

CARDIFF 2004

British HIV Association  
**BHIVA**

# ABSTRACTS

## 10<sup>th</sup> ANNIVERSARY CONFERENCE

OF THE  
BRITISH HIV ASSOCIATION [BHIVA]

Thursday 15 – Saturday 17 April 2004

CITY HALL, CARDIFF

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### Abstract selection

The number of high-quality abstracts submitted for presentation at the Annual Conference of the British HIV Association continues to grow, making the task of selection ever harder. Thanks are due to the Scientific Committee (see below) for all the time and effort they put into overseeing this selection. Unfortunately, due to time and space constraints, it has been necessary to disappoint some potential presenters.

The Scientific Committee hope this will not deter anyone from submitting abstracts for future meetings.

### Abstract citations

All abstracts accepted for both oral and poster presentation will be published in *HIV Medicine*, the BHIVA peer-reviewed journal, in the July 2004 issue. All published citations of abstracts should be made to *HIV Medicine* and not to this conference book.

### Prizes/Scholarships

There will be a BHIVA prize for the best oral presentation and one for the best poster presentation.

Bristol-Myers Squibb Scholarships will be awarded to the five best oral and poster presentations as determined by the Abstract Judging Panel. To qualify for a scholarship, applicants must be of Junior Grade or under 35 years of age. Each scholarship is worth £1000.

BHIVA Science Scholarships will be presented to up to ten scientists studying for a PhD or MD. For those whose abstracts are accepted for presentation (oral or poster), all registration fees, reasonable travel expenses and accommodation costs (maximum two nights at £60 per night) will be paid for by BHIVA.

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#### Abstract Judging Panel

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# EXECUTIVE COMMITTEE

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| Ms R Weston          | (HIVPA)        |

# RESEARCH PRESENTATIONS

FRIDAY 16 APRIL

0830–0930 **Research Presentations: Session 1**  
**Antiretroviral therapy**

Chair: Dr Ed Wilkins  
*North Manchester General Hospital*

**0830–0840 Abstract O1**

Pharmacokinetics (PK) of saquinavir hard gel (SQV-hg)/ritonavir (RTV) with atazanavir (ATV) or fosamprenavir (FPV) in HIV+ patients (pts)  
*M Boffito, Chelsea and Westminster Hospital, London*

**0840–0850 Abstract O2**

Clinical experience of atazanavir: tolerable and effective  
*C McDonald, Brighton and Sussex University Hospitals*

**0850–0900 Abstract O3**

Morbidity of HIV-infected children in Groote Schuur Hospital, Cape Town, South Africa: a tale of the lucky 149  
*LJ Neal, University of Wales College of Medicine, Cardiff*

**0900–0910 Abstract O4**

To err is human: learning from medication errors in HIV  
*H Leake Date, Brighton and Sussex University Hospitals*

**0910–0920 Abstract O5**

Effects of combination antiretroviral therapy (CART) on metabolite levels in children  
*EGH Lyall, St Mary's Hospital, London*

**0920–0930 Abstract O6**

The Stop Study: after discontinuation of efavirenz, plasma concentrations can persist for >2 weeks  
*S Taylor, Birmingham Heartlands Hospital*

0930–1030 **Research Presentations: Session 2**  
**Virology**

Chair: Dr Anna Maria Geretti  
*Royal Free Hospital, London*

**0930–0940 Abstract O7**

Persistence of transmitted resistance-associated HIV-1 mutations in 16 patients  
*D Pao, Brighton and Sussex University Hospitals*

**0940–0950 Abstract O8**

Adjunctive use of the Serological Testing Algorithm for HIV Seroconversion (STARHS) identifies a high and increasing proportion of newly diagnosed infections as incident  
*D Pao, Brighton and Sussex University Hospitals*

**0950–1000 Abstract O9**

Mother-to-child transmission of human herpesvirus-8 (HHV8) in South Africa  
*M Dedicoat, Liverpool School of Tropical Medicine and Hlabisa Hospital*

**1000–1010 Abstract 10**

Is there a significant difference between HIV-1 in the blood and the female genital tract?  
*A Mears, Guy's and St Thomas' Hospitals, London*

**1010–1020 Abstract 11**

Use of coalescence theory to estimate time of introduction of HIV-1 strains into the UK, and subsequent population growth dynamics  
*S Hué, University College London Medical School*

**1020–1030 Abstract 12**

Genotypic resistance to antiretroviral therapy in HIV-1-infected pregnant women taking highly active antiretroviral therapy (HAART) in pregnancy  
*F Lyons, St James's Hospital, Dublin, Ireland*

1630–1730 **Research Presentations: Session 3**  
**Epidemiology**

Chair: Dr Kevin De Cock  
*Centers for Disease Control, Kenya*

**1630–1640 Abstract O13**

Molecular and epidemiological characteristics of primary HIV-1 infections among a cohort of predominantly men who have sex with men (MSM) in a defined geographical area: transmission events associated with high-risk activity and sexually transmitted infections (STIs)  
*D Pao, Brighton and Sussex University Hospitals*

**1640–1650 Abstract O14**

Trends in genotypic resistance in clinical samples submitted for routine HIV resistance analysis  
*NE Mackie, St Mary's Hospital, London*

**1650–1700 Abstract O15**

Late diagnosis of HIV infection among individuals with low or unacknowledged risks in England, Wales and Northern Ireland  
*VL Gilbert, Communicable Disease Surveillance Centre, Health Protection Agency, London*

**1700–1710 Abstract O16**

A comparison of changes in response to HAART over time between regions of Europe: results from the EuroSIDA study  
*W Bannister, Royal Free and UCMS, London*

**1710–1720 Abstract O17**

HIV-infected adolescents: an evolving UK cohort  
*CJ Foster, for the Collaborative HIV Paediatric Study (CHIPS)*

**1720–1730 Abstract O18**

An update of the UK HIV epidemic using national surveillance data  
*K Sinka, Communicable Disease Surveillance Centre, Health Protection Agency, London*

# RESEARCH PRESENTATIONS

SATURDAY 17 APRIL

1030–1230 **Research Presentations: Sessions 4 and 5  
Co-infection**

Chair: Dr Steve Ash  
*Ealing Hospital, London*

**1030–1040 Abstract O19**

Tenofovir in the treatment of hepatitis B (HBV)/HIV co-infected individuals

*Y Gilleece, Chelsea and Westminster Hospital, London*

**1040–1050 Abstract O20**

Acute hepatitis C virus (HCV) in a cohort of HIV-positive men: outcomes and response to pegylated interferon- $\alpha$ 2b (peg-IFN- $\alpha$ 2b) and ribavirin

*S Bhagani, Royal Free Hospital, London*

**1050–1100 Abstract O21**

Tuberculosis and HIV co-infection among healthcare workers in south-west London

*CFJ Rayner, St George's Hospital, London*

**1100–1110 Abstract O22**

Do all HIV-positive patients co-infected with hepatitis C genotypes 2 and 3 require 12 months of treatment with Ribavirin and pegylated (peg) interferon (IFN)?

*C Donnelly, St James's Hospital, Dublin, Ireland*

1110–1150 **Women**

Chair: Dr Margaret Johnson  
*Royal Free Hospital, London*

**1110–1120 Abstract O23**

The impact of an HIV diagnosis on fertility

*S Cliffe, for the UK Collaborative Study of the effect of HIV on pregnancy decisions, Institute of Child Health and Health Protection Agency, London*

**1120–1130 Abstract O24**

Maternal breast-feeding behaviour and prevalence of HIV-1 in rural South Africa

*M Dedicoat, Africa Centre for Health and Population Studies, Somkhele, KwaZulu/Natal, South Africa and Liverpool School of Tropical Medicine*

**1130–1140 Abstract O25**

Pregnancy outcome of HIV-positive women in London, 1998–2002

*L Navaratne, St Thomas' Hospital, London*

**1140–1150 Abstract O26**

Long-term follow-up of HIV-positive pregnant women in London

*F Martin, Homerton University Hospital, London*

1150–1230 **Cancer**

Chair: Dr Gary Brook  
*Central Middlesex Hospital, London*

**1150–1200 Abstract O27**

Is 'high oncogenic risk' human papillomavirus (HR HPV) infection predictive of the evolution of cervical neoplasia in women with HIV?

*BM Holden, St Mary's Hospital, London*

**1200–1210 Abstract O28**

Anti-retroviral treatment regimens and the prevention of systemic HIV-related non-Hodgkin's lymphoma (NHL)

*A Waterston, Chelsea and Westminster Hospital, London*

**1210–1220 Abstract O29**

Highly active antiretroviral therapy (HAART) does not prevent anal cancer

*C Thirlwell, Chelsea and Westminster Hospital, London*

**1220–1230 Abstract O30**

Protease inhibitors potentiate chemotherapy-induced neutropenia

*N McCall-Peat, Chelsea and Westminster Hospital, London*

## 01

## Pharmacokinetics (PKs) of saquinavir hard gel (SQV-hg)/ritonavir (RTV) with atazanavir (ATV) or fosamprenavir (FPV) in HIV+ patients (pts)

M Boffito<sup>1</sup>, DJ Back<sup>2</sup>, M Kurowski<sup>4</sup>, L Dickinson<sup>2</sup>, G Kruse<sup>4</sup>, A Hill<sup>3</sup>, G Moyle<sup>1</sup>, M Nelson<sup>1</sup>, C Higgs<sup>1</sup>, C Fletcher<sup>1</sup>, B Gazzard<sup>1</sup>, A Pozniak<sup>1</sup>  
<sup>1</sup>Chelsea and Westminster Hospital, London, <sup>2</sup>University of Liverpool, Liverpool, <sup>3</sup>Roche, Welwyn, UK; <sup>4</sup>Therapia GmbH, Berlin, Germany

**Background:** Double-boosted protease inhibitor (PI) regimens have shown promising results in HIV+ patients in salvage or when reverse transcriptase inhibitors are no longer a therapeutic option. When combining different cytochrome P450 substrates, the potential for undesirable drug interactions is enhanced.

**Methods:** The PKs of SQV-hg/RTV 1000/100 and 200 mg plus FPV 700mg twice a day ( $n=18$ ) and SQV-hg/RTV/ATV 1600/100/300 mg once a day ( $n=18$ ) was investigated in HIV+ pts. On PK days, blood was drawn predose and 0.5, 1, 2, 3, 4, 6, 8, 12 and 24 hours postdose. Safety analysis was performed at screening, PK days and follow-up. Geometric mean ratios (GMRs) and 95% confidence intervals (CI) were used to compare SQV-PK parameters  $\pm$  FPV or ATV. SQV, RTV, FPV and ATV concentrations were measured by high-performance liquid chromatography (HPLC)-mass spectrometry(MS)/MS.

**Results:** No changes in safety parameters were observed. ATV led to a reversible increase in total and indirect bilirubin after 10 days of therapy. After the addition of FPV, SQV area under the curve ( $AUC_{0-12}$  (GMR, 95% CI: 0.85, 0.74–1.15), plasma drug concentration ( $C_{trough}$  (0.76, 0.64–1.17) and  $C_{max}$  (0.91, 0.79–1.18) were slightly decreased. With a further 100 mg RTV, SQV  $AUC_{0-12}$  (1.09, 0.87–1.65),  $C_{trough}$  (1.02, 0.81–1.74) and  $C_{max}$  (1.19, 0.97–1.67) slightly increased. A statistically significant increase in SQV  $C_{trough}$  (2.12, 1.72–3.50),  $C_{max}$  (1.42, 1.24–1.94) and  $AUC_{0-24}$  (1.60, 1.35–2.43) was observed after the addition of ATV to the once-daily SQV/RTV-containing regimen.

**Conclusions:** SQV use in double-boosted PI-containing regimens is very promising from a safety and PK prospective.

## 02

## Clinical experience of atazanavir: tolerable and effective

C McDonald<sup>1</sup>, N Mackie<sup>2</sup>, C Smyth<sup>1</sup>, N Tamm<sup>2</sup>, R Weston<sup>2</sup>, G Scullard<sup>2</sup>, M Fisher<sup>1</sup>

<sup>1</sup>Brighton and Sussex University Hospitals, <sup>2</sup>St Mary's Hospital, London, UK

**Introduction:** Atazanavir (ATV) is a new protease inhibitor (PI) with potential advantages of once-daily administration, low pill burden and less reported hyperlipidaemia.

**Methods:** Patients attending two HIV clinics and receiving ATV were included. Demographic details, reasons for using ATV, surrogate marker responses and toxicities (pre- and post-ATV) were collected.

**Results:** 76 patients received ATV for a median of 15 weeks (range 1–47). The median time on antiretroviral therapy was 64 months and the duration of prior PI therapy 23 months. Reasons for starting ATV included pill burden (20), once-daily therapy (21), adherence issues (9), hyperlipidaemia (20), gastrointestinal disturbance (11), lipodystrophy (6) and virological failure (13). Two patients died (unrelated to ATV): six stopped ATV because of patient choice (3), hypersensitivity (1), jaundice (1) and myositis (1). One was lost to follow-up. 28 switched to ATV with a viral load of <50 HIV-1 RNA copies/ml, and 27 remain with <50copies/ml; 44 started with detectable viraemia, 22 are now undetectable and the remaining 16 on therapy have experienced significant viral load reductions. Hyperbilirubinaemia occurred in 64%, resolving in 61%; three experienced clinical jaundice. Hyperlipidaemia improved in 61%, with 38% able to stop lipid-lowering agents. Improvements in gastrointestinal symptoms occurred in 54%.

**Conclusion:** ATV is well tolerated, efficacious and enables resolution of PI-related toxicity in many recipients.

## 03

## Morbidity of HIV-Infected children in Groote Schuur Hospital, Cape Town, South Africa: a tale of the lucky 149

LJ Neal<sup>1</sup>, K Yoganathan<sup>2</sup>, P Roux<sup>3</sup>

<sup>1</sup>University of Wales College of Medicine, Cardiff, <sup>2</sup>Singleton Hospital, Swansea, UK; <sup>3</sup>Groote Schuur Hospital, Cape Town, South Africa

**Background:** Globally, HIV infection affects 600,000 children each year, over 90% of whom live in sub-Saharan Africa. It is a huge problem in Cape Town where, annually, Groote Schuur Hospital Paediatric HIV Ward has funding for antiretroviral treatment of only 149 children.

**Methods:** We reviewed 50 children on antiretroviral therapy who were admitted with HIV-related problems during August 2003. Details were recorded of their current admission and a retrospective study was carried out to assess the numbers of previous admissions and the diagnoses present, both before and after antiretroviral therapy.

**Results:** The mean number of admissions per year before and after antiretroviral therapy was 4.5 and 1.2, respectively. Similarly, the mean number of diagnoses per admission fell from 2.1 before to 1.6 after antiretroviral therapy. HIV-related diagnoses included pneumonia, diarrhoea, wasting, haematological abnormalities, candidiasis, lymphocytic interstitial pneumonitis, dermatitis, sepsis and otitis media.

**Conclusions:** The results show that antiretroviral therapy reduces both the number of hospital admissions for HIV-related problems and the number of HIV-related diagnoses present during each admission. We conclude that antiretroviral therapy profoundly improves the health of children with HIV in Cape Town and urge that funding be made available for all HIV-infected children, not just the lucky 149.

## 04

## To err is human: learning from medication errors in HIV

H Leake Date<sup>1</sup>, D Godfrey<sup>2</sup>, Jane Nicholls<sup>3</sup>, on behalf of HIVPA<sup>4</sup>

<sup>1</sup>Brighton and Sussex University Hospitals NHS Trust, <sup>2</sup>Mayday University Hospital, <sup>3</sup>London, Eastern and South East Specialist Pharmacy Services, <sup>4</sup>The HIV Pharmacy Association (HIVPA), UK

**Introduction:** A Department of Health (DH) report on improving medication safety (*Building a Safer NHS for Patients*) highlighted the causes and frequency of medication errors and identified strategies for preventing them. Previous HIVPA research showed that 2.8% HIV outpatient prescriptions contained serious errors.

**Methods:** HIVPA members recorded all serious (moderate, major or catastrophic) medication errors relating to people with HIV for one week [using National Patient Safety Agency (NPSA) criteria] and the results were analysed using Microsoft Excel. All errors were peer-reviewed and 'most likely consequences if not detected' were classified as 'catastrophic' (e.g. could be fatal), 'major' (e.g. could cause virological failure) or 'moderate' (e.g. could cause renal failure).

**Results:** 76 serious errors were detected by 10 centres. 11 (14%) resulted in actual harm, two (3%) caused no harm and 63 (83%) were 'near misses' (detected before the patient received medication). Probable outcomes of all errors if undetected were peer-reviewed as: catastrophic (1.3%), major (54%) and moderate (44.7%).

**Discussion:** The human and financial ramifications of medication errors are enormous. This survey highlights significant clinical risks and training needs for HIV multidisciplinary teams. Strategies are needed to improve patient safety and meet the DH target of a 40% reduction in serious medication errors.

## 05

## Effects of combination antiretroviral therapy (CART) on metabolite levels in children

M Rhoads<sup>1</sup>, CJ Smith<sup>2</sup>, G Tudor-Williams<sup>1</sup>, P Kyd<sup>3</sup>, S Walters<sup>1</sup>, C Sabin<sup>2</sup>, EGH Lyall<sup>3</sup>

<sup>1</sup>Imperial College London, <sup>2</sup>Royal Free and University College London, <sup>3</sup>St Mary's Hospital, London, UK

**Background:** As treated children with HIV survive into adulthood, potential long-term metabolic effects of CART must be considered.

**Methods:** A retrospective longitudinal study of metabolites in children, before and on CART (2000–2003). Non-fasting analyses included cholesterol (total cholesterol (C), high-density lipoprotein (HDL), low-density lipoprotein (LDL)), triglycerides (TG), lactate (L) and glucose (G). Analysis by mixed-effects regression models [Statistical Analysis Systems (SAS) software].

**Results:** 146 children (53% female, 68% African), aged 0.1–16 years (median 6.9), attended 1208 clinic visits. At baseline, 51% were on CART, with higher median total C, HDL and LDL, by 0.7, 0.21 and 0.43 mmol/l, respectively ( $P \leq 0.0003$ ). During a follow-up on CART, in mixed-effects regression, total C increased by 0.07 mmol/l per year of therapy ( $P = 0.0001$ ), and 53 patients (46.1%) had at least one high total C ( $>5$  mmol/l) on treatment. L, TG and G remained stable over time on treatment, but L declined with increased age ( $P = 0.0001$ ). Africans had lower total C, TG, LDL and total C/HDL ratio than Caucasians.

**Conclusions:** In children, CART raises cholesterol above basal levels and this increases over time. Both HIV and CART may increase cardiovascular risk; thus on-going monitoring of lipids in children and adolescents is important. However, lactate need only be measured in those with symptoms.

## 07

## Persistence of transmitted resistance-associated HIV-1 mutations in 16 patients

PA Cane<sup>1</sup>, G Dean<sup>2</sup>, M Fisher<sup>2</sup>, D Pao<sup>2</sup>, S Drake<sup>3</sup>, D Pillay<sup>1,4</sup> and collaborating clinicians

<sup>1</sup>Health Protection Agency Antiviral Susceptibility Reference Unit, Birmingham, <sup>2</sup>Royal Sussex Hospital, Brighton, <sup>3</sup>Birmingham Heartlands Hospital, <sup>4</sup>University College London, UK

**Aim:** To determine the stability of resistance-associated genotypic mutations observed in primary HIV Infection (PHI).

**Methods:** 16 PHI patients with evidence of resistance-associated mutations were followed for up to 3 years

**Results:** The persistence of resistance-associated mutations was variable. Y181C and K219Q in reverse transcriptase disappeared within 25 and 9 months, respectively, while K103N alone was stable for at least for 23 months in one patient. M41L, T69N and T215 variants were stable over the time periods studied up to 3 years, except for T215Y being replaced by T215C in one patient within 21 months. An additional patient was found to have virus showing M41L and T215S 10 years after seroconversion. Three-class resistance in three patients was found to be stable for up to 2 years and was associated with low viral loads, except for one patient showing a change from T215Y to T215C associated with a marked increase in the viral load.

**Conclusions:** Certain resistance-associated mutations are stable in the long term, and may be indicators of infection with drug-resistant virus. However, others may disappear rapidly, possibly as a result of fitness changes. Thus it would be better to undertake resistance testing at the time of diagnosis rather than waiting until treatment is indicated.

## 06

The Stop Study: after discontinuation of efavirenz (EFV), plasma concentrations can persist for  $>2$  weeks

S Taylor<sup>1</sup>, S Allen<sup>2</sup>, E Smit<sup>3</sup>, S Fidler<sup>4</sup>, S Gibbons<sup>5</sup>, S Drake<sup>1</sup>, A Wade<sup>2</sup>, P Cane<sup>3</sup>, J Fox<sup>4</sup>, DJ Back<sup>5</sup>

<sup>1</sup>Birmingham Heartlands Hospital, <sup>2</sup>Coventry and Warwickshire Hospital, <sup>3</sup>Health Protection Agency, Birmingham Heartlands Hospital, <sup>4</sup>Imperial College London, <sup>5</sup>University of Liverpool, UK

**Background:** Current antiretroviral drugs differ in their relative plasma elimination half-lives ( $t_{1/2}$ ). The reported EFV  $t_{1/2}$  is 40–55 hours. Therefore, EFV concentrations may persist at therapeutic levels for greater than 1 week following discontinuation. If drugs with a shorter  $t_{1/2}$  are stopped at the same time as EFV, patients will effectively be receiving monotherapy for a significant period of time.

