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

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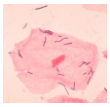
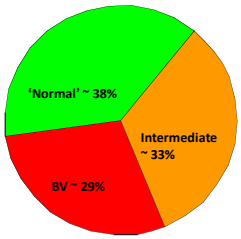
Only a minority of women have a 'normal' lactobacillus-dominated microbiota

Nugent scores 0-3 **'Normal':**
Viscoelastic Mucus
Light gram positive
monoculture
pH ~3.5
~1% Lactic acid
No acetic acid



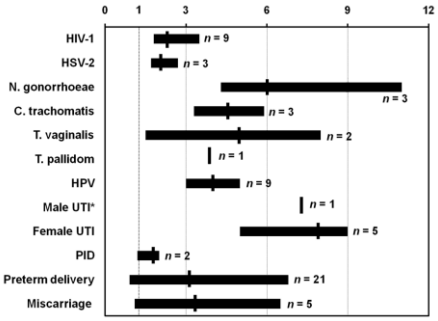
Nugent scores 7-10 **BV:**
Watery discharge
Heavy polyculture
pH ≥4.5
Succinic acid
Acetic acid
Butyric acid
Putrescine
Cadaverine
Tyramine
(fishy odor)



% of U.S.women
on any given day

Allsworth and Peipert, 2007
3,727 women, demographically balanced

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.

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Do lactobacilli *protect* against infections?

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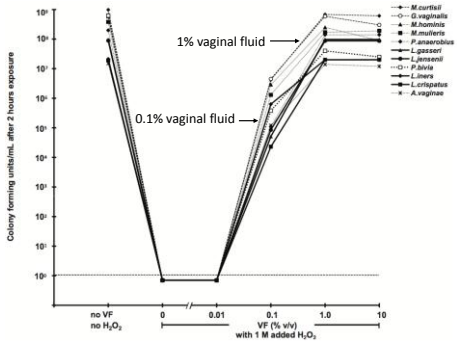
Some lactobacilli produce hydrogen peroxide (H_2O_2).
Does the H_2O_2 they produce protect against infections?

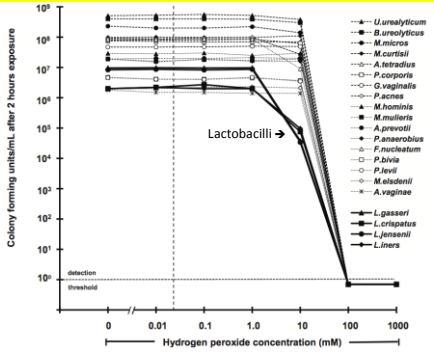
Unfortunately, lactobacilli can only produce H_2O_2 when oxygen is present.
In the hypoxic environment of the vagina, as well as in antioxidant rich vagina fluid, they produce < 1 micro-molar H_2O_2 (our threshold of detection).

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

In the presence of highly diluted vaginal fluid, even **1 Molar** H_2O_2 fails to kill BV bacteria



H_2O_2 kills *lactobacilli* more potently than BV bacteria: How can lactobacilli use it to prevent BV?

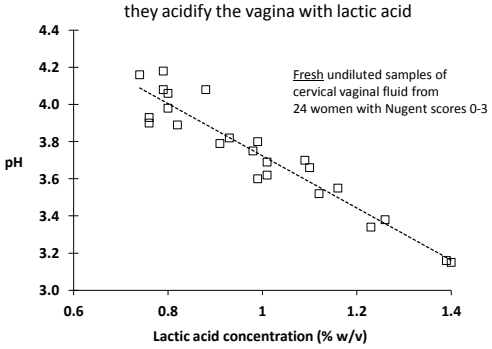


It is improbable that H_2O_2 produced by lactobacilli in the hypoxic vagina, and immersed in antioxidant rich vaginal fluid, can protect against BV, or HIV, or any other STD pathogen. Semen is also antioxidant rich.

However,
H_2O_2 producing lactobacilli are *strongly* associated with reduced BV, and many other infections, but it is likely that H_2O_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 H_2O_2 emerged.)

When lactobacilli dominate (Nugent Scores 0-3) they acidify the vagina with lactic acid



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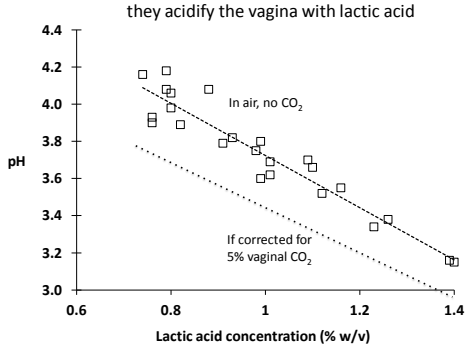
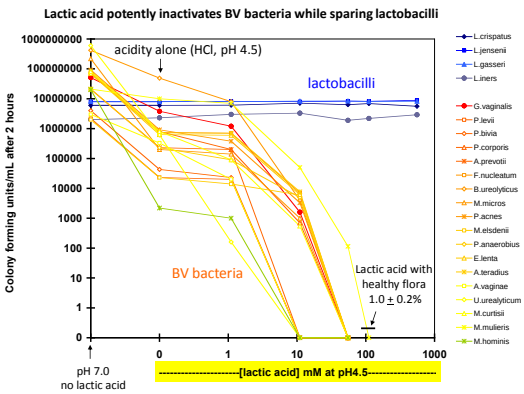
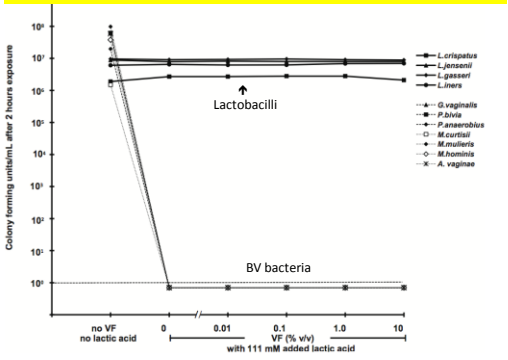


