Vaginal Microbiome: Its Role in Behavior and Infections

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Disclosures

None

Learning Objectives

- Understanding the Human vaginal microbiome
- Vaginal microbiome and relation to menses, reproductive age and menopause
- Relation of vaginal microbiome to infections and STD

The New York Times Magazine

Annals of Science

Germs Are Us

Bacteria make us sick. Do they also keep us alive?

by Michael Specter October 22, 2012

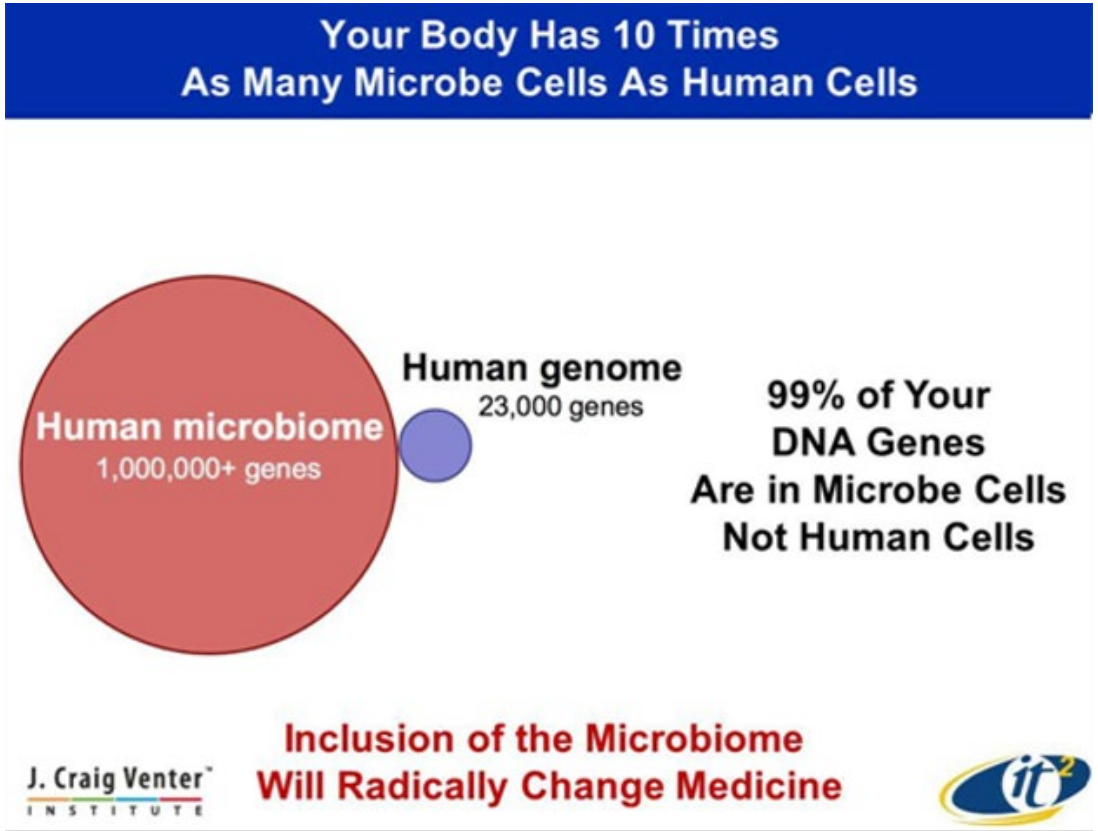
Definition of Microbiota

All the microbes (trillions!) we share our bodies with

Bacteria > Other organisms (e.g. Viruses, Fungi)

We are at least as much "**bacteria**" as we are human!

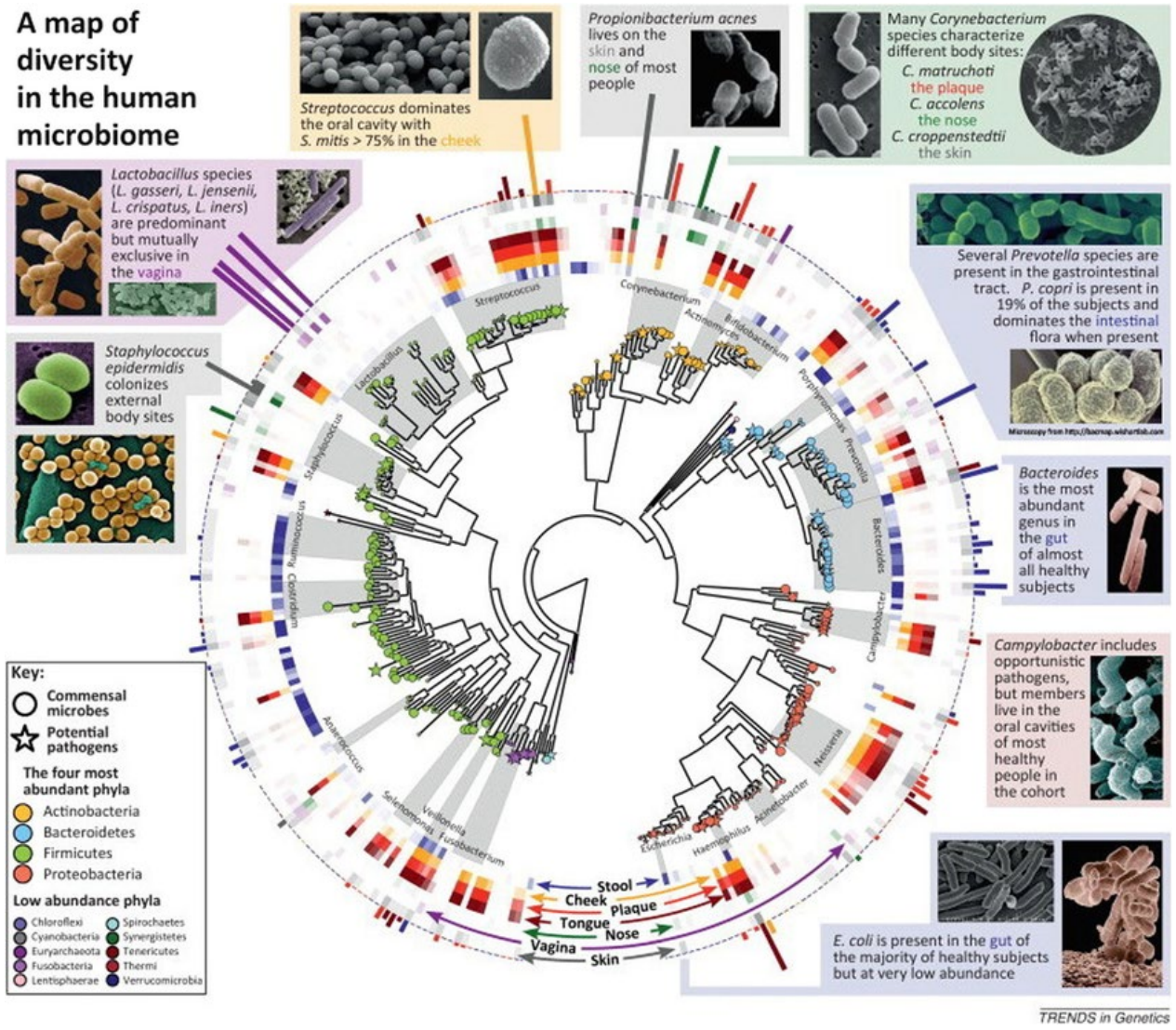
Concept of Supraorganism



No two people have the same gene

The Make-up of the Human Microbiome

We each differ!