**Methods:** 10 HIV-1+ patients took part in a pharmacokinetic (PK) study. Blood was drawn at baseline (day 0) and at days 4, 7, 14 and 21 after stopping EFV. Plasma samples were analysed for EFV concentrations by high-performance liquid chromatography and  $T_{1/2}$  determined by regression analysis. Viral RNA  $\pm$  resistance testing was performed at each time point. A further 25 patients who stopped EFV after short-course antiretroviral therapy following seroconversion were assessed to obtain virological data on patients stopping EFV 7 days prior to nucleoside reverse transcriptase inhibitors (NRTIs). Resistance testing was performed before antiretroviral therapy and 4 weeks after stopping EFV.

**Results:** Five patients had EFV  $T_{1/2}$  within the expected range. However, five had EFV  $T_{1/2} >100$  hours (median 123, range 114–229). Four of these were black African women and three had therapeutic EFV  $>1000$  ng/ml 2 weeks after stopping EFV. Of the 25 patients in the virological study only one had resistance 4 weeks after stopping treatment.

**Conclusions:** Virological data from persons fully suppressed at the time of stopping therapy suggest EFV can be stopped 7 days before other shorter-acting drugs. These extended PK data suggest the stop window should be increased to 2–3 weeks (or switch from EFV to cover this).

## 08

## Adjunctive use of the Serological Testing Algorithm for HIV Seroconversion (STARHS) identifies a high and increasing proportion of newly diagnosed infections as incident

M Fisher<sup>1</sup>, G Dean<sup>1</sup>, V Cooper<sup>2</sup>, G Murphy<sup>3</sup>, D Pao<sup>1</sup>, J Parry<sup>3</sup>

<sup>1</sup>Brighton and Sussex University Hospitals, <sup>2</sup>Brighton University, <sup>3</sup>Health Protection Agency, UK

**Background:** Identification of recent HIV infection (RHI) may enable early intervention and reduce onward transmission. Conventional methods for identifying RHI are limited. STARHS diagnoses infection within the previous 4–6 months. In this study, we determined to what extent adjunctive use of STARHS identified further RHI, and observed RHI trends over time.

**Methods:** Incident cases from 1996 to 2002 were determined by conventional methods (HIV-negative test within 18 months, evolving antibody response or incomplete Western blot), by STARHS and by both methods combined. Trends over time were determined using the Kruskal–Wallis Test (using the Statistical Procedure for the Social Sciences, SPSS).

**Results:** Of 486 individuals newly diagnosed during the study period 387 (89%) underwent STARHS serum analysis. New diagnoses identified as incident by conventional methods increased from 0/50 (1996) to 18/82 (2002). STARHS identified a further 48 incident infections (11% of total new infections; 48% of total incident), ranging from 2/50 (1997) to 14/82 (2002). Using a combination of conventional methods and STARHS, RHI increased over time from 9/50 (1996) to 32/82 (2002) [ $P < 0.001$ ].

**Conclusions:** Adjunctive use of STARHS identified a high and increasing proportion of new HIV diagnoses as incident, which may confirm significant ongoing transmission, enabling early intervention, which could benefit both the individual and the population.

## 09

## Mother-to-child transmission of human herpesvirus-8 (HHV8) in South Africa

M Dedicoat<sup>1,4</sup>, R Newton<sup>2</sup>, J Sheldon<sup>3</sup>, K Alkarsah<sup>3</sup>, I Szabados<sup>3</sup>, B Ndlovu<sup>4</sup>, T Page<sup>4</sup>, C Gilks<sup>1</sup>, S Cassol<sup>4</sup>, T Schulz<sup>3</sup>

<sup>1</sup>Liverpool School of Tropical Medicine and Hlabis Hospital, <sup>2</sup>Cancer Research UK Epidemiology Unit, Oxford, UK; <sup>3</sup>Department of Virology, Hannover Medical School, Hannover, Germany; <sup>4</sup>Africa Centre for Population and Health Research

**Background:** The modes of transmission of HHV8 in Africa are unclear.

**Methods:** To investigate mother-to-child transmission of HHV8 in South Africa, 2546 mother-child pairs were recruited from rural vaccination clinics and tested for antibodies against lytic (K8.1) HHV8 antigens. The HHV8 DNA copy number in saliva was determined for a sample of mothers by quantitative polymerase chain reaction.

**Results:** In children over 1 year of age, the prevalence of HHV8 antibodies was 9% (54/579) if the mother was HHV8 seronegative, and 25% (103/413) if she was seropositive (odds ratio [OR] 3.2, 95% confidence intervals [CI] 2.2-4.7), and increased with increasing maternal antibody titre ( $\chi^2_1=48$ ,  $P<0.001$ ). 15% (145/978) of mothers had detectable HHV8 DNA in saliva (mean viral copy number 488,450 copies/ml, range 1,550-660,000); the prevalence was 10% (51/532) in HHV8 seronegative women and 33% (71/216) in women with the highest antibody titres (OR 4.6, 95% CI 3.0-6.9). The prevalence of anti-HHV8 antibodies in children was 15% (109/735) if the mother had no detectable HHV8 in saliva and 28% (12/43) if the mother had a high HHV8 copy number (>50,000) in saliva (OR 2.2, 95% CI 1.1-4.5).

**Conclusions:** We provide evidence of mother-to-child transmission of HHV8 and show that maternal saliva is a likely route.

## 010

## Is there a significant difference between HIV-1 in the blood and the female genital tract?

A Mears<sup>1</sup>, J Mullen<sup>2</sup>, S O'Shea<sup>1</sup>, I Cormack<sup>1</sup>, V Magaya<sup>1</sup>, S Costelloe<sup>1</sup>, I Chrystie<sup>2</sup>, A de Ruiter<sup>1</sup>

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**Background:** The viral load (VL) and antiretroviral drug resistance in plasma may not reflect HIV-1 activity in the female genital tract (FGT), which is important both for perinatal and heterosexual transmission. A comparative evaluation of HIV-1 activity in the blood and FGT was conducted to characterise HIV-1 and determine whether virus from these two compartments represent distinct populations.

**Methods:** Paired blood and cervicovaginal secretions (CVS) were collected from 41 HIV-1 infected pregnant ( $n=26$ ), and non-pregnant ( $n=15$ ) women using Sno-strips.

**Results:** 94% had a higher VL in plasma (median 4.2 log<sub>10</sub> HIV-1 RNA copies/ml; range <1.7-5.8 log<sub>10</sub>) compared to CVS (median 3.5 log<sub>10</sub> copies/ml; range <2.9-4.7 log<sub>10</sub>). Sixteen women had sufficient FGT VL (>1000 copies/ml) for *pol* gene sequence analysis, and sequence data from paired samples were obtained from 13. Phylogenetic analysis indicated genetic diversity between virus present in the blood and FGT of all 13. Antiretroviral resistance was demonstrated in three women (23%); two had concordant and one discordant resistance mutations in the blood and FGT.

**Conclusions:** These data indicate genetic diversity between viral populations in the blood and FGT. Selection of drug-resistant variants in the blood and FGT can differ, which could impact on postexposure prophylaxis following perinatal and sexual exposure.

## 011

## Use of coalescence theory to estimate time of introduction of HIV-1 strains into the UK, and subsequent population growth dynamics

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**Background:** The population history of HIV-1 can be inferred from viral gene sequences. We investigated the history of the subtype B HIV-1 epidemic in the UK, using recently developed statistical methodologies.

**Methods:** A phylogenetic tree including 1784 *pol* gene sequences from subtype B viruses throughout the world, together with over 1645 sequences from UK isolates, was reconstructed in order to identify independent introductions of HIV-1 within the UK. The dates of introduction of strains, as well as the growth rate of the epidemic, were estimated using a coalescent-based approach, incorporating a calculated rate of nucleotide substitution of the subtype B *pol* gene.

**Results:** Four large viral lineages were identified, indicating multiple, independent introductions of subtype B HIV-1 into the UK, dated to the period 1975-1982. Each strain showed an initial exponential phase of growth from time of introduction until the late 1980s, after which the effective population size appeared to plateau until the present, possibly due to altered sexual behaviour.

**Conclusions:** This is the first estimate of the dates of introduction, and growth rates of the UK HIV-1 epidemic using coalescence theory. We illustrate the important epidemiological information inherent in viral sequence data acquired over time.

## 012

## Genotypic resistance to antiretroviral therapy in HIV-1 infected pregnant women taking highly active antiretroviral therapy (HAART) in pregnancy

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**Background:** HAART, regardless of maternal need for therapy, reduces mother-to-child HIV transmission. Temporary HAART in pregnancy may provide a predisposition to the emergence of genotypic resistance.

**Methods:** Pregnant HIV-1 infected women with a pretreatment CD4 count of >300 cells/ $\mu$ l initiated HAART in the third trimester and discontinued post-partum ( $n=50$ ). Genotypic resistance testing (RT) (HIV-1 TruGene) was performed after HAART cessation and on pretreatment samples when post-partum samples showed primary mutations. Samples with a viral load (VL) of >500 HIV-1 RNA copies/ml were included.

**Results:** 39/50 (78%) sequences were available for analysis, 11/50 (22%) were excluded (nine with a VL <500; two with no sequence). 4/39 (10%) took antiretroviral therapy (ART) in a previous pregnancy [one zidovudine (ZDV), two Combivir, one ZDV/Combivir]. Pretreatment parameters: median CD4 480 cells/ $\mu$ l (range 300-1082); median VL 2689 copies/ml (50-34753). HAART regimens: Combivir/nevirapine (NVP) (28), Combivir/nelfinavir (NLF) (10), didanosine (ddI)/ZDV/NLF (one). Median HAART duration: 70 days (3-114). VL at ~36 weeks: 30/39 (77%) <1000 copies/ml; 7/39 (18%) no result as delivered early (six) or failed to attend (one). Median time from HAART cessation to RT 42 days (13-198). Seven primary mutations (V106A (one), Y181C (two), G190A (one), K101E (one), M184V (one), T215S (one)) were detected in 5/39 (13%) women. 5/5 were on regimens including NVP and were ART-naïve. 4/5 had no mutations detectable pretreatment (one pretreatment RT not available, VL 83 copies/ml).

**Conclusion:** In this cohort, 13% demonstrated primary genotypic resistance post-partum despite HAART.

## 013

**Molecular and epidemiological characteristics of primary HIV-1 infections among a cohort of predominantly men who have sex with men (MSM) in a defined geographical area: transmission events associated with high-risk activity and sexually transmitted infections (STIs)**

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**Background:** It is postulated that onward transmission of HIV-1 is increased during primary HIV infection (PHI) for biological and behavioural reasons. We studied primary infections combining molecular and epidemiological approaches to assess correlates of PHI transmission.

**Methods:** PHI was diagnosed between 1999 and 2003 by one or more of: negative HIV antibody (Ab) within 18 months, evolving Ab response or negative detuned Ab. Epidemiological data were collected and *pol* sequences used to create a phylogenetic tree.

**Results:** Of the 104 subjects with PHI diagnosed between 1999 and 2003, 96% were men with a median age of 36 years; 91% were MSM. 13% of the *pol* sequences had primary antiretroviral resistance. Viruses from 38 individuals (36.5%) appeared within 16 transmission clusters. These associations were significant in the cluster versus non-cluster group: unprotected anal intercourse (UPAI) in the 3 months before PHI diagnosis ( $P=0.03$ ), number of sexual contacts ( $P=0.02$ ), young age ( $P=0.02$ ) and CD4 count ( $P=0.01$ ). Alarmingly high rates of acute STIs were seen (38%).

**Conclusions:** We found high rates of viral clustering in individuals with PHI. The associated behavioural factors we observed can facilitate onward transmission. Increased awareness and targeted identification of individuals during PHI may usefully interrupt transmission networks.

## 014

**Trends in genotypic resistance in clinical samples submitted for routine HIV resistance analysis**

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**Background:** Resistance to antiretroviral drugs is a major factor contributing to failure of therapy.

**Methods:** Genotyping of 795 samples from antiretroviral therapy (ART)-experienced adults submitted from July 1999 to end 2003 was analysed. Frequency of mutations was compared year on year by  $\chi^2$ -tests.

**Results:** Key mutations associated with reduced ART sensitivity were most common in 1999 (85.9%), but declined to 74% in 2003 ( $P=0.06$ ). The prevalence of nucleoside analogue reverse transcriptase inhibitor (NRTI) resistance mutations was relatively constant (average 68.2%). Non-NRTI mutation frequencies (range 45.3–56%) did not change significantly. Mutations associated with protease inhibitor (PI) resistance declined from 56.3% to 17.2% ( $P=0.0001$ ). There were significant declines in two-class (NRTI plus PI) ( $P=0.0001$ ) and three-class resistance ( $P=0.001$ ), while non-B clade HIV and recombinants become increasingly prevalent (21.6%–33.5%,  $P=0.004$ ).

**Conclusions:** Despite some reduction, mutations in HIV *pol* remain common. NRTI-associated mutations are still most common. The reduction in PI-associated mutations may reflect decreased first-line use of PIs, shifts to using more potent boosted-PI regimens and introduction of new agents with less well described mutation pathways. Increasing uptake of resistance testing and alterations in clinic demographics may contribute to some of the changes.

## 015

**Late diagnosis of HIV infection among individuals with low or unacknowledged risks in England, Wales and Northern Ireland**

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**Background:** A small number of UK nationals who have a low or unacknowledged risk of HIV present late in the course of HIV infection, often after frequent attendances to general practitioners (GPs). Late diagnosis may result in avoidable morbidity and premature mortality. **Methods:** Information from in-depth interviews with individuals diagnosed with HIV in England, Wales and Northern Ireland who reported low or unacknowledged risks was analysed. Those diagnosed because of HIV-related symptoms (late diagnoses) were compared with those diagnosed for other reasons.

**Results:** Of the 286 individuals interviewed, 157 (55%) had HIV-related symptoms at the time of diagnosis. A greater proportion of those diagnosed late were male and older, or in a long-standing relationship. Of the 157 late diagnoses, 95 were considered to have acquired HIV heterosexually, 74 in the UK and 21 abroad, 16 through 'high-risk' behaviours, 16 heterosexually by a 'high-risk' partner and the remainder through an unusual, other or unknown route. No partners had informed them of their HIV status.

**Conclusions:** GPs should consider HIV as a possibility when patients without an apparent risk of HIV infection present with symptoms indicative of immune suppression. Sensitive partner-notification practices that enable a greater number of individuals to inform their partners should be explored.

## 016

**A comparison of changes in response to highly active antiretroviral therapy (HAART) over time between regions of Europe: results from the EuroSIDA study**

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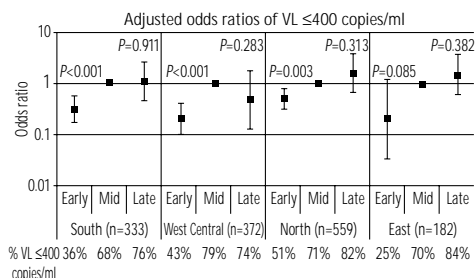
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**Background:** Decreasing response rates to HAART over time may suggest the emergence of primary resistance while regional variation may identify differences in the use of available agents. This study was designed to determine whether any improvements in the response to HAART have been consistent across regions of Europe.

**Methods:** We studied 1713 antiretroviral-naïve patients who started HAART ( $\geq 3$  drugs including protease inhibitor/non-nucleoside reverse transcriptase inhibitor/abacavir) with a viral load (VL) of  $>400$  HIV-1 RNA copies/ml. Response was assessed as the first VL 6–12 months after starting HAART ( $\leq 400$  copies/ml), stratified by region and year started HAART (early 1996–1997, mid 1998–1999, late 2000–2002).

**Results:** Only small improvements in response were observed in later years, more especially in northern and eastern regions, despite new antiretrovirals and better toxicity management.



## 017

## HIV-infected adolescents: an evolving UK cohort

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**Aim:** To describe the demographics, presentation, treatment and outcome for adolescents in CHIPS.

**Methods:** Review of data on HIV-infected adolescents  $\geq 12$  years at one of 18 centres in UK/Ireland in the CHIPS cohort from 1985 to 2003.

**Results:** Of 759 children, 179 (24%) are adolescents (12–19 years), with a median age at last follow-up of 14 [interquartile ratio (IQR) 13–16] years; 56% were female, 61% black African and 27% Caucasian. The median age at presentation was 5.7 years (IQR 1.9–10.7); 15 (8%) children were followed from birth, 67 (37%) were identified after the diagnosis of a family member, three at adoption screening and 71 (40%) presented symptomatically [39 in Centers for Disease Control and Prevention (CDC) category B, 18 in category C]. The median CD4 count at diagnosis was 21% (IQR 12–30%). At the last follow-up, 36 (20%) had never received antiretroviral therapy, 114 (64%) were on highly active antiretroviral therapy (HAART), only 66 (46%) of whom started HAART as their first regimen; the remainder received prior mono- and/or dual therapy. Among 143 treated children, the median number of antiretrovirals was five (range 1–13) and 51 (36%) received all three drug classes. The median CD4 count at last follow-up among those treated was 22% (IQR 14–28%), with 20 (14%) having a CD4 count of  $<10\%$ . 60 (42%) had  $<400$  HIV-1 RNA copies/ml, 31 (66%) having  $<50$  copies/ml. The median current CD4 count in treatment-naïve adolescents was 24% (IQR 19–24%). Since 1996, four adolescents have died, aged 12–14.6 years. 20 transferred to adult services at a median age of 17.0 years (15.3–18.8).

**Conclusions:** HIV-infected children are surviving into adult life. In this cohort, many have been heavily pretreated with antiretroviral therapy with suboptimal responses, and will challenge therapeutics in adult services.

## 018

## An update of the UK HIV epidemic using national surveillance data

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**Background:** National surveillance data on new diagnoses of HIV infection have given a detailed overview of the epidemiology of the epidemic in the UK since 1981. Data to the end of 2003 are used to provide the most recent update.

**Results:** 2003 will again see the highest number of new diagnoses of HIV infection in the UK in a single year, with 5047 reports already received and over 7000 anticipated for the year once delayed reports are received. Behind this figure is a rise in new diagnoses of HIV in men who have sex with men (MSM) and the continuing influence of the global epidemic. Over 2000 new diagnoses are expected in MSM for 2003, giving the highest annual total in this group in the epidemic to date. For the seventh consecutive year, new diagnoses in heterosexual men and women have risen substantially, and the divergence between diagnoses in males and females continues. Since 2001, heterosexual women have been the largest risk group diagnosed, and in 2003, heterosexual women made up 36% (1827) of all new diagnoses so far received, and a further 1000 reports could reasonably be expected. Only part of this increase is explained by increased detection and diagnosis antenatally.

## 019

## Tenofovir in the treatment of hepatitis B (HBV)/HIV co-infected individuals

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**Aim:** To investigate the use of tenofovir in HBV/HIV co-infected individuals.

**Methods:** An open-label study of HBV/HIV co-infected individuals receiving tenofovir.

**Results:** 40 co-infected HBeAg +ve individuals were identified, 39 male and one female, with a median age of 37.5 years. They received tenofovir at 245 mg once a day as part of, or in addition to, their combination antiretroviral therapy. 31 were lamivudine-experienced, with a median exposure of 72 weeks (range 6–270). 60% of those who underwent HBV DNA polymerase sequencing had a mutation in the YMDD motif. The median CD4 count rose from 271 (baseline) to 386 (48 weeks) and 488 cells/ $\mu$ l at 96 weeks. Similarly, the CD4% rose from baseline to 96 weeks (19.2% to 24% to 22.5%). The median HBV DNA level fell from  $250 \times 10^6$  to  $<10,000$  copies/ml at 96 weeks. 25/40 (63%) had an undetectable HBV by 48 weeks. 14/14 (100%) who reached 96 weeks had an undetectable HBV DNA level. Eight individuals became HBeAg-ve between 36 and 96 weeks, and six seroconverted to HBeAb+ve. Three of these six had lamivudine-resistant mutations at baseline. All eight individuals remained HBsAg+ve.

**Conclusion:** Tenofovir is effective against HBV in HIV co-infected lamivudine-experienced individuals.

## 020

Acute hepatitis C virus (HCV) in a cohort of HIV-positive men: outcomes and response to pegylated interferon- $\alpha 2b$  (peg-IFN- $\alpha 2b$ ) and ribavirin

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**Background:** An epidemic of acute HCV has recently been recognised among HIV-positive men in London. We describe their virological outcomes and response to early treatment.

**Treatment:** All patients persistently positive for HCV RNA by reverse transcriptase polymerase chain reaction 12 weeks after presentation were offered peg-IFN- $\alpha 2b$  (1.5  $\mu$ g/kg) and ribavirin ( $>10.6$  mg/kg) for 48 weeks.

