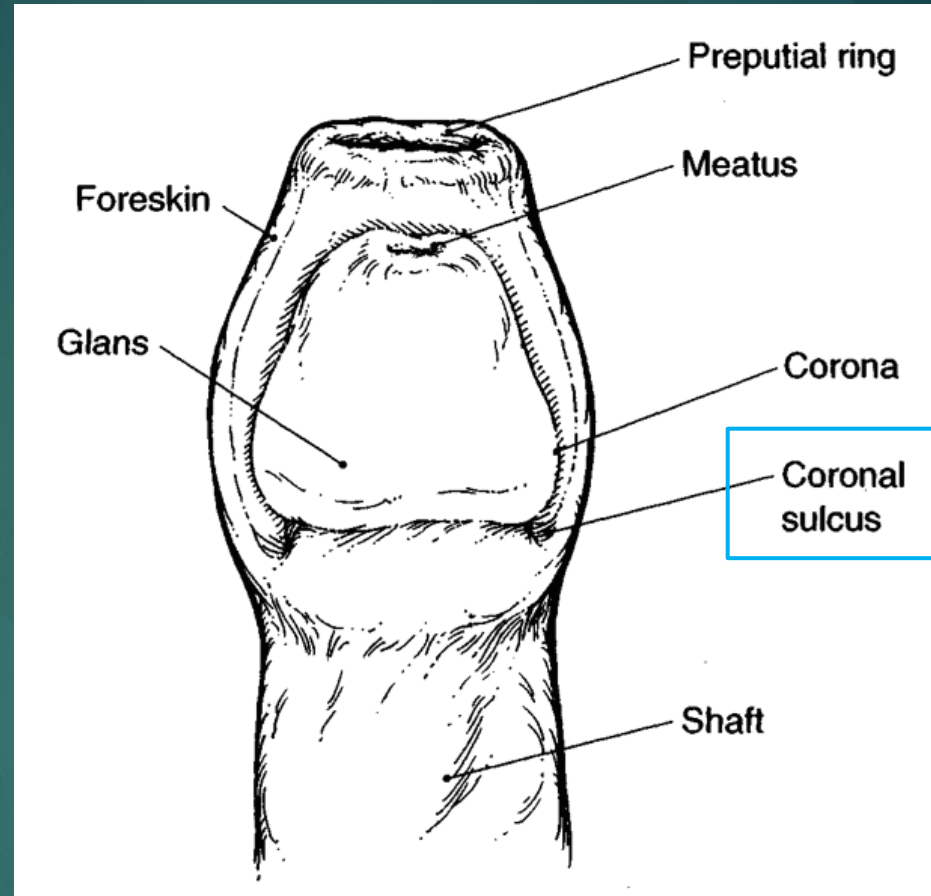
Dysbiosis in the vaginal microbiota



Lactobacilli



Male



- ▶ Foreskin, glans, coronal sulcus, penile shaft

Male genital microbiota

- ▶ Much less studied than the cervicovaginal microbiota
- ▶ Swabs taken from the **coronal sulcus**: reflective of the penile microbiota (similar to those found on the skin including *Corynebacterium* and *Staphylococcus* spp., as well as *Anerococcus*)
- ▶ **Urine** samples: reflective of the urethral microbiota

Female sex hormones

- ▶ Estrogen, progesterone (whether endogenous or exogenous, eg, from use of hormonal contraception)
 - ▶ Affect STI susceptibility
- ▶ Influence of progesterone
 - ▶ Cervicovaginal mucus is thick and viscous
 - ▶ Block the movement of viral particulates, including STIs in female genital tract
- ▶ During ovulation
 - ▶ Increasing estradiol
 - ▶ The mucus thins and becomes less viscous
- ▶ In vitro studies
 - ▶ The cervicovaginal microbiota can modulate the penetration of HIV through mucus to access target cells