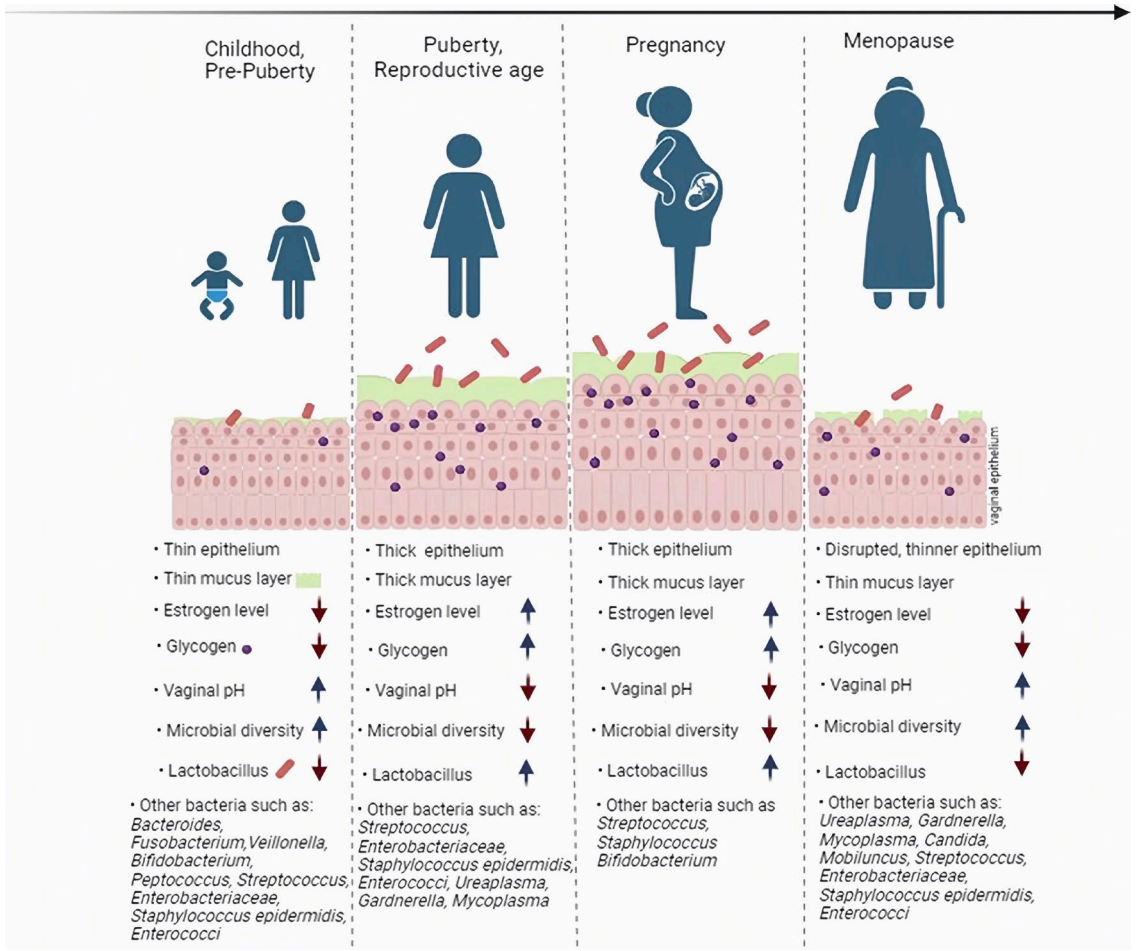
Biodiversity and functional genomics in the human microbiome

Vaginal Microbiome

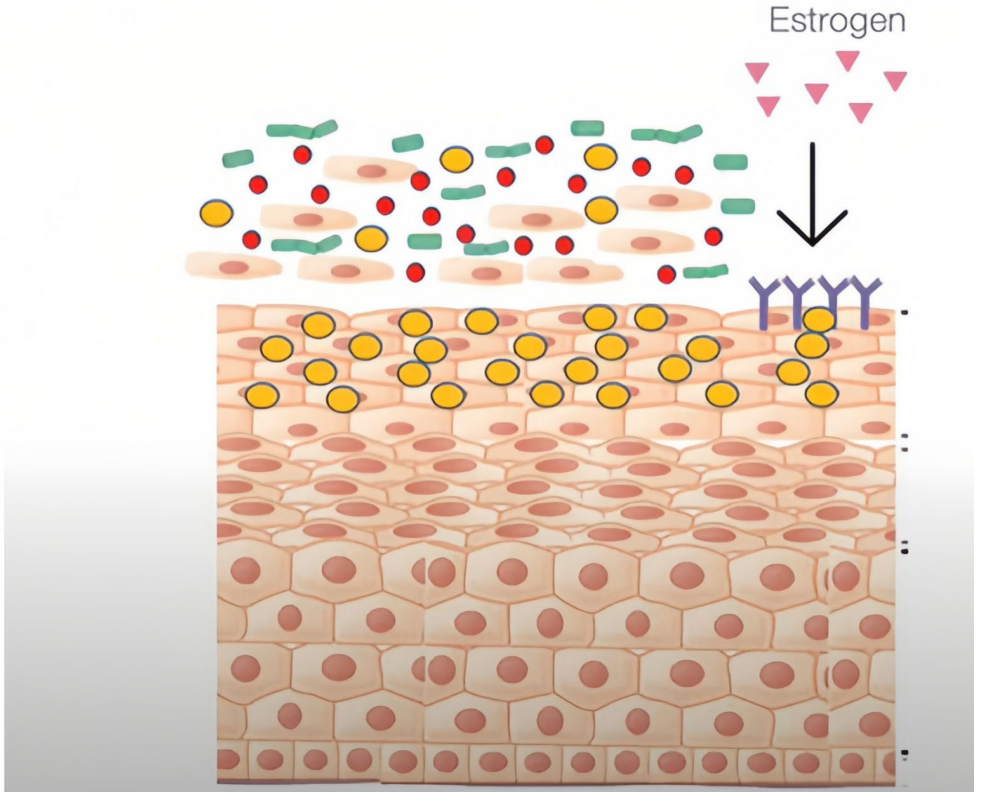
Vaginal Microbiome

- Unique as compared to gut microbiome
- Only one microbiota: Lactobacillus
- Dominance is equivalent to optimal vaginal microbiota
- Lactic acid producers and acidify the vaginal pH<4
- Acidic environment restricts the growth of non-indigenous microbes
- Changes all throughout women's lifespan.