**Results:** 36 cases of acute HCV were identified (mean age 30.5 years, median CD4 count 514 cells/ $\mu$ l); 17 were on HAART. Genotype 1 infection was noted in 21 (58%), genotype 3 in seven (19%), genotype 4 in four (11%) and four could not be typed. In nine patients (25%), HCV cleared spontaneously. 16 patients started treatment [median CD4 514 cells/ $\mu$ l, median HCV viral load (VL) 5.86  $\log_{10}$ ; 12 genotype 1, three genotype 3, one genotype 4]. At week 12, 15 patients were evaluated: 11 (73%) achieved early virological response (HCV VL  $<50$  iu/l or  $>2 \log_{10}$  decrease), two were non-responders, one stopped therapy and one was lost to follow-up. Of the nine patients remaining at week 24, six (66%) had an undetectable HCV-RNA, one stopped treatment and two remain non-responders; two patients stopped therapy at 24–48 weeks and remain undetectable. At week 48, three patients achieved an end-of-therapy response.

**Conclusions:** Spontaneous clearance of HCV is possible, despite HIV co-infection. Initial results suggest a favourable response to early treatment despite unfavourable genotypes and high HCV viral loads.

## 021

### Tuberculosis (TB) and HIV co-infection among healthcare workers in south-west London

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**Background:** The global incidence of TB is increasing. This has coincided with a rise in intercontinental travel and the recruitment of healthcare professionals to the UK from around the world.

**Methods:** To assess the incidence of tuberculosis among healthcare workers, a retrospective interrogation of the SW London TB database for 2002 was performed. Data collected included profession, age, sex, type of disease, HIV status, country of origin, time in the UK, and history of bacille Calmette–Guérin (BCG) vaccination ± scar.

**Results:** 372 patients were diagnosed as having TB. 25 were healthcare workers (6.7%, four doctors, 13 nurses, five healthcare assistants and three healthcare students); 22 (88%) were from overseas (2–22 years in the UK before diagnosis). 18 patients had evidence of BCG vaccination and 17 (68%) had pulmonary TB. Nine patients (36%) were diagnosed HIV antibody-positive.

**Conclusions:** Healthcare workers contribute significantly to the number of patients with TB and a significant proportion is co-infected with HIV. The majority of these patients are migrant workers. The current guidelines for screening healthcare workers state that only those without a BCG scar are tuberculin skin-tested. 52% of our patients would not have required skin testing at initial screening.

## 023

### The impact of an HIV diagnosis on fertility

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**Background:** The impact of HIV on women's reproductive decisions is unclear. Improvements in treatments that delay HIV disease progression and interventions that reduce perinatal transmission of HIV may have altered women's fertility desires.

**Methods:** Self-completion questionnaires were collected from 410 women attending seven HIV-treatment centres in the UK between July 2003 and January 2004.

**Results:** The median age was 35 years. 72% of women were African, 8% had a history of drug use and 29% were diagnosed during pregnancy. 18% of women had had a pregnancy after HIV diagnosis. In univariate analyses, the number of previous children, partnership status, having had an HIV-positive child, young age, years since diagnosis and having a diagnosis during pregnancy were associated with a subsequent pregnancy. 41% of the women (168/410) desired future children, which was associated with having only one or fewer children, partnership status and younger age at diagnosis. Fertility desire was not related to ethnicity nor to disease progression. Although 33% (136/410) indicated that they no longer desired children after their HIV diagnosis, 29% (40/136) and 33% (45/136), respectively, changed their mind in the light of improvements in treatments and interventions.

**Conclusions:** Pregnancy decision-making among HIV-positive women is complex. Many women have had children and many desire to do so in the future. This will have important implications for ongoing HIV education and care provision.

## 022

### Do all HIV-positive patients co-infected with hepatitis C genotypes 2 and 3 require 12 months of treatment with ribavirin and pegylated (peg) interferon (IFN)?

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**Background:** Response rates of up to 80% have been reported in patients mono-infected with hepatitis C genotypes 2 and 3 after 6 months of treatment with ribavirin and peg-IFN. Recent reports of significant relapse rates in HIV co-infected patients treated with 6 months of therapy have raised the question of extending therapy to 12 months in co-infected patients irrespective of genotype.

**Methods:** We report efficacy data for all genotype 2 and 3 co-infected patients treated with ribavirin and peg-IFN- $\alpha$ 2b for 6 months.

**Results:** Of 25 patients who commenced treatment, 16 patients completed 6 months of therapy with ribavirin and IFN. 15/16 patients who had a negative polymerase chain reaction (PCR) at the end of treatment remained PCR-negative 6 months after treatment (sustained virological response, SVR). All patients continued the same dose of IFN and ribavirin and were supported with growth factors, intravenous immunoglobulin and blood products as necessary. One of 16 patients relapsed within 4 weeks of treatment cessation.

**Conclusion:** Six months of treatment for hepatitis C genotype 2 and 3 co-infected patients resulted in an SVR in 94%. All these patients had CD4 counts of  $>200$  cells/ $\mu$ l, negative hepatitis C PCR results after 12 weeks on treatment, and had no dose reduction of their IFN or ribavirin.

## 024

### Maternal breast-feeding behaviour and prevalence of HIV-1 in rural South Africa

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**Aim:** To examine maternal breast-feeding behaviour and the prevalence of HIV-1 in rural South Africa.

**Methods:** Feeding behaviours among HIV-infected and uninfected mothers were compared. The prevalence of HIV among children with HIV-infected mothers was compared between those who had regular mixed-feeding or exclusively breast-feeding at recruitment.

**Results:** Among mothers, the prevalence of HIV infection was 28% (705/2520). Among children of infected mothers, the HIV prevalence was 22% (155/705). For children aged 60 days or under, those with HIV-infected mothers were more than twice as likely to have been introduced to regular mixed feeding compared to children with uninfected mothers [31% (45/146) versus 14% (50/369);  $P < 0.001$ ]. Among children of the same age, born to HIV-infected mothers, there were no statistically significant differences in the prevalence of HIV infection between regular mixed feeding or exclusive breast-feeding.

**Conclusions:** The finding that mothers of young infants are more likely to have regular mixed feeding if they are HIV-infected than if they are not suggests that a policy of exclusive breast-feeding may be difficult to implement among HIV-infected mothers. Furthermore, we find no evidence to support the view that exclusive breast-feeding is associated with a lower prevalence of HIV infection in children.

## 025

## Pregnancy outcome of HIV-positive women in London, 1998–2002

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**Background:** With HIV transmission rates of <1%, mothers and their carers now weigh the risk of additional interventions against potential benefit. In the absence of randomised controlled trials, cohort studies can be informative.

**Methods:** Notes were reviewed for all women diagnosed HIV seropositive ante-partum between the start of 1998 and the end of 2002 in six centres. The women were offered zidovudine (ZDV) monotherapy or three or more antiretroviral drug combinations (CART) and prelabour Caesarian section (PLCS) according to BHIVA guidelines. **Results:** 350 women delivered 362 babies; 84% were black African; 91 took ZDV of whom 80% delivered by PLCS and 10% an emergency Caesarian section (EmgCS). 71% of women on CART also delivered by PLCS and a further 16% by EmgCS. Pre-eclampsia was four times more common in women on CART. No significant trends in PLCS rates or prescribing of ZDV versus CART over 5 years appeared. HIV status is available for 235 babies, among whom one is infected (0.5%), eight are HIV- indeterminate and 22 are missing tests.

**Conclusions:** Pre-eclampsia and EmgCS rates were higher in women taking CART. The continued high PLCS rate in women on CART may reflect the paucity of data on transmission among women on CART with undetectable HIV viraemia.

## 026

## Long-term follow-up of HIV-positive pregnant women in London

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**Background:** Perception of long-term prognosis may influence family planning decisions by HIV-positive women but few studies have investigated the disease-free survival of HIV-infected women following pregnancy.

**Methods:** Notes were reviewed for all women diagnosed HIV seropositive ante-partum between the start of 1998 and the end of 2002 in six centres. Data were analysed by  $\chi^2$ - and *t*-test.

**Results:** 350 women delivered 362 babies; 84% were black African, 10% European and 4% Afro-Caribbean. The only HIV-infection risk in 96.5% was heterosexual intercourse. Compared with women treated with three or more drugs (combination antiretroviral therapy, CART), the 94 women treated with zidovudine monotherapy were younger (mean 28.7 versus 31.1 years,  $P<0.05$ ) had higher CD4 lymphocyte counts (median 460 versus 282 cells/ $\mu$ l,  $P<0.05$ ) and lower HIV loads (median 2279 versus 7800 HIV RNA copies/ml plasma,  $P<0.05$ ). At the last follow-up (mean 26.7 months post-partum), there was no significant difference in CD4 lymphocyte counts (median 484 on monotherapy versus 428 on CART). During 711 person-years of follow-up, five women treated in pregnancy with CART (564 person-years) and one given monotherapy (147 person-years) had an AIDS-defining illness (ADI), but all six women currently have CD4 counts >200 cells/ $\mu$ l.

**Conclusions:** Good immune function is documented up to 5 years post-partum in this cohort with a low incidence of ADIs.

## 027

## Is 'high oncogenic risk' human papillomavirus (HR HPV) infection predictive of the evolution of cervical neoplasia in women with HIV?

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**Background:** HR HPV causes cervical pre-cancer/cancer. We investigated the value of HPV testing in HIV-positive women.

**Methods:** In a prospective cohort of women from a colposcopy clinic, HPV typing (by polymerase chain reaction, using MY09/MY11, Roche reverse line blot) was performed, demographics recorded and the status of cervical disease established at entry to the study.

**Results:** 72 women were recruited over a period of 18 months; 72% were on highly active antiretroviral therapy, 67% had >200 CD4 cells/ $\mu$ l and 42% had an undetectable viral load. The prevalence of HPV was 44%; 24% had eight HR HPV types and 20% of women had untyped HPV. HPV-58 and MM7 were the commonest defined HPVs. There were no 'low oncogenic risk' types. At baseline, 49% had a normal cervix, 43% low-grade changes, 7% had high-grade cervical pre-cancer and there was no biopsy-proven cervical intraepithelial neoplasia (CIN) grade 3. The prevalence of HPV infection by grade of cervical pathology was: 13% with a normal cervix, 61% with low-grade disease and 60% (three of five) had high-grade disease; these latter three women with high-grade squamous intraepithelial lesions (HSILs) all had untyped HPV. Defining new HSILs, loop excision of the transformation zone and cone biopsy as endpoints, only three women progressed, all of whom had loop excision (one HSIL, two low-grade squamous intraepithelial lesions): two were HPV-negative at entry and one had untyped HPV.

**Conclusions:** Use of antiretroviral therapy led to a low average burden of HIV replication. About 7% of women had evidence of HSIL at entry, and 4% developed it during the follow-up. HPV typing is not useful because: (1) untyped/uncommon HPV types are frequent and (2) the test is insensitive in the setting of low-incidence HSIL.

## 028

## Antiretroviral treatment regimens and the prevention of systemic HIV-related non-Hodgkin's lymphoma (NHL)

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**Background:** As HIV increases the risk of NHL, we measured the influence of highly active antiretroviral therapy (HAART) on this risk.

**Methods:** The protective effect of HAART was examined in a prospective cohort of 9621 HIV-infected individuals. Lymphocyte subset data were also examined.

**Results:** 280 patients were diagnosed with lymphoma (206 with systemic NHL, 55 with primary cerebral lymphoma and 19 with Hodgkin's disease). During the HAART era (1996–2003), 5832 individuals were identified as at risk and 102 patients were diagnosed with systemic NHL. Univariate analysis demonstrated that increased age, higher nadir CD4 and CD8 cell counts, CD19 B cell count, CD16/56 natural killer count and exposure to non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI)-containing HAART conferred significant protection against NHL ( $P<0.05$ ). In a multivariate analysis, age, nadir CD4 and CD8 cell counts and exposure to HAART were independent predictors of risk of NHL ( $P<0.02$ ). NNRTI-based HAART [adjusted rate ratio 0.4, 95% confidence interval (CI) 0.3–0.5] had an identical protective effect to PI-based HAART and were both significantly more protective than nucleoside reverse transcriptase inhibitors alone (rate ratio 0.5, 95% CI 0.4–0.7) or no antiretrovirals ( $P<0.001$ ).

**Conclusions:** HAART-induced maintenance of CD4 and CD8 counts protects patients from systemic AIDS-related NHL.

## 029

### Highly active antiretroviral therapy (HAART) does not prevent anal cancer

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**Background:** The incidence of invasive anal carcinoma is increased among people with HIV. HAART has reduced the incidence of both Kaposi's sarcoma and non-Hodgkin's lymphoma, but the effects on anal cancer are unknown.

**Methods:** The anal cancer incidence in our prospective cohort of 8640 HIV-seropositive individuals (40,126 patient-years of follow-up) was measured in pre- (1984–1995) and post- (1996–2003) HAART eras and compared to the age- and sex-matched general population of south-east England for 1995 ( $3.1 \times 10^6$ ) collected by the Thames Cancer Registry.

**Results:** The incidence of anal cancer (diagnosed in 26 patients) in our HIV+ cohort was  $60/10^5$  patient-years. This is 120 times higher than in the matched population. The incidence was 35 [95% confidence interval (CI) 15–72]/ $10^5$  patient-years in the pre-HAART era and 92 (95% CI 52–149)/ $10^5$  patient-years in the post-HAART era. These figures are significantly higher than in the matched population ( $P < 0.001$  for both), and give relative risks of 67 and 176, respectively.

**Conclusions:** HAART has not reduced the incidence of anal cancer. Among possible explanations for this is the lack of clear correlation between anal cancer and the CD4 cell count and the fact that HAART does not cause regression of anal intraepithelial neoplasia, the presumed precursor of anal cancer.

## 030

### Protease inhibitors potentiate chemotherapy-induced neutropenia

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**Background:** Pharmacokinetic interactions between chemotherapy and highly active antiretroviral therapy (HAART) are described but their clinical relevance has largely been overlooked.

**Methods:** 46 patients with non-Hodgkin's lymphoma were treated with concomitant HAART and infusional cyclophosphamide, doxorubicin, etoposide (CDE) chemotherapy. A total of 190 cycles of CDE were administered, 48 with a protease inhibitor (PI) (11 patients) and 142 (35 patients) with PI-sparing HAART regimens. Neutrophil counts were measured on days 1, 7, 10, 14, 21 and 28 and the number of days of granulocyte colony-stimulating factor (G-CSF) recorded for each cycle.

**Results:** There were no significant differences in CD4 count, HIV viral load, lymphoma stage, histological subtype or international prognostic index group or in the presence of bone marrow infiltration by lymphoma between the two groups (all  $P > 0.05$ ). The day 10 neutrophil count nadir was significantly lower in patients receiving PIs ( $P = 0.012$ ), although there was no difference in the number of days of G-CSF administered between groups ( $P = 0.16$ ). Infectious episodes were recorded for 66% cycles with PIs and 27% cycles without PIs ( $P < 0.0001$ ).

**Conclusions:** PI-based HAART potentiates the myelotoxicity of CDE chemotherapy and this is believed to be a consequence of microsomal enzyme inhibition reducing the metabolism of cytotoxics, particularly etoposide in this regimen.

## P1

## Simplification to Trizivir in patients with an undetectable viral load

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**Background:** While simplification of antiretroviral therapy with Trizivir has been advocated as a way of reducing pill burden and improving concordance, it is unclear whether a durable response to therapy can be maintained.

**Methods:** We identified 50 patients who switched to a combination of zidovudine, lamivudine and abacavir with a viral load <50 HIV-1 RNA copies/ml, and assessed subsequent changes in viral load, CD4 count and clinical events.

**Results:** The patients had received highly active antiretroviral therapy for a median of 20 months, using a median of 4 drugs; 46 had received non-nucleoside reverse transcriptase inhibitors and 31 protease inhibitors. Over a median follow-up of 16 months, 19 patients made at least one change to their regimen (11 stopped abacavir, 12 stopped zidovudine, nine stopped lamivudine and seven added in another drug). Eleven of the 50 patients had a viral blip of >50 copies/ml; this was sustained in seven patients. The median time to a blip was 5.5 months. No new AIDS event occurred following the switch and a median rise in the CD4 count of 90 cells/ $\mu$ l was seen in the first six months post switch.

**Conclusions:** Although a sustained viral rebound was seen in 22% of these patients, there were no new AIDS events and CD4 counts continued to increase.

## P2

## The effect of gender on haemoglobin as a marker of HIV disease progression in the era of highly active antiretroviral therapy (HAART)

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**Introduction:** While haemoglobin was strongly associated with disease progression and death pre-HAART, its role in patients receiving HAART is unclear.

**Methods:** Changes in haemoglobin were investigated in 645 antiretroviral-naïve patients from the Royal Free Hospital who started HAART between 1996 and 2003. Relationships between haemoglobin levels and disease progression were investigated using Cox models.

**Results:** Median pre-HAART haemoglobin levels were 13.8 g/dl in men and 11.4 g/dl in women. Levels were significantly lower in women ( $P<0.0001$ ) and in those of non-white ethnicity ( $P=0.002$ ), and were positively correlated with the CD4 count ( $P<0.0001$ ) and negatively with age ( $P=0.0005$ ). Although there was little overall change in haemoglobin levels 1 year after HAART, women had a 1.29 g/dl greater increase in Hb than men ( $P<0.0001$ ); increases were also related to age, risk group and pre-HAART haemoglobin levels. There was a decline in anaemia in both sexes ( $P<0.0001$ ). Haemoglobin changes were correlated with changes in the CD4 count over 1 year. Time-updated haemoglobin was related to time to AIDS/death (hazard ratio 0.59,  $P<0.0001$ ), independently of the CD4 count (0.59,  $P<0.0001$ ) and a previous AIDS diagnosis (0.49,  $P<0.002$ ). The prognostic value of haemoglobin did not differ by sex.

**Conclusions:** Haemoglobin changes following HAART vary by sex, age and risk group, but remain significantly associated with prognosis in both sexes.

## P3

## Renal dysfunction with tenofovir DF (TDF)-containing highly active antiretroviral therapy (HAART) regimens is not observed more frequently: a cohort and case-control study

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**Background:** Despite recent case reports, there are no data on the overall incidence and risk of renal dysfunction in individuals receiving TDF.

**Methods:** Data from the Chelsea and Westminster cohort were analysed to identify HIV-positive individuals with creatinine >120  $\mu$ mol/l at any time and to classify them according to HAART exposure and time exposed. A matched case-control study was performed, comprising patients who had received TDF and subsequently developed creatinine >120  $\mu$ mol/l, against controls who had been treated with TDF and not experienced creatinine elevation.

**Results:** From 4183 HIV-infected patients, 1175 were identified as having a recorded creatinine >120  $\mu$ mol/l. Comparison of HAART-naïve patients, and patients exposed to TDF and non-TDF containing regimes revealed a lower rate ratio and probability of developing creatinine >120  $\mu$ mol/l in patients exposed to TDF (rate ratio versus no antiretrovirals 0.22, 95% confidence interval 0.07–0.69,  $P<0.001$ ) with no significant difference between HAART regimens, corrected for duration of exposure. Of the 1058 patients exposed to TDF, 84 (8%) experienced creatinine >120  $\mu$ mol/l subsequent to exposure. An alternative aetiology for renal dysfunction was found in 75 (90%) individuals.

**Conclusions:** TDF is not associated with renal dysfunction more frequently than other antiretrovirals and the occurrence of renal dysfunction in this context is a rare and idiosyncratic event.

## P4

## Tenofovir use and creatinine clearance in an unselected cohort of HIV positive patients

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**Background:** Tenofovir has been widely used in our cohort. There have been reports of renal toxicity. We reviewed tenofovir use and evidence of nephrotoxicity.

**Methods:** A retrospective case-note review was done in patients receiving tenofovir. Creatinine clearance (CrCl) was calculated (Cockcroft and Gault equation) at baseline, 3, 6 and 12 months. The number of previous regimens and the antiretroviral combination was recorded.

**Results:** 70 patients received tenofovir and 33 patients had completed treatment for 12 months or more at the time of the study. Nine patients received tenofovir as part of their first antiretroviral regimen, 14 in their second regimen and 47 in their third regimen or as salvage. Tenofovir was used in combination with protease inhibitors (PIs) in 24 patients, in 27 patients taking non-nucleoside reverse transcriptase inhibitors (NNRTIs), in 14 taking nucleoside reverse transcriptase inhibitors (NRTIs) only and in five on a PI/NNRTI combination. Virological suppression was achieved in 51 (73%). Mean CrCl was 77 ml/min (SD 17) at baseline, 75 ml/min (SD 19) at 3 months, 78 ml/min (SD 15) at 6 months and 76 ml/min (SD 20) at 12 months. Two patients discontinued treatment due to nephrotoxicity: Fanconi's syndrome developed in one case and a 72% drop in CrCl in the other.

