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# HIV/Sexual Health Clinical Education Session



<http://courses.ashm.org.au/HIV/hiv-sexual-health-clinical-education-session/>

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# Journal Club

Journal of infections Disease



Prepared by **Dr Chris Bourne**  
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October 2018



## JID

- since 1904
- premier global journal for original research on infectious diseases.
  - Major Articles and Brief Reports
  - microbiology, immunology, epidemiology, and related disciplines, on the pathogenesis, diagnosis, and treatment of infectious diseases;
  - on the microbes that cause them;
  - and on disorders of host immune responses.

June – November 2018

9 issues, 2 supplements



## Nov 2018, Volume 218, Issue 10

### **Liposome-Encapsulated Human Immunodeficiency Virus-1 gp120 Induces Potent V1V2-Specific Antibodies in Humans**

Rao et al

- 2 adjuvants (Al OH & Liposomal MPL) better than 1

### **Trajectories and Predictors of Longitudinal Preexposure Prophylaxis Adherence Among Men Who Have Sex With Men.** Pasipanodya et al

- N=181, RCT SMS PREP adherence 48wk. Risk – minority, yg, baseline depression, subst use, sexual risk



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## Nov 2018, Volume 218, Issue 10

### **Effects of Substance Use and Sex Practices on the Intestinal Microbiome During HIV-1 Infection** Fulcher et al

- N=37 MSM, different drug use and sex behavior (survey and swab/urine) assoc different microbiome variations



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## Nov 2018, Volume 218, Issue suppl\_2

### Advances & Controversies in Our Understanding of Herpes Zoster

- H z vaccine effectiveness – models
- Epidemiological Links With Stroke and Myocardial Infarction
- Zoster vaccine, live attenuated [ZVL] vs recombinant subunit vaccine (HZ/su)- less senescence; > efficacy (51/65% vs 90%) for HZ and post herpetic neuralgia



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## Nov 2018, Volume 218, Issue 9

### Balancing Benefits and Risks of Antibiotic Use (ed)

#### Highly Attenuated Infection With a *vpr*-Deleted Molecular Clone of Human Immunodeficiency Virus-1. Ali et al

- Case report. 48 yo woman NSI, *vpr*-deletion (nef) HIV clone. Seroconversion delayed, durable HIV suppression, N CD4, Nab, CD8 = unremarkable

#### Levonorgestrel and Female Genital Tract Immunity: Time for a Closer Look Miguel et al (letter)

- LNG-IUS/DMPA-susceptibility to/impaired clearance of CT (nose/genitals)/not PID in mice, baboons- conflicting results of studies.
- Mice in estrus part of cycle are protected?



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## Oct 2018, Volume 218, Issue 8

### **Recurrence of Genital Infections With 9 Human Papillomavirus (HPV) Vaccine Types (6, 11, 16, 18, 31, 33, 45, 52, and 58) Among Men in the HPV Infection in Men (HIM) Study**

- 31% prior prevalent, 20% prior incident HPV recurred.
- Highest rate among prevalent, HPV 52, 45, 16, 58, and 6
- among incident, HPV 58, 52, 18, 16, and 11

### **Influenza Viral Shedding in a Prospective Cohort of HIV-Infected and Uninfected Children and Adults in 2 Provinces of South Africa, 2012–2014**

- No difference

## Oct 2018, Volume 218, Issue 7

### **Detection of Incident Anal High-Risk Human Papillomavirus DNA in Men Who Have Sex With Men: Incidence or Reactivation?**

- highly sexually exposed, HIV+, penile HPV positively associated with incident anal HPV detection; BUT
- Incident anal hrHPV detection common in recently non-exposed MSM→reactivated latent HPV instead of an incident infection may underlie incident HPV detection

## Sept 2018, Volume 218, Issue 6

### Identification of Key Bacteria Involved in the Induction of Incident Bacterial Vaginosis: A Prospective Study. Christina A Muzny et al