The Vaginal Microbiota through the Lifespan

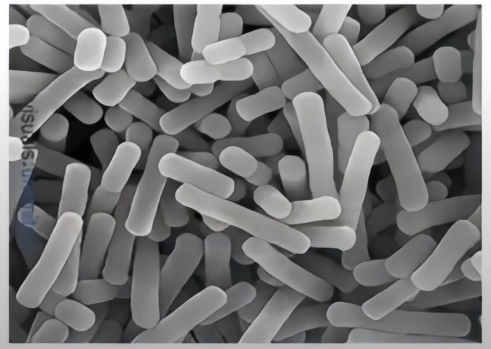


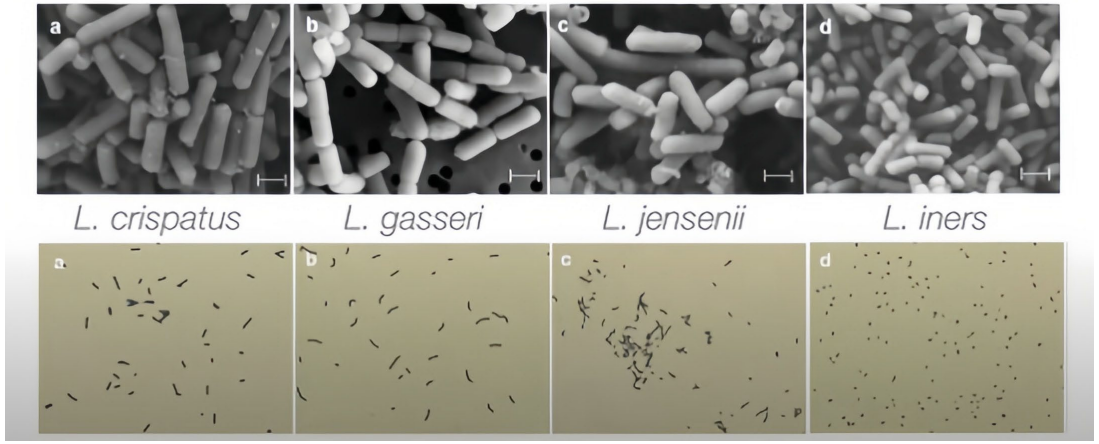
Estrogen and Epithelial Cell Maturation



Vaginal Lactobacilli

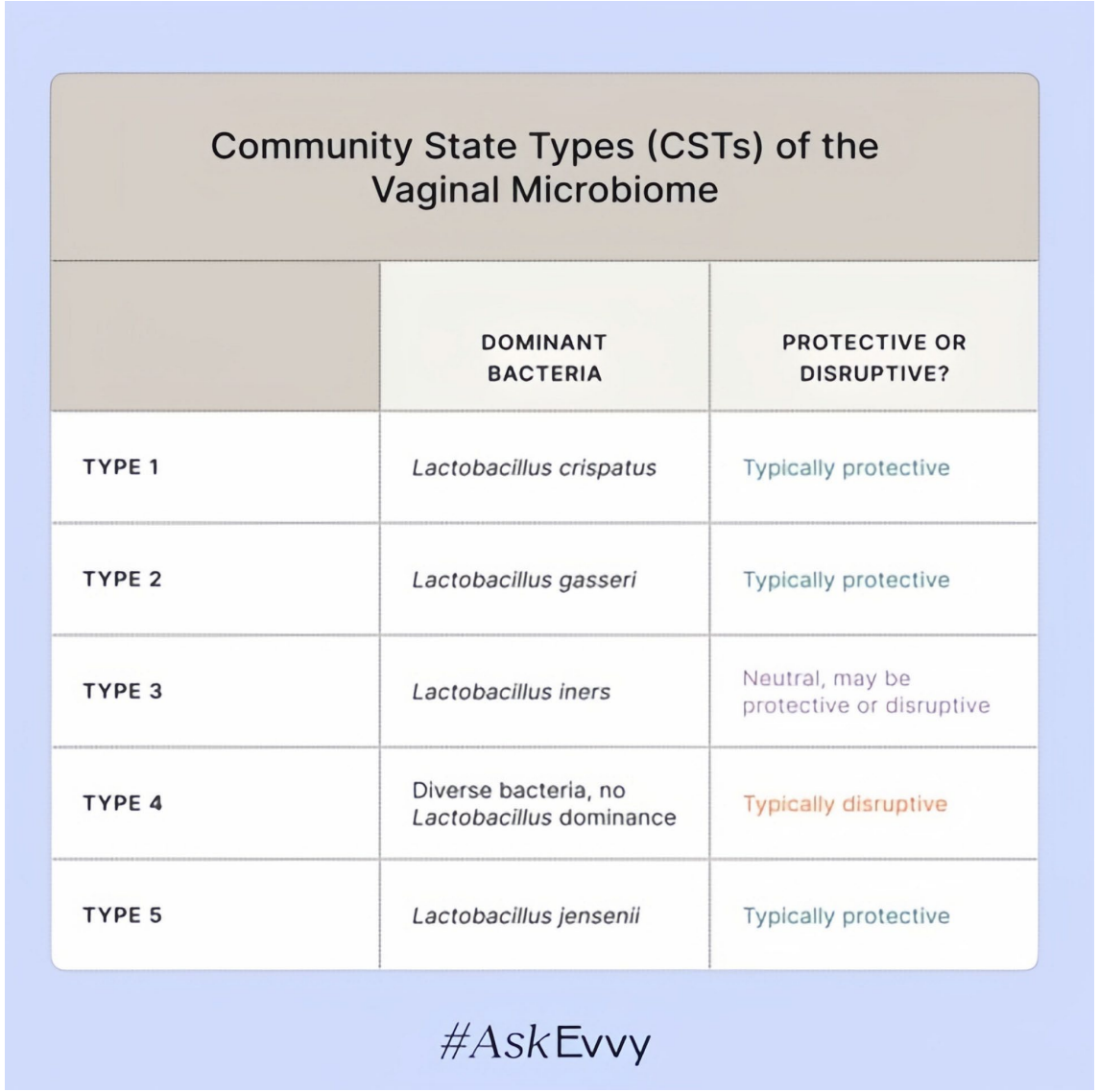
- Gram positive
- Facultative or microaerophilic anaerobe
- Rod shaped
- Non-spore forming





- Produces lactic acid
- Reduces pH
- Produces bacteriocins and anti-microbial products (H2O2)
- Prevents pathogens colonization

Community State Types (CST) of Vaginal Microbiome



Community State Types (CSTs) of the Vaginal Microbiome

	DOMINANT BACTERIA	PROTECTIVE OR DISRUPTIVE?
TYPE 1	*Lactobacillus crispatus*	Typically protective
TYPE 2	*Lactobacillus gasseri*	Typically protective
TYPE 3	*Lactobacillus iners*	Neutral, may be protective or disruptive
TYPE 4	Diverse bacteria, no *Lactobacillus* dominance	Typically disruptive
TYPE 5	*Lactobacillus jensenii*	Typically protective

#AskEvvy

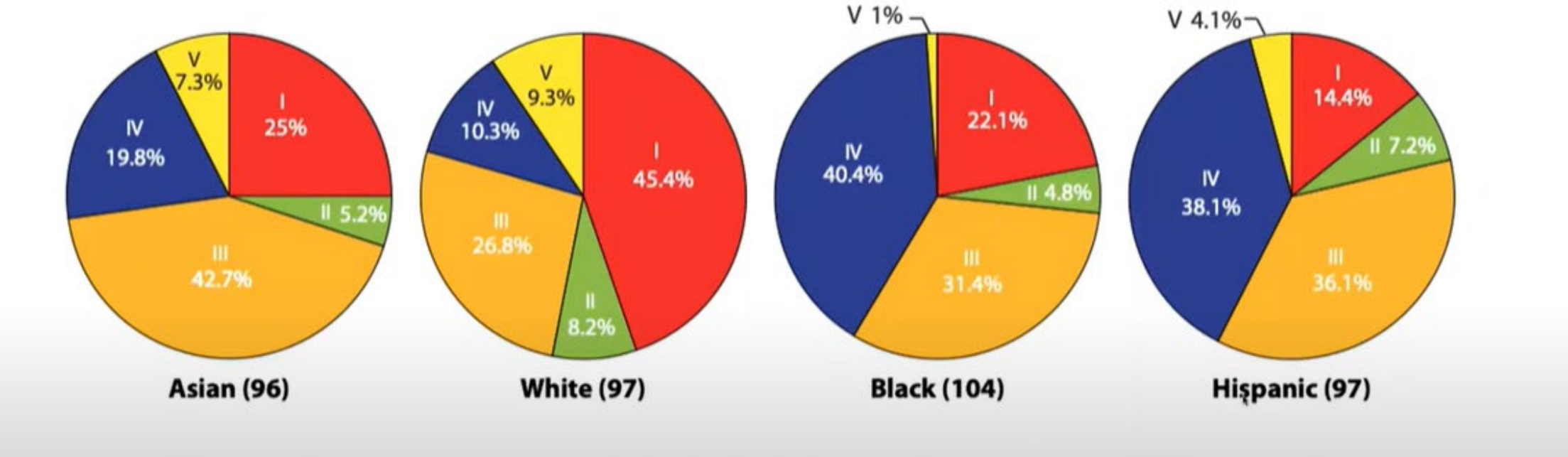
Factors that Influence the Normal Vaginal Microbiome

Ethnicity	Diet	Exercise and Body Mass index	Stress
Smoking	Hygiene practices	Sexual intercourse	Menstrual cycle
Contraception	Pregnancy	Menopause	Hygiene practices

