

**9<sup>th</sup>**  
**ANNUAL CONFERENCE**  
OF THE  
**BRITISH HIV ASSOCIATION [BHIVA]**

**24–26 April 2003**

**UNIVERSITY OF MANCHESTER,  
INSTITUTE OF SCIENCE & TECHNOLOGY (UMIST)  
MANCHESTER**

*Including*

**MRC Clinical Trials Unit Annual Centres Meeting  
Thursday 24 April 2003**

**UMIST, Manchester**

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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 in to 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 2003 issue. All published citations of abstracts should be made to *HIV Medicine* and not to this conference book.

## Prizes / Scholarships

Bristol-Myers Squibb Travelling Scholarships will be awarded to the five best oral and poster presentations as determined by the Judging Panel. To qualify for a scholarship, applicants must be of Junior Grade or under 35 years of age. Each scholarship is worth £1,000

Abbott Travelling Scholarships will be awarded to three overseas delegates who submitted abstracts for presentation at the conference. These prizes are worth £1,000 each and are intended to enable attendance at international meetings.

BHIVA Science Scholarships will be presented to up to ten scientists studying for a PhD or MD. For those abstracts accepted for presentation (oral or poster), all registration, travel and accommodation will be paid for by BHIVA.

BHIVA Community Scholarships will be presented to up to ten community registrants. Scholarship winners will have registration, travel and accommodation paid for by BHIVA.

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# RESEARCH PRESENTATIONS

FRIDAY 25 APRIL

1145–1245 **Research Presentations: Session 1**  
**Mother-to-child transmission**

Chair: Dr Gareth Tudor-Williams  
*Imperial College and St Mary's Hospital, London*

**1145–1155 Abstract O1**

AIDS-free survival of 218 HIV-infected women following pregnancy  
*H Lyall, St Mary's Hospital, London*

**1155–1205 Abstract O2**

Seminal super shedding of HIV: implication for sexual transmission  
*S Taylor, Birmingham Heartlands Hospital*

**1205–1215 Abstract O3**

Sperm washing in the UK: evidence of safety and efficacy  
*C Gilling-Smith, Chelsea & Westminster Hospital, London*

**1215–1225 Abstract O4**

An estimation of the UK demand for fertility services in HIV-positive couples  
*L Frodsham, Chelsea & Westminster Hospital, London*

**1225–1235 Abstract O5**

Neurological and developmental outcomes in HIV-infected children presenting before 3 years of age  
*R Biggs, St Mary's Hospital, London*

**1235–1245 Abstract O6**

Migration and HIV: impact on service delivery  
*J Dhar, Leicester Royal Infirmary*

1445–1545 **Research Presentations: Session 2**  
**Antiretroviral therapy**

Chair: Dr Ed Wilkins  
*North Manchester General Hospital*

**1445–1455 Abstract O7**

Durability of efavirenz compared to nevirapine with long-term follow-up of an antiretroviral-naïve patient cohort  
*C Orkin, Chelsea & Westminster Hospital, London*

**1455–1505 Abstract O8**

The success of tenofovir (TNF) and didanosine (ddI) when dosed together using low-dose didanosine 250 mg  
*M Tung, Chelsea & Westminster Hospital, London*

**1505–1515 Abstract O9**

Efavirenz: what happens in the long term?  
*L Swaden, Royal Free Hospital, London*

**1515–1525 Abstract O10**

Optimising outcomes to antiretroviral therapy: a comprehensive multidisciplinary approach  
*H Leake Date, Brighton General Hospital*

**1525–1535 Abstract O11**

Dose escalation or immediate full dose when switching from efavirenz- to nevirapine-based HAART?  
*A Winston, Chelsea & Westminster Hospital, London*

**1535–1545 Abstract O12**

Impact of archived NRTI resistance mutations on maintenance of virological control after switching from stavudine to tenofovir with an undetectable viral load  
*C McDonald, King's College Hospital, London*

1605–1705 **Research Presentations: Session 3**  
**Opportunistic infections**

Chair: Dr Martin Fisher  
*Brighton General Hospital*

**1605–1615 Abstract O13**

CDE chemotherapy plus HAART for AIDS-related non-Hodgkin's lymphoma  
*C Thirwell, Chelsea & Westminster Hospital, London*

**1615–1625 Abstract O14**

Pegylated interferon (PIFN) and ribavirin (RBV) in the treatment of acute hepatitis C in individuals co-infected with HIV  
*C Orkin, Chelsea & Westminster Hospital, London*

