Second Joint Conference

*of the British HIV Association **[BHIVA]***
and the
*British Association for Sexual Health and HIV **[BASHH]***

20-23 April 2010, Manchester Central Convention Complex

SECOND JOINT CONFERENCE OF BHIVA AND BASHH 2010

Dr Steve Taylor

Birmingham Heartlands Hospital

COMPETING INTEREST OF FINANCIAL VALUE ≥ £1,000:	
Speaker Name	**Statement**
Dr Steve Taylor:	Dr Taylor has received educational research grants, travel grants for attending conferences and honoraria from Abbott, Boehringer Ingelheim, Bristol-Myers Squibb Pharmaceuticals, Gilead Sciences, MSD, Tibotec and ViiV Healthcare
Date	13 April 2010

20-23 April 2010, Manchester Central Convention Complex

DEPARTMENT OF **SEXUAL HEALTH** AND **HIV MEDICINE**

The TOP TEN Papers 2009-2010

Dr Stephen Taylor, FRCP, PhD
Department of Sexual Health and HIV Medicine
Directorate of Infection
Birmingham Heartlands Hospital

BIRMINGHAM HEARTLANDS **HIV SERVICE**

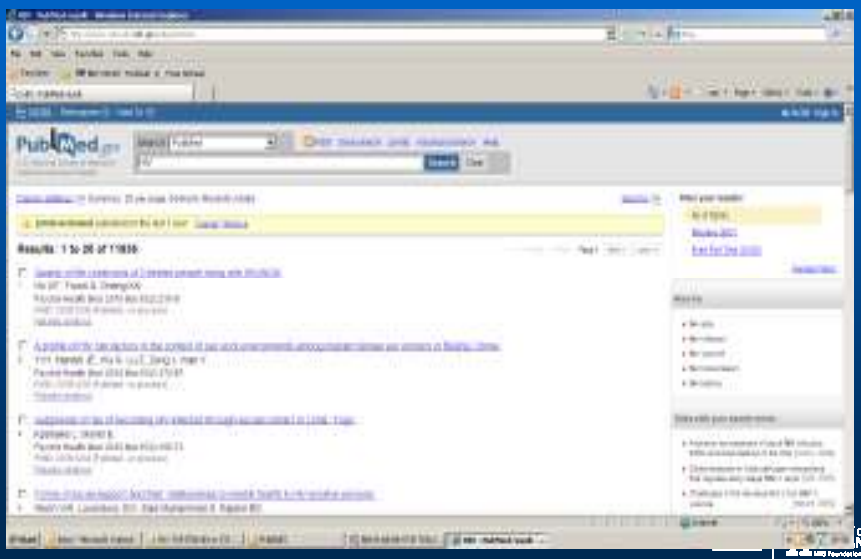
We couldn't think of a better person …

Go ahead have a drink …it's not poison!

BHIVA 2009 TOP 10 – Dr Andrew Ustianowski

"It really aged me …"

HIV: 11,836



Sexually Transmitted Infections : 6835

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HIV and STIs : 5707

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So after reading those ….

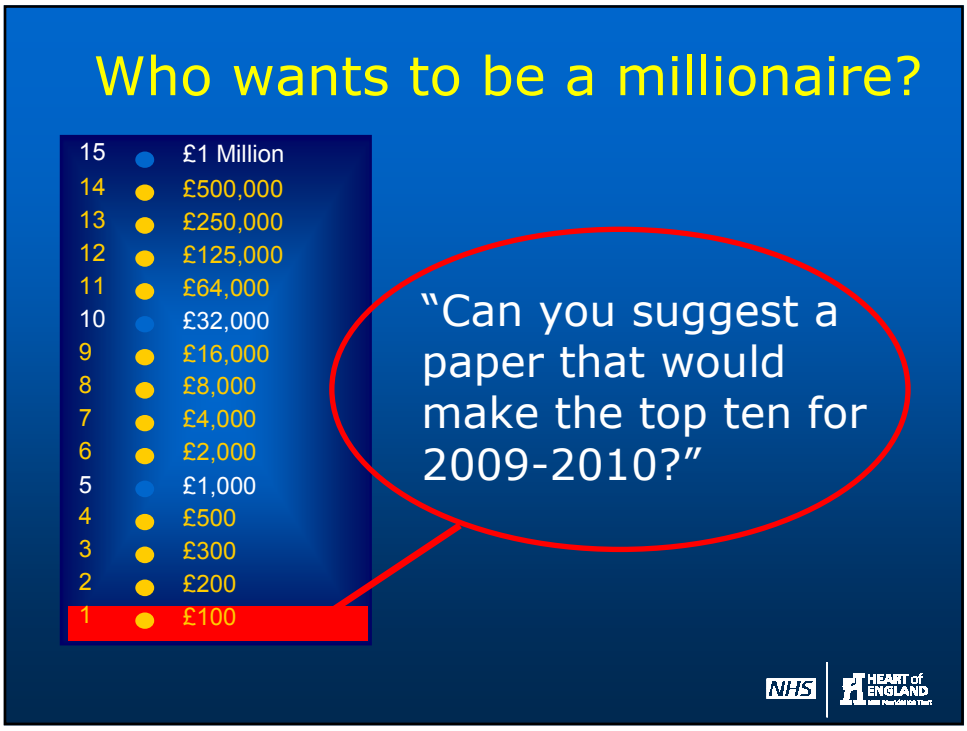
- NATURE
- SCIENCE
- NEJM
- LANCET
- AIDS
- JAIDS
- HIV MEDICINE
- STI
- STD
- IJSTDA
- JID
- CID
- JAC
- AAC
- BMJ