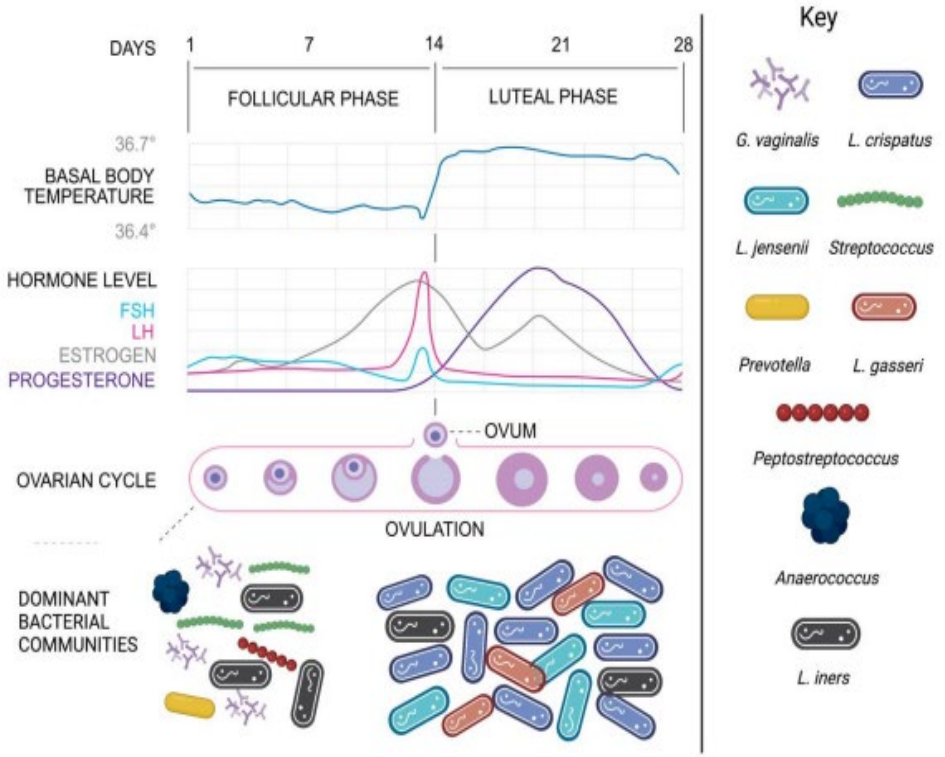
Disruption of the Vaginal Ecosystem

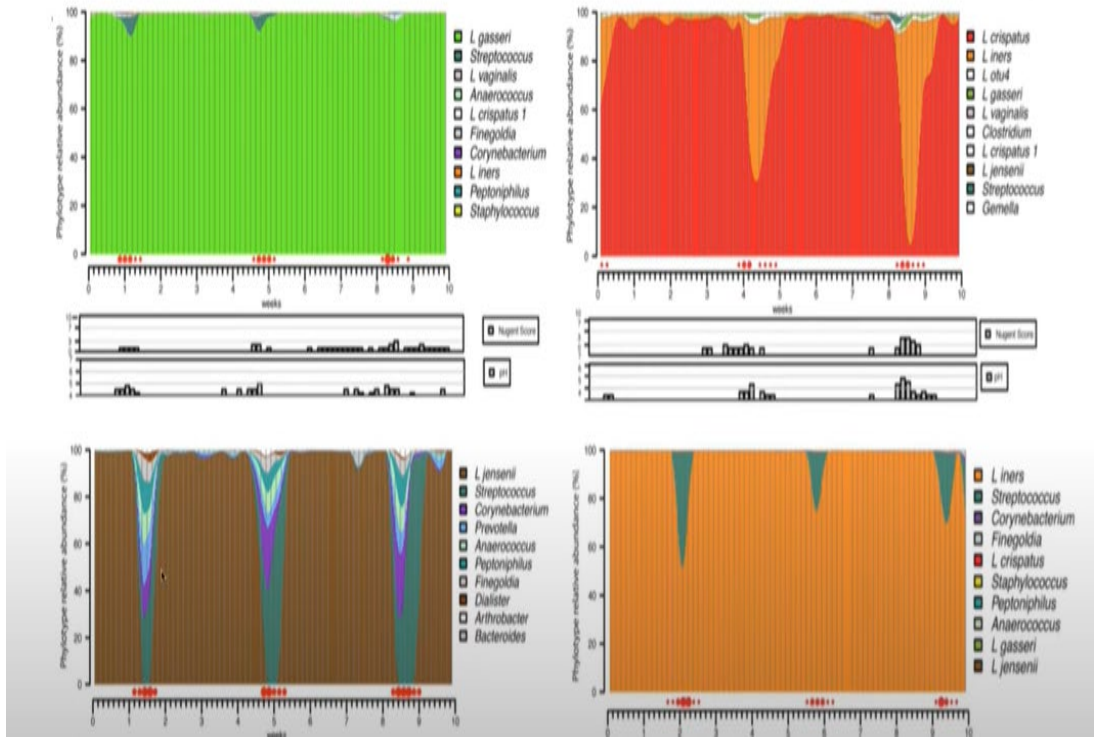
- Vaginal Infections
- Bacterial Vaginosis
- Candidiasis
- Urinary tract infections
- Sexually transmitted infections
- Pelvic Inflammatory Disease
- Complications of fertility and pregnancy

Frequency of CST in Ethnic Groups- *Ravel et al.*

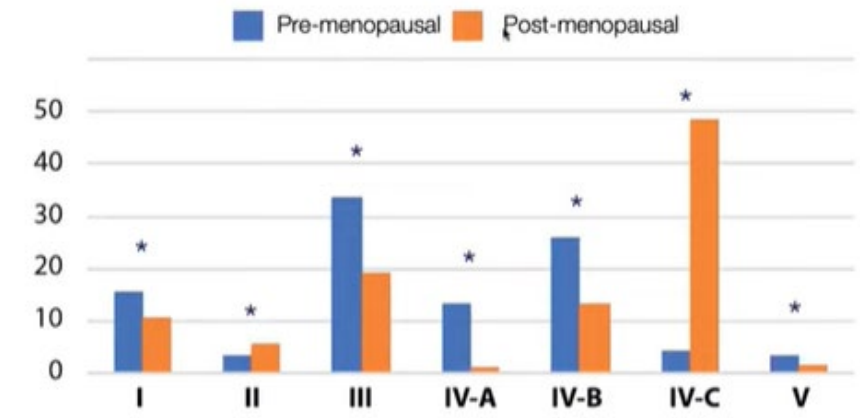


Menstrual Cycle





Vaginal Microbiota in Menopause



- CST frequency in pre and post menopausal women

Menopause: The Journal of The North American Menopause Society
Vol. 21, No. 5, pp. 450-458
DOI: 10.1097/gme.0b013e3182a4690b

Association between the vaginal microbiota, menopause status, and signs of vulvovaginal atrophy

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Factors that Influence the Normal Vaginal Microbiome

- Diet- Increased CHO intake fuels lactobacillus sp.

  High glycemic index, fats, low micronutrient intake- Vit A, C, D Folate and calcium- favors BV.

- BMI- Raglan et al. studied Obese vs non-Obese woman
- Stress- Chronic stress, Pregnancy, Psychosocial and community stress- increases cortisol and BV.

Factors that Influence the Normal Vaginal Microbiome

Smoking - 3 mechanisms by which tobacco affects the human body and predisposes to BV

- Nicotine accumulates in cervical mucus
- Accumulation of vaginal amines and anti-estrogenic effect
- Trace amounts of Benzo pyrene diol epoxide (BPDE): Increase bacteriophage induction of lactobacilli

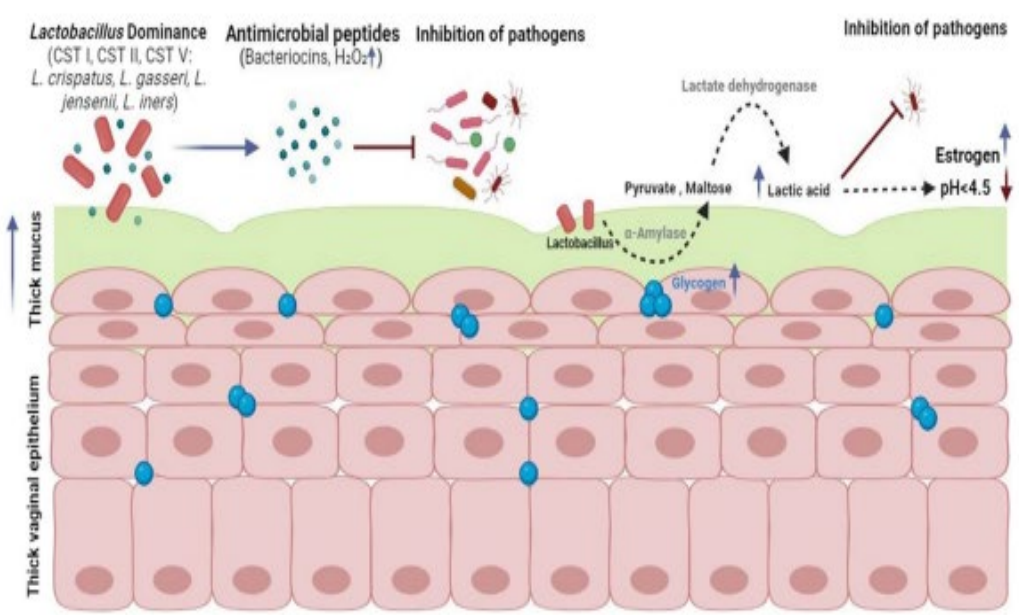
Impact of Vaginal Microbiome on Health

Bacterial Vaginosis

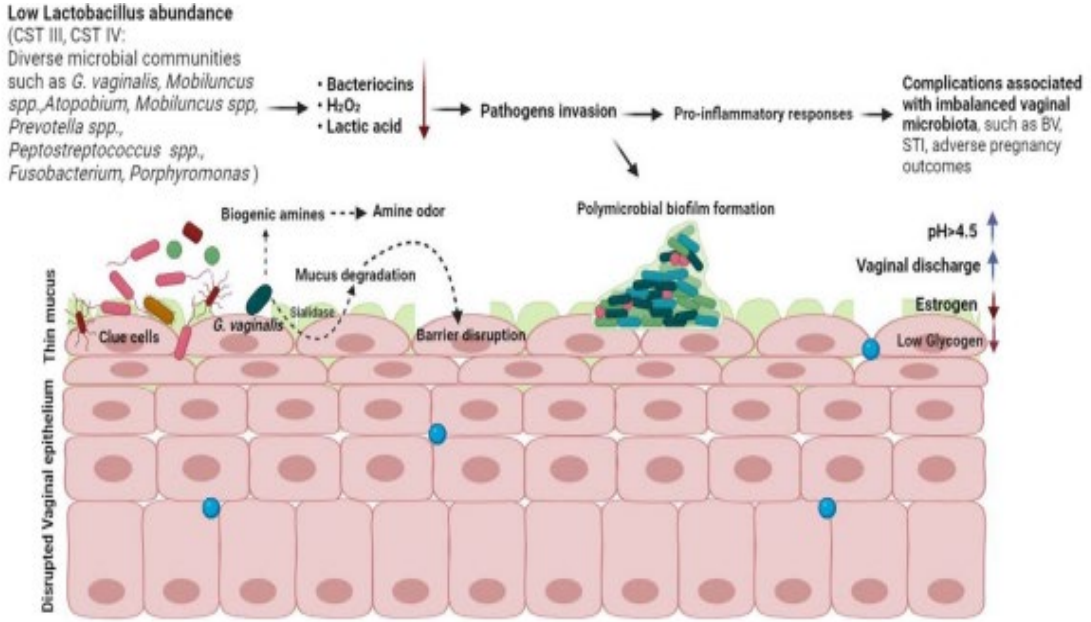
- Inflammatory condition caused by vaginal dysbiosis
- Imbalance between lactobacilli and anerobic bacteria (G.Vaginalis, prevotella, mobiluncus)
- 10-15 million doctor visits per year in the US, economic burden 4.8 billion USD
- BV can be symptomatic but often asymptomatic
- Report of symptoms include thin, gray, white or green vaginal discharge, foul smelling “fishy” vaginal odor, vaginal itching and burning during urination.