**1625–1635 Abstract O15**

Co-infection with HIV-1 and hepatitis C does not ablate the allostimulatory function of dendritic cells  
*S Portsmouth, Chelsea & Westminster Hospital, London*

**1635–1645 Abstract O16**

Increasing incidence of acute hepatitis C in HIV-positive men secondary to sexual transmission: a new epidemic?  
*R Browne, Chelsea & Westminster Hospital, London*

**1645–1655 Abstract O17**

Outcome of acute hepatitis C in HIV-positive homosexual men  
*RM Lascar, Mortimer Market Centre, London*

**1655–1705 Abstract O18**

Survival in HIV-infected individuals following liver transplantation is influenced by viral co-infection: the negative impact of HCV infection  
*C McDonald, King's College Hospital, London*

# RESEARCH PRESENTATIONS

## SATURDAY 26 APRIL

### 1020–1120 **Research Presentations: Session 4** **Science and side effects**

Chair: Dr Barry Peters  
*St Thomas's Hospital, London*

#### **1020–1030 Abstract O19**

Growth hormone and effective antiretroviral therapy augment immune function of HIV-1 infected individuals

*A Pires, Imperial College, London*

#### **1030–1040 Abstract O20**

The heat shock protein receptor CD91 is up-regulated in monocytes of HIV-1-infected 'true' long-term non-progressors

*J Stebbing, Chelsea & Westminster Hospital, London*

#### **1040–1050 Abstract O21**

The impact of antiretroviral therapy and/or immunotherapy on the levels of circulating B-chemokines and IL-16 in HIV-1 infected individuals

*C Burton, Imperial College, London*

#### **1050–1100 Abstract O22**

Atorvastatin and pravastatin for hypercholesterolaemia in HIV-positive patients receiving HAART

*NP Smith, Chelsea & Westminster Hospital, London*

#### **1100–1110 Abstract O23**

Exocrine pancreatic insufficiency in HIV-positive patients

*DA Price, Newcastle General Hospital*

#### **1110–1120 Abstract O24**

Changing mortality patterns in the HAART era

*J Ashby, Chelsea & Westminster Hospital, London*

### 1430–1530 **Oral research presentations: Session 5** **Ethnicity and service delivery**

Chair: Dr Jane Anderson  
*St Bartholomew's Hospital, London*

#### **1430–1440 Abstract O25**

Is it time to rethink the roles of the health professionals in the HIV outpatient setting?

*K Miles, Mortimer Market Centre, London*

#### **1440–1450 Abstract O26**

Missed opportunities to diagnose HIV infection

*L Adejolu, Ealing Hospital, London*

#### **1450–1500 Abstract O27**

National Strategy does not ensure PCT-level priority or national equity for HIV services

*L Power, Terrence Higgins Trust*

#### **1500–1510 Abstract O28**

CD4 cell counts in HIV-infected adults at HIV diagnosis in England and Wales, 1990 to 2001

*T Chadborn, CDSC PHLS, London*

#### **1510–1520 Abstract O29**

South Asians with HIV infection in London: a growing epidemic?

*G Sethi, St Mary's Hospital, London*

#### **1520–1530 Abstract O30**

HIV and black Caribbeans in the UK

*S Dougan, CDSC, London*

## 01

**AIDS-free survival of 218 HIV-infected women following pregnancy**

GP Taylor<sup>1</sup>, L Sarner<sup>2</sup>, W Khan<sup>3</sup>, L Navaratne<sup>4</sup>, D Mercey<sup>5</sup>, EGH Lyall<sup>6</sup>, A Fakoya<sup>2</sup>, D Hawkins<sup>3</sup> and A de Ruiter<sup>4</sup>  
*Imperial College<sup>1</sup>, Newham Healthcare NHS Trust<sup>2</sup>, Chelsea and Westminster Hospital<sup>3</sup>, St Thomas's Hospital<sup>4</sup>, Mortimer Market Centre<sup>5</sup> and St Mary's Hospital<sup>6</sup>, London, UK*

**Background:** The number of HIV-infected women becoming pregnant in the UK has increased dramatically over the last few years. Few studies have addressed the long-term outcome of these women. We have therefore initiated a multicentre, prospective cohort study of pregnant women in London.

**Methods:** Chart review of all women diagnosed HIV positive ante partum in five London centres between 01/1998 and 12/2001 with follow up recorded prospectively.

