the *vaginal microbiome* after menopause

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# Urogenital symptoms of menopause

<table>
<thead>
<tr>
<th>Urogenital symptoms</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urogenital symptoms</td>
<td>50%</td>
</tr>
<tr>
<td>Recurrent urinary tract infections</td>
<td>5-17%</td>
</tr>
<tr>
<td>Vaginal dryness or itching</td>
<td>47%</td>
</tr>
<tr>
<td>Painful sex</td>
<td>15-35%</td>
</tr>
</tbody>
</table>
Prepuberty

- High pH
- Diverse microbiota
- Low levels of estrogen
- Mucus
- Squamous epithelium
- Low levels of glycogen
- Thin vaginal mucosa

Adult

- Low pH
- H₂O₂
- L. iners
- L. crispatus
- Mucus
- Thick vaginal mucosa
- Glycogen
- Deposition of glycogen
- Degradation to glucose

Postmenopause

- High pH
- Diverse microbiota
- Low levels of estrogen
- Mucus
- Squamous epithelium
- Low levels of glycogen
- Thin vaginal mucosa

Petrova et al. FEMS Microbiol Rev 2013
AVOTE FOR BLUE
IS A VOTE FOR YOU

THE REDOLUTION IS NOW!

VOTE RED
Which species dominate the vaginal microbiome after menopause?

Lactobacilli

Anaerobes
Vagal Microbiome and Epithelial Gene Array in Post-Menopausal Women with Moderate to Severe Dryness

Ruben Hummelen¹,², Jean M. Macklaim¹,³, Jordan E. Bisanz¹,⁴, Jo-Anne Hammond¹,⁵, Amy McMillan¹,⁴, Rebecca Vongsa⁶, David Koenig⁶, Gregory B. Gloor¹,³, Gregor Reid¹,⁴

32 women after menopause

- 8 with symptoms
- 8 without symptoms

Follow-up every 2 weeks for 10 weeks
- Microbial profile
- Symptoms
Microbiome after menopause

Same players – different constitution
Lactobacilli dominate the vaginal microbiome
Which species are associated with urogenital symptoms of menopause?

*Prevotella*

*Gardnerella*
Inverse correlation between lactobacilli and symptoms

*Prevotella* and *Peptoniphilus* associated with severe symptoms
Association between the vaginal microbiota, menopause status, and signs of vulvovaginal atrophy

Rebecca M. Brotman, PhD, MPH,1,2 Michelle D. Shardell, PhD,2 Pawel Gajer, PhD,1 Doug Fadrosh, MS,1 Kathryn Chang, RN,3 Michelle I. Silver, ScM,3 Raphael P. Viscidi, MD,4 Anne E. Burke, MD, MPH,5 Jacques Ravel, PhD,1,6 and Patti E. Gravitt, PhD, MS3

<table>
<thead>
<tr>
<th>Vaginal atrophy</th>
<th>CST I (Lactobacillus crispatus)</th>
<th>CST II (Lactobacillus gasseri)</th>
<th>CST III (Lactobacillus iners)</th>
<th>CST IV-A (low Lactobacillus diverse)</th>
<th>CST IV-B (Atopobium, Gardnerella)</th>
<th>CST V (Lactobacillus jensenii)</th>
<th>P^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>21 (84.0)</td>
<td>6 (100.0)</td>
<td>21 (91.3)</td>
<td>2 (22.2)</td>
<td>8 (61.5)</td>
<td>2 (66.7)</td>
<td>0.002</td>
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<tr>
<td>Mild</td>
<td>3 (12.0)</td>
<td>0 (0.0)</td>
<td>2 (8.7)</td>
<td>3 (33.3)</td>
<td>4 (30.8)</td>
<td>1 (33.3)</td>
<td></td>
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<tr>
<td>Moderate</td>
<td>1 (4.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>4 (44.4)</td>
<td>1 (7.7)</td>
<td>0 (0.0)</td>
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<tr>
<td>Vaginal dryness</td>
<td>None</td>
<td>23 (92.0)</td>
<td>21 (91.3)</td>
<td>5 (55.6)</td>
<td>10 (76.9)</td>
<td>2 (66.7)</td>
<td>0.011</td>
</tr>
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<td>1 (4.0)</td>
<td>0 (0.0)</td>
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<td>4 (44.4)</td>
<td>0 (0.0)</td>
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<tr>
<td>Severe</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (7.7)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
</tbody>
</table>

Symptoms associated with IV-A type microbiota

Menopause
The Journal of The North American Menopause Society
Low in lactobacillus and high in *Prevotella* and *Peptostreptococcus*.
How stable is the vaginal microbiome after menopause?

A unique individual microbiome exists

Species are transient
Microbiome dynamics

Diversity did not change significantly over time
Can probiotics colonize the vaginal tract?

Yes, for several weeks

Not at all
A Systems Biology Approach Investigating the Effect of Probiotics on the Vaginal Microbiome and Host Responses in a Double Blind, Placebo-Controlled Clinical Trial of Post-Menopausal Women

14 women after menopause

7 women probiotics

washout period

7 women placebo

7 women placebo

washout period

7 women probiotics
Lactobacillus rhamnosus GR-1
Lactobacillus reuteri RC-14

Placebo administered
Probiotic administered

Lactobacillus rhamnosus GR-1
Lactobacillus reuteri RC-14
Can the vaginal microbiome be changed by probiotics?

Yes, reduction of anaerobes

Nope
Probiotics increase abundance of *Lactobacillus*
Decrease abundance of *Atopobium*, trend to decrease *Prevotella* and *Gardnerella*
Can probiotics reduce the genitourinary symptoms of menopause?

Yes, reduction of urinary tract infections

Nope
Lactobacilli vs Antibiotics to Prevent Urinary Tract Infections

A Randomized, Double-blind, Noninferiority Trial in Postmenopausal Women

Mariëlle A. J. Beerepoot, MD; Gerben ter Riet, MD, PhD; Sita Nys, PhD; Willem M. van der Wal, PhD; Corianne A. J. M. de Borgie, MD, PhD; Theo M. de Reijke, MD, PhD; Jan M. Prins, MD, PhD; Jeanne Koeijers, MD; Annelies Verbon, MD, PhD; Ellen Stobberingh, PhD; Suzanne E. Geerlings, MD, PhD

252 women after menopause with >3 urinary tract infections/year
Randomized to oral lactobacilli (GR-1 and RC-14) or prophylactic antibiotics

Before prophylaxis patients reported 7 urinary tract infections per year

During the study the mean number of recurrences was 2.9 in the antibiotics groups vs 3.3 in the probiotics group per year (P = 0.4)
Lactobacilli vs Antibiotics to Prevent Urinary Tract Infections

A Randomized, Double-blind, Noninferiority Trial in Postmenopausal Women

Mean time to recurrence was 3 months in the probiotic group vs 6 months in the antibiotic group
Original Investigation

Lactobacilli vs Antibiotics to Prevent Urinary Tract Infections

A Randomized, Double-blind, Noninferiority Trial in Postmenopausal Women

Antibiotics

Lactobacilli
The postmenopausal vaginal microbiome...

same players – different constitution
is stable
lactobacilli inversely related to symptoms
Prevotella and Peptinophilus are not
can be transiently colonized by probiotics