Tried a scoring system…

Categories: each scoring 0-5 points

- S
- C
- H
- P
- P
- Interesting
- Patient centred
- Personal opinion

After 39 papers scored more than 30 points!
I gave up ……


Who wants to be a millionaire?
15 £1 Million
14 £500,000
13 £250,000
12 £125,000
11 £64,000
10 £32,000
9 £16,000
8 £8,000
7 £4,000
6 £2,000
5 £1,000
4 £500
3 £300
2 £200
1 £100
"Can you suggest a paper that would make the top ten for 2009-2010?"
NHS
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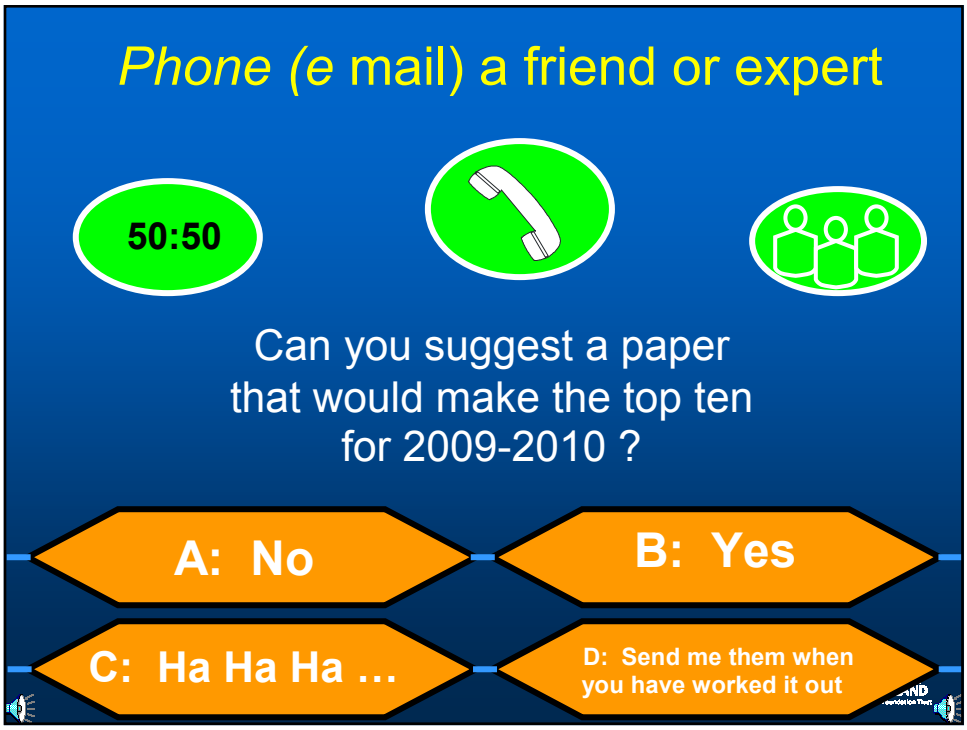
Phone (e mail) a friend or expert
50:50
Can you suggest a paper that would make the top ten for 2009-2010 ?
A: No
B: Yes
C: Ha Ha Ha …
D: Send me them when you have worked it out

The friends /experts phoned

- John Watson
- Chris Pilcher
- Rob Miller
- Bob Coombs
- Marc Lipman
- Martin Fisher
- Myron Cohen
- John White
- Ian Williams
- Jonathon Ross
- Scott Letendre
- Ras Smit
- Andy Ustinowski
- Pietro Vernazza
- Nicola Steedman
- Martin Dedicoat
- Steven Welch
- Roget le Banc
- Colm O' Mahoney
- Nicola Mackie
- Gus Cairns
- David White
- Clare Robertson
- Ras Smit
- Duncun Churchill
- Mark Mascolini
- Edwin Bernard
- David Back
- Simon Collins
- Penny McDuff
- Katy Hayward
- Gary Rubin
- Sarah Barrett

Expert Rating

THANKYOU +++

Only 8 to go…

3. REVIEWS
4. HERPES, ACICLOVIR AND HIV
5. DEVELOPING WORLD
6. CHLAMYDIA

7/8 HEPATITIS C and B

9. HPV
10. THE TOP TEN PAPER OF 2009-2010

NUMBER 3

3

Reviews

Science
AAAS

The Challenge of Finding a Cure for HIV Infection
Douglas D. Richman, *et al.*
Science **323**, 1304 (2009);
DOI: 10.1126/science.1165706

The Challenge of Finding a Cure for HIV Infection

Douglas D. Richman,[1*] David M. Margolis,[2] Martin Delaney,[3†] Warner C. Greene,[4] Daria Hazuda,[5] Roger J. Pomerantz[6]

1

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International AIDS Society–USA *Topics in HIV Medicine*

HIV–Related Internet Resources Volume **17** Issue **5** December **2009**

Review

HIV–Associated Resources on the Internet

Wendy S. Armstrong, MD, and Carlos del Rio, MD

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Table **1.** Selected Web Sites Providing HIV-Related Clinical Guidelines

Table 1. Selected Web Sites Providing HIV-Related Clinical Guidelines

Title of Web Site, in Alphabetical Order	Uniform Resource Locator	Source or Sponsor	Description
Guidelines Published in the United States			
AIDSinfo	http://www.aidsinfo.nih.gov http://www.aidsinfo.nih.gov/Guidelines/Default.aspx?MenuItem=Guidelines	US Department of Health and Human Services (DHHS)	Links to guidelines, including treatment (adult, pediatrics, perinatal), postexposure prophylaxis, opportunistic infections, testing
HIV Medicine Association of the Infectious Diseases Society of America Practice Guidelines	http://www.idsociety.org/Content.aspx?id=1922	HIV Medicine Association of the Infectious Diseases Society of America	Guidelines for HIV primary care, management of dyslipidemia, chronic kidney disease, and others in HIV-infected patients
International AIDS Society–USA	http://www.iasusa.org/guidelines/index.html	International AIDS Society–USA	Antiretroviral therapy and resistance testing guidelines originally published in JAMA and Clin Infect Dis
US Health Resources and Services Administration	http://hab.hrsa.gov/publications.htm	DHHS	Guidelines and protocols for HIV primary care, hepatitis C virus and HIV coinfection, others
Guidelines Published Outside the United States			
British HIV Association	http://www.bhiva.org http://www.bhiva.org/cms1191540.asp		

Table 2: Resistance + Interactions

Table 2. Selected Web Sites Providing HIV-Related Literature Citations and Other Educational Materials (cont'd)

Title of Web Site, in Alphabetical Order	Uniform Resource Locator	Sponsor (Type/Sponsor)	Description
Specialized Sites			
HIVandHepatitis.com	http://www.hivandhepatitis.com/	Commercial/Supported by pharmaceutical sponsors	Treatment issues in HIV and hepatitis B or C virus–coinfected patients, conference updates; CME credits available
HIV Drug Interactions	http://www.hiv-druginteractions.org/	Academic/University of Liverpool	HIV pharmacology resource, offers drug-interaction charts, pharmacology fact sheets
HIV French Resistance	http://www.hivfrenchresistance.org	Government/French National Agency for AIDS Research (ANRS) Resistance Group	Drug resistance algorithms for genotypic data
HIV Transplant	http://www.hivtransplant.com/	Government/US National Institute of Allergy and Infectious Diseases	Solid Organ Transplantation in HIV Study protocol, pilot data, links to posters and literature from the study
National HIV/AIDS Clinicians' Consultation Center	http://www.nccc.ucsf.edu/Infolindex.html	Academic/University of California San Francisco	Links to guidelines, resistance cases, and other information; links to sites below
• PEPline: The National Clinicians' Post-Exposure Prophylaxis Hotline	http://www.nccc.ucsf.edu/Hotlines/PEPline.html		• Postexposure prophylaxis hotline for treating clinicians; related links
• Warmline: The National HIV Telephone Consultation Service	http://www.nccc.ucsf.edu/Hotlines/Warmline.html		• Advice to clinicians with questions about HIV and HIV care; related links
• Perinatal HIV Hotline: The National Perinatal HIV Consultation and Referral Service	http://www.nccc.ucsf.edu/Hotlines/Perinatal.html		• Consultation and advice on management of HIV in pregnancy and HIV-exposed infants
Stanford University HIV Drug Resistance Database	http://hivdb.stanford.edu/	Academic/Stanford University	HIV drug resistance database with genotypic, phenotypic, and clinical correlations and resistance algorithms