Mechanism of Action: G Vaginalis

Normal vaginal microbiota and Lactobacillus mechanism of action



Dysbiosis of vaginal microbiota and mechanisms of G. vaginalis virulence



Diagnostic Criteria for BV

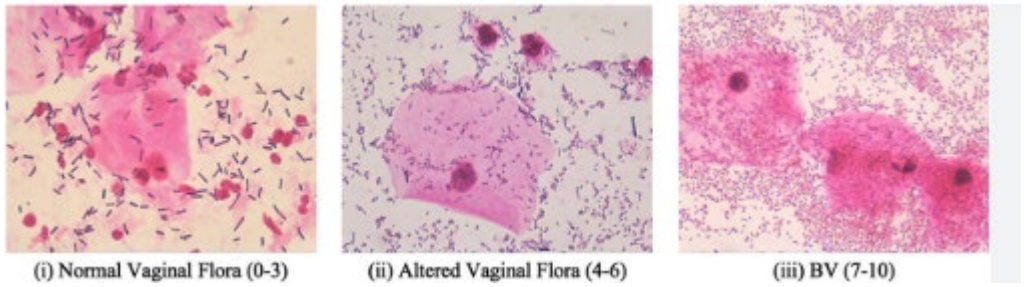
- Thin, white, homogenous discharge
- Clue cells on wet mount microscopy
- pH of vaginal fluid >4.5
- Whiff test- positive for amines

Point-of-care test

- FemExam card- measures amines, pH, peptides
- OSOM BV Blue- measures sialidase

Nugent score: Alternative

- Gram stain microscopy
- Compares lactobacilli vs Gardnerella sp



Molecular Diagnostics: PCR

- **NuSwab- BV** (Atopobium vaginae, BVAB-2, Megaspherae-1), Candida albicans, Candida glabrata, Trichomonas vaginalis. Results 3-5 days
- **NuSwab Plus**- BV (Atopobium vaginae, BVAB-2, Megaspherae-1), Candida albicans, Candida glabrata, Trichomonas vaginalis, Chlamydia trachomatis, Neisseria gonorrhea.
- **SureSwab**- qPCR: BV (Atopobium vaginae, G vaginalis, Megaspherae-1), Candida albicans, Candida glabrata, Trichomonas vaginalis, Chlamydia trachomatis, Neisseria gonorrhea and lactobacillus sp (crispatus, Jensenii). Results in 1-2 days.
- **BD max vaginal panel**: L. jensenii and L. crispatus and four BV associated microorganisms (G. vaginalis, BVAB2, Megasphaera type 1, and A. vaginae), candida sp and antimicrobial resistance (by reporting C Kruseii and Glabrata)

BV Treatment

- **Antibiotics** - metronidazole, clindamycin
- **Antibiotics alternatives** - Tinidazole, secnidazole
- **Newer therapies** - probiotics, prebiotics, boric acid, DNases, antiseptics, acidifying agents, retrocyclins, vaginal microbiota transplantation, and natural antimicrobial agents.
- **Biofilm-disrupting agents** - Lauramide Arginine Ethyl Ester, Endolysin (subtilosin, polylysine), Thymol, and Boric Acid
- **Combining antibiotics** with biofilm-disrupting agents
- **Postmenopausal woman** - Estradiol treatment.

Recommended and Alternative Regimens

Metronidazole 500 mg orally 2 times/day for 7 days

OR

Metronidazole gel 0.75% one full applicator (5 g) intravaginally, once a day for 5 days

OR

Clindamycin cream 2% one full applicator (5 g) intravaginally at bedtime for 7 days

Clindamycin 300 mg orally 2 times/day for 7 days

OR

Clindamycin ovules 100 mg* intravaginally once at bedtime for 3 days

OR

Secnidazole 2 g oral granules in a single dose†

OR

Tinidazole 2 g orally once daily for 2 days

OR

Tinidazole 1 g orally once daily for 5 days

Recurrent BV Treatment

Extended Metronidazole regimen:

- **Induction**- Oral metronidazole or tinidazole 500mg twice daily for 7 days (tinidazole is not for use in pregnancy and lactation)

  OR

  Metrogel 0.75% (5g) dose intravaginally twice daily for 7 d

Followed by

- **Maintenance**

  Metrogel 0.75% (5g) dose intravaginally twice weekly for 4-6 month (prophylaxis for recurrence).

Vaginal Boric acid regimen:

- **Induction-** Oral metronidazole or tinidazole 500mg twice daily for 7 days

  PLUS

  Vaginal boric acid 600mg inserted daily at night

Followed by

- **Maintenance**

  After nitromidazole treatment is stopped, continue vaginal boric acid for a total of 30 days.

- **Optional Suppression**

  Metrogel 0.75% (5g) dose intravaginally twice weekly for 4-6 month

Male Partner Treatment- Prevent Recurrent BV

Male-Partner Treatment to Prevent Recurrence of Bacterial Vaginosis

Authors: Lenka A. Vodstrcil, Ph.D. , Erica L. Plummer, Ph.D., Christopher K. Fairley, Ph.D., Jane S. Hocking, Ph.D., Matthew G. Law, Ph.D., Kathy Petoumenos, Ph.D., Deborah Bateson, M.D., +6 , for the StepUp Team* Author Info & Affiliations