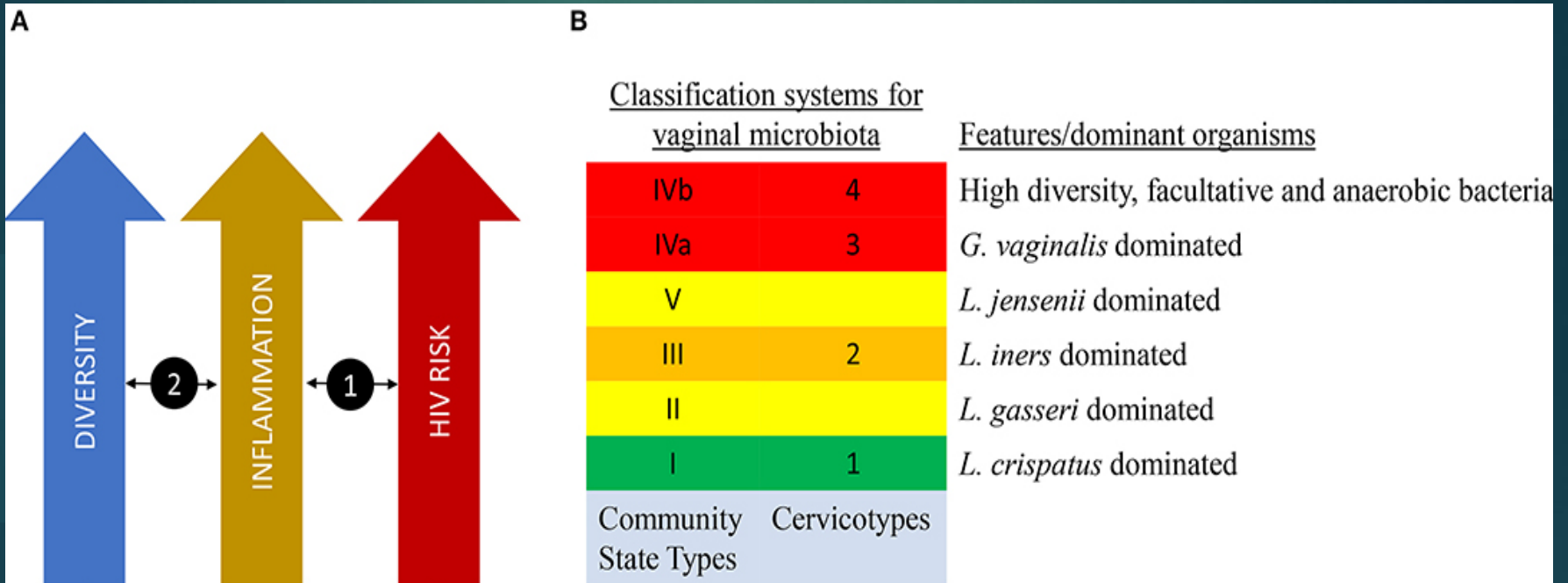
Bacterial vaginosis

- ▶ 27% of women in the United States: BV
- ▶ 50% of women with BV are symptomatic
 - ▶ Vaginal odor and discharge
- ▶ BV
 - ▶ Increased risk of several adverse reproductive health outcomes
 - ▶ Preterm birth, low birth weight, upper reproductive tract infections
- ▶ Current guidelines recommend treatment of BV only in women complaining of symptoms
- ▶ Both symptomatic and asymptomatic BV
 - ▶ Increased acquisition and transmission of STIs and HIV

Bacterial vaginosis (Amsel-BV)

- ▶ BV is diagnosed in the clinical setting using Amsel's criteria defined by the presence of at least 3 of the following:
 - ▶ Thin homogenous vaginal discharge
 - ▶ Vaginal pH > 4.5
 - ▶ Positive "whiff " test with addition of KOH to vaginal secretions
 - ▶ Presence of clue cells on microscopy