Table 3. Selected Web Sites of HIV-Related Scientific Conferences

Title of Conference Web Site, in Alphabetical Order	Uniform Resource Locator	Description
Conference on Retroviruses and Opportunistic Infections (annual)	http://www.retroconference.org	Free access to Webcasts, posters, searchable abstracts; links to previous conferences
Infectious Diseases Society of America Annual Meeting	http://www.idsociety.org/Content.aspx?id=12006	General conference information
International AIDS Conference (even years)	http://www.aids2010.org/	Free abstracts; some Webcasts and Podcasts of presentations
International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention (odd years)	http://www.ias2009.org/	Free Webcasts, abstracts
International HIV Drug Resistance Workshop (annual)	http://www.informedhorizons.com/resistance2009/index.html	Content 2002–2009 available with abstracts and some presentations
International Workshop on Adverse Drug Reactions & Co-Morbidities in HIV (annual)	http://www.intmedpress.com/lipodystrophy/default.cfm?itemtypeid=1&title=Home	Link to 2008 abstracts from link to Webcasts and videos
Interscience Conference on Antimicrobial Agents and Chemotherapy (annual)	http://www.icaac.org/	Sponsored by American Society for Microbiology; digital recordings available for purchase, free searchable posters for attendees

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Table 5: Journals

Table 5. Selected Web Sites of Major Journals Specializing in or Including HIV-Related Content

Journal Title, in Alphabetical Order	Uniform Resource Locator	Publisher; Access
HIV and Infectious Diseases Specialty Journals		
AIDS	http://journals.lww.com/aidsonline/pages/default.aspx	Lippincott Williams & Wilkins; requires subscription for full access
AIDS Clinical Care	http://aids-clinical-care.jwatch.org/	Massachusetts Medical Society; requires subscription for full access
AIDS Research and Human Retroviruses	http://www.liebertonline.com/loi/aid	Mary Ann Liebert, Inc; requires subscription for full access
AIDS Research and Therapy	http://www.aidsrestherapy.com/	BioMed Central; open access
Antiviral Therapy	http://www.intmedpress.com/index.cfm?pid=12	International Medical Press; requires subscription for full access
Clinical Infectious Diseases	http://www.journals.uchicago.edu/toc/cid/current	University of Chicago Press; requires subscription for full access
Current Opinion in HIV and AIDS	http://journals.lww.com/co-hivandaids/pages/default.aspx	Lippincott Williams & Wilkins; requires subscription for full access
Journal of Acquired Immune Deficiency Syndromes	http://journals.lww.com/jaids/pages/default.aspx	Lippincott Williams & Wilkins; requires subscription for full access
Journal of Infectious Diseases	http://www.journals.uchicago.edu/toc/jid/current	University of Chicago Press; requires subscription for full access
Topics in HIV Medicine	http://www.iasusa.org/pub/	International AIDS Society–USA; open access

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Table 4: Images and case studies

Table 4. Selected Web Sites with HIV-Related Images and Case Studies

Title of Web Site, in Alphabetical Order	Uniform Resource Locator	Sponsor	Description
Images			
AIDS Images Library	http://www.aids-images.ch/	Geneva University Hospital, Switzerland	Maintained by HIV expert; free registration
AIDS Imaging	http://members.xoom.virgilio.it/Aidsimaging/	Casa del Sole Hospital, Palermo, Italy	Clinical, radiologic, and histologic images of AIDS and sexually transmitted diseases; last update 2002
Public Health Image Library	http://phil.cdc.gov/phil/home.asp	US Centers for Disease Control and Prevention	Photographs, illustrations, and multimedia files on a variety of medical topics
The Internet Pathology Library WebPath	http://library.med.utah.edu/WebPath/TUTORIAL/AIDS/HIV.html	University of Utah Eccles Health Sciences Library and Mercer University School of Medicine	HIV tutorial and many images of pathology with limited text
US Department of Veterans' Affairs HIV/AIDS Image Library	http://www.hiv.va.gov/value/pagewire-00-00	US Department of Veterans Affairs	> 200 images of clinical symptoms of HIV infection; available free for downloading
Case Studies			
Clinical Care Options HIV-Management Series	http://www.clinicaloptions.com/HIVManagement%20Series.aspx	Commercial site supported by pharmaceutical and biotechnology companies	Free continuing medical education (CME) credits offered through accredited providers
HIV Web Study: A Case-Based Clinical Curriculum	http://depts.washington.edu/hivwebs/	University of Washington and Northwest AIDS Education and Training Center	> 65 case-based modules; free CME credits
International AIDS Society–USA Cases on the Web	http://www.iasusa.org/cow/	International AIDS Society–USA	> 40 Cases on the Web interactive presentations; free CME credits

Antiretroviral drug concentrations in the male and female genital tract: implications for the sexual transmission of HIV

Stephen Taylor[a,b] and Sophia Davies[a]

Purpose of review

To summarize the recent literature (2008–2010) on antiretroviral (ARV) drug disposition into the male and female genital tract.

Recent findings

Current Opinion in HIV and AIDS 2010, 5:

Summary

There appear to be several patterns of drug penetration into the male and female genital tract. In addition there appear to be different patterns of genital shedding under the influence of antiretroviral therapy. What effect this will have on the sexual transmission of HIV or the evolution and transmission of resistant HIV remains to be seen.

Keywords

antiretroviral drug concentrations, female genital tract, HIV-1, male genital tract

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NUMBER 4

3 studies on herpes, HIV and aciclovir …

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Acyclovir and Transmission of HIV-1 from Persons Infected with HIV-1 and HSV-2

C. Celum, A. Wald, J.R. Lingappa, A.S. Magaret, R.S. Wang, N. Mugo, A. Mujugira, J.M. Baeten, J.J. Mullins, J.P. Hughes, E.A. Bukusi, C.R. Cohen, E. Katabira.