When lactobacilli dominate (Nugent scores 0-3):

- Vaginal pH = **3.5 ± 0.3** (pH range 3.0-3.9)
- Vaginal lactic acid concentration = **1.0 ± 0.2%**
- Acetic acid < 0.003%
- H_2O_2 < 1 x 10^{-6} molar



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

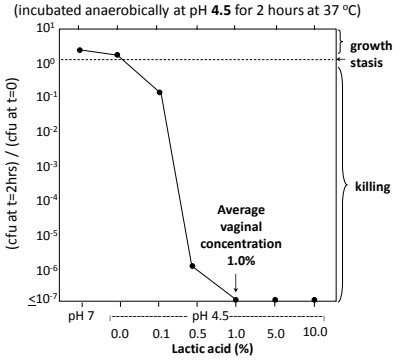


Lactic acid preserves food.

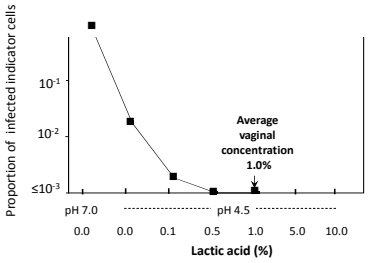
Carcasses are sprayed with lactic acid as a preservative.

Effect of lactic acid on ***Neisseria gonorrhoeae***

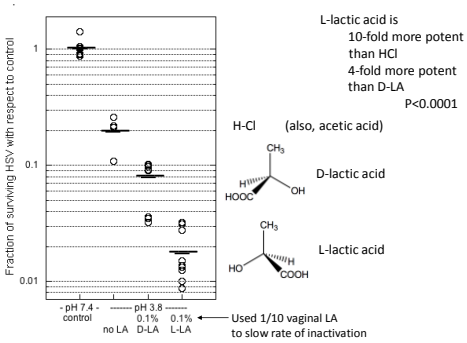
(incubated anaerobically at pH **4.5** for 2 hours at 37 °C)



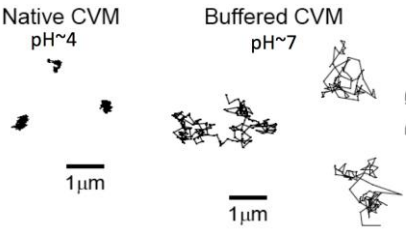
Effect of lactic acid on **HSV-2** incubated at **pH 4.5** for 20 minutes at 37C as discovered by Deirdre O'Hanlon



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

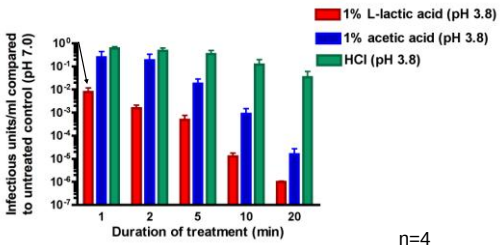


HIV is trapped in acidic cervicovaginal mucus (CVM), but not in neutralized mucus



Lai, Hida, Shukair, Wang, Figueiredo, Cone, Hope, Hanes: J Virol. 2009

HIV_{Ba-L} inactivation by 1% L-LA is more rapid and potent than low pH alone and 1% acetic acid



n=4

37 C

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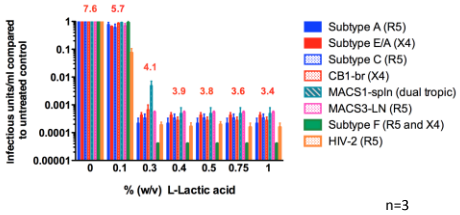
L-LA inactivates different HIV-1 subtypes, X4 and R5 strains, patient isolates and HIV-2



n=3

30min at 37°C

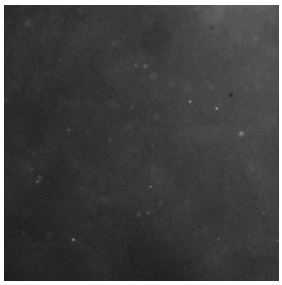
Gilda Tachedjian

SUMMARY

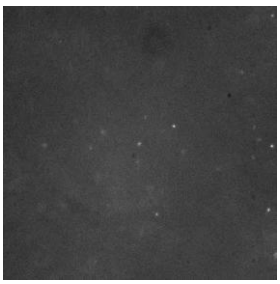
- Lactic acid as produced by lactobacilli in the vagina, but not H_2O_2, can inactivate BV bacteria without inactivating lactobacilli.
- Even at pH 4.5, 1% lactic acid completely inactivates all 17 BV-associated bacteria tested to date.
- When lactobacilli dominate, they produce lactic acid rapidly enough 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.

CONCLUSIONS

- 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.



HIV in normal vaginal mucus with lactic acid



HIV in neutralized vaginal mucus

Human immunodeficiency virus type 1 is trapped by acidic but not by neutralized human vaginal mucus. Lai, Hida, Shukair, Wang, Figueiredo, Cone, Hope, Hanes. J Virol. 2009 Nov;83(21):11196-200.