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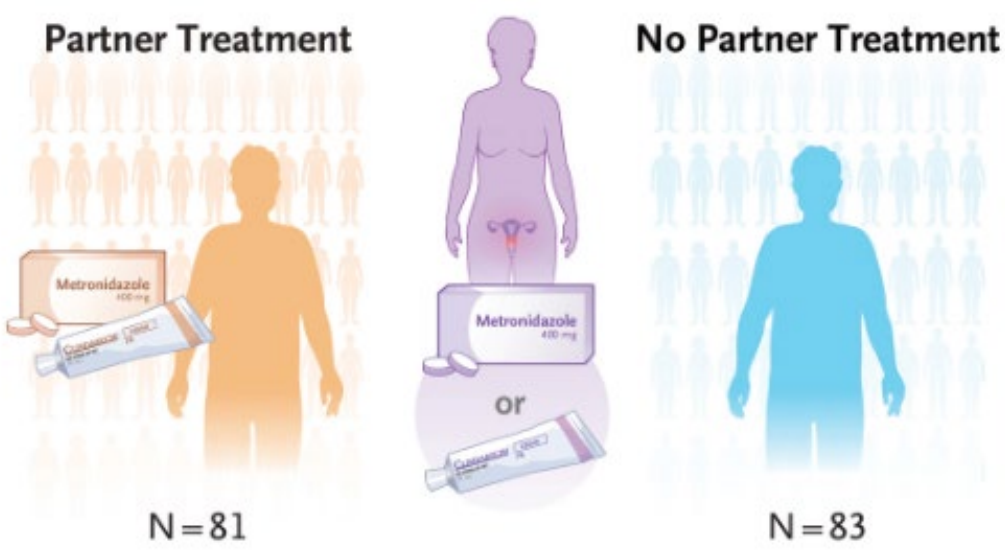
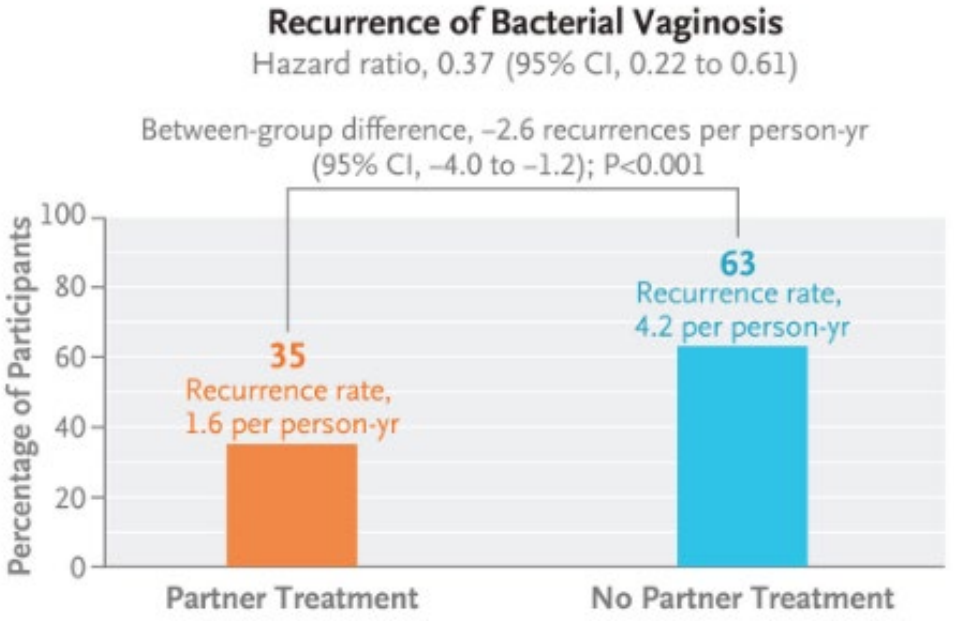
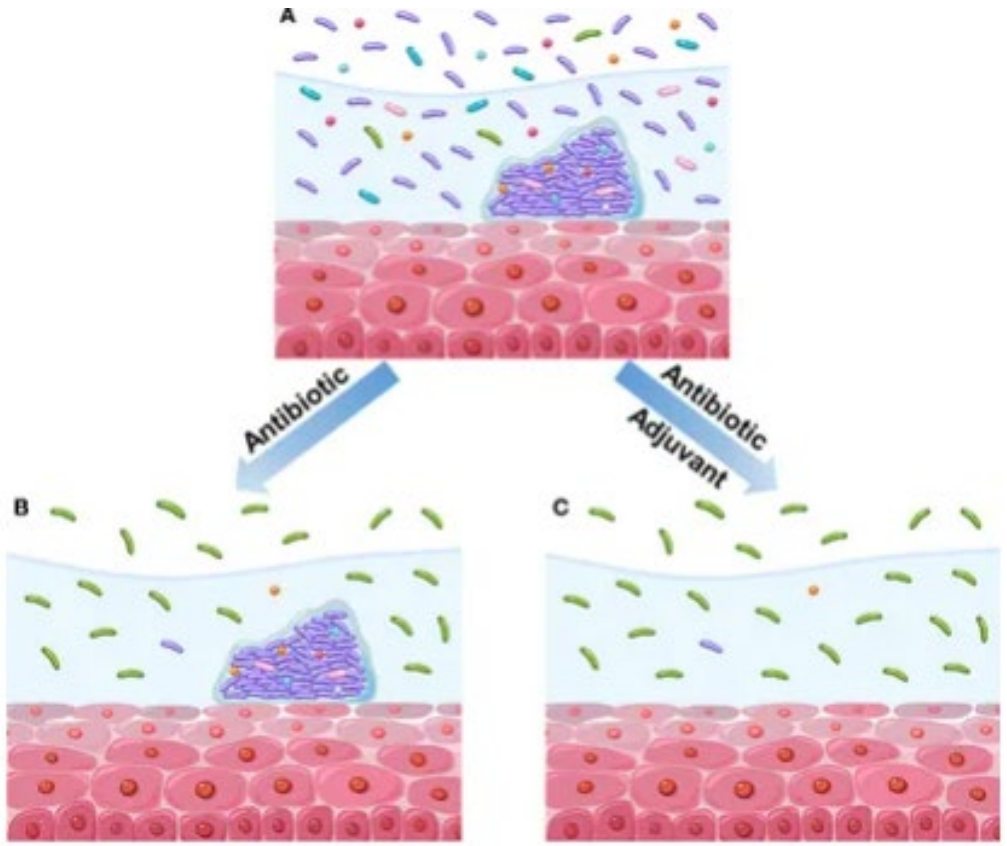
Male Partner Treatment- Prevent Recurrent BV





Probiotics

- Live microorganisms
- Investigational
- Oral or vaginal lactobacillus
- Efficacious when combined with antibiotics
- L acidophilus (LACTIN V), L rhamnosus GR-1 and L reuteri RC-14 strains
- Used for a total of 12 weeks after vaginal metrogel of 5 days
- Natural dairy foods - yogurt, Kefir, cheese, buttermilk.
- Natural fermented foods- sauerkraut, kimchi, kombucha, pickles, cider vinegar.



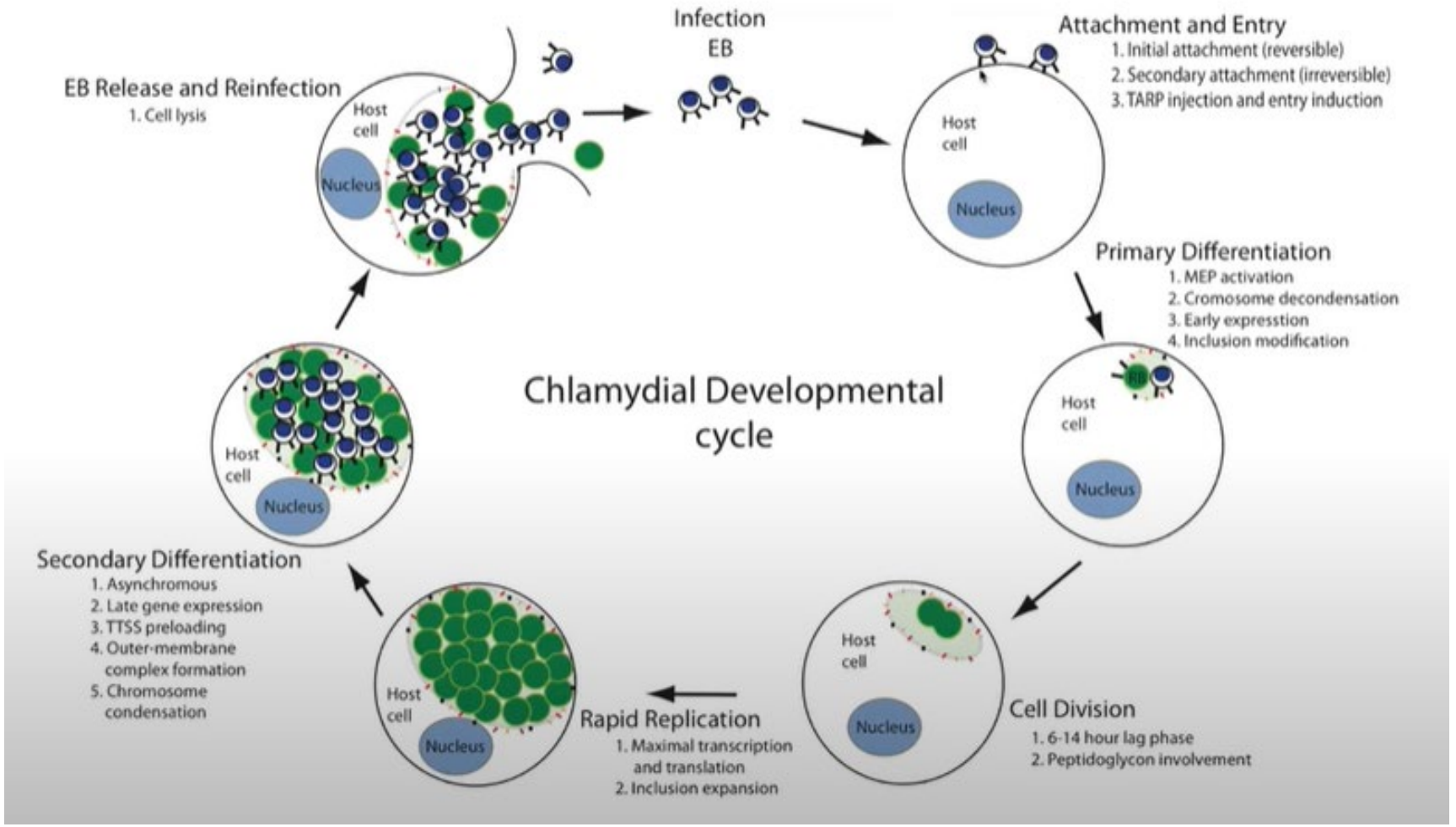
Consequences of Dysbiosis

BV-Associated Diseases

- Increases risk of STI - HSV2, HIV, HPV, Chlamydia, Gonorrhea and Trichomonas
- PID and adverse reproductive outcomes - Infertility, chronic pelvic pain and ectopic pregnancy
- Obstetric outcomes - Late miscarriage, preterm birth and maternal infections