- N=204, AA WSW, 90 day FU. 45% developed iBV.
- Mean relative abundance *Prevotella bivia*, *Gardnerella vaginalis*, *Atopobium vaginae*, and *Megasphaera* type I became significantly higher among women 4 days before (*P. bivia*), 3 days before (*G. vaginalis*), and on the day of (*A. vaginae* and *Megasphaera* type I) incident bacterial vaginosis- ?significant role in iBV

## Aug 2018, Volume 218, Issue 4

### Eradication of Hepatitis C Virus (HCV) Reduces Immune Activation, Microbial Translocation, and the HIV DNA Level in HIV/HCV-Coinfected Patients

### First-in-Human Randomized, Controlled Trial of Mosaic HIV-1 Immunogens Delivered via a Modified Vaccinia Ankara Vector

## Aug 2018, Volume 218, Issue 3

### Prevalence and Epidemiologic Profile of Oral Infection with Alpha, Beta, and Gamma Papillomaviruses in an Asian Chinese Population

- Chinese/HK general pop(n=1426, 61% participation, ave age 46.3y)
- HRHPV 0.8%; 16, 0.4%
- Assoc *alpha*- HPV smoking, drinking, oral sex, and more sexual partners; teeth brushing before sleep protective *beta/gamma* HPV



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## Aug 2018, Volume 218, Issue 3

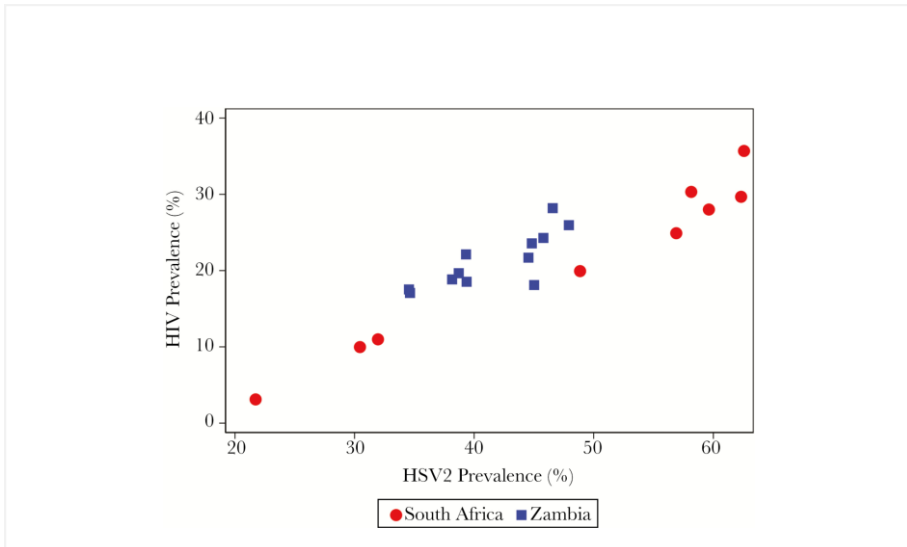
### Sexually Transmitted Bedfellows: Exquisite Association Between HIV and Herpes Simplex Virus Type 2 in 21 Communities in Southern Africa in the HIV Prevention Trials Network 071 (PopART) Study

- n=2000 adults (18–44y) randomly each community, n=38691
- HSV-2 prevalence: Zambia/SAfr-women 50/62%, men 22/27%
- Incidence women; men: 8/100 py (CI:6.8-9.3); 1.76 py (CI1.3-2.2)
- 6X AOR HIV both women and men with HSV
- Strong linearity at community level ( $\rho = 0.92$ ;  $P < .001$ )



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From: Sexually Transmitted Bedfellows: Exquisite Association Between HIV and Herpes Simplex Virus Type 2 in 21 Communities in Southern Africa in the HIV Prevention Trials Network 071 (PopART) Study  
 J Infect Dis. 2018;218(3):443-452. doi:10.1093/infdis/jiy178  
 J Infect Dis | © The Author(s) 2018. Published by Oxford University Press for the Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.