N Engl J Med 2010;362:427-39.

W.L.H. Whittington, M.J. McElrath, L. Barnes, R. Ridzon, and L. Corey, for the Partners in Prevention HSV/HIV Transmission Study Team*

1

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BACKGROUND

Most persons who are infected with human immunodeficiency virus type 1 (HIV-1) are also infected with herpes simplex virus type 2 (HSV-2), which is frequently reactivated and is associated with increased plasma and genital levels of HIV-1. Therapy to suppress HSV-2 reduces the frequency of reactivation of HSV-2 as well as HIV-1 levels, suggesting that suppression of HSV-2 may reduce the risk of transmission of HIV-1.

METHODS

We conducted a randomized, placebo-controlled trial of suppressive therapy for HSV-2 (acyclovir at a dose of 400 mg orally twice daily) in couples in which only one of the partners was seropositive for HIV-1 (CD4 count, ≥250 cells per cubic millimeter) and that partner was also infected with HSV-2 and was not taking antiretroviral therapy at the time of enrollment. The primary end point was transmission of HIV-1 to the partner who was not initially infected with HIV-1; linkage of transmissions was assessed by means of genetic sequencing of viruses.

RESULTS

A total of 3408 couples were enrolled at 14 sites in Africa. Of the partners who were infected with HIV-1, 68% were women, and the baseline median CD4 count was 462 cells per cubic millimeter. Of 132 HIV-1 seroconversions that occurred after randomization (an incidence of 2.7 per 100 person-years), 84 were linked within couples by viral sequencing: 41 in the acyclovir group and 43 in the placebo group (hazard ratio with acyclovir, 0.92; 95% confidence interval [CI], 0.60 to 1.41; P=0.69). Suppression with acyclovir reduced the mean plasma concentration of HIV-1 by 0.25 $\log_{10}$ copies per milliliter (95% CI, 0.22 to 0.29; P<0.001) and the occurrence of HSV-2–positive genital ulcers by 73% (risk ratio, 0.27; 95% CI, 0.20 to 0.36; P<0.001). A total of 92% of the partners infected with HIV-1 and 84% of the partners not infected with HIV-1 remained in the study for 24 months. The level of adherence to the dispensed study drug was 90%. No serious adverse events related to acyclovir were observed.

CONCLUSIONS

Daily acyclovir therapy did not reduce the risk of transmission of HIV-1, despite a reduction in plasma HIV-1 RNA of 0.25 $\log_{10}$ copies per milliliter and a 73% reduction in the occurrence of genital ulcers due to HSV-2. (ClinicalTrials.gov number, NCT00194519.)

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Daily aciclovir for HIV-1 disease progression in people dually infected with HIV-1 and herpes simplex virus type 2: a randomised placebo-controlled trial

Jairam R Lingappa, Jared M Baeten, Anna Wald, James P Hughes, Katherine K Thomas, Andrew Mujugira, Nelly Muga, Elizabeth A Bukusi, Craig R Cohen, Elly Katabira, Allan Ronald, James Kiarie, Corey Fong-Ibar, Grace John Stewart, Joseph Makhema, Myron Essex, Edwin Were, Kenneth H Mayer, Guy de Bruyn, Glenda E Gray, James A McIntyre, Rachel Manongi, Saidi Kapiga, David Coetzee, Susan Allen, Marleena Inambao, Kayitesi Kayitenkore, Etienne Karita, William Kanweka, Sinead Delany, Helen Rees, Bellington Vwalika, Amalia S Magaret, Richard S Wong, Lara Kidoguchi, Linda Barnes, Renee Ridzon, Lawrence Corey, Connie Celum, for the Partners in Prevention HSV/HIV Transmission Study Team*

Lancet 2010; 375: 824–33

Published Online

February 15, 2010

2

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AIDS 2009, **23**:

HSV suppression reduces seminal HIV-1 levels in HIV-1/HSV-2 co-infected men who have sex with men

Richard A. Zuckerman[a], Aldo Lucchetti[b], William L.H. Whittington[c], Jorge Sánchez[b], Robert W. Coombs[c,d], Amalia Magaret[d,f], Anna Wald[c,d,e,f], Lawrence Corey[c,d,f] and Connie Celum[c,e,g]

3

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HSV suppression reduces seminal HIV-1 levels in HIV-1/HSV-2 co-infected men who have sex with men

Objectives: Suppressive herpes simplex virus (HSV) therapy can decrease plasma, cervical, and rectal HIV-1 levels in HIV-1/HSV-2 co-infected persons. We evaluated the effect of HSV-2 suppression on seminal HIV-1 levels.

Design: Twenty antiretroviral therapy (ART)-naive HIV-1/HSV-2 men who have sex with men (MSM) in Lima, Peru, with CD4 >200 cells/μl randomly received valacyclovir 500 mg twice daily or placebo for 8 weeks, then the alternative regimen for 8 weeks after a 2-week washout. Peripheral blood and semen specimens were collected weekly. Anogenital swab specimens for HSV DNA were self-collected daily and during clinic visits.

Methods: HIV-1 RNA was quantified in seminal and blood plasma by TaqMan real-time polymerase chain reaction (RT-PCR) or Roche Amplicor Monitor assays. HSV and seminal cytomegalovirus (CMV) were quantified by RT-PCR. Linear mixed models examined differences within participants by treatment arm.

Results: Median CD4 cell count of participants was 424 cells/μl. HIV-1 was detected in 71% of 231 semen specimens. HSV was detected from 29 and 4.4% of swabs on placebo and valacyclovir, respectively ($P < 0.001$). Valacyclovir significantly reduced the proportion of days with detectable seminal HIV-1 (6.3% during valacyclovir vs. 78% during placebo; $P = 0.04$). Seminal HIV-1 quantity was 0.25 $\log_{10}$ copies/ml lower [95% confidence interval (CI) −0.40 to −0.10; $P = 0.001$] during the valacyclovir arm compared with placebo, a 44% reduction. CD4 cell count ($P = 0.32$) and seminal cellular CMV quantity ($P = 0.68$) did not predict seminal plasma HIV-1 level.

Conclusions: Suppressive valacyclovir reduced seminal HIV-1 levels in HIV-1/HSV-2 co-infected MSM not receiving ART. The significance of this finding will be evaluated in a trial with HIV-1 transmission as the outcome.