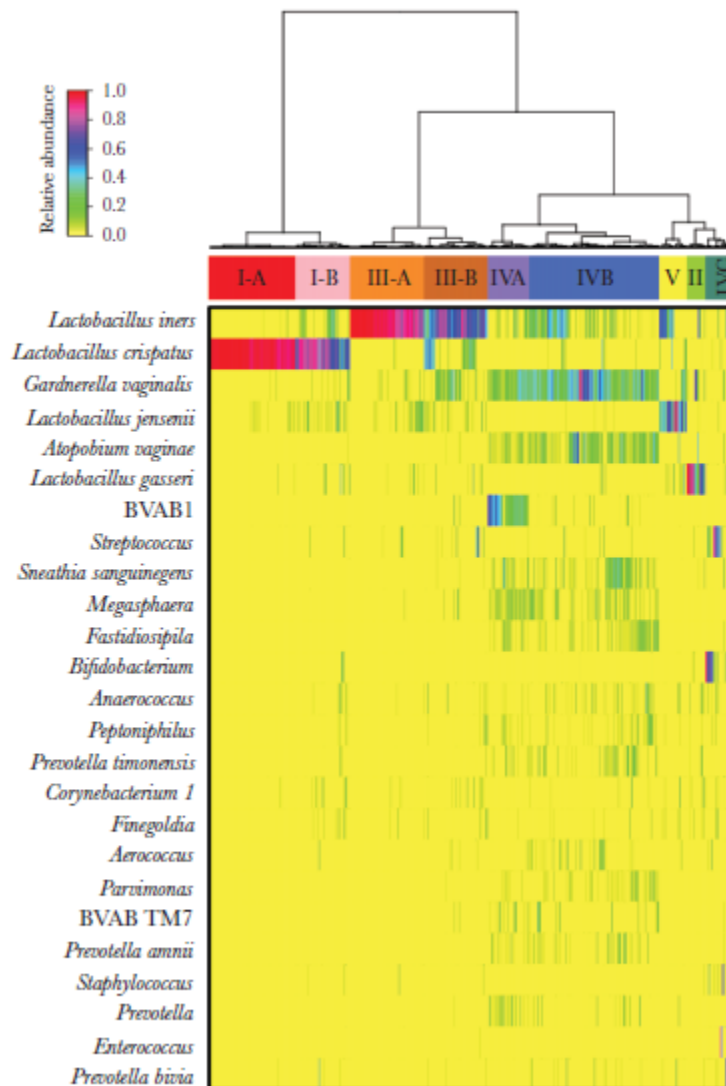
Community state types (CSTs)



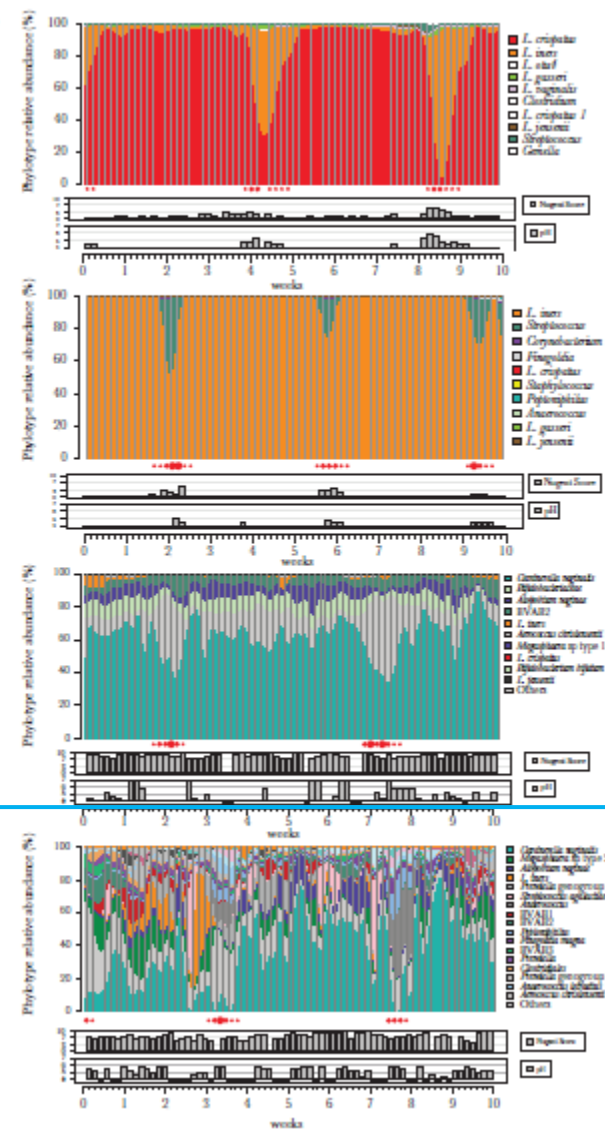
- 1 Elevated genital concentrations of HIV target cell-recruiting chemokines and a genital inflammatory profile contributes to the high risk of HIV acquisition in African women (Masson et al 2015)
- 2 Unlike the gut, high-diversity cervicovaginal communities are pro-inflammatory; specific bacteria induce cytokine production from genital APCs and epithelial cells (Anahtar et al 2015)
- 3 Women with high-diversity genital bacterial communities acquire HIV at 4× higher rates; specific genital bacterial taxa are linked with reduced or elevated HIV acquisition (Gosmann et al 2017)