**Conclusions:** There was no overall decline in CrCl; however, nephrotoxicity did occur but was rare.

## P5

## Participation in clinical trials at the Royal Free Hospital: characteristics of those included and impact on treatment outcomes

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**Introduction:** We investigated the characteristics and outcomes of patients starting first-line highly active antiretroviral therapy (HAART) according to participation in a randomised controlled trial (RCT).

**Methods:** Previously treatment-naïve individuals starting HAART were included. Patients starting HAART while participating in an RCT were identified. The impact of being in an RCT on the response to HAART was investigated.

**Results:** 176/589 (30%) started HAART while participating in an RCT. Risk group was associated with inclusion in an RCT ( $P=0.01$ ). Those participating in an RCT were likely to have more CD4 counts and viral load measurements taken. 153/176 (87%) and 319/413 (63%) achieved a viral load <400 HIV-1 RNA copies/ml within 48 weeks of starting HAART (odds ratio 1.97; 1.13–3.43;  $P=0.02$ ). 127/176 (72%) in the RCT group had a CD4 increase of >100 cells/μl within 48 weeks compared to 273/413 (66%) not in an RCT (odds ratio 1.28; 0.83–1.96;  $P=0.3$ ). 68/176 (39%) in the RCT group compared to 185/413 (45%) discontinued an antiretroviral during the first 48 weeks (hazard ratio 0.73; 0.55–0.87;  $P=0.002$ ).

**Discussion:** Patients included in first-line HAART RCTs are reflective of the cohort, except for risk group. Those in an RCT were less likely to discontinue an antiretroviral and may have an improved short-term virological response but a similar immunological response compared to those starting HAART as part of routine clinical care.

## P6

## Trizivir and tenofovir (TT): a simple regimen for salvage therapy

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**Background:** The aim was to describe a simple regimen, TT, for salvage. **Methods:** A retrospective analysis of TT in patients having virologically failed at least one antiretroviral regimen, identified via the clinic database.

**Results:** 122 patients were identified, with a mean of four previous regimens, a mean CD4 count of 221 cells/μl (median 170) and a viral load of 109,267 HIV-1 RNA copies/ml (median 35,745). 87% had previously received lamivudine, 77% zidovudine, 55% abacavir and 26% tenofovir. At 6 months there were 31 dropouts (eight lost to follow-up, six virological failures, 12 for adverse drug reactions, five by patient request); the mean CD4 increase was 80 cells/μl. 62% of patients achieved an undetectable viral load. 28 patients followed up for 1 year or more had a mean CD4 increase of 124 cells/μl, and 54% were undetectable. The M184V mutation had no impact on outcome, but four or more thymidine analogue mutations (TAMs) increased the chance of viral failure. Four of six viral failures had resistance test data available; at failure, only one of four patients had more TAMs than at baseline. A 0.5 mmol/l fall in total cholesterol was seen at 6 months, from a mean baseline cholesterol of 4.6 mmol/l.

**Conclusions:** A simple regimen of Trizivir/tenofovir is associated with improvement in outcome in heavily pretreated patients, provided there are less than four TAMs in their resistance history. TT does not adversely affect total cholesterol.

## P7

## Ritonavir-boosted double protease inhibitors in salvage therapy

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**Aim:** To review the efficacy of double boosted protease inhibitors.

**Methods:** Retrospective analysis of patients who received lopinavir/ with amprenavir (LPV/APV) or saquinavir (LPV/SQV) with or without other antiretrovirals, identified via the clinic database.

**Results:** 47 patients received LPV/APV; their baseline median viral load (VL) was 39,638 HIV-1 RNA copies/ml and their mean number of previous regimens was 8.3. At week 24, 23 of these patients remained on treatment and 35% had a VL of <50 copies/ml. Among 35 patients who received LPV/SQV, the baseline median VL was 41,848 copies/ml, the mean number of previous regimens was 8.8 and at week 24, 20 patients remained on treatment, 45% of whom had a VL of <50 copies/ml. The number of previous protease mutations had no impact on the efficacy of LPV/APV. For LPV/SQV, at week 24, those patients with four or fewer protease mutations were more likely to have a VL of <500 copies/ml than those with more than four mutations (14 of 25 versus three of 15,  $P=0.026$ ). For both regimens, the median number of active drugs for patients who achieved a VL of <50 copies/ml was three, and two in patients who did not achieve a VL of <50 copies/ml. **Conclusions:** Double boosted protease inhibitors have limited efficacy in salvage therapy, but are more effective in patients with three or more active drugs within the regimen. Patients on LPV/SQV-containing regimens are less likely to succeed if they have more than four protease mutations.

## P8

## A high percentage of patients on highly active antiretroviral therapy (HAART) consistently have undetectable viral loads

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**Background:** HAART has been prescribed widely for many years, with the London centres reporting good viral suppression. We looked at the potency and durability of HAART in our cohort of patients.

**Methods:** Information on all patients on HAART was retrieved on a 6-monthly basis, starting on 1 July 2002 and repeated on 1 January 2003 and 1 July 2003. Time on current treatment plus most recent HAART regimen, CD4 count and viral load (VL) were recorded. For the purpose of the audit, only patients who had been on their present HAART regimen for  $\geq 3$  months were deemed to have been on HAART for sufficient time to reach viral suppression.

**Results:** Patient numbers on treatment were 65, 85 and 90, respectively, for the three time periods. Of these, 64, 82 and 85 had been on their present treatment for  $\geq 3$  months. Concentrating on these patients, 83%, 90% and 92% had a VL of <50 HIV-1 RNA copies/ml with an additional 8%, 1% and 2% having a VL of 50–100 copies/ml. Of the patients with a VL of <50 copies/ml, 83%, 79% and 80% were on three drugs, while 17%, 21% and 20% were on four to six drugs.

**Conclusions:** In all three data collections, over 80% of patients on HAART for longer than 3 months had a VL of <50 copies/ml, and consistently over 90% had a VL of <100 copies/ml.

## P9

## Treatment of primary HIV infection: a local experience

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**Introduction:** Management of primary HIV infection is under debate, with guidelines suggesting enrolment in trials. Some patients identified with seroconversion illness or within 6 months of seroconversion opted for a 6-month course of HAART. Can any benefit be shown?

**Methods:** Notes of patients treated during primary infection were analysed with respect to initial CD4 count, viral loads (VL) before and after treatment, genotypic resistance profiles and highly active antiretroviral therapy (HAART) regimens.

**Results:** Seven patients were identified, the average CD4 count at presentation being 581 cells/ $\mu$ l (range 193–1195), and the VL being >750,000 HIV-1 RNA copies/ml in four cases. Two patients had wild-type virus, one had M41L, D67N and T69D mutations (intermediate to high resistance to reverse transcriptase inhibitors), two showed V179D [low-level non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance] and two showed V106I (potential low-level NNRTI resistance). All patients commenced Trizivir (stopped in two cases because of abacavir hypersensitivity, substituted by Kaletra, didanosine and stavudine). In all seven patients, VLs were suppressed to <50 copies/ml. Six months after HAART cessation, the VL remained 1 log<sub>10</sub> below presentation levels in only three of the seven patients. The average CD4 count was 680 cells/ $\mu$ l.

**Conclusion:** The benefit of short-course HAART in acute primary infection remains unclear and points to the need for local availability of clinical trials.

## P10

## A review of tenofovir (TDF) use in the Edinburgh HIV cohort

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**Background:** TDF is a potent antiretroviral that has shown efficacy in clinical trials, both in treatment-naïve and -experienced patients [including those with nucleoside reverse transcriptase inhibitor (NRTI) resistance]. Our objective was to review the use of TDF in our clinical practice.

**Methods:** Case notes and laboratory reports were reviewed for all patients currently or previously prescribed TDF as part of combination antiretroviral therapy.

**Results:** 118 patients have been prescribed TDF (93 current, 25 past). Of the 25 patients who discontinued TDF, two developed toxicity (both renal tubular acidosis), three had virological failure (associated with the K65R mutation), four stopped due to data on reduced efficacy of triple NRTI regimens and 16 stopped due to lack of tolerability or to patient choice. 31 patients (26%) took TDF as part of a once-daily combination. 71 patients (60%) had three-class antiretroviral experience and 71 patients (60%) had previous mono-/dual-NRTI therapy. 76 (82%) of those currently on TDF had <50 HIV-1 RNA copies/ml. 24/27 (89%) of patients with two or more nucleotide-associated mutations (NAMs) had <50 HIV-1 RNA copies/ml. 10 patients co-infected with hepatitis B were on TDF (six with lamivudine) and nine of the 10 had undetectable hepatitis B DNA (<50 copies/ml).

**Conclusion:** The effectiveness of TDF in clinical trials is also apparent in routine clinical practice.

## P11

## Efficacy, tolerability and durability of second-line protease inhibitor (PI)-based therapy following failure of first-line non-nucleoside reverse transcriptase inhibitor (NNRTI)-based therapy in an ethnically mixed cohort

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**Background:** Durability of PI-based therapy is dependent on potency as well as adherence and tolerability.

**Method:** Prospective observational study at five London clinics.

**Results:** We studied 143 patients (55% male and 45% female; 55% African, 34% white and 6% Caribbean). The median time to failure of first-line therapy [two nucleoside reverse transcriptase inhibitors (NRTIs) + one NNRTI] was 57 weeks (mean 69.7). Second-line therapy included low-dose ritonavir/lopinavir (r/LPV) (36%), nelfinavir (31%), low-dose ritonavir/saquinavir (r/SQV) (18%) and low-dose ritonavir/indinavir (r/IDV) (6%), with a mean of two NRTIs, and was started at a median of 4.3 log<sub>10</sub> HIV-1 RNA copies/ml and 194 CD4 cells/ $\mu$ l. After a median of 50 weeks (mean 68.4), two patients had been lost to follow-up, 71 (50%) discontinued therapy [within <6 months (18%), 6–12 months (10%) or >12 months (22%)], due to side effects in 31 (22%), patient's choice in 27 (19%) and virological failure in 13 (9%). Common adverse events causing discontinuation included gastrointestinal toxicity (14/31) and lipodystrophy or hyperlipidaemia (10/31). 72 patients remained on therapy with a median viral load (VL) decline of 2.4 log<sub>10</sub> copies/ml; 81% had a VL of <400 and 67% <50 copies/ml. The rate of failure (intent to treat, two consecutive VLs of >400 copies/ml) was 85/143 (59%).

**Conclusions:** A high rate of discontinuation of second-line therapy mostly reflected intolerance/poor adherence, not virological failure.

## P12

## Comparison of standard laboratory lactate analysis with a rapid finger-prick lactate measurement in a cohort of HIV-infected individuals

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**Background:** Highly active antiretroviral therapy-induced lactic acidosis has a significant morbidity of up to 80% with lactate levels greater than 10 mmol/l. Measuring lactate is not straightforward: venepuncture must be undertaken without a tourniquet, and samples must be stored on ice and transferred immediately to the laboratory.

**Aims:** We aimed to validate the hand-held rapid finger-prick lactate device currently used to aid training in athletes. We propose that this device may be a useful adjunct to standard laboratory testing, particularly in the out-patient clinic setting.

**Methods:** Serum lactate and two finger-prick lactates were measured in a total of 45 patients, 44 patients attending routine clinic appointments and one admitted with lactic acidosis. Where multiple lactate levels were measured, only the highest dataset was used from each patient.

**Results:** The data were analysed statistically, using limits of agreement (95%). With the mean of two finger-prick measures, the average difference was 0.2 (-0.9 to 0.5). When only the first finger-prick was compared to the laboratory values, the difference was 0.3 (-1.1 to 0.5).

**Conclusion:** The hand-held finger-prick lactate device can be effectively used in monitoring serum lactate levels in HIV-infected individuals, particularly in the out-patient setting. It appears to have a tendency to overestimate the result, which should be recognised.

## P13

## Late presenters with HIV in the era of HAART: how effective is therapy?

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**Background:** We investigated the characteristics of patients presenting for care with low CD4 counts (<50 cells/ $\mu$ l) and described their clinical, immunological and virological outcomes.

**Methods:** Patients presenting late at the Royal Free Hospital between 1996 and 2002 were identified. Follow-up was maintained until December 2002 or death.

**Results:** 100/677 (14.8%) patients presenting for care over the period were late presenters; late presenters were more likely to be female (33% versus 26%), heterosexual (50% versus 39%) and black African (39% versus 29%). Over a median follow-up of 2.7 years, 71% developed at least one AIDS condition and 14% died. The majority of AIDS events (87 events) occurred at presentation. 80 patients attended at least one follow-up out-patient visit (median 21 visits, range 0–130), and 52 were admitted as an in-patient at least once. 89 started antiretroviral treatment; among these patients, the median CD4 counts increased from 22 (100% <200) cells/ $\mu$ l at 0–2 months after presentation to 180 (55% <200) cells/ $\mu$ l at 1 year, and median viral loads dropped from 4.8 to 1.7 log<sub>10</sub> HIV-1 RNA copies/ml. The median time to a viral load of <50 copies/ml was 8 months.

**Conclusion:** Late presenters may make large demands on clinical resources, particularly in the early months after presentation.

## P14

## The durability of tenofovir (TDF) and didanosine (ddl) when dosed together using low-dose ddl (250 mg)

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**Background:** Pharmacokinetic studies have shown that when TDF is co-administered with 400 mg ddl, plasma ddl concentrations are increased by up to 60%. Reducing the ddl dose to 250 mg has been suggested in combination with TDF to minimise this interaction. There have been few comparative data assessing the use of the two doses of ddl in clinical practice.

**Methods:** We performed a retrospective analysis of patients who commenced an antiretroviral regimen containing TDF plus ddl at either 400 mg or 250 mg for the first time. All patients were virologically successful (viral load <50 HIV-1 RNA copies/ml). All patients who had to switch regimens due to side effects or experienced virological failure were documented.

**Results:** A total of 45 patients started regimens containing TDF and ddl at 400 mg, compared to 33 patients who started TDF and ddl at 250 mg. The mean duration of treatment was 215 days on 400 mg ddl and 356 days on 250 mg ddl. The time from below the level of virological detection to treatment failure between the two groups was statistically significant ( $P=0.005$ ), showing that patients taking TDF plus ddl at 250 mg were significantly more likely to remain on treatment.

**Conclusions:** Our clinical cohort has shown that using TDF plus ddl at 250 mg is a safe, well-tolerated and effective combination.

## P15

## Tolerability and durability of non-nucleoside reverse transcriptase inhibitors (NNRTIs) and reasons for changing the 'backbone': 5-year observational cohort data

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**Aims:** (1) To analyse a clinical database of antiretroviral-naïve patients who have started therapy since 1998; (2) to calculate virological and toxicity outcomes in patients treated with NNRTI-containing regimens; and (3) to evaluate reasons for and outcome of switching drugs other than the NNRTI (the 'backbone').

**Methods:** Data were collected retrospectively from the clinic database, which is updated in real time in the course of patients' out-patient care. All events from 1 January 1998 to 1 September 2003 were included in the analysis. Demographic and surrogate marker data, changes in treatment and reasons for switching were tabulated and analysed.

**Results:** 294 patients started an NNRTI-containing regimen (190 efavirenz, 104 nevirapine). The subjects were 70.4% black, 20.4% white, 52.7% male and 79.3% heterosexual. Other components of their regimens were two nucleoside reverse transcriptase inhibitors (NRTIs) (224 cases), three NRTIs (51 cases) and protease inhibitors (PIs) with or without NRTIs (19 cases). 37.4% of patients discontinued NNRTI (median follow-up 130 weeks). Reasons included toxicity (17.3%), failure (7.5%) and poor adherence (8.1%). 105 patients changed the 'backbone', usually as a result of suspected toxicity, generally without loss of virological control.

**Conclusions:** NNRTI-containing regimens were commonly used in this cohort of mainly black, heterosexual patients, were durable and had rates of toxicity comparable to published data.

## P16

## The effect of CD4 cell nadir on the toxicity profiles of antiretroviral regimens

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**Background:** It has been suggested that a lower CD4 nadir before starting highly active antiretroviral therapy (HAART) may lead to a greater risk of experiencing HAART-related toxicity. We investigated the relationship between the pre-HAART CD4 nadir, HAART and the occurrence of laboratory-defined toxicities.

**Methods:** Antiretroviral-naïve patients starting HAART were included. Discontinuation of any antiretroviral, the occurrence of laboratory-defined hypercholesterolaemia (>6.2 mmol/l), hepatotoxicity (aspartate aminotransferase/alanine aminotransferase over five times the upper limit of normal) and anaemia (haemoglobin <14 g/dl) were assessed.

**Results:** 195/766 (25%) individuals starting HAART stopped an antiretroviral within the first 48 weeks; 40/260 (15%), 21/167 (13%) and 46/339 (14%) with a CD4 nadir of 0–100, 100–200 and 200+ cells/ $\mu$ l, respectively, stopped for toxicity reasons; and 26/260 (10%), 17/167 (10%) and 45/339 (13%) stopped for efficacy reasons ( $P=0.6$ ). Lower CD4 nadirs were not associated with a greater rate of discontinuing antiretrovirals for any reason [adjusted hazard ratio (HR) 1.04 per 100 cells/ $\mu$ l higher; 95% confidence interval (CI) 0.99–1.10;  $P=0.1$ ]. Reasons for stopping were similar between groups. Lower CD4 nadirs were not associated with an increased risk of hypercholesterolaemia (HR 0.99; 95% CI 0.88–1.11;  $P=0.8$ ) or hepatotoxicity (HR 0.83; 0.64–1.07;  $P=0.2$ ), but were associated with increased incidence of anaemia (HR 0.78; 0.71–0.86;  $P<0.0001$ ).

**Discussion:** Lower CD4 nadirs were not found to be associated with either a higher risk of toxicity or of discontinuing an antiretroviral.

## P17

### Immunological success in HIV-infected patients starting highly active antiretroviral therapy (HAART) with a CD4 count of <200 cells/ $\mu$ l

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**Aim:** To compare immunological responses to highly active antiretroviral therapy (HAART) in treatment-naive patients with a baseline CD4 of <200 cells/ $\mu$ l.

**Design and methods:** Longitudinal data were obtained from a prospective database. Treatment-naive patients with a CD4 count of <200 cells/ $\mu$ l who had commenced HAART since 1996 were identified. Regimens were compared using the log-rank  $\chi^2$ -test.

**Results:** 561 of 1747 patients starting HAART since January 1996 met the study criteria. 86.1 % were male, the mean age was 37.9 years and the median (interquartile ratio) baseline CD4 count and viral load were 89 cells/ $\mu$ l and 140,338 HIV-1 RNA copies/ml, respectively. 62.8% of the subjects had commenced HAART with two nucleoside reverse transcriptase inhibitors (NRTIs) plus a non-nucleoside reverse transcriptase inhibitor (NNRTI) [34% nevirapine (NVP), 66% efavirenz (EFV)], 33.2% with two NRTIs plus a protease inhibitor (PI) and 4.1% with two NRTIs plus a boosted PI. A multivariate analysis showed that a regimen of two NRTIs plus one PI was less likely to achieve immunological success [adjusted hazard ratio (HR) 0.68, 95% confidence interval (CI) 0.43–1.05] than two NRTIs plus EFV, while commencing with two NRTIs plus a boosted PI was as likely to succeed (adjusted HR 1.62, 95% CI 0.98–2.66) as was two NRTIs plus NVP (adjusted HR 0.91, 95% CI 0.65–1.26).

**Conclusions:** This study shows a better immunological response to NNRTI or boosted-PI based HAART compared with a single PI. It also shows that boosted-PI regimens are at least as effective as those that are EFV-based and that NVP has similar immunological success to EFV.

## P18

### Epidemiological and clinical trends in levels of antiretroviral therapy uptake, using national surveillance data (1998–2002)

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**Background:** The proportion of individuals reported to the annual Survey of Prevalent HIV Infections Diagnosed (SOPHID) who received triple therapy (TT) or more has increased over the past few years. We aimed to identify new treatment starters and describe trends in epidemiology and clinical status over 5 years.

**Methods:** SOPHID data for the years 1998–2002 were matched on Soundex, date of birth and sex. Individuals who started treatment were identified and further matched to the CD4 surveillance scheme.

**Results:** Of 13,624 individuals who started treatment between 1998 and 2002, 93% (12,636) received TT, with an increasing trend from 88% to 95% ( $P<0.001$ ). Of those on TT, 33% had AIDS (unchanged over time,  $P=0.21$ ); 35% had pre-AIDS symptoms (falling from 41% to 31%,  $P<0.001$ ); and 29% were asymptomatic (increasing from 24% to 31%,  $P<0.001$ ). Of the TT starters, 6769 had a CD4 count available; 54% had a count of <200 cells/ $\mu$ l (rising from 46% to 60%,  $P<0.001$ ); and 21% had a count of  $\geq 350$  cells/ $\mu$ l (falling from 25% to 19%,  $P<0.001$ ).

**Conclusions:** A third of individuals starting TT had AIDS, reflecting late presentation. Within each clinical stage there was a trend towards lower CD4 counts at the start of TT. Additionally, there was a trend towards starting treatment while patients were asymptomatic.