AIDS 2009, **23**:000–000

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Journal of Infectious Diseases 2009 Apr 1;199(7):923-5

Effect of HSV-2 serostatus on acquisition of HIV by young men: results of a longitudinal study in Orange Farm, South Africa

Sobngwi-Tambekou J, Taljaard D, Lissouba P, Zarca K, Puren A, Lagarde E, Auvert B.

NHS | HEART of ENGLAND

J Infect Dis. 2009 Apr 1;199(7):923-5.

Effect of HSV-2 serostatus on acquisition of HIV by young men: results of a longitudinal study in Orange Farm, South Africa.

- Sobngwi-Tambekou J, Taljaard D, Lissouba P, Zarca K, Puren A, Lagarde E, Auvert B.
- BACKGROUND: The objectives of this study were to assess the impact among young men of herpes simplex virus type 2 (HSV-2) status on the acquisition of human immunodeficiency virus (HIV) and on the protective effect of male circumcision against HIV acquisition. METHODS: We used data collected during a male circumcision trial conducted in Orange Farm, South Africa. We estimated adjusted incidence rate ratios (IRRs) for HIV acquisition, using survival analysis and background characteristics, HSV-2 status, male circumcision status, and sexual behavior as covariates. RESULTS: Compared with subjects who remained HSV-2 negative throughout the study, subjects who were HSV-2 positive at enrollment had an adjusted IRR of 3.3 (95% confidence interval [CI], 1.5-7.4; P=.004), and those who became HSV-2 positive during follow-up had an adjusted IRR of 7.0 (95% CI, 3.9-12.4; P<.001). The population fraction of incident HIV infection attributable to HSV-2 was 27.8% (95% CI, 17.7%-37.2%). Intention-to-treat analysis of the protective effect of male circumcision on HIV acquisition was the same among men with and men without HSV-2 (0.38 vs. 0.37; P=.93). CONCLUSIONS: This study shows that HSV-2 has a substantial impact on HIV acquisition among young South African men. It suggests that HSV-2 infection enhances HIV acquisition and is responsible for approximately 25% of incident cases of HIV infection. However, the protective effect of male circumcision against HIV acquisition appears independent of HSV-2 serostatus.

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Talk and References

www.sexual**health**birmingham.co.uk

PROFESSIONAL

Presentations by the Department of Sexual Health and HIV Medicine *click here*

YouTube

LOGON : **TALKS**

PASSWORD : **SLIDES**

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NUMBER 5

4 from the developing world

Lancet. 2010 January 9; 375(9709): 123–131.

Routine versus clinically driven laboratory monitoring of HIV antiretroviral therapy in Africa (DART): a randomised non-inferiority trial

Lancet. 2010 January 9; 375(9709): 123–131.

DART Trial Team‡

1

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DART points the way for HIV treatment programmes

Published Online December 9, 2009 DOI:10.1016/S0140-6736(09)61964-9

See Articles page 233

In much of sub-Saharan Africa, the scale-up of use of antiretroviral therapy has been so far achieved without routine laboratory monitoring of drug toxicity and efficacy. Until now, there has not been substantive evidence about the consequences of delivering antiretrovirals without such routine monitoring.

In The Lancet today, the DART Trial Team[1] present the Development of AntiRetroviral Therapy in Africa (DART) trial. In DART at enrolment, all participants started triple-drug antiretroviral therapy and were randomised to clinically driven monitoring versus laboratory plus clinical monitoring for toxicity (haematology and biochemistry) and efficacy (CD4-cell counts). Over 5 years, the proportions who had one or more serious adverse events were almost identical, while there was a somewhat higher proportion in the group on clinically driven monitoring who had disease progression or death (28%, compared with 23% in the other group; hazard ratio 1·31, 95% CI 1·14–1·51). This benefit of laboratory plus clinical monitoring is probably due to the use of CD4 count rather than presence of clinical symptoms alone to decide on when to switch to a second-line regimen. This criterion for switching on the basis of CD4 count is just one of the CD4-count switch criteria recommended by WHO; the other criteria (on the basis of CD4-count change from baseline and from peak) are problematic to implement without a baseline CD4 count and frequent CD4 counts being available thereafter.[1]

The other particularly striking result from DART is the 5-year survival in both groups: 67% for clinical monitoring and 90% for laboratory plus clinical monitoring. Such rates of survival are for people in whom

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Timing of Initiation of Antiretroviral Drugs during Tuberculosis Therapy

Salim S. Abdool Karim, M.B., Ch.B., Ph.D., Kogieleum Naidoo, M.B., Ch.B., Anneke Grobler, M.Sc., Nesri Padayatchi, M.B., Ch.B., Cheryl Baxter, M.Sc., Andrew Gray, M.Sc. (Pharm.), Tanuja Gengiah, M.Clin.Pharm., M.S. (Epi.), Gonasagrie Nair, M.B., Ch.B., Sheila Bamber, M.B., Ch.B., Aarthi Singh, M.B., Ch.B., Munira Khan, M.B., Ch.B., Jacqueline Pienaar, M.Sc., Wafaa El-Sadr, M.D., M.P.H., Gerald Friedland, M.D., and Quarraisha Abdool Karim, Ph.D.

N ENGL J MED 362;8 NEJM.ORG FEBRUARY 25, 2010

2

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Timing of Initiation of Antiretroviral Drugs during Tuberculosis Therapy

BACKGROUND

The rates of death are high among patients with coinfection with tuberculosis and the human immunodeficiency virus (HIV). The optimal timing for the initiation of antiretroviral therapy in relation to tuberculosis therapy remains controversial.

METHODS

In an open-label, randomized, controlled trial in Durban, South Africa, we assigned 642 patients with both tuberculosis and HIV infection to start antiretroviral therapy either during tuberculosis therapy (in two integrated-therapy groups) or after the completion of such treatment (in one sequential-therapy group). The diagnosis of tuberculosis was based on a positive sputum smear for acid-fast bacilli. Only patients with HIV infection and a CD4+ cell count of less than 500 per cubic millimeter were included. All patients received standard tuberculosis therapy, prophylaxis with trimethoprim–sulfamethoxazole, and a once-daily antiretroviral regimen of didanosine, lamivudine, and efavirenz. The primary end point was death from any cause.

RESULTS

This analysis compares data from the sequential-therapy group and the combined integrated-therapy groups up to September 1, 2008, when the data and safety monitoring committee recommended that all patients receive integrated antiretroviral therapy. There was a reduction in the rate of death among the 429 patients in the combined integrated-therapy groups (5.4 deaths per 100 person-years, or 25 deaths), as compared with the 213 patients in the sequential-therapy group (12.1 per 100 person-years, or 27 deaths); a relative reduction of 56% (hazard ratio in the combined integrated-therapy groups, 0.44; 95% confidence interval, 0.25 to 0.79; P=0.003). Mortality was lower in the combined integrated-therapy groups in all CD4+ count strata. Rates of adverse events during follow-up were similar in the two study groups.