CSTs

A



B



Factors Associated With Female Genital Microbiota Structure and Stability

Increased Risk of BV/Vaginal Microbiota Instability

Menses

New sexual partner

Condomless vaginal sex

Uncircumcised male partner

Female partner with BV

Black race

Smoking

Lubricant use

Douching

Decreased Risk of BV/Vaginal Microbiota Instability

Estrogen

Hormonal contraception

Circumcised male partner

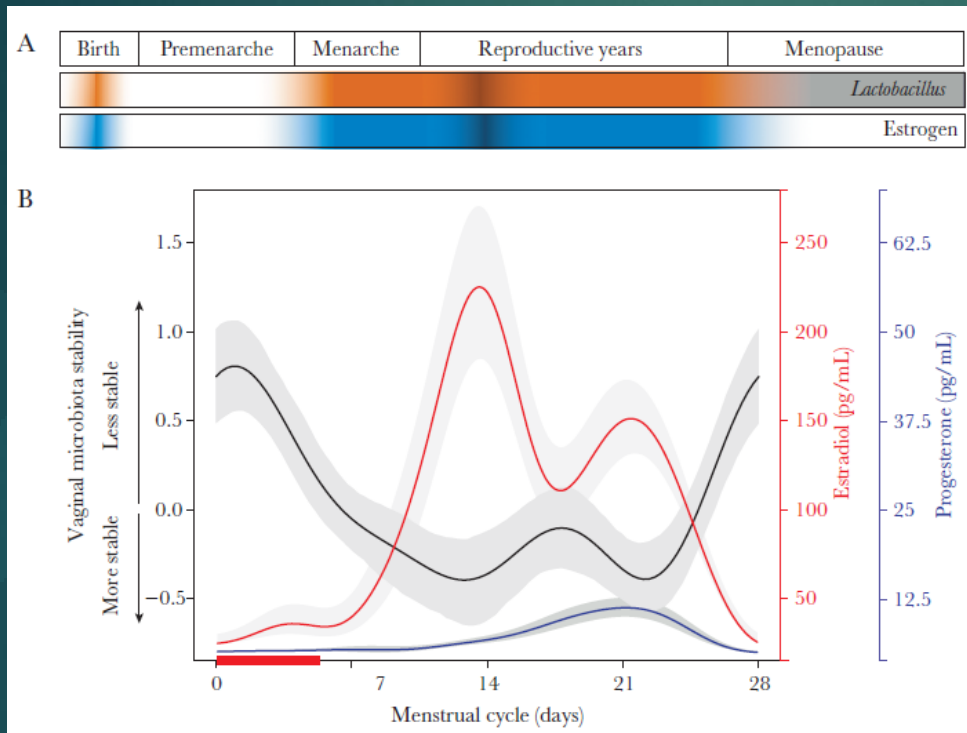
Pregnancy

Antibiotics

Abbreviation: BV, bacterial vaginosis.

- ▶ **Estrogen**: promote the production of glycogen by vaginal epithelial cells -> support the growth of lactobacilli and other bacteria

Estrogen level and Microbiota



- ▶ Estrogen levels throughout the life cycle are mirrored by corresponding changes in the vaginal microbiota

Female genital microbiota and STIs

- ▶ Gonorrhea
- ▶ Chlamydia, Trichomoniasis, Mycoplasma genitalium
- ▶ HPV, HSV, HIV

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Bacterial vaginosis and HIV acquisition: A meta-analysis of published studies