## P19

### The psychological impact of HIV-related lipodystrophy

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**Background:** Since the late 1990s, new combinations of treatment for HIV patients have emerged. The use of highly active antiretroviral therapy (HAART) has been associated with a group of side effects that can alter the way fats are distributed in the body. This is known as HIV-related lipodystrophy (HIVLD). HIVLD can result in changes in body shape that are noticeable to the patient and to others. Anecdotal evidence suggests that body-shape changes can be associated with psychological and social difficulties.

**Methods:** In this qualitative study, we explored the psychological experience of HIV-infected adults with lipodystrophy. Semistructured interviews were conducted with seven patients at a London HIV treatment centre to elicit their experiences of the psychological impact of HIVLD.

**Results:** Thematic analysis of the interviews gave rise to a number of categories of psychological experience that were affected by HIVLD. These categories proved similar to those observed in other conditions where there is disfigurement.

**Conclusions:** The implications for counselling psychology and medical practice are discussed. Suggestions are made regarding adherence, assessment and psychological approaches to treatment.

## P20

### Sexual dysfunction in HIV-infected men: a cohort analysis

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**Background:** Erectile dysfunction and a low level of sexual desire has been reported in HIV-infected men. Sexual dysfunction in other medical settings, namely hypertension and depression, is associated with a detrimental effect on adherence to therapy. The aetiology of sexual dysfunction in HIV infection is unclear: psychological and organic mechanisms have been muted.

**Aim:** The aim of this study was to evaluate the nature of sexual dysfunction in patients referred to a dedicated HIV-sexual dysfunction clinic, and identify any possible aetiological factors.

**Methods:** A database analysis and retrospective analysis of patients' notes were performed.

**Results:** 72/82 patients reported erectile dysfunction, 30/82 low sexual desire and 6/82 retarded ejaculation. Reports of depression (21/72), peripheral neuropathy (6/72), lipodystrophy (15/72) and NNRTI-use (37/72) were correlated with erectile dysfunction. Nevirapine use was associated with high oestradiol levels.

**Conclusions:** Depression, peripheral neuropathy, lipodystrophy and antiretroviral use, with or without elevated oestradiol levels, are possible aetiological factors in HIV-associated male sexual dysfunction. Sexual dysfunction may impact upon adherence to highly active antiretroviral therapy and must be considered in clinical practice.

## P21

## Are HIV/AIDS services in Leeds able to meet the needs of asylum-seekers?

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**Background:** Yorkshire and Humberside had the second highest number of asylum-seekers after London, with 7330 in 2001, of whom Leeds took 1100. A significant proportion of asylum-seekers came from areas of high HIV prevalence, with consequent pressure on HIV-related care and health services in Leeds. The provision of sexual health services for this client group needs to be evaluated.

**Aims:** To develop a method of determining whether existing HIV/AIDS services in Leeds meet the needs of HIV-positive asylum-seekers.

**Methods:** A qualitative study using semistructured interviews was performed. The participants were seven service providers and 14 HIV-positive patients at the Leeds Centre for Sexual Health, of whom six were asylum-seekers.

**Results:** Asylum-seekers and UK residents were equally satisfied with HIV/AIDS services at the Leeds Centre for Sexual Health. Other agencies such as the Health Access Team and Terrence Higgins Trust had different strengths, which provided valuable support for this client group. Unmet needs of asylum-seekers were identified, such as specialist services for torture victims and opportunities for education. In areas of asylum-seeker dispersal with increased case loads, this methodology may assist the development of client-centred care networks.

## P22

## Cost-effectiveness of first-line regimens of highly active antiretroviral therapy (HAART) in the UK: non-nucleoside reverse transcriptase inhibitors (NNRTIs) versus protease inhibitors (PIs)

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**Aim:** Cost-effectiveness of two nucleoside reverse transcriptase inhibitors (NRTIs) plus one NNRTI versus two NRTIs plus one PI for first-line HAART.

**Methods:** Disease progression and direct costs per annum were estimated by stage of HIV infection, comparing two NRTIs plus one NNRTI with two NRTIs plus one PI, using data for 1996–2000 from 10 HIV units. Survival analyses were adjusted for baseline CD4 counts, age, sex and CD4 nadir, and analysed using the log-rank  $\chi^2$ -test.

**Results:** Centers for Disease Control and Prevention (CDC) Group A: Of 106 patients, 16 (15.1%) progressed and one died, with no differences between regimens (likelihood ratio  $\chi^2=8.4$ ,  $P=0.68$ ). Costs were £10,800 for an NNRTI-containing compared with £12,800 for a PI-containing regimen. CDC Group B: 12 of 48 patients (25%) progressed and four died, with no differences in progression (likelihood ratio  $\chi^2=10.9$ ,  $P=0.45$ ). Costs were £13,000 per annum for NNRTIs compared with £15,000 for a PI regimen. CDC Group C: Of 223 AIDS patients, 17 (7.6%) died, with no differences in progression between regimens (likelihood ratio  $\chi^2=7.3$ ,  $P=0.77$ ). Costs were £21,700 for NNRTIs compared with £23,700 per annum for a PI regimen.

**Conclusions:** First-line NNRTI- and PI-containing HAART regimens had similar effectiveness, but the NNRTI regimens were less expensive than the PI regimens. Cost is also an important factor in selecting HAART regimens.

## P23

## High level of social need among asylum-seekers in south London

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**Aim:** To describe the spectrum of social problems among HIV-1 infected patients in south London.

**Methods:** Cross-sectional questionnaire survey of 324 HIV-infected patients attending King's College Hospital on seven areas of social need: immigration, finance, housing, transport, child-care, mental health and knowledge of HIV.

**Results:** Of the 312 patients with complete data, 193 (62%) were male; 133 (43%) were white, 115 (36%) were black African and 26 (8%) black Caribbean. 55.5% were born outside the UK. 97 (67.8% of non-UK born) patients were seeking asylum or leave to remain in the UK. The most common social problems were: finance (47.1%), mental health (46.2%), housing (45.8%), transport (36.2%) and immigration (20.8%). 41.3% had experienced problems in more than three areas, and these patients were more likely to be female ( $P=0.002$ ), from sub-Saharan Africa ( $P=0.02$ ) and seeking asylum ( $P<0.001$ ). Patients seeking asylum (compared with those not seeking asylum) reported more frequent problems with housing (78.4% versus 33%,  $P<0.001$ ), finance (92% versus 39%,  $P<0.001$ ), mental health (62% versus 50%,  $P=0.2$ ), transport (65% versus 30%,  $P<0.001$ ) and child care (35% versus 5%,  $P<0.001$ ). Commonly cited immigration problems included long delays in processing applications, restrictions on seeking work and separation from children.

**Conclusions:** This study highlights the high level and complexity of social problems especially among HIV-positive asylum-seekers in south London.

## P24

## Uptake of HIV testing in a busy south London genitourinary medicine (GUM) clinic: will we reach National Sexual Health Strategy targets and are we testing those at risk?

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**Background:** The National Sexual Health Strategy states that all new attenders at GUM clinics should be offered an HIV test, with uptake of 40% by December 2004 and 60% by 2007. We aimed to determine whether we had reached this target, and whether there were ethnic differences given a higher HIV seroprevalence in black Africans and increasing rates in black Caribbeans.

**Methods:** All new patients attending our GUM clinic in July 2003 were reviewed to determine whether an HIV test was offered and accepted. Data were collected on sex, age, ethnicity, sexuality, presenting complaint and sexually transmitted infection (STI) diagnosis, and were analysed using the  $\chi^2$ -test.

**Results:** 627 men and 447 women were included in the study (96.8% eligible cases). 98.4% men and 95.1% women were offered a test. Of those, 60.7% of men and 56.5% of women were tested. There was no significant difference in uptake between Caucasian, black Africans, black Caribbeans, black British, Asian or mixed ethnicity (men  $P=0.764$ , women  $P=0.718$ ). There was no difference in uptake between heterosexual and gay men. There was no correlation between diagnosis of STI and test acceptance. Nine patients tested HIV-positive.

**Conclusions:** We have already exceeded the targets set by the National Sexual Health Strategy across higher-risk ethnic groups and gay men, but these groups should be targeted further.

## P25

## One size fits all? The changing needs of HIV-positive teenagers

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**Aim:** To identify teenagers' views on healthcare concerns and service provision within two London HIV clinics.

**Methods:** Self-administered, anonymous patient questionnaire.

**Results:** 19 teenagers were identified (10 male, nine female), with a median age of 16 years (range 13–19); eight were aged <16 years (younger teenagers, YTs) and 11 were aged ≥16 years (older teenagers, OTs). Most teenagers requested general information on healthy living and sexual development and education. OTs also highlighted the need for more information on antiretroviral therapy and HIV disclosure. Most teenagers were given their HIV diagnosis in the presence of a healthcare professional. There was wide variation on their views at which age this was best done. OTs highlighted the need to understand the implications of HIV disclosure. The services were rated highly by all but one teenager. Service priorities for all teenagers included meeting the doctor alone and knowing clinic staff, with OTs also wanting teenager-only clinics operating outside college hours and YTs wanting a gradual introduction to adult services. Teenagers' concerns varied widely (OTs: relationship issues, HIV transmission, becoming a parent; YTs: managing work and HIV secrecy at school, arguments with parents).

**Conclusions:** These youngsters welcomed the opportunity to comment on their care. While healthcare concerns and service needs varied between younger and older teenagers, the common theme was around opportunities that increase independence and choice.

## P26

## Relieving the burden: could nurse practitioners take on routine HIV out-patient care for select cohorts?

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**Background:** In-house audit demonstrated that a high proportion of patients attending routine HIV out-patient care have needs that could be met by other healthcare professionals. We therefore evaluated the potential development and acceptability of nurse practitioner roles.

**Methods:** Qualitative data were collected through 26 consultation observations, 25 patient interviews, two patient focus groups, 22 provider interviews and eight provider focus groups. Quantitative data were collected through database analyses, waiting time surveys and workload reviews. Service users were key members of the evaluation team.

**Results:** A 225% increase in numbers of HIV-positive individuals has occurred since 1992. There are growing concerns about appointment availability and maintaining high-quality care. Nurse practitioners were perceived as an acceptable development for distributing the workload. Three roles emerged: managing an asymptomatic cohort, shared care with a physician and implementing episodes of treatment support. Key considerations included training, supervision and practice limitations. The potential role of 'expert patients' in approaches to care also became apparent.

**Conclusions:** Proposals to develop alternative models of care were welcomed. Ongoing work will determine the model of care most suitable. Evaluation will determine impact on service utilisation, health and economic outcomes. The role of the 'expert patient' warrants further investigation.

## P27

## Comparing HIV and highly active antiretroviral therapy (HAART) with other National Health Service (NHS) priority diseases and their associated treatments

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**Background:** Until April 2002, HIV budgets were 'ring-fenced' for NHS providers, guaranteeing funds for HIV services. Now, primary care trusts (PCTs) receive unified budgets and are given commissioning autonomy to decide how budgets are allocated across therapy areas. Many of these (Mental Health, CHD, Cancer, Diabetes) are linked to NHS priorities/targets. Resources are therefore being diverted to prioritised areas/diseases/interventions. There is a need to understand the burden of HIV on patients relative to other diseases and to appreciate the value of HAART relative to treatments for other conditions.

**Methods:** A literature review was performed of HIV/HAART publications with a focus on cost-effectiveness (CE) and quality of life (QoL). A review of the National Institute of Clinical Excellence (NICE) published guidance was undertaken to compare the CE of HAART with that of approved therapies.

**Results:** The review uncovered evidence that HIV/AIDS is characterised by worse QoL than epilepsy, prostate cancer, diabetes and multiple sclerosis. These are all NHS priorities and receive considerably more focus/resourcing than HIV. Relative to NICE-approved interventions (which, as a result of approval, guarantees funding), HAART was also shown to be an efficient intervention.

**Conclusions:** The evidence indicated that HIV patients are constrained by a poorer QoL than patients in many NHS priority diseases. HAART is efficient relative to NICE-approved interventions.

## P28

## Current National Health Service (NHS) priorities towards sexual health and HIV/AIDS: implications for HIV treatment

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**Background:** The NHS is largely managed through use of central guidance, targets and performance indicators. Very few of these initiatives are focused on sexual health or HIV. Discontinuation of ring-fenced funds for HIV has further deprioritised its status. This investigation explored the implications for HIV treatment in England.

**Methods:** Key decision-makers involved in HIV/AIDS were selected for qualitative one-on-one discussions to explore service delivery issues. Interviewees were drawn from strategic health authorities (StHAs) and primary care trusts (PCTs). Interviews were conducted from December 2003 to January 2004, and were supplemented by a full review of the content of StHA local delivery plans (LDPs).

**Results:** There was a general paucity of HIV Commissioning Leads; many were part-time posts filled by individuals with little experience in the area. Only seven of 28 StHAs included HIV/AIDS in their LDPs. Antiretrovirals represented a cost pressure for most PCTs, with many forced to provide funding through development money or by re-prioritising existing budgets.

**Conclusions:** The current failure to designate HIV as a government priority may result in restrictions on whom and when to treat with antiretrovirals, irrespective of treatment guidelines. Re-instatement of HIV as a government priority may be necessary to ensure appropriate provision and delivery of HIV care.

## P29

### Health planning systems fail to provide appropriate resources and responses to sexual ill health in England

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**Background:** HIV/sexually transmitted infection (STI) clinicians are concerned about rising patient numbers and lack of prioritisation of sexual health services. *Per capita* funding appears to be decreasing while waiting lists grow. BHIVA, the National Association of Providers of AIDS Care and Treatment (PACT) and the THT undertake an annual snapshot analysis of the situation in order to formulate policy.

**Methods:** Twin postal surveys were undertaken of primary care trust (PCT) Chief Executives and BHIVA member clinicians in August 2003. Responses were augmented by questionnaires at BHIVA's Autumn Conference. Results were analysed and compared to each other and to the 2002 survey. These were published as *More Disturbing Symptoms* in November 2002.

**Results:** Almost a third of PCTs have no sexual health needs assessment. Less than 10% include patients in sexual health planning teams and clinic waiting times are increasing, up to 15 times the proposed government target. More than two-thirds of clinicians feel services are worsening and only one in eight have enough resources to manage their workloads.

**Conclusion:** The health planning system continues to fail to give sexual health and HIV appropriate attention, resulting in long-term public health costs.

## P31

### Is dispersal of HIV-positive persons with insecure immigration seeking asylum (PIISAs) appropriate? A postal survey of genitourinary medicine (GUM) clinics

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**Background:** The National Asylum Support Service (NASS) aims to disperse away from London at least 50% of the 500 HIV-positive PIISAs entering the UK annually. We investigated attitudes to dispersal among HIV physicians.

**Methods:** Anonymous postal questionnaire of all lead GUM clinicians in England.

**Results:** Of 75 questionnaires distributed, 55 (73%) were returned (35 from outside London). 45/55 (78%) physicians had direct experience of dispersal, a third of whom (13/45) had patients dispersed both to and from their centre. Centres reported increases in their HIV cohort, attributable to dispersal, of between 11 and 140% (median 36%). 38/55 (69%) of centres disagreed with dispersal in any situation. Problems encountered included PIISAs without medical care arranged prior to dispersal (90%), complicated patients (being investigated/treated by more than one speciality) (95%) and PIISAs with previous psychological trauma (89%). Six (11%) centres mentioned dispersal of pregnant women (two attributing birth of an HIV-positive baby as a consequence), four reported unintentional discontinuation of HAART and two reported an HIV-related death.

**Conclusions:** The data suggest that there are problems with dispersal of HIV-positive PIISAs. HIV specialists should work with NASS to ensure that PIISAs are dispersed in a safe and medically justifiable manner.

## P30

### What factors may impact on the ability of African patients to get the most from their HIV service?

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**Background:** Black Africans make up 25% of HIV-positive patients attending the Royal Free Hospital. African patients' ability to access care can be compromised by language barriers, health beliefs and cultural attitudes to sex. There is a lack of evidence of what may help in achieving good health outcomes among this heterogeneous patient group.

**Methods:** A patient study using a self-completed questionnaire to identify patients' health needs was undertaken. 135 black African patients (30% of all African patients) were chosen at random on attendance at the clinic. The sample was 60% female and 40% male.

**Results:** Only 30% spoke English as their first language, 10% spoke French and 9.6% spoke Shona. 30% wished to keep their diagnosis private; 17% have difficulty discussing safer sex with a partner; 94% have children; 13% are known to be HIV-positive and 18% are currently trying to have children. Patients on antiretrovirals accounted for 70%, while 51% were not willing to take part in a drug trial.

**Implementations:** The following have been implemented: advocacy and interpreter service, cultural and language-appropriate patient information, staff training in cultural and sexual practices; and a culturally targeted male/female condom pack. These results have implications for service developments to meet the HIV and sexual health needs of African patients.

## P32

### Attitudes of HIV-positive women to cervical screening

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**Introduction:** Immunosuppression increases the risk of cervical intraepithelial neoplasia; thus, participation of HIV-positive women in cervical screening programmes is imperative.

**Aim:** To identify negative attitudes and experiences of HIV-positive women to cervical screening and factors associated with these.

**Methods:** Women attending the Royal Free Hospital who had a previous colposcopy were given a questionnaire. Demographic variables and responses were compared using  $\chi^2$ -tests.

**Results:** 78/104 questionnaires (75%) were returned. The women were mainly of black ethnicity (68%), did not speak English as a first language (59%) and were taking antiretrovirals (76%). Responses to most questions were similar. 93% agreed that regular smears and 81% that regular colposcopy was valuable. 82% preferred a female examiner. Women of white ethnicity (87%) and those speaking English as a first language (74%) were more likely to dislike colposcopy versus those of non-white ethnicity (25%,  $P=0.0007$ ) and not speaking English as a first language (26%,  $P=0.002$ ). Those of white ethnicity were more likely to find smears and colposcopy painful (60%, 73%) versus those of black ethnicity (46%, 51%;  $P=0.47$ , 0.28, respectively). Telephone interviews of a sample of non-attenders revealed a preference for screening at general practitioners' clinics because of geographical convenience.

**Conclusion:** Cultural differences and language are important factors in women's perception of cervical screening.

## P33

## HAART in Canada: cost-effectiveness 1991–2001

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**Aim:** To compare additional costs per life-year gained (LYG) for non-AIDS and AIDS patients between 1997–2001 (period 2) and 1991–1995 (period 1).

**Methods:** Mean in-patient (IP) days and out-patient (OP) visits per patient-year (PPY) were assessed for non-AIDS and AIDS groups; costs of hospital care were estimated. Disease progression was controlled for baseline CD4 count, sex, age and risk factors.

**Results:** Non-AIDS IP days were 1.9 (period 1) and 0.9 PPY (period 2); OP visits increased from 2.8 to 5.6 PPY; costs were US\$5268 (period 1) and US\$11,462 PPY (period 2), of which 64% (period 1) and 84% (period 2) was spent on antiretroviral therapy; the median progression time was 6.3 years (period 1) compared with 12.5 years (period 2; log-rank  $\chi^2$ -test  $P < 0.001$ ); the additional cost per LYG was US\$17,614 for non-AIDS IPs. For AIDS patients, mean IP days decreased from 14.4 (period 1) to 4.3 PPY (period 2); OP visits increased from 7.9 to 9.2 PPY; costs increased from US\$11,409 to US\$14,184 PPY; expenditure on antiretroviral therapy increased from 29% (period 1) to 72% (period 2); the median progression time was 3.8 years (period 1), which increased to 13.3 years (period 2; log-rank  $\chi^2$ -test  $P < 0.001$ ) at an additional cost of US\$15,289 per LYG.

**Conclusion:** HAART was a cost-effective intervention for HIV patients in Canada.

## P34

## HIV testing in tuberculosis (TB) patients: meeting the London standard

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**Background and methods:** The London Regional Office has stated that all TB patients of unknown HIV status should be offered an HIV test. We sought to implement this using a standard protocol where TB nurses or medical staff discussed testing with patients early in their treatment.

**Results:** Between July 2002 and July 2003, there were 236 TB notifications of unknown HIV status. 131 (56%) were offered an HIV test. 103 (79%) took this up and 18 (17%) were found to be HIV-positive. Of 178 out-patients, 88 (49%) were offered a test, and 61 (69%) accepted; one (2%) was HIV-positive. There were 58 in-patients. HIV testing was discussed with 43 (74%). 42 (98%) had a test and 17 (40%) were HIV-positive. The latter individuals were predominantly black Africans often with severe systemic symptoms. Subjects who declined a test often did so because they felt they were at low risk of HIV, or did not want a possible dual diagnosis at that stage.

**Discussion:** Our results indicate that we are far from achieving 100% coverage. Improvements may arise from using alternative testing strategies and qualitative analysis of decision-making by healthcare professionals and patients in the two settings.

## P35

## The outcome of patients with HIV-related germ-cell tumours (GCTs): a case-control study

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**Background:** Testicular GCT is not an AIDS-defining illness despite an increased incidence in men with HIV infection. Many clinicians feel that the prognosis of testicular cancer may be worse among men with HIV infection.

**Methods:** We performed a matched case-control study, comparing outcomes in 35 HIV-positive men and in an HIV-negative control group derived from a large prospective cohort from one treatment centre, using three age- and stage-matched controls for each case.