CONCLUSIONS

The initiation of antiretroviral therapy during tuberculosis therapy significantly improved survival and provides further impetus for the integration of tuberculosis and HIV services. (ClinicalTrials.gov number, NCT00398996.)

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Timing of Initiation of Antiretroviral Drugs during Tuberculosis Therapy

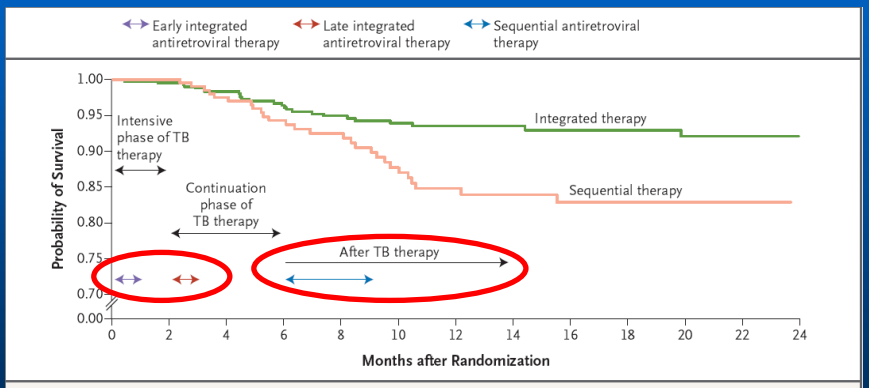

Figure 2. Kaplan–Meier Survival Curves.

ORIGINAL RESEARCH

PENTA 2009 guidelines for the use of antiretroviral therapy in paediatric HIV-1 infection

PENTA Steering Committee

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Antiretroviral Therapy and Mortality among HIV-Infected Infants

Avy Violari, F.C.Paed., Mark F. Cotton, M.Med., Ph.D., Diana M. Gibb, M.D., Abdel G. Babiker, Ph.D., Jan Steyn, M.Sc., Shabir A. Madhi, F.C.Paed., Ph.D., Patrick Jean-Philippe, M.D., and James A. McIntyre, F.R.C.O.G., for the CHER Study Team*

N Engl J Med. 2010 Mar 4;362(9):812-22.

A trial of a 7-valent pneumococcal conjugate vaccine in HIV-infected adults.

French N, Gordon SB, Mwalukomo T, White SA, Mwafulirwa G, Longwe H, Mwaiponya M, Zijlstra EE, Molyneux ME, Gilks CF.

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N Engl J Med. 2010 Mar 4;362(9):812-22.
A trial of a 7-valent pneumococcal conjugate vaccine in HIV-infected adults.
French N, Gordon SB, Mwalukomo T, White SA, Mwafulirwa G, Longwe H, Mwaiponya M, Zijlstra EE, Molyneux ME, Gilks CF.

BACKGROUND: Streptococcus pneumoniae is a leading and serious coinfection in adults with human immunodeficiency virus (HIV) infection, particularly in Africa. Prevention of this disease by vaccination with the current 23-valent polysaccharide vaccine is suboptimal. Protein conjugate vaccines offer a further option for protection, but data on their clinical efficacy in adults are needed. METHODS: In this double-blind, randomized, placebo-controlled clinical efficacy trial, we studied the efficacy of a 7-valent conjugate pneumococcal vaccine in predominantly HIV-infected Malawian adolescents and adults who had recovered from documented invasive pneumococcal disease. Two doses of vaccine were given 4 weeks apart. The primary end point was a further episode of pneumococcal infection caused by vaccine serotypes or serotype 6A. RESULTS: From February 2003 through October 2007, we followed 496 patients (of whom 44% were male and 88% were HIV-seropositive) for 798 person-years of observation. There were 67 episodes of pneumococcal disease in 52 patients, all in the HIV-infected subgroup. In 24 patients, there were 19 episodes that were caused by vaccine serotypes and 5 episodes that were caused by the 6A serotype. Of these episodes, 5 occurred in the vaccine group and 19 in the placebo group, for a vaccine efficacy of 74% (95% confidence interval [CI], 30 to 90). There were 73 deaths from any cause in the vaccine group and 63 in the placebo group (hazard ratio in the vaccine group, 1.18; 95% CI, 0.84 to 1.66). The number of serious adverse events within 14 days after vaccination was significantly lower in the vaccine group than in the placebo group (3 vs. 17, P=0.002), and the number of minor adverse events was significantly higher in the vaccine group (41 vs. 13, P=0.003). CONCLUSIONS: The 7-valent pneumococcal conjugate vaccine protected HIV-infected adults from recurrent pneumococcal infection caused by vaccine serotypes or serotype 6A. (Current Controlled Trials number, ISRCTN54494731.) 2010 Massachusetts Medical Society

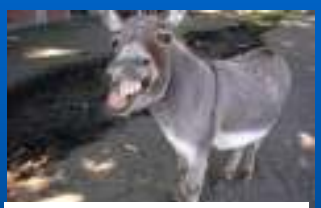
NHS | HEART of ENGLAND

NUMBER 6

4 Studies on Chlamydia

Which is the odd one out ?….

Dr Robertson's Daleks



Dr Watson's Donkey

Dr White's Cactus

Dr Barrett's Tomatoes

International Journal of STD & AIDS Volume 21 March 2010

A pilot qualitative analysis of the psychosocial factors which drive young people to decline chlamydia testing in the UK: implications for health promotion and screening

D Richardson MRCP*, **K Maple** MBBS†, **N Perry** MSc*, **E Ambler** RN*, **C Jurd** RN* and **M Fisher** FRCP*

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International Journal of STD & AIDS Volume 21 March 2010

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D Richardson MRCP*, **K Maple** MBBS†, **N Perry** MSc*, **E Ambler** RN*, **C Jurd** RN* and **M Fisher** FRCP*

Summary: The main objectives of this study are to investigate the psychosocial issues for young people who decline chlamydia testing as part of the national chlamydia screening programme in the UK and to consider the implications for future opportunistic screening. Transcripts of qualitative semi-structured interviews were analysed using interpretative phenomenological analysis to identify themes. The study involved 14 young people aged 16–24 years who declined chlamydia tests in non-health-care settings as part of the chlamydia screening programme. The study was conducted in educational settings where chlamydia screening is available. Four interlinked themes were identified: stigmatization of young people with chlamydia and who take a test, the feeling of embarrassment, their perception of risk and their beliefs of what the test involves. These beliefs and feelings were pervasive and negatively affected their personal decisions of having a test. In conclusion, understanding psychosocial cultural phenomena in the context of screening programmes for sexually transmitted infections (STIs) in young people are important for their success. Chlamydia and STIs remain stigmatized; testing is poorly understood and embarrassing for young people, which impacts the poor uptake for opportunistic screening. Strategies are needed to normalize and de-stigmatize chlamydia and the chlamydia test.