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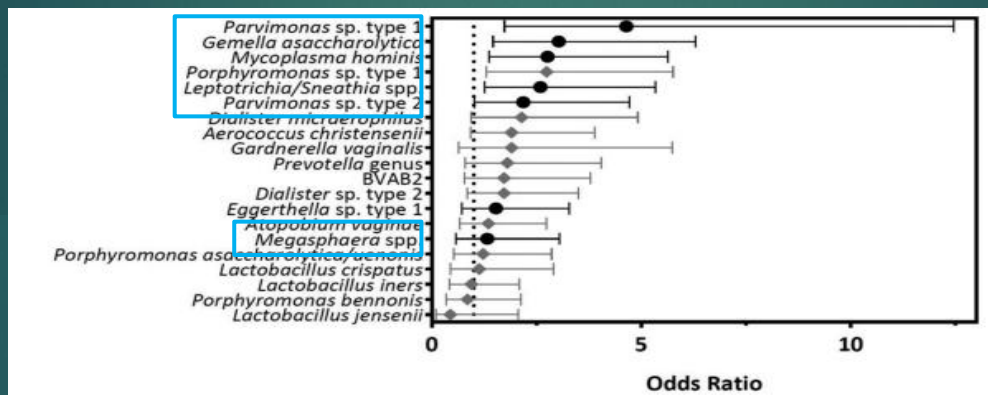
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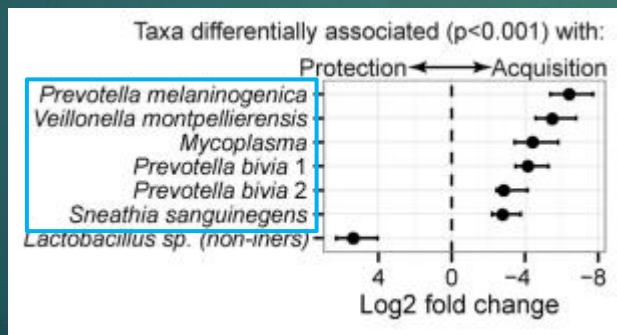
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Specific bacteria associated with BV

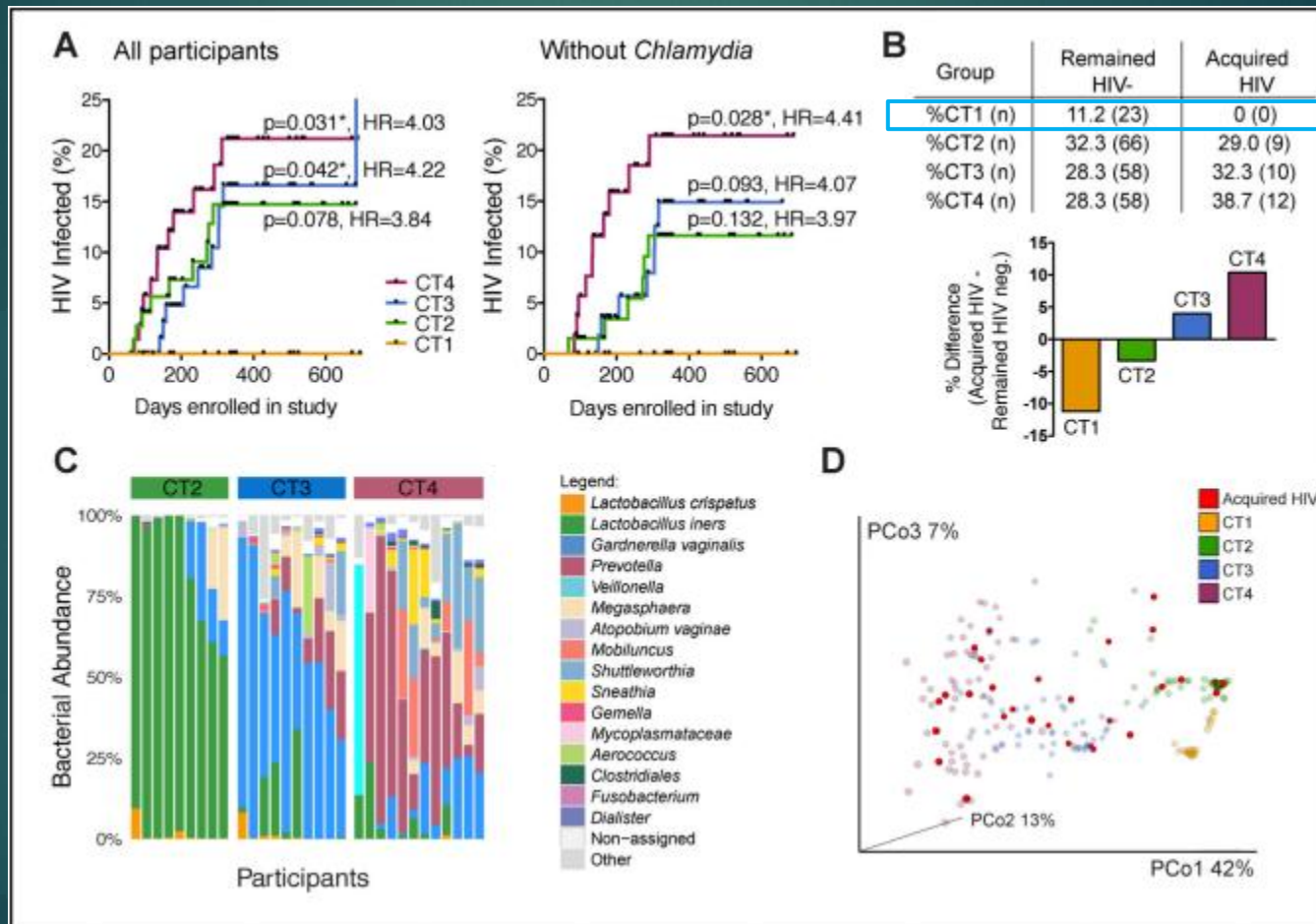
- ▶ 55 women who acquired HIV vs 55 women who remained uninfected (African)



