

# **Bacterial Vaginosis and Risk of HIV-1 Infection**

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# Bacterial Vaginosis (BV)

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- Changes in vaginal flora result in loss of lactobacilli, increase in predominantly anaerobic flora, and increase in vaginal pH.
- Hydrogen peroxide ( $H_2O_2$ )-producing strains of lactobacilli play an important protective role against BV and the acidic environment of the normal flora inhibits colonization by potentially pathogenic bacteria.
- Low pH inactivates both HIV-1 and T lymphocytes in vaginal fluid and impedes growth. Therefore, women with higher vaginal pH such as in BV could be more susceptible to HIV infection.

# Today's Questions

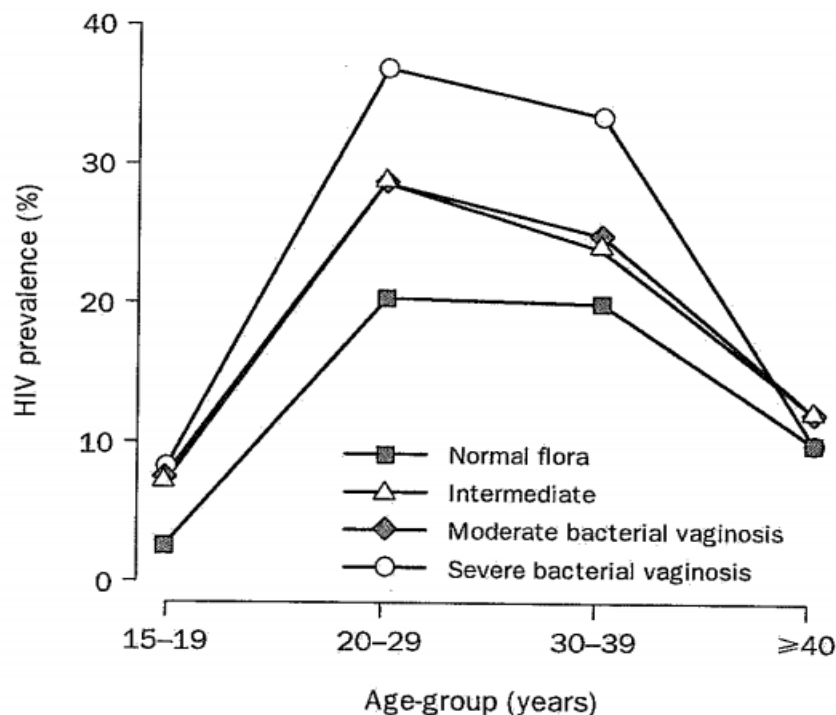
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- Is there an association between abnormal vaginal flora and HIV acquisition?
- Could these abnormal flora impact the effectiveness of vaginal microbicides?

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**Share some historical perspectives**

# Data from Rakai, Uganda – 1997: HIV-1 infection associated with abnormal vaginal flora morphology and bacterial vaginosis



## Age-specific prevalence of HIV infection associated with vaginal flora morphology scores

Normal=0-3; intermediate=4-6; moderate bacterial vaginosis=7-8; severe bacterial vaginosis=9-10.

- HIV-1 frequency 14.2% in women with normal vaginal flora and 26.7% in women with severe BV ( $p < 0.0001$ )
- Increased HIV infection among young women but not among women older than 40 years
- Adj. OR of HIV infection associated with any vaginal flora abnormality (score 4-10) was 1.52; for moderate BV (score 7-8) was 1.50; and for severe BV (score 9-10) was 2.08
- Data suggest that loss of lactobacilli or presence of bacterial vaginosis may increase susceptibility to HIV.
- Nelson Sewankambo, et al. *Lancet* 1997; 350: 546-50.

# Longitudinal Data from Blantyre, Malawi (N=1173)

## Age-Specific HIV Incidence Rates

(Women Followed 1990-1995)

Age group	New HIV infections	Person years of follow-up	Incidence rate (Per person yr %)	95% CI
< 20	30	502	5.98	5.84-8.12
20-24	32	699	4.58	2.99-6.17
25-29	21	496	4.23	2.42-6.04
30-34	12	343	3.50	1.60-5.40
35+	2	262	0.76	0.01-1.81

Taha TE et al. HIV incidence among pregnant and postpartum women in urban Malawi. *AIDS*: 1998; 12:197-203.

# Longitudinal Data from Blantyre, Malawi

## HIV Incidence in Cohorts of Pregnant Women Recruited in 1990 and 1993 in Malawi

	<b>New HIV Infections</b>	<b>Person Years</b>	<b>Incidence Rate (Person Yrs %)</b>	<b>95% CI</b>
<b>Antenatal<sup>¶</sup></b>	<b>27</b>	<b>338</b>	<b>7.9</b>	<b>4.9-11.0</b>
<b>Postnatal <sup>§</sup></b>	<b>97</b>	<b>2,684</b>	<b>3.6</b>	<b>2.9-4.3</b>

<sup>¶</sup> 1, 196 HIV seronegative women enrolled at first antenatal visit and followed for a median of 3.4 months during pregnancy.

<sup>§</sup> Follow-up of 1,169 HIV seronegative women was continued for a median duration of 2.5 years after delivery.

Taha TE et al. BV and disturbances of vaginal flora association with increased HIV acquisition. AIDS: 1998; 12:1699-1706.