**Results:** There was no difference in the 5-year GCT-free survival between cases [82%; 95% confidence interval (CI) 69–95] and controls 80% (95% CI 72–88). However, overall survival was significantly decreased in the cases (log-rank  $P = 0.03$ ). HIV was responsible for 70% of this mortality. The relapse-free survival for stage I patients treated with orchidectomy and surveillance was not affected by HIV status (log-rank  $P = 0.68$ ). There was no difference in disease-free survival in patients with metastatic disease (log-rank  $P = 0.78$ ). The overall survival has not improved since the introduction of highly active antiretroviral therapy (log-rank  $P = 0.4$ ).

**Conclusion:** HIV-related GCT is not more aggressive than GCT in the general population.

## P36

## Cancer in rural KwaZulu/Natal, South Africa

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**Background:** The incidence of cancer in rural sub-Saharan Africa in the era of the HIV/AIDS epidemic is unknown.

**Methods:** To investigate cancer incidence, a registry was established in Hlabisa District, KwaZulu/Natal, South Africa. A registrar was employed to find all cancer cases presenting to the district hospital and clinics, by active case-finding.

**Results:** During 18 months of registration, information was collected on 118 cancers in men and 106 in women. In men, the most frequently diagnosed cancers were Kaposi's sarcoma (40%;  $n = 47$ ) and lung cancer (20%;  $n = 24$ ), followed by cancers of the liver (9%;  $n = 11$ ) and oesophagus (7%;  $n = 8$ ). In women, the most frequent cancers were Kaposi's sarcoma (41%;  $n = 43$ ) and cancer of the uterine cervix (33%;  $n = 35$ ), followed by other female genital tumours (6%;  $n = 6$ ) and colorectal cancer (4%;  $n = 4$ ).

**Conclusions:** Cancers of the lung and cervix are relatively frequent in KwaZulu/Natal, reflecting the prevalence of risk factors such as tobacco and human papillomavirus infection. Kaposi's sarcoma has increased in frequency with the recent spread of HIV infection. The impact on health of sexually transmitted infections and tobacco are clearly evident in these cancer registration data, but cancer incidence represents only a small proportion of morbidity and mortality associated with these factors.

## P37

### Study of fine-needle aspirations and lymph-node biopsies in HIV-infected patients

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**Background:** Lymphadenopathy in HIV-positive people is commonly of no clinical consequence if it is in the form of persistent generalised lymphadenopathy (PGL). We remarked that a large number of fine-needle aspirations (FNAs) and lymph-node biopsies (LNBs) were reported as consistent with PGL. We considered the possibility of patients with PGL being overinvestigated and whether there are markers that could be used to identify those more likely to have a significant diagnosis. There are no guidelines on the indications for lymph-node investigations in HIV-positive patients.

**Methods:** We studied all patients who had undergone a LNB or FNA over a year. Details of symptoms, signs, laboratory and radiological investigations, surrogate markers, antiretroviral therapy and final diagnoses were collected.

**Results:** 44 patients were identified, 10 of whom had a significant diagnosis. These patients did have certain characteristics compared to those with PGL: they were more likely to be in-patients, have documented fever, be anaemic, have a CD4 count of <200 cells/ $\mu$ l, a viral load of >100,000 HIV-1 RNA copies/ml, C-reactive protein >7, albumin <25 g/l and have splenomegaly.

**Conclusions:** Using these as indicators of a more significant underlying pathology and hence the need to investigate further, the number of unnecessary lymph-node investigations could be reduced in those with PGL as the cause.

## P38

### Resolution of AIDS-related Castleman's disease with anti-CD20 monoclonal antibodies is associated with declining interleukin (IL)-6 and tumour necrosis factor (TNF)- $\alpha$ levels

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**Background:** Multicentric Castleman's disease (MCD) is a lymphoproliferative disorder characterised by lymphadenopathy with angiofollicular hyperplasia and plasma cell infiltration. In the context of HIV-1, Kaposi's sarcoma-associated herpesvirus (KSHV) has been identified as a potential causative agent and lymph nodes of patients with MCD specifically harbour the virus in B cells that stain positively for the CD20 surface antigen.

**Methods:** A 32-year-old HIV-1 positive man was diagnosed with MCD following a long history of constitutional symptoms and generalised lymphadenopathy. Primary therapy with single agent rituximab, a humanised monoclonal antibody to CD20, was associated with a near complete clinical response.

**Results:** During this time, his KSHV viral load decreased and we also observed immediate, large and sustained decreases in interleukin-6 (IL-6) and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) levels. This is consistent with recent data demonstrating that IL-6 levels may be a surrogate marker of KSHV viral load and that decreases in IL-6 reflect response to therapy.

**Conclusion:** Rituximab was effective therapy in this patient and the response was associated with declines in KSHV viral titres and circulating cytokines.

## P39

### Case history: regression of advanced conjunctival carcinoma in patient on antiretroviral therapy

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**History:** A 52-year-old African lady attended a genitourinary medicine clinic, was diagnosed with HIV (CD4 count 56 cells/ $\mu$ l, viral load >100,000 HIV-1 RNA copies/ml) and was commenced on Combivir and efavirenz. Her medical history included 3 months of orbital pain and blurred vision of the left eye, which had been diagnosed as infected pterygium but had not responded to treatment. An ophthalmology referral was made. Vulvar intraepithelial neoplasia (VIN) and cervical intraepithelial neoplasia (CIN) grade 3 were diagnosed also. A conjunctival biopsy revealed a highly aggressive squamous cell carcinoma. A computed tomography scan suggested orbital margin invasion. The patient declined radical orbital exenteration, which carried a poor prognosis, relying on faith alone. Palliative care personnel were contacted, as the pain was now severe. The patient's immune function gradually improved, and after 1 year, her CD4 count was 221 cells/ $\mu$ l and her viral load was undetectable. The eye swelling and pain began to diminish rapidly. After 16 months, the eye appeared normal and she was persuaded to re-attend the ophthalmology department, who agreed that, incredibly, there was no longer any evidence of malignancy.

**Discussion:** Unprecedented tumour regression may be related to immune recovery. A human papilloma virus (HPV) aetiology is possible in orbital carcinoma (work ongoing). Only the patient's religious faith (against medical advice) prevented ultimately unnecessary mutilative surgery.

## P40

### The value of anal cytology and human papilloma virus (HPV) typing in the detection of anal intraepithelial neoplasia: a review of cases from an anoscopy clinic

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**Background:** Anal intraepithelial neoplasia (AIN) is usually detected by chance during routine haemorrhoidectomy or excision of anal warts. It is unclear whether individuals who practice anoreceptive sexual intercourse should be screened for AIN. A prerequisite before this can occur is validation of cytology as a screening tool.

**Methods:** We undertook 156 anoscopic procedures in 100 patients, 89 of whom were HIV-1 positive. A comparison was made between the anal cytology results (obtained with the Palefsky sampling method) and the histological findings of biopsies taken from abnormal areas seen on a high-resolution anoscopic examination of the anal canal. Swabs taken concurrently with the cytology were analysed for the presence of HPV DNA and compared with the cytological and histological findings.

**Results:** The sensitivity of the cytology was 82%, and the specificity 45%, compared with the histology. Of the patients with no detectable AIN, 75% had a high-risk HPV type (hrHPV) in the anal canal, rising to 94% in patients with high-grade AIN (HG-AIN). There were no significant differences in the prevalence of hrHPV genotypes between different cytological or histological grades of abnormalities.

**Conclusion:** Anal cytology by the Palefsky method is simple to undertake, has a sensitivity and specificity comparable with cervical cytology and can therefore be used as the basis of a pilot screening project in centres with large cohorts of HIV-positive homosexual men who have a high risk of developing anal carcinoma. HPV genotyping is not a useful adjunct to cytological screening.

## P41

## Invasive anal cancer: single institution experience

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**Background:** Many clinicians believe the prognosis for anal cancer in HIV-positive patients is poor.

**Methods:** 26 patients (25 male) with histologically confirmed invasive anal cancer were identified.

**Results:** The median age was 43 years (range 28–56) and CD4 cell count 206 cells/ $\mu$ l (16–749). 12 were receiving highly active antiretroviral therapy (HAART), but only five (42%) had undetectable viral loads. 22 patients were treated with chemoradiotherapy, two tumours confined to the anal verge were completely excised and two patients received palliative care only. The median follow-up was 4.8 years, 11 patients have died (seven from anal cancer and four in remission). The overall survival at 5 years is 47% (95% confidence interval 24–70%). Five patients (23%) relapsed after chemoradiotherapy and all died of anal cancer. There was no difference in overall survival between the pre- and post-HAART eras (log-rank  $P=0.19$ ).

**Conclusions:** This cohort study is the largest series reported so far. The 5-year overall survival is worse than for the general population; however, the 2-year survival rate is 74%, with no relapses of anal cancer occurring after this time and all subsequent deaths attributed to HIV infection. These results are encouraging as they include two patients who received palliative care only.

## P42

## End-stage liver disease was the primary cause of mortality in HIV-positive patients

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**Background:** The introduction of highly active antiretroviral therapy (HAART) has been associated with a significant reduction in mortality rate in cohorts studied. Previous analysis of mortality rates in this institution had identified decreasing trends for the years 1995–1998.

**Methods:** A retrospective analysis of causes of mortality for the period 1 January 1999 to 31 March 2002 was undertaken, using patients' charts, HIPE system and the departmental database. The data were analysed with Epi-info 2000.

**Results:** 89 patients (28 females, 61 males) died in the study period, 79 as in-patients, four in other hospitals, two in a hospice and four in the community. The mean age at death was 41 years (range 21–58). The mode of HIV acquisition included intravenous drug use (IVDU) in 47 (53%), men having sex with men 16 (18%) and heterosexual five (6%). The mean viral load was 108,770 HIV-1 RNA copies/ml, range (<50 to 430,000), and the mean CD4 count was 79 cells/ $\mu$ l (range 9–754). The mean time between first registration with the service and time of death was 7.7 years (SD  $\pm$  4.17 years, range <1 month to 14 years). Among patients who died in the hospital, 70% had previous antiretroviral therapy (ART) experience and 51% were on ART. End-stage liver disease (ESLD) was a cause of death in 43 patients (48.3%), who were also hepatitis C co-infected (41 IVDUs and two haemophiliacs). Active chronic hepatitis B infection was diagnosed in two of the 41 IVDUs. Only eight of the 43 patients who died from ESLD had problematic alcohol-drinking. The other common causes of mortality were HIV-associated malignancy (four lymphoma, one Kaposi's sarcoma), end-stage HIV disease (five), opportunistic infections (one) and accidental death (four). Two patients died from lactic acidosis secondary to ART, one compounded by acute hepatitis A.

## P43

Pegylated interferon- $\alpha$ 2b and ribavirin for chronic hepatitis c virus (HCV) infection in individuals with HIV/HCV co-infection

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**Background:** End-stage liver disease has become a leading cause of morbidity and mortality in patients with HCV/HIV co-infection, emphasising the importance of treatment of chronic hepatitis C in these patients.

**Methods:** 12 haemophilic and 14 non-haemophilic (six female) HCV/HIV co-infected individuals have been treated with pegylated interferon- $\alpha$ 2b (1.5  $\mu$ g/kg) and ribavirin (10.6 mg/kg). Patients with genotypes (G) 1/4 were treated for 48 weeks and those with G 2/3 for 24 weeks.

**Results:** The cohort has a median age of 40 years (range 28–48); all had a CD4 count of >200 cells/ $\mu$ l; the pretreatment median HCV viral load was 891,000 iu/ml (range 18,500–13,300,000); 12 patients were G1, four G2, nine G3 and one G4. Nine were antiretroviral-naive. A sustained virological response (SVR) was found in 10/26 patients (39%) of all genotypes, in 7/13 (54%) with G2/G3 and in 4/13 (31%) with G1/G4 (31%). After achieving an end-of-therapy response, 4/13 (31%) with G2/G3 relapsed. Anaemia was universal but did not require any erythropoietin support nor any ribavirin dose reduction. No adverse drug interactions were noted. Three female patients developed symptomatic hypothyroidism. In this cohort of patients, pegylated interferon- $\alpha$ 2b and ribavirin are safe and well tolerated. The SVR was lower in G 1/4 patients, and there was a high relapse rate (31%) in G2/3 patients treated for 24 weeks.

## P44

## Hepatitis B virus (HBV) re-activation during combination chemotherapy for AIDS-related lymphoma is uncommon and does not adversely affect outcome

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**Background:** HBV re-activation and subsequent liver damage during anticancer chemotherapy has been reported in a number of studies. As co-infection with HBV and HIV-1 is common, we examined the incidence and degree of HBV re-activation in a cohort of individuals with AIDS-related lymphoma.

**Methods:** We measured HBV core antibody, surface antigen and HBV viral loads in 60 individuals before, during and after cytotoxic chemotherapy.

**Results:** All 60 were hepatitis B surface antigen-negative and HBV DNA was undetectable prior to chemotherapy. 30 were positive prior to chemotherapy for HBV core antibody. During chemotherapy, re-activation, as defined by a detectable HBV DNA, was observed in only five out of these 30 patients (17%) and only two demonstrated subsequent surface positive antigenaemia. Two of the five patients whose disease was re-activated were receiving concurrent lamivudine and/or tenofovir disoproxil fumarate. There were no differences in overall or disease-free survival between patients who were HBV core antibody-negative, those who were core antibody-positive with no re-activated disease and those whose disease was reactivated.

**Conclusions:** HBV re-activation during chemotherapy for AIDS-related lymphoma appears uncommon. In HBV surface antigen-negative HIV-1 infected individuals with AIDS-related lymphoma, the risk of HBV-related hepatitis during chemotherapy appears insignificant.

## P45

### Hepatitis C (HCV) viral kinetics in patients co-infected with HIV treated with pegylated interferon and ribavirin

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**Background:** Early prediction of failure to respond to pegylated interferon and ribavirin for HCV treatment would reduce cost and toxicity. We examined quantitative HCV viral load responses in 11 HIV co-infected patients during treatment with pegylated interferon- $\alpha$ 2b and ribavirin.

**Methods:** 11 co-infected patients were treated and a quantitative HCV viral load was measured every 4 weeks using the Roche monitor assay. Qualitative HCV polymerase chain reaction was checked when the quantitative assay was below the limit of detection (<600 IU/ml).

**Results:** Nine patients were genotype 1 and two patients genotype 3. The median HCV viral load at baseline was 379,000 IU/ml (range 17,400 to 1,000,000). At week 12, an undetectable HCV viral load and greater than a 2 log<sub>10</sub> drop was seen in eight patients, and at week 24 this was seen in six patients. Three patients achieved an undetectable HCV viral load at the end of treatment and one patient had an undetectable HCV viral load at week 36, but discontinued treatment at this time. Sustained response results are awaited. Individual virological HCV profiles will be presented.

**Conclusions:** A detectable viral load at week 12 predicted a lack of response but an undetectable viral load at week 12 or 24 could not accurately predict the response at 48 weeks.

## P46

### Hepatitis C (HCV) and HIV in the Regional Infectious Diseases Unit Edinburgh (RIDU): who is a candidate for HCV treatment?

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**Aim:** To identify patients suitable for HCV treatment.

**Methods:** HCV antibody-positive patients were identified and their current/previous HCV polymerase chain reaction (PCR) status was recorded. Patients' notes were examined to assess their suitability for HCV therapy. Patients who were HCV PCR-positive were included. Patients excluded from consideration for HCV treatment were those with a CD4 count of <200 cells/ $\mu$ l, current intravenous drug use (IVDU) and any absolute contra-indication to interferon or ribavirin (EASL guidelines).

**Results:** Within the current cohort ( $n=428$ ), 173 (40%) patients are HCV antibody-positive. Of these, 130 (75%) are HCV PCR-positive, 38 (22%) PCR-negative and five (3%) had no PCR recorded. 47 (36%) of the HCV PCR-positive patients were excluded: 31 had a CD4 count of <200 cells/ $\mu$ l, two were considering pregnancy, four were ongoing IVDUs, nine had severe neuropsychiatric illness and one had terminal malignancy. 83 (64%) met the inclusion criteria. However, 53 of these (41%) were not suitable for treatment: 31 declined (11 had previously had liver biopsy), six had poor attendance, two had failed interferon therapy and declined further treatment, 10 had deferred treatment following a liver biopsy and five had not responded to treatment with pegylated interferon and ribavirin. 30 (23%) patients were thus suitable for treatment and two are currently receiving treatment.

**Conclusions:** In this cohort, HCV treatment is currently appropriate in only 30 patients (23%). This low figure reflects patients with a CD4 count of <200 cells/ $\mu$ l and those who declined further assessment or treatment (24%). The reasons for the latter warrant further study.

## P47

### Experience of hepatitis C virus (HCV) treatment in the Edinburgh HIV cohort

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**Background:** Individuals co-infected with HIV and HCV have a lower response rate to HCV treatment in clinical trials than those without HIV infection. Our objective was to assess the outcomes of HCV treatment in our cohort of co-infected individuals.

**Methods:** Medical notes were reviewed for all co-infected patients treated for HCV at the Regional Infectious Diseases Unit in Edinburgh. **Results:** 18 co-infected patients received HCV treatment between 1994 and 2004; 17 patients had a pretreatment liver biopsy, six had cirrhosis and 10 had fibrosis. Six of the 18 patients have had more than one course of therapy: 28 courses of treatment have been completed (12 interferon; nine interferon/ribavirin; one pegylated-interferon; six pegylated-interferon/ribavirin); two patients are currently receiving pegylated-interferon and ribavirin. One patient had a sustained virological response (SVR) to pegylated-interferon and ribavirin. Three patients had an end-of-treatment response but no SVR. Two other patients received a full course of treatment with no response. All other courses were discontinued early, due to poor tolerability or toxicity.

**Conclusions:** The outcomes of HCV treatment in co-infected patients are poor. There is an urgent need to determine how the results of recent studies involving pegylated interferon and ribavirin can be applied to clinical practice.

## P48

### Viral tropism and endogenous interferon production in patients with acute hepatitis C virus (HCV)

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**Background:** HCV has been demonstrated in peripheral blood mononuclear cells (PBMCs), in chronic HCV models, but the tropism for individual leucocyte populations has not been established. PBMCs from acute HCV/HIV co-infected and chronic HCV patients were isolated and the presence of HCV determined. Dendritic cell (DC) numbers and interferon (IFN)- $\alpha$  levels were obtained, to correlate plasmacytoid DC numbers to the amount of IFN- $\alpha$  produced.

**Methods:** The Miltenyi bead system was used to separate the CD3, CD14, CD19, CD56 and DC populations from two acutely infected co-infected and four chronic HCV patients. The presence of HCV RNA was detected by nested polymerase chain reaction. Fluorescein-activated cell-sorter (FACS) analysis was used to determine DC numbers. IFN- $\alpha$  levels were determined by enzyme-linked immunosorbent assay (ELISA).

**Results:** HCV genomic RNA was detected only in CD3 cells in two co-infected patients with acute HCV, being cleared in the patient who subsequently cleared HCV. This is in contrast to the situation in four patients with chronic HCV. IFN- $\alpha$  levels were raised with respect to controls, in acute HCV, where the patients went on to clear the virus.

**Conclusions:** The presence of HCV in T cells confirms the importance of the T-cell response in acute HCV. IFN- $\alpha$  levels rise in acute HCV, which may play a role in subsequent viral clearance.

## P49

Use of ultrasensitive mutation detection system to identify the *in vivo* efficacy of tenofovir against lamivudine-resistant and -susceptible hepatitis B virus (HBV) subpopulations in lamivudine-experienced HBV/HIV-1 co-infected individuals

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**Background:** We developed a supersensitive system for detection of HBV drug-resistant mutants, down to 1:10,000 plasma viruses, in order to assess the response of individual quasispecies to antiviral therapy.

**Methods:** We studied eight lamivudine-experienced HBV/HIV-1 co-infected patients switching anti-HBV therapy to tenofovir. Plasma samples were assessed for HBV viral load by real-time polymerase chain reaction (PCR), and the relative proportions of lamivudine-resistant mutants and wild-type viruses were assessed by a real-time PCR-based amplification refractory mutation system (ARMS).

**Results:** The median baseline HBV DNA was  $4.3 \times 10^7$  IU/ml. Tenofovir therapy led to a median 4.9 log<sub>10</sub> reduction in the HBV DNA viral load over 24 weeks. At baseline, all samples exhibited lamivudine-resistant mutations M204V or I, and L180M in HBV polymerase, with the mutant : wild-type ratios ranging between 50 and 99.9%. During the first 16 weeks of viral load decline, these proportions remained similar within each individual. However, suppression of mutant virus then overtook wild-type suppression, so that the mutant : wild-type ratios at week 24 ranged from 0.1 to 50%.

**Conclusion:** Our results are compatible with an equivalent potency of tenofovir against lamivudine-sensitive and -resistant viruses, with the fitness deficit of the latter further reducing mutant concentrations after 16 weeks.