## Aug 2018, Volume 218, Issue 3

### Acute HIV Infection Results in Subclinical Inflammatory Cardiomyopathy

N= 49, increased N-terminal prohormone brain natriuretic peptide (myocardial function surrogate) & troponin T → functional & morphological impairment, reversible





## July 2018, Volume 218, Issue 2

### Abacavir Induces Arterial Thrombosis in a Murine Model

- through interference with purinergic (ATP<sub>P2c</sub>) signalling; cf other RTIs

### What Is the Best Model for HIV Primary Care? Assessing the Influence of Provider Type on Outcomes of Chronic Comorbidities in HIV Infection

N= 916, ave age 53, ave >1 comorbidity, trend towards improved outcomes in those with PCP- in or outside HIV clinic. DM well controlled overall but not HT, Hyperchol (trend towards PCP); screening better overall if PCP but after MVA no difference in outcomes by provider.



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## July 2018, Volume 218, Issue 1

### Increased Risk of HIV Acquisition Among Women Throughout Pregnancy and During the Postpartum Period: A Prospective Per-Coital-Act Analysis Among Women With HIV-Infected Partners

- 2751 HIV-serodiscordant couples- 2xRCT-PIP(HSV/HIV), PrEP, prob HIV acquisition women/ sex act in early pregnancy, late pregnancy, postpartum period, and non-pregnant period
- 686 pregnancies, 82 incident HIV
- late pregnancy (aRR], 2.82; P = .01): postpartum period (aRR, 3.97; P = .01) cf nonpregnant period.
- 25-y woman not on PrEP, condomless sex act HIV+ male VL10 000

Pregnancy period	Probability/ condomless sex act
Non-pregnant	0.0011 (95% CI, 0.0005–0.0019)
early pregnancy	0.0022 (95% CI, 0.0004–0.0093)
late pregnancy	0.0030 (95% CI, 0.0007–0.0108)
postpartum	0.0042 (95% CI, 0.0007–0.0177)

## July 2018, Volume 218, Issue 1

### **Efficacy, Immunogenicity, and Safety of a 9-Valent Human Papillomavirus Vaccine: Subgroup Analysis of Participants From Asian Countries**

efficacious, immunogenic, and well-tolerated: India, Hong Kong, South Korea, Japan, Taiwan, and Thailand



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## May 2018, Volume 217, Issue 11

### **Nonreactive HIV-1 Rapid Tests After Sustained Viral Suppression Following Antiretroviral Therapy Initiation During Primary Infection**

- PHI –NAT + before seroconversion, 18% of participants were nonreactive with fourth-generation (4thG) IA and 11% seroreverted after 24 weeks of ART (deSouza)
- N= 44, France
- (all gp41) HIV self-tests 30% and point-of-care tests 7%–9% were negative
- DONOT retest after ARV initiation!
- More people on PREP now



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# Comparable Serologic Responses to 2 Different Combinations of Inactivated Hepatitis A Virus Vaccines in HIV-Positive Patients During an Acute Hepatitis A Outbreak in Taiwan

Sept 2018, Volume 218, Issue 7

Kean-Yin Lin, et al



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## Background

- HAV outbreaks occurring in MSM
- HAVx effective and recommended for MSM
- Immunogenic, generally (>95%) and in HIV+ (96%)
- Outbreaks can lead to supply issues, interchangeability qs
- RCT comparable seroconversion rates, higher titres in VAQTA

Aim:

evaluate the serological responses 2 diff HAVx in HIV+ people during outbreak



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## SUBJECTS & METHODS: Study Setting & patients

- Mid 2015 - late 2017, 1500 AHAV infections, Taiwan
- >1/2 MSM & or HIV+
- HAV seronegative people advised to have HAVx, 0,6 mths

Retrospective study:

- Include: HIV+, HAV-, >19y, June 1 2015-Sept 30 2016
- Excluded: one dose HAVx
- Ethics approval/informed consent waived not required- PH response