# **Blantyre, Malawi HIV Incidence and Associated Factors**

- **High HIV incidence in pregnant and postpartum women: why? What are the underlying risk factors?**
- **What is the role of genital tract infections – BV and conventional STIs?**
- **Era of no ARTs; large STI treatment clinical trials to reduce HIV incidence; in Blantyre: Wash study just completed and a penile wipe topical microbicide was being discussed .....**

# Longitudinal Data from Blantyre, Malawi, 1990-95

## Risk Factors Associated with HIV Seroconversion among Pregnant Women\*

<b>Risk factors</b>	<b>Unadjusted OR (95% CI)</b>	<b>Adjusted** OR (95% CI)</b>
<b>Disturbance of vaginal flora:</b>		
None	1.00	1.00
One criterion	1.55	1.54
Two criteria	2.40	2.37
3+ (BV)***	3.72	3.68
<i>Linear trend</i>	<i>P=0.03</i>	<i>P=0.04</i>
Gonorrhoea	4.78 (1.36-16.81)	4.34 (1.20-5.70)
Trichomoniasis	1.68 (0.74-3.82)	
Syphilis	3.65 (1.22-10.93)	
Candidiasis	0.90 (0.31-2.65)	
Age (1 yr increase)	1.00 (0.94-1.06)	
Have electricity§	2.13 (0.64-7.13)	
Sexual partners $\geq 2$	1.95 (0.66-5.77)	
Time to delivery¶	1.39 (1.25-1.83)	1.45 (1.08-1.95)

\* Logistic regression analysis. \*\* Variables included in the final stepwise regression model.  
§ Index of high SES. ¶ Time in months.

Taha TE et al. BV and disturbances of vaginal flora association with increased HIV acquisition. AIDS: 1998; 12:1699-1706.



# Longitudinal Data from Blantyre, Malawi, 1990-95

## Association of Risk Factors with HIV Seroconversion among Postpartum Women\*

<b>Risk factors</b>	<b>Unadjusted OR (95% CI)</b>	<b>Adjusted** OR (95% CI)</b>
<b>Disturbance of vaginal flora:</b>		
None	1.00	1.00
One criterion	1.31	1.32
Two criteria	1.72	1.74
3+ (BV)***	2.25	2.30
<i>Linear Trend</i>	<i>P=0.04</i>	<i>P=0.03</i>
Gonorrhea	3.11 (0.76-12.79)	
Trichomoniasis	1.88 (1.32-3.38)	
Syphilis	1.04 (0.24-4.28)	
Candidiasis	0.84 (0.40-1.76)	
Age (1 yr increase)	0.91 (0.87-0.95)	0.91 (0.87-0.95)
Have electricity§	2.19 (1.00-4.80)	
Sexual partners $\geq 2$	1.28 (0.58-2.82)	

\* Proportional hazards analysis. \*\* Variables included in the final stepwise regression model.  
§ Index of high socioeconomic status.

Taha TE et al. BV and disturbances of vaginal flora association with increased HIV acquisition. AIDS: 1998; 12:1699-1706.

# The METRO Trial: Mass Treatment of BV, Blantyre, Malawi 2007

- Large randomized, double-masked, placebo-controlled trial among 842 HIV-uninfected and 844 HIV-infected non-pregnant women.
- Mass treatment with intravaginal metronidazole gel (0.75 MetroGel-vaginal) compared to placebo gel – each once a day for 5 consecutive nights every 3 mo for 1 yr.
- Primary aim: cross-sectional and longitudinal comparisons of BV frequency at baseline, 1 mo after product dispensation, and every quarterly visit.

# Frequency of BV and normal vaginal flora by study arm among HIV-uninfected women

Taha TE et al. PLOS Clinical Trials 2007

Visit	Treatment % BV (N)	Placebo % BV (N)	P-value†	Treatment % Normal (N)	Placebo % Normal (N)	P-value†
<b>Quarterly visits</b>						
V1.0	45.9 (418)	46.8 (417)	0.84	36.8 (418)	36.0 (417)	0.83
V2.0	38.4 (365)	45.7 (363)	0.05	41.6 (365)	32.8 (363)	0.01
V3.0	34.4 (320)	36.7 (324)	0.56	43.4 (320)	41.1 (324)	0.58
V4.0	22.4 (277)	27.8 (284)	0.15	54.1 (277)	50.4 (284)	0.40
V5.0‡	24.7 (275)	28.8 (285)	0.29	56.4 (275)	51.2 (285)	0.24
<b>Post-treatment evaluation visits</b>						
V1.9	35.0 (389)	48.7 (394)	<0.0001	42.9 (389)	31.5 (394)	0.001
V2.9	28.0 (336)	37.6 (327)	0.01	46.7 (336)	39.5 (327)	0.06
V3.9	23.6 (292)	32.7 (297)	0.02	50.7 (292)	44.1 (297)	0.12
V4.9	23.6 (250)	30.4 (253)	0.09	58.0 (250)	52.2 (253)	0.21

# Conclusion: METRO Trial, Blantyre, Malawi 2007

- In both arms, over time, there were reductions in frequency of BV accompanied by restoration and maintenance of normal flora.
- Use of a gel can change vaginal flora probably as a lubricant or as a chemical or physical barrier.
- What will be the experience with other microbicides?