## P50

## A cohort study to review the efficacy of the total lymphocyte count (TLC) as a predictor of AIDS-defining opportunistic infection (ADOI) in HIV-infected patients

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**Methods:** A Chelsea and Westminster HIV cohort was used to identify patients with first episodes of ADOI. Corresponding CD4 counts/TLCs used were those recorded 3 months before diagnosis or at the time of prescribing first prophylaxis. Patients without ADOI were considered the 'at risk' group. The TLC/CD4 values used were obtained from the last clinic appointment or the date of death. Event time was defined as the period since the TLC/CD4 result and development of the first ADOI, clinic visit or death date. Cut-off values for TLCs/CD4 counts were estimated using receiver operating characteristic (ROC) curves. The likelihood of a first ADOI was estimated using Cox's proportional hazards method.

**Results:** A significant linear correlation was found between the log<sub>10</sub> CD4 count and the TLC ( $r=0.70$ ,  $P<0.001$ ). 1097 patients (19%) developed ADOI. The cut-off value for the TLC (where the error rate is minimum/sensitivity maximum) was 1500 cells/ $\mu$ l. Individuals with a TLC of 1000-1500 were 40% more likely to experience ADOI compared to those with a TLC of >1500 [sensitivity (95% confidence interval) 68.6 (65.7-71.3), specificity 66 (64.6-67.3)]. The risk of an opportunistic infection was almost threefold higher with a TLC of 500-1000 than with >1000. The cut-off value for the CD4 count was 200 cells/ $\mu$ l. Individuals with a CD4 count of 150-200 cells/ $\mu$ l were 34% more likely to develop ADOI than those with a CD4 count of >200 cells/ $\mu$ l (sensitivity 73.8 (71.2-76.4), specificity 75.6 (74.4-76.8)]. The area under the ROC curve for TLC was 10% lower than that for the CD4 count.

**Conclusions:** A TLC is only moderately less reliable than a CD4 count.

## P51

## Chemokine receptor analysis of a UK cohort with chronic HIV-1 infection

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**Background:** CCR5, a chemokine co-receptor for HIV-1, is mutated in a small number of individuals due to a 32-basepair deletion. Homozygosity for the  $\Delta$ 32 mutation permits resistance to HIV-1 infection, and heterozygous individuals show a limited resistance to disease progression. A variant of CCR2 (CCR2-64I) is associated with a delay in disease.

**Methods:** 40 HIV-1-positive and 135 HIV-negative subjects were genotyped for  $\Delta$ 32 and CCR2-64I. Plasma HIV-1 RNA and T-cell subsets were measured in the HIV-1-positive subjects.

**Results:** Two of 40 HIV-1-positive subjects were heterozygous for  $\Delta$ 32. 19/135 HIV-negative controls were heterozygous and 10/135 were homozygous for  $\Delta$ 32. One patient had CCR2-64I: she was Caucasian and had been diagnosed with HIV-1 infection for 12 years; she had a stable viral load (~16,000 HIV-1 RNA copies/ml) and an average CD4 count decline of only 36 cells/ $\mu$ l per year despite the absence of therapy.

**Conclusions:** In this study, numbers of HIV-negative  $\Delta$ 32 heterozygous individuals were higher than published values, possibly due to ethnic differences. Lower numbers were seen in the HIV-1-positive subjects. Our CCR2 data support the findings of others. Published data have indicated a link between chemokine receptor mutations and the failure of viral suppression by antiretroviral therapy. We have shown that  $\beta$ -chemokine levels are altered by the choice of antiretroviral therapy. We propose that knowledge of the effects of  $\beta$ -chemokines and chemokine-receptor mutation may become important for new classes of antiretroviral therapy.

## P52

High levels of HIV-1 infection of CD8 lymphocytes expressing CD4 *in vivo*

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**Background:** CD8 lymphocytes express CD4 and become susceptible to HIV-1 infection during intrathymic development and on activation. The extent of CD8 lymphocyte infection and the relative contribution of intrathymic- versus activation-related infection was assessed in subjects at various HIV disease stages.

**Methods:** The HIV proviral load was quantified by polymerase chain reaction in CD8 lymphocyte subsets isolated by fluorescence-activated cell sorting from blood of 16 HIV-infected subjects. The differentiation phenotype of CD8 lymphocytes expressing CD4 was assessed by flow cytometry.

**Results:** 13 subjects had detectable provirus in CD8 lymphocytes (median 8 viral copies/million cells), with an inverse correlation between the CD8 lymphocyte proviral load and the CD4 count ( $R=-0.73$ ,  $P<0.01$ ). Strikingly, much higher proviral loads were found in CD8 lymphocytes expressing CD4 (median 1197 proviral copies/million cells,  $n=5$ ). CD8 lymphocytes expressing CD4 represented between 0.8 and 3.3% of total CD8 lymphocytes and were more frequent in memory than either antigen-naive or effector subsets ( $P<0.05$ ,  $P<0.01$ , respectively).

**Conclusion:** Infection of activated cells rather than intrathymic cells is the major route of production of circulating HIV-infected CD8 lymphocytes. The high HIV proviral loads in CD8 lymphocytes expressing CD4 suggest targeted infection of CD8 lymphocytes responding to antigen.

## P53

## Function and distribution of natural killer (NK) cell subsets in HIV-1 positive individuals in the presence and absence of viraemia

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**Background:** NK cells are a subset of lymphocytes that are important in the innate control of viral infection, responding through cytolytic activity, cytokine and chemokine secretion. It has been shown recently that there is an imbalance in NK cell redistribution and function, which persists even following successful depression of the HIV-1 viral load with antiretroviral therapy. Others have shown that certain NK cell subsets fail to return with antiretroviral therapy and that interferon- $\gamma$  production is impaired.

**Methods:** We analysed the changes in distribution of the CD3-CD56<sup>high</sup>CD16- and CD3-CD56<sup>low</sup>CD16<sup>high</sup> NK subsets within a group of patients undergoing temporary interruption of antiretroviral therapy through an unstructured treatment interruption. We will be presenting flow cytometric analysis and enzyme-linked immunosorbent assay (ELISA) data, which were used to analyse the production of cytokines and chemokines in patients with plasma HIV-1 viral loads (VL) of <50 HIV-1 RNA copies/ml and those with >1000 copies/ml.

**Results:** We have shown that there are decreases in absolute numbers of NK cells and an altered distribution of cytolytic CD16<sup>high</sup> and cytokine-producing CD16- NK cell subsets in patients undergoing a treatment interruption, correlating with an increased viral load.

**Conclusions:** Increases in the viral load are associated with decreases in absolute numbers of NK cells and a deficient redistribution of their subsets.

## P53a

## Prevalence of skin dysplasia and malignancy in HIV-positive individuals

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**Background:** Recent studies have suggested that certain non-AIDS-defining cancers may be becoming more prevalent in the HIV+ population due to improved survival.

**Aim:** To describe the prevalence and character of malignant or dysplastic skin lesions in a London HIV clinic.

**Methods:** Prospective data were collected, including a history of, and known risk factors for, skin malignancy in patients attending for out-patient care.

**Results:** Data were collected on 294 patients (15% of the total clinic population). 16/294 (5.4%) had had skin malignancy or dysplasia, 13 after an HIV diagnosis. The median CD4 count was 260 cells/ $\mu$ l (range 100–570), the median age was 41 years and eight were on highly active antiretroviral therapy at the time of the diagnosis of skin cancer. All patients were Caucasian, and the prevalence of skin cancer was 7.3% (16/219). There were nine with basal cell carcinoma, three with dysplastic naevi, two with malignant melanoma (MM), one with Bowen's disease, one with squamous cell carcinoma, one with dermatofibrosarcoma and one with anal intra-epithelial neoplasia. 11/16 patients (68.8%) had at least one risk factor for skin malignancy (family history of MM, sunbed use or lived in tropics). Cases were significantly more likely to have used a sunbed (72.7% versus 48.3%;  $P=0.04$ ).

**Conclusions:** Both HIV and ultraviolet radiation may contribute to reduced tumour surveillance in the skin. Our data highlight the need for clinicians to advise patients about risk factors and monitor them in order to diagnose skin cancers promptly.

## P54

## Retrospective study of antiretroviral therapy in HIV-infected children at the Royal Free Hospital

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**Background:** The Paediatric Department provides a key service for HIV-positive families. To describe our cohort, we studied children attending the centre from January 1994 to January 2004. The aim was to identify the antiretroviral regimens used and their impact on surrogate markers.

**Methods:** We performed a retrospective cohort study on 30 patients. 19 patients received antiretroviral therapy during the defined period. From these patients, we identified the antiretroviral regimens received, reasons for switching, time to an undetectable viral load (VL) and duration of a detectable VL.

**Results:** 30 antiretroviral regimens were received by 19 patients with a mean age of 8.7 years and a mean nadir CD4 of 14.3%. 14 regimens were protease inhibitor-based and 13 were non-nucleoside reverse transcriptase inhibitor (NNRTI)-based. Two patients received a dual nucleoside reverse transcriptase inhibitor (NRTI) regimen and one received a triple NRTI regimen. The mean time to an undetectable VL (<400 HIV-1 RNA copies/ml) was 16 weeks (range 8–24 weeks). The nadir CD4 percentage increased by a mean of 14.8 (range 5–26%). The duration of a detectable VL on therapy ranged from 3 months to 5 years (mean 18 months).

**Conclusions:** Difficulty adhering to complex regimens was the prime reason for uncontrolled viral suppression, resulting in either rapid cycling of antiretroviral agents or continuation of a partially resistant regimen.

## P55

## Teaching pill-swallowing in HIV-infected children revisited

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**Background:** One of the significant practical struggles in treating paediatric HIV infection is ensuring that children can follow strict medication regimens, which often include swallowing multiple, large capsules every day for an unlimited time, with as little fuss possible. There is considerable evidence supporting the efficacy of *in vivo* behavioural treatments in the training of children to take pills.

**Methods:** 24 4- to 14-year-old children with HIV infection who were naive to pill-swallowing or who had difficulty with pill-swallowing were seen. The modelling was done by a psychologist and used a shaping technique to teach the swallowing of progressively larger placebo capsules.

**Results:** 17 children learned to swallow large capsules and were able to comply with their combination antiretroviral regimen for at least 6 months. All 17 of these children learned with one 20–30 minute training session. Of those children who were unable to complete the task, most continued to manage a liquid/crushed tablet regimen.

**Conclusions:** Details and difficulties of the technique will be discussed.

## P56

## Follow-up of children exposed to antiretroviral therapy in pregnancy (CHART): a role for HIV physicians?

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**Introduction:** In the UK, most uninfected children born to diagnosed HIV-infected women have been exposed to antiretroviral therapy (ART) *in utero*, and there is concern about possible long-term side effects.

**Methods:** A protocol based on routine surveillance through the National Study of HIV in Pregnancy and Childhood (NSHPC) has been established to maintain contact with uninfected children (CHART). Parental consent for inclusion in CHART is requested via the notifying paediatrician. Annual follow-up information is collected by short standard questionnaire.

**Results:** By December 2003, paediatricians had been approached to enrol 889 children. Of these children, 29% were enrolled, 11% lost to follow up, 1% known to have left the UK and 5% of parents had declined. The remainder were still in process. Among the enrolled children, 64% were exposed to combination therapies *in utero*, 30% to monotherapy and 5% were born to women who had no antenatal antiretroviral therapy. Increasingly, paediatricians are referring us to an HIV physician for information.

**Conclusions:** Developing a practical, acceptable method of follow-up is necessary in light of the variety of antiretroviral therapy regimens, increasing numbers of antiretroviral-exposed children and implications for workloads. Involvement of HIV physicians may increase as enrolled children are discharged from paediatric care.

## P57

## Patterns of attendance post-delivery for antenatally diagnosed HIV positive women

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**Background:** All obstetric departments in the UK should be offering screening for HIV infection to >90% of antenatal attenders, in order to reduce the rate of mother-to-child transmission (MTCT). Those women diagnosed positive at this time have an enormous care input prior to delivery, but often are unprepared for routine care afterwards. We have looked at follow-up patterns and factors that may determine outcomes in this group.

**Methods:** A retrospective case-note review was performed for all women antenatally diagnosed HIV-positive giving live birth from January 1999 to December 2003 at the Whittington Hospital.

**Results:** 39 women were identified, with a mean age of 26.2 years (range 18–41). 70.5% were from Africa, 52.9% had a partner in the UK and 29.4% were single. Of those with partners, 42% were unaware of the HIV diagnosis. 76.4% had CD4 counts over 350 cells/ $\mu$ l, and 33% had viral loads greater than 10,000 HIV-1 RNA copies/ml. 47% returned for their routine appointment post-delivery. Non-return was associated with late diagnosis, non-disclosure to a partner, a high CD4 count and being a prisoner. Reasons for eventual return included feeling ready and being symptomatic. Only 35% returned within 3 months for their next follow-up.

**Conclusions:** Regular attendance after delivery for these women is poor for many reasons. Having integrated clinics and identifying those most likely to be lost may improve their health outcome.

## P58

## Identification of discordant women in a dedicated HIV-positive women's clinic: a descriptive analysis

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**Aims:** Developing strategies to minimise HIV transmission in HIV-discordant couples requires the identification of this high-risk group, so that interventions such as condom use, postexposure prophylaxis (PEP) awareness and sexually transmitted infection (STI) diagnosis and treatment can be applied with the aim of preventing HIV transmission to negative partners.

**Methods:** A retrospective notes review of women's clinic attendances between December 2002 and November 2003 was performed.

**Results:** 62 case-notes were reviewed. The average age of sexually active women was 32 years and 87% ( $n=33$ ) were black African in origin; 39% ( $n=15$ ) had HIV-infected male partners, while 61% ( $n=23$ ) of women viewed their partners' status as negative or untested.

|             | Sero-discordant<br>( $n=23$ ) | Sero-concordant<br>( $n=15$ ) | Not sexually<br>active<br>( $n=24$ ) | Total<br>( $n=62$ ) |
|-------------|-------------------------------|-------------------------------|--------------------------------------|---------------------|
| Condoms     | 11                            | 3                             | 5                                    | 19                  |
| No. on ART  | 17                            | 7                             | 13                                   | 12                  |
| Average CD4 | 374                           | 272                           | 296                                  | 314                 |
| STIs        | 8                             | 5                             | 2                                    | 15                  |
| PEP aware   | 14                            | 3                             | 11                                   | 28                  |

ART, antiretroviral therapy.

**Discussion:** In this cohort, serodiscordant women had a greater awareness of PEP, reported greater use of condoms and were more likely to be taking highly active antiretroviral therapy than seroconcordant women. However, both groups had similar proportions of acute STIs (35% and 33%). Targeted women's services that promote safer sex, PEP awareness and STI screening may reduce HIV transmission to negative partners, by encouraging health-seeking behaviour for the rapid treatment of STIs.

## P59

## Adapting to changing needs: 10 years of a family clinic

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**Background:** Started in 1994, this multidisciplinary team (MDT) provides a holistic family approach with adult and paediatric services in one clinic. Developmental and psychosocial care are integrated into medical monitoring and treatments

**Results:** Since 1994, 700 families have attended, 85% of whom originated from other countries. Social and family stressors remain high. Fathers are difficult to engage but this is improving. Attendance is good, with a high level of satisfaction expressed. At present, over 160 HIV-positive children, most perinatally infected, attend the clinic.

- 75% are on antiretroviral therapy, but adherence is variable.
- 10% have severe neurological/developmental difficulties.
- 40% need learning support in school.
- Few have serious emotional/behavioural difficulties.
- Two-thirds of the older children have had an open discussion of the diagnosis.
- A new young persons' service has been established (25% are over 11 years of age).

**Conclusions:** The multidisciplinary family approach has been an effective way of delivering medical, social and psychological care. It is now adapting its approach in response to the changing needs of families and older children.

## P60

### Setting standards: analysis of the effectiveness of the care pathway for HIV-infected pregnant women

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**Introduction:** We have previously discussed and presented a care pathway for optimising the management of HIV-infected pregnant women in Leicestershire. Following its implementation in December 2000, an analysis of the outcome has been carried out against BHIVA guidelines.

**Methods:** Data were collected from all women whose pregnancy ended in live births from December 2000 until September 2003.

**Results:** Data were available from 29/26 (81%) women identified. 23/29 (87%) were detected by antenatal screening. 11/29 were diagnosed in the second trimester. The pathway requires discussion and provision of care at antenatal, intra-partum and post-partum stages. The documentation showed discussion of vertical transmission in 25/29 (86%), maternal and neonatal highly active antiretroviral therapy (HAART) in 13/29 (45%), mode of delivery in 28/29 (97%) and avoidance of breast-feeding in 25/29 (86%). 28/29 (97%) had a sexual health screen. All had CD4 counts and viral load monitoring and received HAART. Further details will be presented.

**Conclusions:** All females received care in line with BHIVA guidelines. The care pathway enabled us to achieve the above-mentioned standards, and allowed us to audit the outcome. Inconsistencies in documentation were noted, and recommendations will be discussed.

## P60a

### Dedicated services for HIV positive adolescents: why bother?

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**Aims:** To describe 2 years' experience of a dedicated adolescent HIV out-patient service based at a Central London teaching hospital.

**Methods:** A prospective data collection was made, using a standardised database, between October 2001 and 2003.

**Results:** 15 adolescents were seen (six female, nine male). Most (87%) were black African and had been vertically infected outside the UK. The median age at diagnosis was 11 years (range 4–16), and at the time of transition, 16 years (range 15–19). 53% (8/15) had had an AIDS-defining illness and 87% (13/15) were taking antiretroviral therapy according to BHIVA guidelines. The median CD4 count was 380 cells/ $\mu$ l (range 10–510). The median duration on antiretroviral therapy was 43 months (range 2–128). During follow-up, 54% (7/13) had episodes of intermittent non-adherence and 50% (7/14) of adolescents ever having taken antiretroviral therapy had resistance to one or two classes of drugs. Despite this, 62% (8/13) currently have a viral load of <50 HIV-1 RNA copies/ml and all remain under active follow-up. Three of the 15 adolescents live independently and four report being sexually active.

**Conclusions:** Increasing numbers of HIV-infected, multidrug class-experienced children will be surviving into adolescence and becoming sexually active. There is an urgent need to further develop dedicated adolescent services to minimise loss to follow-up, encourage adherence to antiretroviral therapy and prevent the transmission of drug-resistant virus in this vulnerable group.

## P61

### Sexual health in HIV-positive patients attending an infectious diseases unit

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**Aim:** To assess the sexual health of HIV-positive patients by an anonymous survey.

**Methods:** For 1 month, a sexual-health questionnaire was given to all HIV-positive patients attending the clinic. The questionnaire asked about numbers of partners, condom use, previous sexually transmitted infections (STIs) and current symptoms of possible STIs. It asked for patients' preferences for the setting in which sexual screening would take place (e.g. RIDU, local genitourinary (GU) medicine clinic or general practice), what service they wanted (full screen, *Chlamydia* only, no extra service) and the frequency of screening.

**Results (provisional):** This study is ongoing. With 27% of questionnaires returned, 61% of participants are male, 48% heterosexual, 9% bisexual and 43% are men who have sex with men. 56% of patients practice safe sex (always using condoms for penetrative anal, vaginal and oral sex), and 61% of patients want STI screening to be at RIDU, i.e. in the same place as HIV care. 83% want a complete GU screen: when symptomatic, 39%; yearly, 43%; at every visit 9%; and 9% had no preference.

**Conclusions:** In this survey, most patients want sexual-health screening to take place in the same setting as HIV care. This is not being met by our current service. The survey highlights ongoing transmission risks of both STIs and HIV, with 44% of patients not always using condoms for penetrative sex.

## P62

### A retrospective audit of the management of hepatitis C (HCV) and HIV co-infection: How close is current practice to the BHIVA guidelines and audit standards?

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**Aim:** To assess current management of HIV/HCV co-infection.

**Methods:** Patients with anti-HCV antibody, a positive HCV polymerase chain reaction (PCR) or abnormal alanine aminotransferase levels (anti-HCV negative) were identified from our database. Patients' notes were reviewed. The current cohort includes 428 patients.

**Results:** 173 patients were anti-HCV positive. Of these, 97% had HCV PCR measured. 130 (75%) were HCV PCR-positive; 62% had HCV genotype results available, 52 (40%) had had a liver biopsy (19% showed cirrhosis) and 17 (13%) had received anti-HCV treatment.

|  |                    |       |
|--|--------------------|-------|
| Screen all HIV+ patients for HCV   |                    | 99.8% |
| All HCV+ patients not immune to HBV should be vaccinated (PCR+)            | Vaccinated         | 8%    |
|  | Previous infection | 75%   |
| All HCV+ patients not immune to HAV should be vaccinated (PCR+)            | Vaccinated         | 11%   |
|  | Serology awaited   | 10%   |
|  | Immune             | 11%   |
| Alcohol avoidance documented   |                    | 66%   |
| HCV PCR on all patients with unexplained liver disease (anti-HCV negative) |                    | 30%   |
| Risks of transmission documented   |                    | 21%*  |
| Clear treatment plan   |                    | *     |
| Attempts to notify sexual/parental contacts documented                     |                    | *     |

\*All HIV+ patients are counselled with reference to transmission of HIV/blood-borne viruses and attempts made to notify contacts.