## Exposures & Outcomes

- Mid May 2016- VAQTA replaced HAVRIX due to shortage
- 3 groups: H-H, V-H, VV -0,6mth
- H-H excluded because only 19
- Anti-HAV IgG week 4, 24, 28-36, 48
- Follow up- AHAV, death, lost, or the end of the study

Outcomes:

1. Primary- IgG wk 28-36 (7-8mths)
2. Secondary- IgG wk 4, 24 & 48; AHAV

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2. Secondary- IgG wk 4, 24 & 48; AHAV
3. response estimated ITT with last-observation-carried-forward (LOCF) analysis and per-protocol (PP) analysis

## Lab investigations

- Serum anti-HAV IgG (Architect, Abbott), S/C >1= +

## Statistical analysis

- 2 groups by 1-way analysis of variance, with Bonferroni tests for multiple pair-wise comparisons.
- MVA- generalized estimating equation (GEE) model, 2tailed,  $P < .05$
- STATA

## Results

- N=946; 395 (42%) H-V, 551 (58%) V-V

**Table 1.**  
Comparison of Clinical Characteristics and Outcomes Between the Havrix-Vaqta and Vaqta-Vaqta Groups

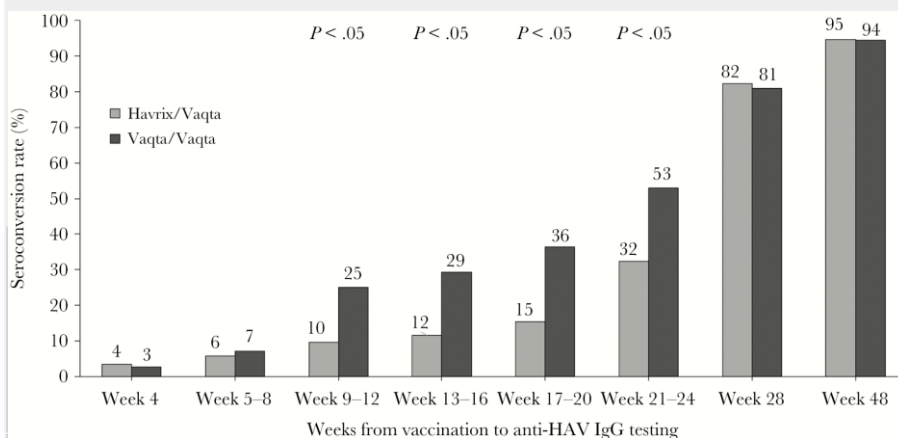
CHARACTERISTIC	HAVRIX-VAQTA	VAQTA-VAQTA	P
Age, y	35 (30–41)	34 (29–42)	.265
MSM	373/395 (94.4)	531/551 (96.4)	.153
Current smoker	109/395 (27.6)	141/551 (25.6)	.837
HBsAg positive	44/395 (11.1)	53/551 (9.6)	.447
Anti-HCV positive	17/395 (4.3)	37/551 (6.7)	.115
Receiving immunosuppressant <sup>a</sup>	4/395 (1.0)	2/551 (0.4)	.214
<b>Receiving cART at vaccination</b>	<b>385/395 (97.5)</b>	<b>534/551 (96.9)</b>	<b>.614</b>
<b>CD4<sup>+</sup> T-cell count at vaccination</b>			
Overall, cells/ $\mu$ L	571 (437–748)	577 (441–743)	.779
>350 cells/ $\mu$ L	349/395 (88.4)	487/551 (88.4)	.989
<b>Plasma HIV RNA load at vaccination</b>			
Overall, copies/mL	UD <sup>b</sup>	UD <sup>b</sup>	.859
<20 copies/mL	337/395 (85.3)	468/551 (84.9)	.871
Receiving cART at wk 28–36	389/395 (98.5)	539/551 (97.8)	.464
CD4 <sup>+</sup> T-cell count at wk 28–36, cells/ $\mu$ L	585 (460–781)	617 (480–781)	.355
<b>Plasma HIV RNA load at wk 28–36</b>			
Overall, copies/mL	UD <sup>b</sup>	UD <sup>b</sup>	.336
<20 copies/mL	355/395 (89.9)	501/551 (90.9)	.197
<b>Syphilis during follow-up</b>	<b>115/395 (29.1)</b>	<b>140/551 (25.4)</b>	<b>.205</b>