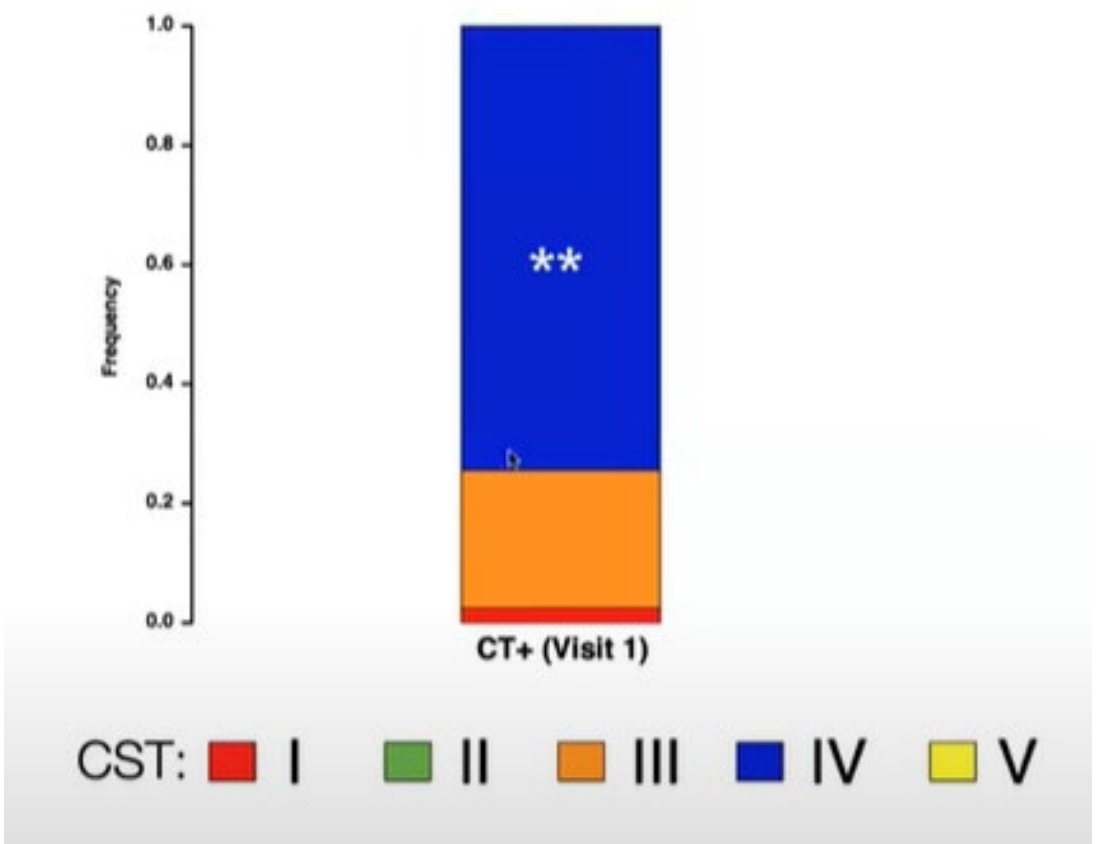
STI and the Vaginal Microbiota

Chlamydia Infection



Vaginal Microbiota and Chlamydial Infection

- 150 CT + woman
- Azithromycin treated
- Resampled 3 months later



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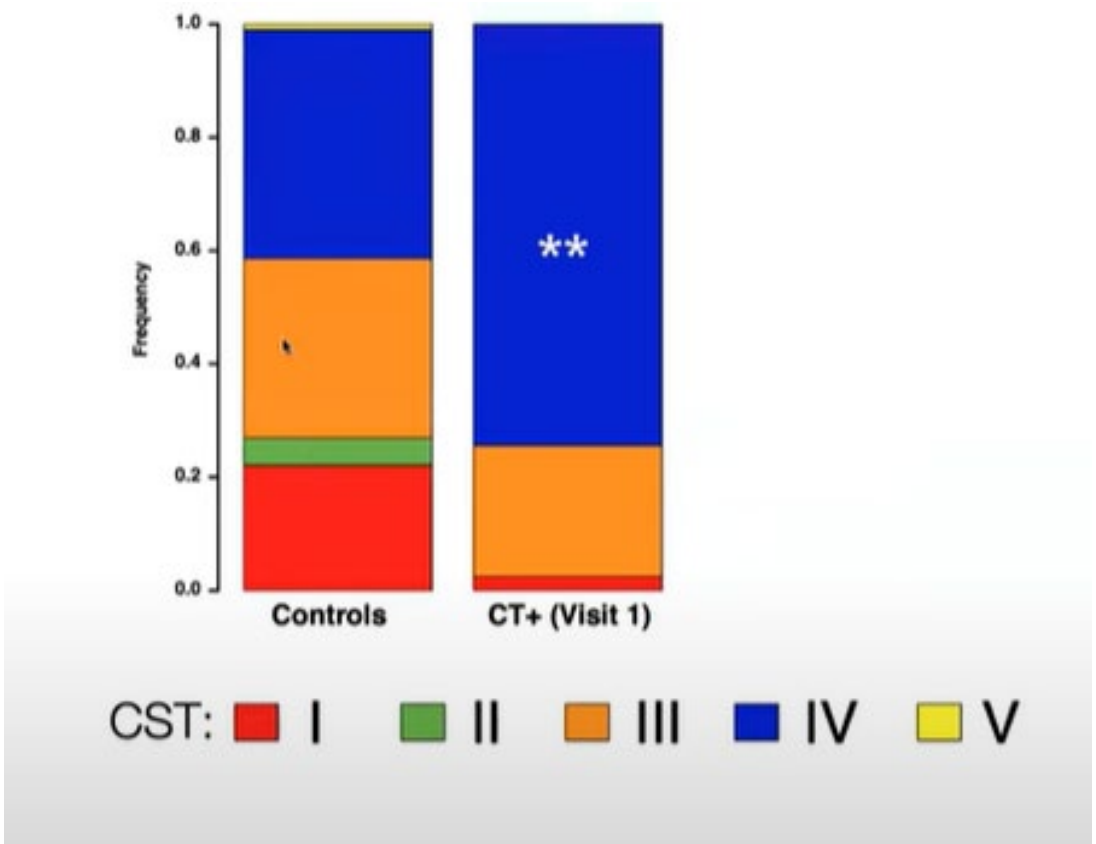