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Clinical Infectious Diseases 2009; 49:000–000

Chlamydia trachomatis and *Neisseria gonorrhoeae* Transmission from the Oropharynx to the Urethra among Men who have Sex with Men

Kyle T. Bernstein,[1] Sally C. Stephens,[1] Pennan M. Barry,[1,3] Robert Kohn,[1] Susan S. Philip,[1] Sally Liska,[2] and Jeffrey D. Klausner[1,3]

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Background. Limited data exist on the risk of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* transmission from oropharynx to urethra. We examined urethral *C. trachomatis* and *N. gonorrhoeae* positivity among men who have sex with men (MSM) seen at San Francisco City Clinic (San Francisco, CA) during 2007.

Methods. All patients who sought care at the San Francisco City Clinic (the only municipal sexually transmitted disease clinic in San Francisco) received a standardized interview conducted by clinicians. We estimated urethral *C. trachomatis* and *N. gonorrhoeae* positivity for 2 groups of visits by MSM who visited during 2007: (1) men who reported their only urethral exposure was receiving fellatio in the previous 3 months and (2) men who reported unprotected insertive anal sex in the previous 3 months. Additionally, urethral *C. trachomatis* and *N. gonorrhoeae* positivity was estimated, stratified by human immunodeficiency virus infection status, urogenital symptom history, and whether the patient had been a contact to a sex partner with either chlamydia or gonorrhea.

Results. Among MSM who reported only receiving fellatio, urethral *C. trachomatis* and *N. gonorrhoeae* positivity were 4.8% and 4.1%, respectively. These positivity estimates were similar to positivity found among MSM who reported unprotected insertive anal sex.

Conclusions. A more complete understanding of the risks of transmission of *C. trachomatis* and *N. gonorrhoeae* from oropharynx to urethra will help inform prevention and screening programs.

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High Prevalence of Anorectal Chlamydial Infection in HIV-Infected Men Who Have Sex with Men in Switzerland

Thanh Dang,[1] Katia Jaton-Ogay,[2] Markus Flepp,[3] Helen Kovari,[4] John-Marc Evison,[5] Jan Fehr,[6] Patrick Schmid,[7] Emmanuelle Boffi El Amari,[8] Matthias Cavassini,[1] Massimo Odorico,[9] Philip E. Tarr,[10] Gilbert Greub,[1,2] and the Swiss HIV Cohort Study

[1]Infectious Diseases Service, University Hospital Center, and [2] Institute of Microbiology, University of Lausanne and University Hospital Center, Lausanne, [3]Center for Infectious Diseases, Klinik im Park, and [4]Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, Zurich, [5]Department of Infectious Diseases, University Hospital Bern, Bern, [6]Division of Infectious Diseases, University Hospital Basel, Basel, [7]Infectious Disease Unit, Hospital St-Gall, St-Gall, [8]HIV-AIDS Unit and Infectious Disease Consultations, University Hospital Geneva, Geneva, [9]Infectious Disease Service, Hospital Lugano, Lugano, and [10]Infectious Diseases Service, Kantonsspital Bruderholz, University of Basel, Bruderholz, Switzerland

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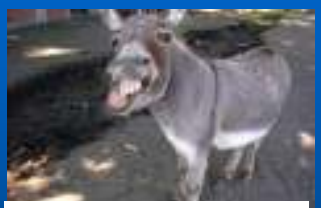
BRIEF REPORT

High Prevalence of Anorectal Chlamydial Infection in HIV-Infected Men Who Have Sex with Men in Switzerland

Which is the odd one out ?....

Dr Robertson's Daleks



Dr Watson's Donkey

Dr White's Cactus

Dr Barrett's Tomatoes

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International Journal of STDs & AIDS Volume 19

Unusual transmission route of Lymphogranuloma venereum; following sexual contact with a female donkey

Farzin Khorvash MD*, **Ammar H Keshteli** MD†, **Hassan Salehi** MD*, **Levente Szeredi** DVM PhD‡ and **Servaas A Morré** PhD§¶††

*Department of Infectious and Tropical Diseases, School of Medicine; †Medical Students' Research Center, Isfahan University of Medical Sciences, Isfahan, Iran; ‡Central Agricultural Office, Veterinary Diagnostic Directorate, Budapest, Hungary; §Department of Pathology, Laboratory of Immunogenetics; ¶Department of Internal Medicine, Section Infectious Diseases, VU University Medical Center, Amsterdam; ††Department of Medical Microbiology, University Hospital Maastricht, Maastricht, The Netherlands

Summary: Here, we present a 20-year-old man who presented with painful inguinal and femoral masses. He gave a history of sexual contact with a mare 14 days before his recent illness. He was diagnosed with lymphogranuloma venereum based on the histopathological findings and a high titre of IgG (1:1400).

Keywords: lymphogranuloma venereum, *Chlamydia trachomatis*, transmission route

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NUMBER 7&8

3 studies on hepatitis C/B

NHS | HEART of ENGLAND

CONCISE COMMUNICATION

Delayed anti-HCV antibody response in HIV-positive men acutely infected with HCV

Emma C. Thomson, Eleni Nastouli, Janice Main, Peter Karayiannis, Joseph Eliahoo, David Muir and Myra O. McClure

AIDS 2009, **23**:89–93

1

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Objective: An epidemic of acute hepatitis C virus (HCV) infection among HIV-positive men who have sex with men is occurring in urban centers in Western Europe and the United States. Early diagnosis and treatment of HCV results in improved sustained virological response rates. This study compared the sensitivity of reverse transcriptase PCR (RT–PCR) versus antibody screening for the diagnosis of early HCV infection in HIV-positive patients and estimated the length of time from HCV infection to the development of anti-HCV antibodies.

Design: Patients from the St Mary's Acute Hepatitis C Cohort (SMACC) were recruited retrospectively and prospectively between 2004 and 2008.

Methods: Archived plasma samples, obtained at 1–3 monthly intervals for routine monitoring of HIV viral load were assayed retrospectively for HCV in order to assess the sensitivity of RT–PCR and enzyme-linked immunosorbent assay (ELISA).