- ▶ 31 women who acquired HIV vs 205 women who remained uninfected (African)



Lactobacillus crispatus : rare HIV



Factors Associated With Male Genital Microbiota Structure

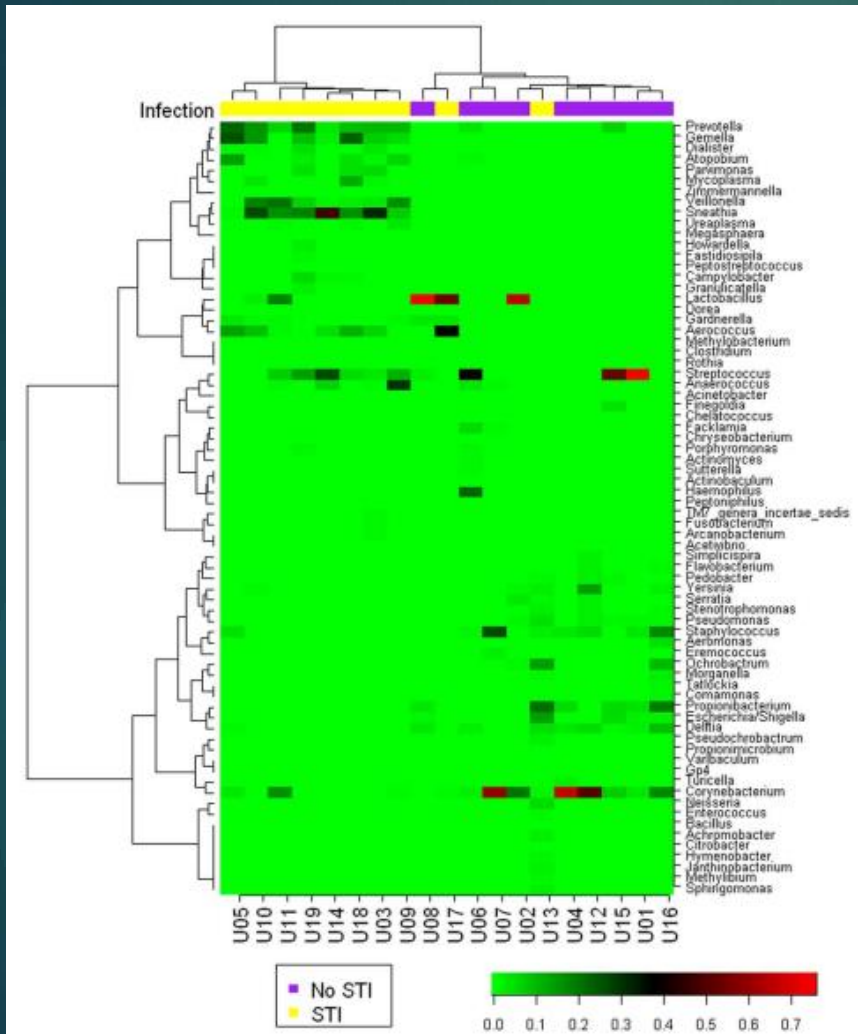
Increased Anaerobes/BV-Associated Bacteria	Decreased Anaerobes/BV-Associated Bacteria
Uncircumcised penis	Circumcised penis
Female partner with BV	Female partner without BV

Abbreviation: BV, bacterial vaginosis.