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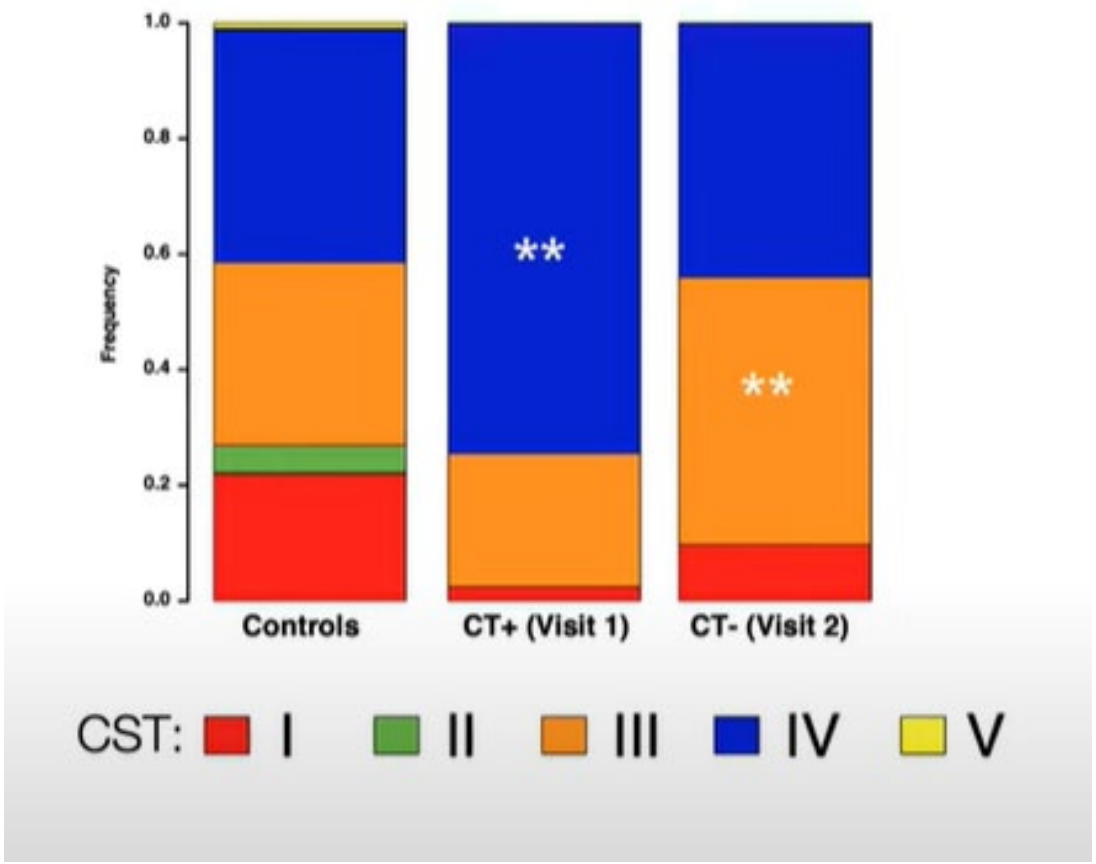
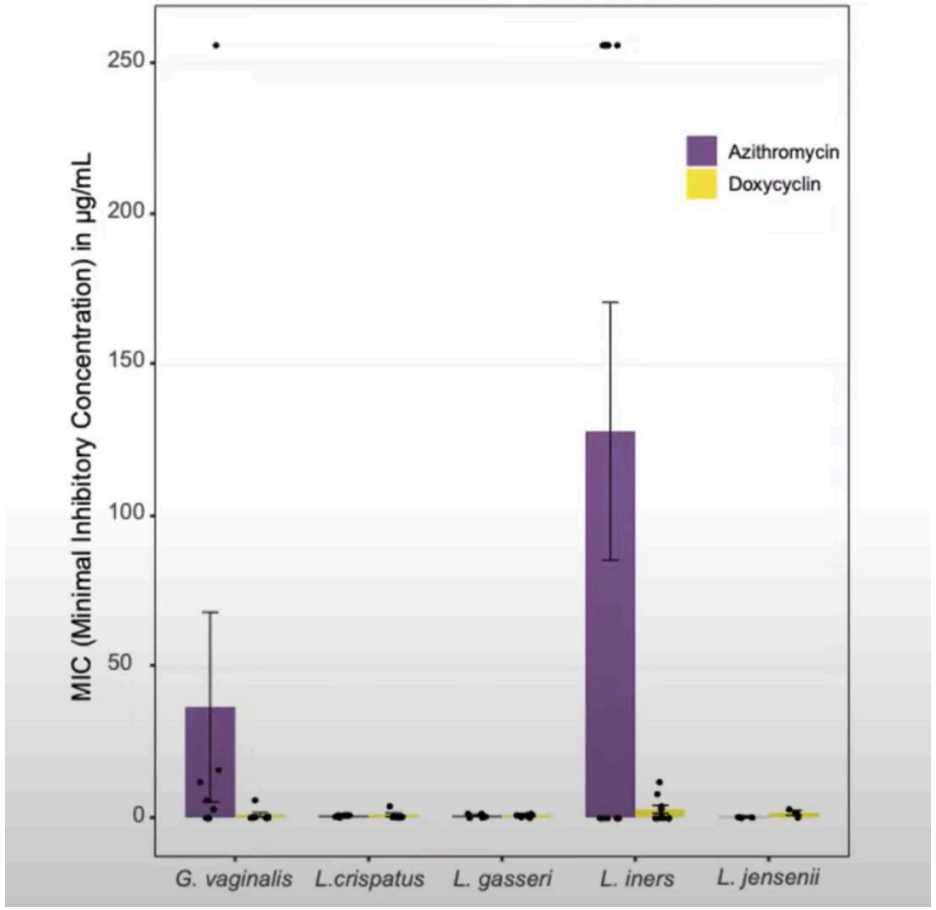
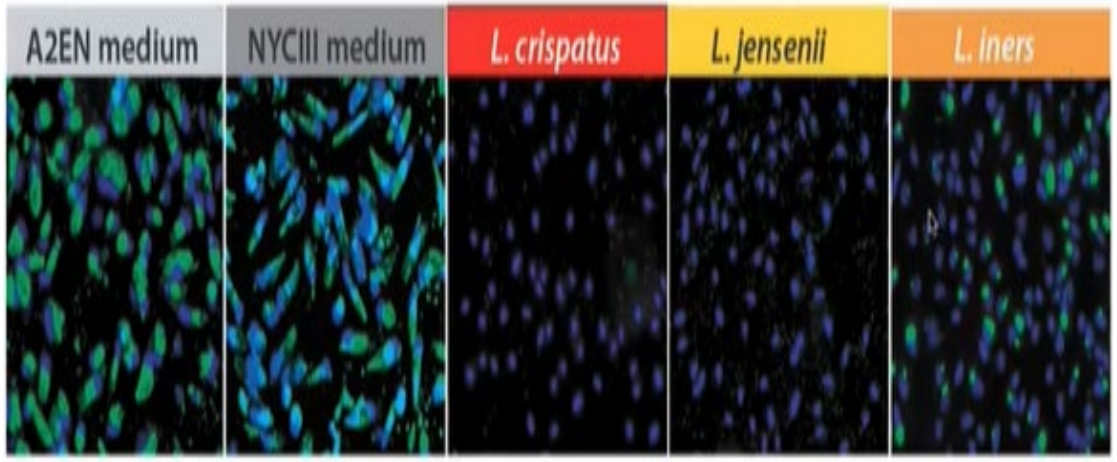


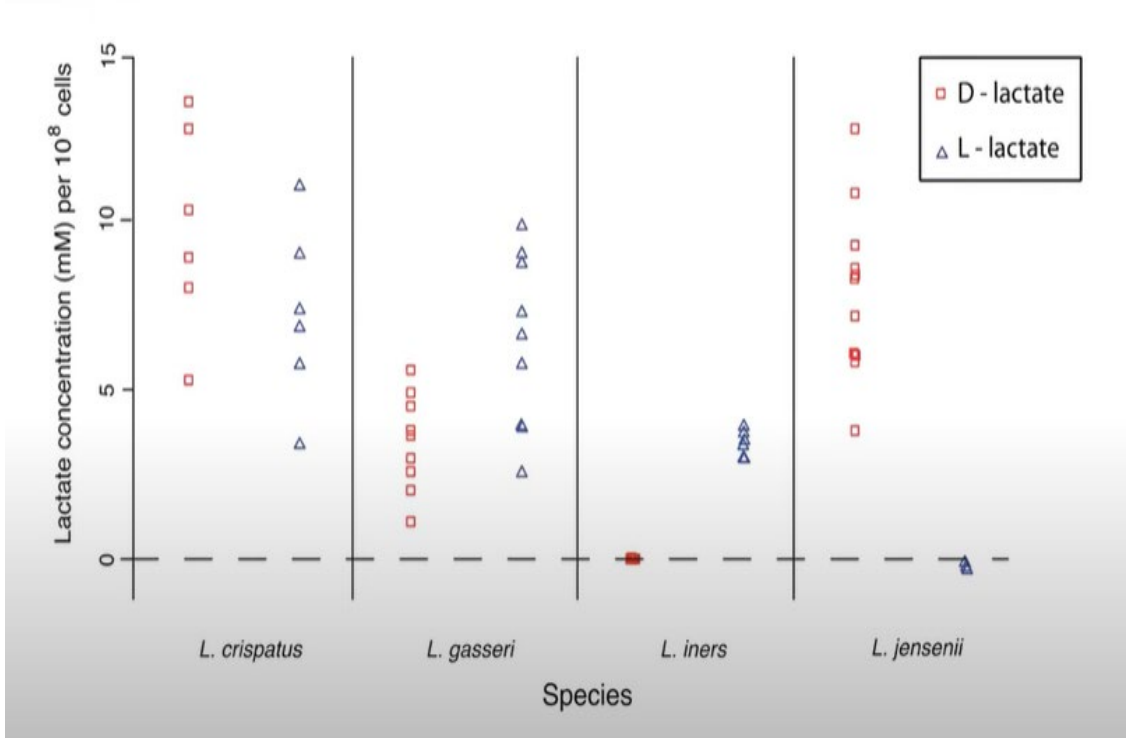
Vaginal Bacteria Antimicrobial Resistance



- AZT is resistant to G Vaginalis and L Iners.
- Doxycycline is sensitive to all species of bacteria.

Lactobacillus sp Affect Chlamydia in Vitro





Conclusion

- Different types of vaginal microbiota that differ in bacterial composition and protection against infections.
- Hygiene practices, sexual practices, smoking, obesity, contraception, and lubricant use, among others, can affect the composition of vaginal microbiota.
- Lactic acid is an essential metabolite that can affect host physiology and resistance to STIs such as chlamydia.

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Questions?