Results: Forty-three HIV-positive patients with early HCV infection were identified. The median CD4 cell count was 370 cells/μl. The median alanine transaminase at the time of the first positive HCV PCR was 65 IU/ml. At this time, 75% of patients had a negative HCV antibody test. Three months later, 37% of patients still had a negative result. After 9 months, 10% of patients had a negative test and 5% remained negative after 1 year.

Conclusion/discussion: Delayed seroconversion in HIV-positive individuals with acute HCV may result in delayed diagnosis and treatment. Where there is a clinical suspicion of recent HCV infection, for example, elevated alanine transaminase levels, HIV-infected patients should be screened for HCV RNA by RT–PCR.

AIDS 2009, **23**:89–93

Keywords: acute hepatitis C, antibody, HIV

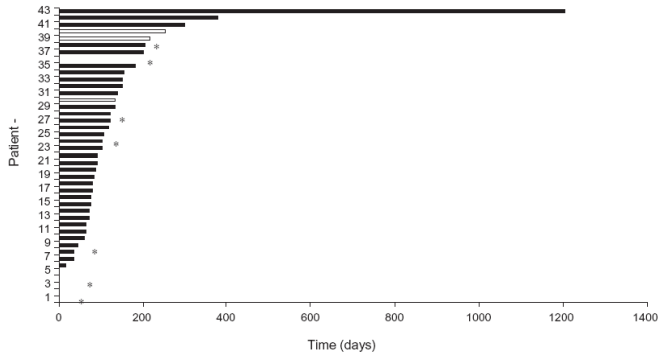

Fig. 1. Time to seroconversion. Seroconversion time (days) was calculated as the time from the first PCR positive sample to the first positive antibody (range 0–1206 days). Four patients (patients 30, 36, 39 and 40 shown in white) did not produce an antibody by 133, 183, 205 and 218 days of follow-up. Seven patients (asterisked) spontaneously cleared the infection, two of whom did not produce an antibody response.

nature Vol 461|17 September 2009

Genetic variation in *IL28B* predicts hepatitis C treatment-induced viral clearance

Dongliang Ge[1], Jacques Fellay[1], Alexander J. Thompson[2], Jason S. Simon[3], Kevin V. Shianna[1], Thomas J. Urban[1], Erin L. Heinzen[1], Ping Qiu[3], Arthur H. Bertelsen[3], Andrew J. Muir[2], Mark Sulkowski[4], John G. McHutchison[2] & David B. Goldstein[1]

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people worldwide and is the leading cause of cirrhosis in North America[1]. Although the recommended treatment for chronic infection involves a 48-week course of peginterferon-α-2b (PegIFN-α-2b) or -α-2a (PegIFN-α-2a) combined with ribavirin (RBV), it is well known that many patients will not be cured by treatment, and that patients of European ancestry have a significantly higher probability of being cured than patients of African ancestry. In addition to limited efficacy, treatment is often poorly tolerated because of side effects that prevent some patients from completing therapy. For these reasons, identification of the determinants of response to treatment is a high priority. Here we report that a genetic polymorphism near the *IL28B* gene, encoding interferon-λ-3 (IFN-λ-3), is associated with an approximately twofold change in response to treatment, both among patients of European ancestry ($P = 1.06 \times 10^{-25}$) and African-Americans ($P = 2.06 \times 10^{-3}$). Because the genotype leading to better response is in substantially greater frequency in European than African populations, this genetic polymorphism also explains approximately half of the difference in response rates between African-Americans and patients of European ancestry.

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Journal of Infect Dis. 2009 Sep 28

Antibody Levels and Protection after Hepatitis B Vaccine: Results of a 22-Year Follow-Up Study and Response to a Booster Dose.

McMahon BJ, Dentinger CM, Bruden D, Zanis C, Peters H, Hurlburt D, Bulkow L, Fiore AE, Bell BP, Hennessy TW.

3

NUMBER 9

1 study on HPV

Sexually Transmitted Infections. 85(7)(pp 499-502), 2009.

Rapid decline in presentations of genital warts after the implementation of a national quadrivalent human papillomavirus vaccination programme for young women.

Fairley C.K., Hocking J.S., Gurrin L.C., Chen M.Y., Donovan B., Bradshaw C.S.

Sexually Transmitted Infections. 85(7)(pp 499-502), 2009.

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Fairley C.K., Hocking J.S., Gurrin L.C., Chen M.Y., Donovan B., Bradshaw C.S.

Objective:

This study aimed to determine if the Australian human papillomavirus (HPV) vaccination programme has had a population impact on presentations of genital warts. Methods: Retrospective study comparing the proportion of new clients with genital warts attending Melbourne Sexual Health Centre (MSHC) from January 2004 to December 2008. Australia provided free quadrivalent HPV vaccine to 12-18-year-old girls in a school-based programme from April 2007, and to women 26 years and younger through general practices from July 2007. Results: 36 055 new clients attended MSHC between 2004 and 2008 and genital warts were diagnosed in 3826 (10.6%; 95% CI 10.3 to 10.9). The proportion of women under 28 years with warts diagnosed decreased by 25.1% (95% CI 30.5% to 19.3%) per quarter in 2008. Comparing this to a negligible increase of 1.8% (95% CI 0.2% to 3.4%) per quarter from the start of 2004 to the end of 2007 also in women under 28 years generates strong evidence of a difference in these two trends ($p<0.001$). There was no evidence of a difference in trend for the quarterly proportions before and after the end of 2007 for any other subgroup, and on only one occasion was there strong evidence of a trend different to zero, for heterosexual men in 2008 in whom the average quarterly change was a decrease of 5% (95% CI 0.5% to 9.4%; $p=0.031$). Conclusions: The data suggest that a rapid and marked reduction in the incidence of genital warts among vaccinated women may be achievable through an HPV vaccination programme targeting women, and supports some benefit being conferred to heterosexual men.

Finally.....

At number 10...

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 19, Number 5, 2003, pp. 000-000
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Identification of a Transmission Chain of HIV Type 1 Containing Drug Resistance-Associated Mutations

and DEENAN PILLAY[1]

UNIVERSITY OF BIRMINGHAM
BIRMINGHAM HEARTLANDS HOSPITAL

ABSTRACT

We have investigated a potential transmission chain of HIV-1 with drug resistance-associated mutations between three individuals over a period of 5 years by use of cloning and sequencing of viral genes, and phenotypic characterization. Viruses containing reverse transcriptase drug resistance-associated mutations were transmitted sequentially between three homosexual men (A, B, and C), and persisted in one individual for at least 4 years, despite intermittent therapy and reduced viral replicative capacity compared with wild-type

Professor; Head Virology, UCL

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