CHARACTERISTIC	HAVRIX-VAQTA	VAQTA-VAQTA	P
<b>SEROLOGIC RESPONSE AT WK 28–36<sup>c</sup></b>			
ITT with LOCF analysis	325/395 (82.3)	446/551 (80.9)	.301
<b>Per-protocol analysis</b>	<b>293/318 (92.1) 20% loss</b>	<b>331/348 (95.1) 40% loss</b>	<b>.056</b>
<b>Serologic response at wk 48<sup>d</sup></b>			
ITT with LOCF analysis	374/395 (94.7)	520/551 (94.4)	.418
<b>Per-protocol analysis</b>	<b>307/322 (95.3) 18% lost</b>	<b>229/243 (94.2) 54% lost</b>	<b>.278</b>
<b>Acquisition of acute hepatitis A</b>	<b>0/395 (0)</b>	<b>0/551 (0)</b>	

## RESULTS

- See figure 1 - next slide
- 5 individuals received only 1 dose HAVx acquired AHAV, not included in the analysis; of them, 3 received Havrix and 2 received Vaqta.
- S/CO IgG titres were higher throughout for V vs H, remained highest for V-V
- Multivariate
  - Younger (AOR, 1.06/1-year decrease; 95% CI, 1.02–1.11)
  - higher CD4+ (AOR, 1.04/10-cells/ $\mu$ L increase; 95% CI, 1.02–1.05)
  - UDVL at vaccination (AOR, 2.92; 95% CI, 1.38–6.18)

Figure 1. Seroconversion rates after hepatitis A virus (HAV) vaccination at different follow-up intervals in the Havrix-Vaqta and Vaqta-Vaqta groups. Data are from the intention-to-treat with last-observation-carried-forward analysis. IgG, immunoglobulin G.



From: Comparable Serologic Responses to 2 Different Combinations of Unadjuvanted Hepatitis A Virus Vaccines in HIV-Positive Patients During an Acute Hepatitis A Outbreak in Taiwan  
 J Infect Dis. 2018;218(5):734-738. doi:10.1093/infdis/jiy224

## DISCUSSION

- Similar seroconversion rates after different 2 dose HAVx in HIV + MSM at 28-36wk during HAV outbreak- interchangeable
- 1 dose VAQTA- faster, better response (early and late)
- Yger and higher CD4 better
- Other studies-difficult to compare viral protein equivalents, different EIA for serology, higher titre response to VAQTA, 'non-inferiority/interchangeability for 2<sup>nd</sup> dose' in HIVneg
- HIV+ poorer response, Vaqta better to get rapid protection
- Limitations:

## DISCUSSION

- Limitations:
  - Vax, serology 'conducted at regular intervals' not fixed times- observational
  - Convenience sample, no sample size calculations, was powered showing non-inferiority
  - Serology follow-up 'may have led to missing data points in V-V gp' after dose 2
  - Serology - vaccination or natural infection? Syphilis similar both gps
- Conclusion: 2 dose H-V & V-V similar



## My appraisal

### Question:

- aim reasonable

### Methodology:

- Study population – convenient, appropriate
- data sources- retrospective
- case definition- reasonable
- exclusion criteria- reasonable

## My appraisal

### Statistics:

- Standard statistics
- 'intention-to-treat (ITT) with last-observation-carried-forward (LOCF) analysis'- veracity debatable; 'over reporting efficacy or underreporting harmful safety problems'
- Wk 4-21, no. tested data not shown

### Did it answer the question?:

- yes a little

### Usefulness:

- Give two doses HAVx in HIV+
- ?VAQTA for quicker and stronger immune response in HIV+ but non-inferior after 2 doses.