**Conclusions:** Improvements are needed in hepatitis A (HAV) vaccine coverage. At present we have no formal documentation of this ongoing process. The documented episodes are for patients with ongoing risks.

## P63

### A regional audit of the antenatal and perinatal management of HIV-infected women, and the postnatal management of their children in the north-west of England, 2002-2003

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**Background:** The requirement for antenatal, perinatal and postnatal HIV services in the north-west has increased dramatically in recent years. Although national guidelines exist for the HIV management of pregnant women and their infants, these are not universally accepted as optimal practice, implementation is not compulsory and there is disparity in their interpretation. Recently, there has also been concern over the use of nevirapine to prevent mother-to-child-transmission.

**Methods:** Using retrospective case-note reviews and a centre survey, we performed an audit focused on the appropriateness and effectiveness of local practice between 2002 and 2003, and its consistency across six acute NHS trusts in relation to BHIVA guidelines. **Results:** Interpretation of guidance varied across the trusts involved, and within trusts, compliance with existing policy was not absolute. The majority of women were started on or switched to nevirapine-based highly active antiretroviral therapy at or after 13 weeks, irrespective of the viral load. Several instances of incorrect management were identified, which related to delays in arrival of case-notes, inadequate drug stocks on delivery wards, miscalculation of doses or poor communication between disciplines. However, the majority of women were being identified early on in pregnancy, were able to access appropriate antiretroviral regimens and were managed according to local or national guidelines.

**Conclusions:** This audit has underlined the importance of a multidisciplinary approach to maternal and neonatal care, the need for well-circulated and agreed guidelines, and regular staff training to convey best practice.

## P64

### Adherence services in practice

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**Background:** In March 2001, a *Protocol for Clients Starting HAART* was written and implemented by the local Adherence Multidisciplinary Team (AMDT). This protocol stipulated that there should be formal referral for adherence counselling before starting highly active antiretroviral therapy (HAART) to assess readiness, individualise the treatment plan and provide patient education. Draft *BHIVA Guidelines on the Provision of Adherence Support* were published in 2002.

**Aim:** To audit the uptake and implementation of our local protocol.

**Methods:** Retrospective case-note review of all patients on HAART for:

- documentation of adherence assessment by a doctor in the previous 3 months;
- consultation with a member of the AMDT; and
- referral to AMDT before commencing HAART.

**Results:** 63% of patients on HAART had documentation by a doctor of an assessment of adherence in the previous 3 months. One-quarter of these were quantitative provider estimates. 77% were seen by the dietitian to discuss aspects of their treatment adherence. 85% were referred to the AMDT before commencing HAART. A telephone follow-up by the adherence nurse was not implemented, as the funding for the post was withdrawn.

**Conclusions:** Implementation of a local HAART adherence protocol is achievable. We met the BHIVA guidelines for patients commencing HAART. However, we were unable to provide ongoing assessment and support to maintain adherence, due to inadequate staff resources.

## P65

### An audit of baseline history, examination and investigations of patients infected with HIV: a comparison of practices between departments of genitourinary medicine (GUM) and infectious diseases (ID)

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**Background:** We conducted an audit to compare the recording of baseline history, examination and investigations performed at diagnosis of HIV in two adjacent units.

**Methods:** A retrospective case-note review was performed.

**Results:** 166/318 (52%) of notes were reviewed randomly (97 GUM and 69 ID). At least 80% of patients had smoking and sexual histories recorded. 72% of GUM patients were asked about recreational drug use (46% ID). Both departments were poor at recording a past history of tuberculosis, vaccinations and risk factors for heart disease, and < 20% of patients had their teeth examined. 59% of GUM versus 19% of ID patients had a screen for sexually transmitted infections. 95% of patients had baseline CD4 counts, viral loads, full blood counts, renal and liver function tests recorded. Both teams were poor at performing baseline lipids and glucose. ID was more likely to perform fundoscopy, chest X-ray, toxoplasma and cytomegalovirus screening, whereas GUM was more likely to perform herpes simplex virus and varicella zoster virus screens. More patients were screened for hepatitis B and C than hepatitis A in both departments.

**Conclusions:** A universal patient proforma would aid equality of documentation and care for newly diagnosed HIV patients in the two units, as well as providing an audit tool in the face of new BHIVA guidelines.

## P66

### An audit of out-patient management and screening investigations of patients infected with HIV: a comparison of practices between departments of genitourinary medicine (GUM) and infectious diseases (ID)

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**Background:** Out-patient management of HIV-infected patients allows for screening of infections and malignancies as well as monitoring disease progression and adherence to treatment.

**Methods:** A retrospective case-note review was performed of HIV-infected patients in adjacent units of GUM and ID; all visits were in 2001-2002.

**Results:** 166/318 (52%) notes were randomly reviewed, 97 GUM and 69 ID. GUM patients were reviewed more frequently than ID (mean interval 1.7 months (SD 1.96) versus 2.4 months (SD 1.49)), but the mean interval between CD4 counts and viral loads was similar (GUM 3.2 months versus ID 3.8 months,  $P>0.5$ ). 60% of GUM patients and 52% of ID patients had repeat syphilis and hepatitis serology documented in the last 2 years. 36% of ID women had a yearly cervical smear recorded, compared to 66% of GUM women. In their last 3 out-patient visits, 2% of ID patients and 16% of GUM patients were asked a repeat sexual history. Adherence to antiretroviral therapy was documented in 44% of ID and 32% of GUM patients.

**Conclusions:** Both departments are poor at documenting repeat screening investigations, assessment of risk for sexually transmitted infections and treatment adherence. A 'reminder' proforma will be introduced and outcomes audited again against the new guidelines produced by BHIVA.

## P67

## HIV-related pulmonary hypertension: a case report and literature review

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**Background:** Isolated pulmonary hypertension is a rare manifestation of HIV infection, with a reported frequency of 0.5% among HIV-infected patients. The prognosis is unfavourable (mean survival of 6 months). The effect of highly active antiretroviral therapy (HAART) is unknown.

**Aim:** To report a case of HIV-related pulmonary hypertension.

**Case presentation:** A 36-year-old male, a heavy smoker, was diagnosed HIV-positive 5 years ago (Centers for Disease Control and Prevention stage C3), with poor compliance to treatment. In the out-patient clinic, he was asymptomatic, with normal vital signs, except for an O<sub>2</sub> saturation of 85%. A physical examination, laboratory tests and electrocardiograph were unremarkable. His CD4 count was 24 cells/μl and he had 1,500,000 HIV-1 RNA copies/ml. A high-resolution chest computed tomography scan showed emphysematic lungs and spirometry revealed final bronchiolar disease without obstructive pulmonary disease. The transthoracic echocardiogram showed severe pulmonary hypertension (systolic pulmonary arterial pressure ~63 mmHg). He refused pulmonary catheterisation. Other causes of secondary pulmonary hypertension were excluded (intravenous drug abuse, interstitial pulmonary disease, chronic obstructive pulmonary disease or infection). He was treated with diltiazem and a HAART regimen, but once discharged from the unit, he did not adhere to treatment. He died 9 months later, hospitalised with worsening dyspnoea.

**Conclusions:** HIV-associated pulmonary hypertension should be included in the differential diagnosis in patients with pulmonary hypertension and respiratory failure, despite the absence of typical symptoms.

## P68

## Elevated intracranial pressure and immune reconstitution inflammatory syndrome complicating cryptococcal meningitis

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**Introduction:** Elevated intracranial pressure (ICP) and the immune reconstitution inflammatory syndrome (IRIS) are recognised complications in the management of cryptococcal meningitis. We report a case highlighting this.

**Case presentation:** A 34-year-old black Caribbean woman presented with advanced HIV disease (CD4 count 9 cells/μl, viral load 515,000 HIV-1 RNA copies/ml) and a cerebrospinal fluid (CSF) culture confirmed the presence of *Cryptococcus neoformans*. She had CSF protein of 290 mg/l, glucose of 3.1 mmol/l, cryptococcal antigen (Cr Ag) titre of 1:640. Her initial CSF opening pressure (OP) was normal (9.5 cm). There was good clinical response to a 2-week course of amphotericin B and flucytosine, and initiation of highly active antiretroviral therapy (zidovudine, lamivudine and nevirapine). One month later she developed papilloedema (CSF OP 39.5 cm, CSF Cr Ag 1:20 but a culture was negative). The CSF OP remained above 35 cm despite serial lumbar punctures. She was re-treated with a 4-week course of amphotericin B and flucytosine. A lumbar drain was inserted, followed by a lumboperitoneal shunt. This was ligated after a week because of overdrainage. She continued on fluconazole (800 mg daily), but 2 months later she re-presented with headaches and a raised CSF OP, above 40 cm, but a negative CSF culture [CD4 59 cells/μl (12%) and viral load <50 copies/ml]. A lumbar drain was reinserted. One day later she had a respiratory arrest and died. A postmortem showed evidence of rupture of a cryptococcoma.

**Conclusions:** This case highlights the complex interpretation and management of a possible IRIS, causing sustained high ICP in cryptococcal disease.

## P69

## The bottom line: a case of tuberculosis (TB) in the buttock of a patient co-infected with HIV

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**Case presentation:** We describe the case of a 27-year-old Somali-born UK resident presenting with right-sided chest pain and left hip discomfort. He had been diagnosed with HIV 2 years earlier, following a fully treated episode of nodal TB and had been prescribed Combivir/nevirapine since; his CD4 count was 116 cells/μl (16%) and viral load <50 HIV-1 RNA copies/ml. X-rays of the hip were unremarkable, but a chest X-ray showed a right apical shadow. A chest computed tomography scan revealed a destructive lesion of the rib, confirmed by increased uptake on a bone scan. He experienced swinging fevers. A biopsy of the rib showed acid-fast bacilli. He was commenced on antituberculous therapy and 14 days later developed a large grapefruit-sized abscess of the left buttock. Subsequently, a large fluctuant right-sided posterior auricular node emerged. This paradoxical worsening of presumed *Mycobacterium tuberculosis* (MTB) was managed with corticosteroids, and then percutaneous aspirations. A culture confirmed fully sensitive MTB. He developed sinuses at the aspiration sites. Magnetic resonance imaging of the pelvis showed extensive sacro-iliac joint destruction and a large collection.

**Discussion:** We will display photographs, radiographs and discuss the optimal investigation and management (steroids, aspiration, surgical drainage) of paradoxical reactions. We will also debate the value of secondary prophylaxis for MTB, which may have prevented such a case.

## P70

## Case report: bilateral psoas abscesses in an HIV-positive patient

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**Case report:** Patients with HIV can often present a diagnostic challenge and may have atypical presentations of more common diseases. This case demonstrates such a scenario: we describe a 35-year-old man with a recent diagnosis of HIV infection complaining of backache, anorexia and weight loss. On investigation he was found to have bilateral tuberculous abscesses. These were treated by computed tomography-guided percutaneous drainage and antituberculous therapy with a good result.

**Discussion:** A review of the literature shows that this is a rare presentation of an already unusual problem (<3% of psoas abscesses are bilateral), with subtle signs requiring a high index of clinical suspicion. Historically, tuberculous psoas abscesses were seen following a spread of *Mycobacterium tuberculosis* from spinal tuberculosis, Pott's disease, but this has become extremely rare in developed countries. Currently in Europe, a psoas abscess is most commonly seen secondary to a spread of infection from a gastrointestinal source such as inflammatory bowel disease, whereas in the developing world, it is most commonly a primary infection due to *Staphylococcus aureus*.

**Conclusion:** As the prevalence of tuberculosis among HIV-positive patients is high, and extrapulmonary presentations are more common, there is a need for increased awareness of this diagnosis.

## P71

## Complicated varicella zoster virus (VZV) infection in an AIDS patient

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## P72

## Herpes simplex virus (HSV) infection of the central nervous system (CNS) in HIV

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## P73

## Increased prevalence of reverse transcriptase (RT) mutation Q207D/E in lamivudine (3TC)-experienced versus treatment-naïve patients suggests a role in nucleoside reverse transcriptase inhibitor (NRTI) resistance

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## P74

## Therapeutic drug monitoring (TDM) in patients taking fosamprenavir and Kaletra as dual protease inhibitor (PI)-based antiretroviral therapy

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St Mary's Hospital, London, UK**Background:** The choice of treatment for antiretroviral-experienced patients failing their current regimen is problematic. For such patients, innovative strategies such as double-boosted PI-containing regimens have been used.**Methods:** On the basis of information from genotypic analysis and drug history, seven patients were commenced on a regimen including both fosamprenavir (700 mg twice a day), Kaletra (four capsules twice a day for five patients, three capsules twice a day for two patients) plus one or two nucleoside reverse transcriptase inhibitors and tenofovir. TDM occurred at least 2 weeks after commencing the regimens. Trough concentrations were measured by validated assays 12 hours after the dose for amprenavir and lopinavir.**Results:** The patients had used a mean of six previous combinations, and a mean of two PIs; they had a mean of two primary mutations in HIV protease at baseline. In one patient, therapeutic amprenavir levels were achieved after increasing the fosamprenavir dose to 1050 mg twice a day. All seven patients achieved a viral load of <400 HIV-1 RNA copies/ml by 6 months, with six reaching <50 copies/ml.

|            | Mean<br>$C_{\min}$ (12 h)<br>(ng/ml) | Range<br>(ng/ml) | SEM    | Consensus<br>therapeutic<br>level |
|------------|--------------------------------------|------------------|--------|-----------------------------------|
| Amprenavir | 2085                                 | 508–5492         | 747.8  | 400                               |
| Lopinavir  | 4707                                 | 1255–10218       | 1263.0 | 1000                              |

**Discussion:** We conclude that in this heavily treatment-experienced sample, Kaletra/fosamprenavir in combination is effective providing TDM is used to ensure a 12-hour trough concentration [ $C_{\min}$  (12 h)] within the therapeutic range.

## P75

## Is there evidence for weight-adjusted dosing of Kaletra?

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**Background:** Kaletra is a coformulation of lopinavir (LPV) and ritonavir (RTV). In a Kaletra monotherapy study (Gathe *et al.*, 43rd ICAAC, 2003, Abstr. H845), subjects were commenced on weight-based regimens of 400/100 mg ( $\leq 70$  kg) or 533/133 mg ( $> 70$  kg) twice daily. The relationship between LPV concentrations and body weight was investigated in samples received by the Liverpool Therapeutic Drug Monitoring Service.

**Methods:** A retrospective analysis was performed on trough samples (10–14 hour post dose) from adults receiving LPV at 400 mg twice a day. Plasma concentrations of  $< 50$  ng/ml were excluded due to possible non-adherence.

**Results:** Trough LPV concentrations were significantly reduced in low body-weight males; however, no difference was observed in females, possibly due to small numbers (see table).

|        | Weight (kg) | n   | Median (range) LPV (ng/ml)      |
|--------|-------------|-----|---------------------------------|
| Male   | $\leq 70$   | 122 | 5,614 (56–35,791)*              |
|        | $> 70$      | 123 | 4,434 (178–14,917)              |
| Female | $\leq 70$   | 33  | 6,429 (206–13,286) <sup>†</sup> |
|        | $> 70$      | 16  | 8,274 (1,044–13,153)            |

\* $P < 0.007$ . <sup>†</sup> $P = 0.390$ .

The proportion of concentrations below the therapeutic range (1,000–10,000 ng/ml) was not significantly different between the two weight groups in males. A greater proportion of low body-weight males (compared to  $> 70$  kg) had concentrations  $> 10,000$  ng/ml (17.2% versus 4.8%,  $P = 0.002$ ).

**Conclusions:** LPV exposure appears to be affected by body weight. The clinical relevance of these findings should be explored further.

## P76

## Saquinavir hard gel (SQV-hg)/ritonavir (RTV) pharmacokinetics (PKs): effect of high-fat meals, plasma concentration diurnal variation and inpatient variability

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**Background:** The amount of fat required in a meal to absorb SQV-hg or inpatient variability in PK may be useful to better manage HIV-positive patients and interpret therapeutic drug monitoring results.

**Methods:** The effect of 40 g versus 20 g of fat in meals on SQV-hg/RTV exposure was investigated in 10 and eight patients on SQV-hg/RTV (either 1000/100 mg twice a day or 1600/100 once a day). Day versus night PKs were measured in 18 patients. Inpatient variability in SQV-hg/RTV PKs (three determinations) was calculated over 14 days ( $n = 16$ ) and expressed as a coefficient of variation (CV). Geometric mean ratios (GMR) and 95% confidence intervals (CIs) were used to compare SQV/RTV PKs on different days. SQV/RTV concentrations were measured by high-performance liquid chromatography–mass spectrometry (MS)/MS.

**Results:** No difference was observed in SQV and RTV areas under the curve (AUCs) after SQV-hg/RTV plus 40 or 20 g fat in meals (GMR, 95% CIs: SQV 0.63, 0.37–1.19; 1.18, 0.71–1.89; RTV: 0.89, 0.64–1.42; 1.26, 0.69–2.15, respectively). A statistically significant higher trough plasma concentration ( $C_{trough}$ ) was measured 12 hours after the evening dose for both SQV (2.25, 1.39–4.50) and RTV (1.66, 1.40–2.38). Median (range) values for SQV/RTV day  $C_{trough}$ , maximum plasma concentration ( $C_{max}$ ) and  $AUC_{0-12h}$  CV were: 40% (3–94), 33% (9–57), 23% (10–53) and 30% (7–57), 22% (10–41), 22% (9–42), respectively. **Conclusions:** SQV-hg/RTV absorption is not dependent on the amount of fat contained in a meal. Significant diurnal variations and wide inpatient variability have been observed in SQV and RTV  $C_{trough}$ .

## P77

## Repeated pharmacokinetics (PKs) of tenofovir disoproxil fumarate (TDF) in HIV-infected adults receiving saquinavir hard gel (SQV)/ritonavir (RTV) at 1000/100 mg twice a day

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**Background:** Tenofovir plasma PKs following oral administration have been well characterised. The aim of this analysis was to measure tenofovir plasma PKs 2 days after TDF initiation and at steady-state (day 13) in HIV-positive adults receiving SQV/RTV twice a day.

**Methods:** On PK days, blood was drawn pre-dose and 0.5, 1, 2, 3, 4, 6, 8, 12 and 24 hours after the dose from 18 subjects (mean age 44 years). Tenofovir was determined by high-performance liquid chromatography. Data were analysed by non-compartmental PK methods. Geometric mean ratios (GMRs) and 95% confidence intervals (CIs) were measured to calculate differences between the two PK days.

**Results:** At screening, the mean  $\pm$  SD CD4 count was  $497 \pm 244$  cells/ $\mu$ l and the plasma viral load  $< 200$  HIV-1 RNA copies/ml. TDF was well tolerated and no significant changes in laboratory parameters were observed. On day 2 of TDF intake, the GM area under the curve, maximum and minimum plasma drug concentrations, half life and time to maximum concentration ( $AUC_{0-24h}$ ,  $C_{max}$ ,  $C_{trough}$ ,  $t_{1/2}$ ,  $T_{max}$ ) were 2733 ng/hour per ml, 268 ng/ml, 56 ng/ml, 16 hours and 2.0 hours, respectively. On day 13, the corresponding values were: 3005 ng/hour per ml, 287 ng/ml, 64 ng/ml, 14 hours and 1.7 hours. On day 13, slight increases in  $AUC_{0-24h}$ ,  $C_{max}$  and  $C_{trough}$  (10%, 7%, 15%) and a slight decrease in  $t_{1/2}$  and  $T_{max}$  (11%, 16%) were observed, compared to day 2. **Conclusions:** Tenofovir  $t_{1/2}$  and overall exposure were comparable with previously published data. SQV/RTV does not appear to have any impact on tenofovir PKs.

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# HIV Resistance and Clinical Pharmacology Workshops 2004



*Faculty:*

Professor Clive Loveday, FRCPath, PhD  
*Clinical Director, International Clinical Virology Centre (ICVC)*  
 Dr Stephen Taylor, MRCP, PhD  
*Consultant Physician, Birmingham Heartlands Hospital*

|                  |                |            |
|------------------|----------------|------------|
| <b>Course 2:</b> | 17-18 June     | Manchester |
| <b>Course 3:</b> | 25-26 November | London     |

These are interactive workshops for those involved in the management and care of HIV+ve patients. The objectives of the workshops are to de-mystify resistance and pharmacological assessment.

The workshops include a refresher on the basic principles of resistance testing and HIV pharmacology. They will also include discussions of the latest trials and studies affecting patient care.

There will be 4 sessions of interactive case discussions, including:

- Basic virology and pharmacology
- Resistance testing
- Therapeutic drug monitoring
- Resistance and TDM in clinical practice

During the sessions we will cover:

- Interpretation of resistance and TDM reports
- Theoretical case scenarios
- Real-life patient case discussions
- How resistance testing and TDM can help difficult cases

Places are limited to 25 per workshop and a nominal charge of £90 will be made. This figure covers hotel accommodation, dinner, breakfast, lunch and study materials.

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Surname: .....

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*(The above information will be used on your name badge and an attendance list to be handed out at the event)*

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