- ▶ Foreskin ≠ Coronal sulcus
 - ▶ Removal of the foreskin during male circumcision: dramatic changes in the penile microbiota
- ▶ Circumcision
 - ▶ Penile microbiota density and diversity decline, anaerobes decrease significantly
 - ▶ Dominated by members of the genera *Staphylococcus* and *Corynebacterium*, but in low absolute abundances
 - ▶ Reduce HIV, herpes simplex 2 (HSV2), human papillomavirus (HPV) acquisition in men and decreased BV in female partners

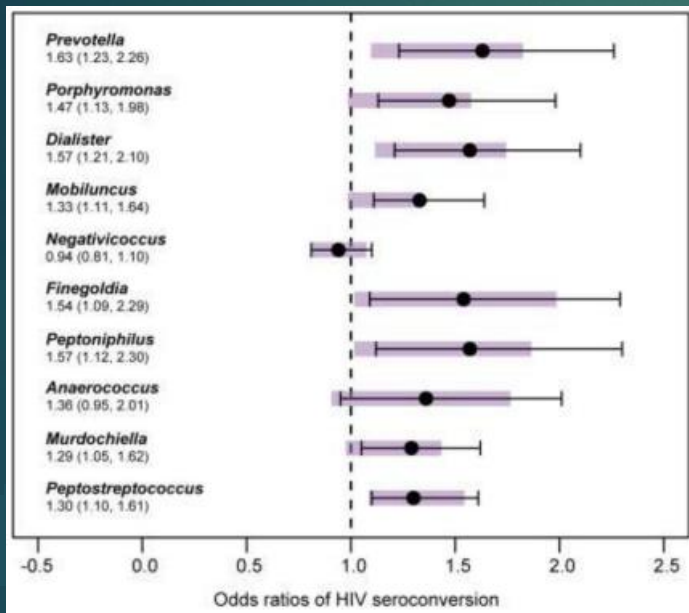
Penile microbiota and STIs: Urine

- ▶ Men with asymptomatic STIs (gonorrhea and chlamydia) were more likely to have urine microbiota dominated by **fastidious, anaerobic, and uncultivated** bacteria (potentially reflective of urethral colonization) than those without STI

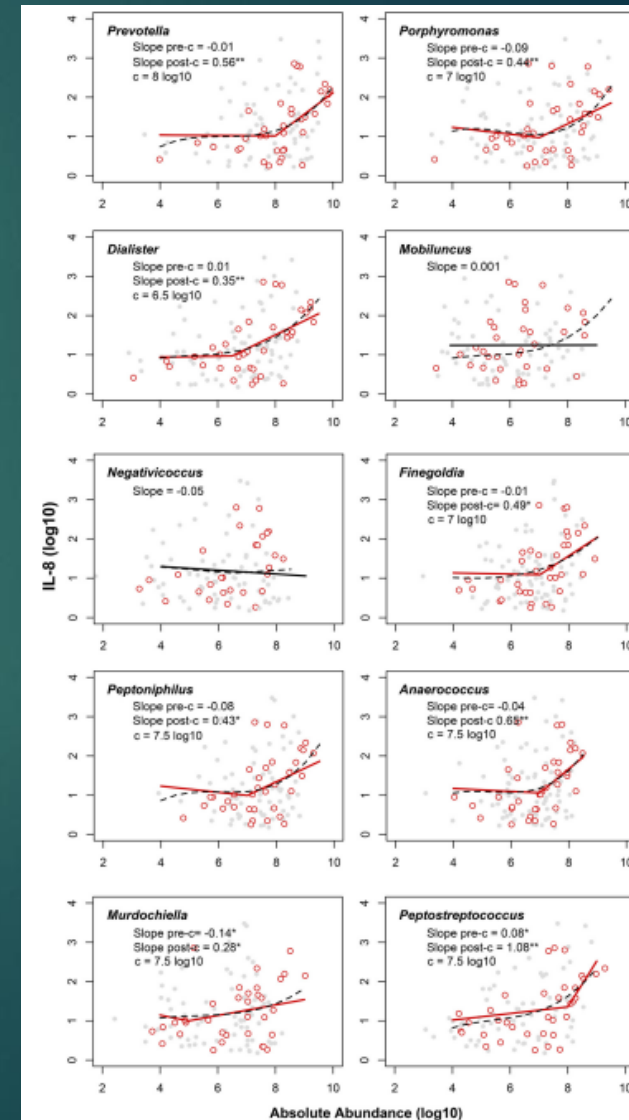


Penile microbiota and HIV

(182 uncircumcised men, the 46 men who became HIV infected)