**Results:** 218 women delivered, 24 in 1998, 48 in 1999, 67 in 2000 and 79 in 2001. 180 were black African, 25 were European of which 4 were or had been injecting drug users. Mean age at delivery was 30.2 years. First antenatal clinic visit: CDC status A 164, B 24, C 16; mean CD4 count 345 cells/ $\mu$ l, median viral load (VL) 4780 copies/ml. 42 mothers were already on triple therapy (group I) CD4 204, VL <50. 58 mothers took zidovudine monotherapy (group II), CD4 435, VL 2238. 103 commenced triple therapy (group III), CD4 288, VL 14820. The mean follow-up (FU) is 20.5 months. During 347 person-years of follow-up, three women have had an AIDS-defining infection, one from each group. All were African, had CD4 counts >200 and two had tuberculosis. Only one group II mother has started triple therapy (ART) post-partum but only 74 women remained on ART at last FU; 43 women discontinued triple therapy within 1 month of delivery. Mean CD 4 count of the cohort at last FU was 437 cells/ $\mu$ l. Group III  $n = 469$ , group II 535, group III 449.

**Conclusions:** These data demonstrate good maternal health for up to 4 years following the management of HIV infection in pregnancy.

## 02

**Seminal super-shedding of HIV: implications for sexual transmission**

S Taylor<sup>1,3</sup>, T Sadiq<sup>2</sup>, D White<sup>1</sup>, C Sabin<sup>2</sup>, P Cane<sup>1,3</sup>, S Drake<sup>1</sup> and D Pillay<sup>2</sup>

<sup>1</sup>Birmingham Heartlands Hospital, Birmingham, <sup>2</sup>Royal Free and University College Medical School, University College London, and <sup>3</sup>University of Birmingham, UK

**Background:** We identified patients who shed HIV into their seminal plasma (SP) at levels in excess of their blood plasma (BP). We termed them 'seminal super-shedders' (SSS) of HIV-1 and postulate that they may represent a group at increased risk of transmitting HIV-1.

**Methods:** 72 HIV +ve men not on therapy were enrolled. They produced matched BP and SP samples at the same time as undergoing tests for urethritis. Viral load was determined by NASBA. Variables considered were: age, CDC status, CD4 count, BP viral load (VL) >100,000 copies/ml and the presence of urethritis. SSS was defined as SPVL/BPVL ratio >1. **Results:** No men had BPVL <400 copies/ml. In contrast 22/72 (30%) had SPVL <400 copies/ml despite detectable BPVL (non-shedders). Men who shed virus into semen had significantly higher BPVL than non-shedders; 5.01 log<sub>10</sub> copies/ml (range 3.4-6.3) versus 4.2 log<sub>10</sub> copies/ml (3.0-5.5),  $P < 0.0001$ . Nine met the SSS criteria. These had significantly higher SPVL compared with non-SSS; 5.6 log<sub>10</sub> copies/ml (4.1-6.7) versus 3.4 log<sub>10</sub> copies/ml (2.6-6.2),  $P < 0.001$ . Their BPVL was not significantly different. SSS were generally older; 48 versus 35 years ( $P < 0.02$ ) and the presence of urethritis was significantly over-represented in the SSS group: 3/9 (33%) versus 3/63 (4.8%) in other groups ( $P = 0.02$ ). BPVL >100,000, CD4 counts and CDC status were not significantly different between SSS and SS.

**Conclusions:** 12% of this cohort were SSS as defined by the reversed SP:BP ratio. We postulate that within these individuals viral replication is occurring locally within the genital tract. Furthermore, when virus is produced at a high concentrations, these individuals may have a high probability of transmitting HIV during sexual acts.

## 03

**Sperm washing in the UK: evidence of safety and efficacy**

C Gilling-Smith, B Tamberlin, A Cox, G Rozis, JR Smith, S Barton and PA Almeida  
*Chelsea and Westminster Hospital, London, UK*

**Background:** HIV-discordant couples where the male partner is HIV-positive have an option to reproduce safely through the technique of sperm washing. Unfortunately, few centres in the UK offer this service and health authority funding remains limited. We have provided a sperm-washing programme since 1999 and report on the safety and efficacy of this service.

**Methods:** 53 HIV-1 positive men with seronegative partners have been treated. Following a sexual health and fertility screen on each partner, sperm washing was performed with intrauterine insemination (IUI) if there were no fertility factors or *in vitro* fertilisation (IVF)/ICSI if a fertility factor was diagnosed.

