When lactobacilli dominate they inactivate HIV and BV bacteria with lactic acid

D.E. O’Hanlon (JHU), G. Tachedjian (Burnet), T.R. Moench (ReProtect), and R.A. Cone (JHU and ReProtect)

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Increased risks if BV is present on day of entry into n prospective trials

BV increases several factors that may increase susceptibility to infections, e.g., inflammatory cytokines, degraded mucus, weak acidity.

Do lactobacilli protect against infections?

Some lactobacilli produce hydrogen peroxide (H$_2$O$_2$). Does the H$_2$O$_2$ they produce protect against infections?
Unfortunately, lactobacilli can only produce \( \text{H}_2\text{O}_2 \) when oxygen is present. In the hypoxic environment of the vagina, as well as in antioxidant rich vagina fluid, they produce < 1 micro-molar \( \text{H}_2\text{O}_2 \) (our threshold of detection).

(O’Hanlon, Lanier, Moench, and Cone, BMC Infect Dis 2010)

\[ \text{H}_2\text{O}_2 \text{ kills lactobacilli more potently than BV bacteria. How can lactobacilli use it to prevent BV?} \]

It is improbable that \( \text{H}_2\text{O}_2 \) produced by lactobacilli in the hypoxic vagina, and immersed in antioxidant rich vaginal fluid, can protect against BV, or HIV, or any other STD pathogen. Semen is also antioxidant rich.

However, \( \text{H}_2\text{O}_2 \) producing lactobacilli are strongly associated with reduced BV, and many other infections, but it is likely that \( \text{H}_2\text{O}_2 \) producing lactobacilli are best at producing something else - - - like lactic acid???

Does lactic acid produced by lactobacilli protect against infections? (As believed for most of the past century, but not after \( \text{H}_2\text{O}_2 \) emerged.)
When lactobacilli dominate (Nugent Scores 0-3):
- Vaginal pH = 3.5 ± 0.3 (pH range 3.0-3.9)
- Vaginal lactic acid concentration = 1.0 ± 0.2%
- Acetic acid < 0.003%
- $\text{H}_2\text{O}_2 < 1 \times 10^{-6}$ molar

Lactic acid potently inactivates BV bacteria while sparing lactobacilli.

The presence of vaginal fluid does not diminish the microbicidal effect of lactic acid.

Lactic acid preserves food.

Carcasses are sprayed with lactic acid as a preservative.
Effect of lactic acid on Neisseria gonorrhoeae

(incubated anaerobically at pH 4.5 for 2 hours at 37°C)

| pH 7 | pH 4.5 | Lactic acid (%) | growth | stasis | killing
|------|--------|----------------|-------|--------|-------
| <10^-7 | <10^-6 | <10^-5 | <10^-4 | <10^-3 | <10^-2 | <10^-1 |

Average vaginal concentration 1.0%

Effect of lactic acid on HSV-2 incubated at pH 4.5 for 20 minutes at 37°C as discovered by Deirdre O’Hanlon

Fraction of HSV-2 that remains infectious after 30 min exposure to pH 3.8 with HCl, D-lactic acid, and L-lactic acid

L-lactic acid is 10-fold more potent than HCl
4-fold more potent than D-LA

P<0.0001

L-lactic acid is used 1/10 vaginal LA to slow rate of inactivation

HIV is trapped in acidic cervicovaginal mucus (CVM), but not in neutralized mucus


L- LA inactivates different HIV-1 subtypes, X4 and R5 strains, patient isolates and HIV-2

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Lactic acid as produced by lactobacilli in the vagina, but not H$_2$O$_2$, can inactivate BV bacteria without inactivating lactobacilli.

- Even at pH 4.5, 1% lactic acid completely inactivates all 17 BV-associated bacteria tested to date.
- When lactobacilli dominate, they produce lactic acid rapidly enough to maintain the vagina at a mean pH of 3.5 with 1% lactic acid.
- Lactic acid potently inactivates HIV, HSV, and Neisseria gonorrhoeae.
- Lactic acid inactivates HIV in the presence of seminal and vaginal fluid, and BV-associated bacteria in the presence of vaginal fluid.

SUMMARY

- At pH 3.5, vaginal lactic acid will likely inactivate most acid-sensitive pathogens shed vaginally by infected females and reduce female-to-male transmission of infections.
- Semen transiently alkalinizes the vagina, but lactobacilli may restore acidity in the epithelium rapidly enough to help reduce male-to-female transmission of acid-sensitive pathogens.

CONCLUSIONS