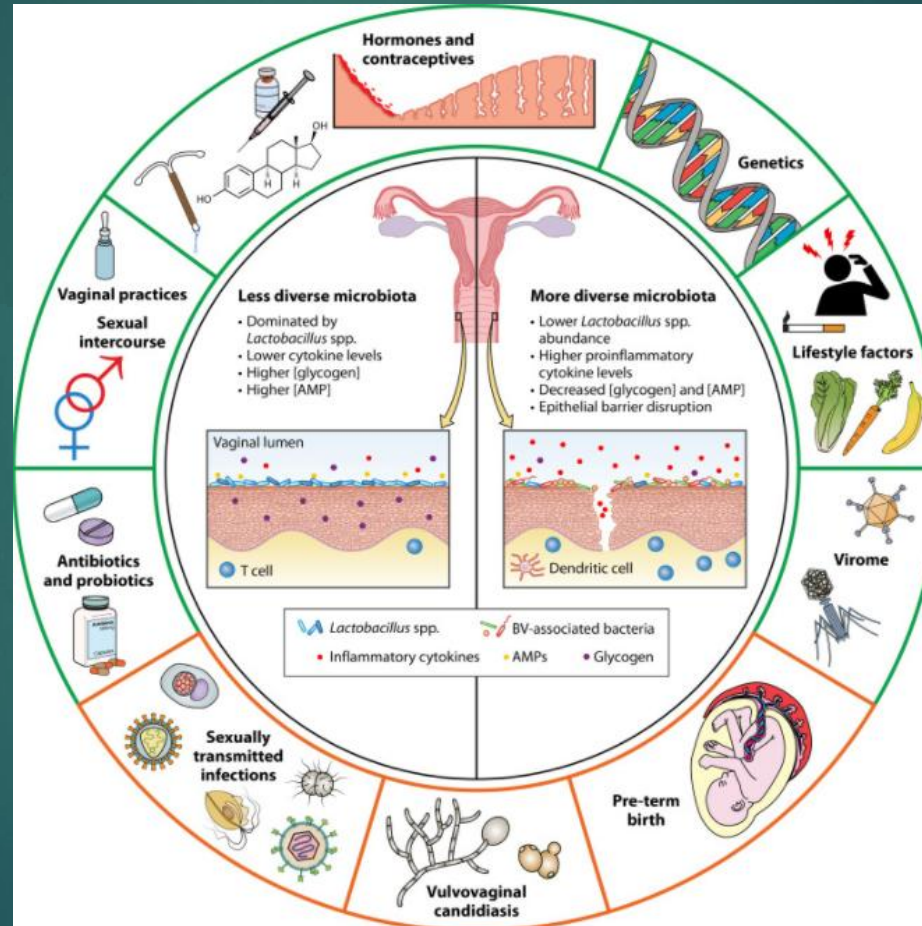
- Colonization with BV-associated organisms may lead to increased inflammation in the male genital tract, hence leading to increased susceptibility to HIV.



Limitation

- ▶ Whether the microbiota of the **coronal sulcus** (on which most existing studies are based) or that of the **urethra** plays a greater role in STI vulnerability is unclear.
- ▶ Many early epidemiologic studies linking STIs and the vaginal microbiota have been cross-sectional, making causal inferences difficult.
- ▶ More research to understand factors associated with **stability of the vaginal microbiota and STI risk** is needed, study design is difficult given that frequent longitudinal sampling prior to infection would be required.

“Reset” of the vaginal microbiota



Future direction

- ▶ Antibiotic-sparing approaches
 - ▶ Rising STI rates and challenges surrounding antibiotic resistance
- ▶ Combinations of treatments
 - ▶ Transplants of healthy vaginal fluid, synthetic or rationally assembled consortia of bacteria (next-generation live biotherapeutics)
 - ▶ Small molecules that target biofilm or specific pathogens
- ▶ Target both the male and female microbiota at the same time



Thank you for your attention!