**Results:** 38 couples had 94 cycles of IUI and 30 couples had 42 cycles of IVF or ICSI. All sperm samples were verified HIV-1 negative with NASBA assay before treatment. Ongoing pregnancy/live-birth rates per cycle were 10.6% (10/94) for IUI and 23.8% (10/42) for IVF/ICSI. 15 healthy children have been born with no seroconversions in either female partner or child on rigorous follow-up. Eight couples had satellite arrangements for investigations and scanning. Only five couples received NHS funding and over 40% of patients referred did not proceed to treatment for financial reasons.

**Conclusions:** Sperm washing in a specialist centre is safe and effective as a risk-reduction treatment. Lack of NHS funding for this service may force couples to consider unprotected intercourse. Health Authorities must address this issue.

## 04

**An estimation of the UK demand for fertility services in HIV-positive couples**

LCG Frodsham, F Boag, S Barton and C Gilling-Smith  
*Chelsea and Westminster Hospital, London, UK*

**Introduction:** Demand for assisted conception in HIV discordant/concordant couples is rising due to increased HIV prevalence in the heterosexual population and the effect of antiretroviral drugs on life expectancy and vertical transmission risk. The reduction in vertical transmission from 20-30% to less than 1% has encouraged HIV-positive women to consider their reproductive potential. Further demand in women can be expected according to data from Africa, which demonstrate relative subfertility in HIV-positive women. To date, there has been no survey of the demand for assisted conception and/or risk reduction (sperm washing) in HIV-discordant or -concordant couples.

**Methods:** A postal survey of the 294 genitourinary medicine (GUM) clinics registered in the AGUM directory (2000) elicited a 63% response rate (186/294).

**Results:** 83/186 clinics had received requests for advice on conceiving. 15,211 HIV patients were registered in 81/83 of these clinics. 16% of the women and 4% of the men requested advice on fertility services and/or risk reduction. 49/83 units (59%) had referred men for sperm washing and 42/83 (51%) had referred women for assisted conception. 12/83 units (14%) had had success in obtaining HIV-prevention funds from local health authorities for sperm washing. 80/83 clinics (96%) felt that a UK database of units providing treatment would be of benefit in referring patients.

**Conclusions:** The demand for fertility services in HIV-infected couples is high. Our survey reinforces the need to improve current services to meet the demand and improve the information available to referring physicians.

## 05

## Neurological and developmental outcomes in HIV-infected children presenting before 3 years of age

EGH Lyall, C Foster, D Melvin and R Biggs

*Family Clinic, Department of Paediatrics, St Mary's Hospital, London, UK*

**Background:** Even with improved prognosis for HIV-infected children, developmental monitoring remains important.

**Aim:** To compare neurological and early developmental outcome of two groups of children, group 1 presenting with severe HIV disease other than encephalopathy (category C, CDC Classification 1994) and group 2 presenting with mild/moderate disease (category A/B).

**Methods:** Systematic evaluations of neurological and developmental functions, with neurological examination by a paediatric physiotherapist and paediatrician. Development was assessed using the Bayley Scales of Infant Development II by a clinical psychologist and paediatric physiotherapist.

**Results:** Neurology: group 1 ( $n=32$ ), mean age at assessment 16 months (range 7–26), 43% (13/32) had abnormal neurological signs, mostly spastic diplegia. Group 2 ( $n=31$ ), mean age at assessment 18 months (8–33), 7% (2/31) had abnormal neurological signs, both mild diplegia ( $\chi^2 P<0.05$ ).

**Developmental scores:** 20% of group 1 and 61% of group 2 scored within the average range (+1 to -1 SD score) in both mental and motor functions ( $\chi^2 P<0.05$ ). Group 2 scores were more normally distributed around the mean; in group 1 a higher number of children had scores of over -3 SD.

**Conclusions:** Severe early HIV disease is related to abnormal neurology with motor impairment and developmental delays. Our results emphasise the need for regular developmental monitoring and have implications for community services.

## 06

## Migration and HIV: impact on service delivery

C Chapman and J Dhar

*Department of Genito-Urinary Medicine, Leicester Royal Infirmary, Leicester, UK*

**Background:** Since 2000, antenatal screening for HIV infection has been implemented nationally. As the new HIV diagnoses have risen by 61% during that time in our area, the aim of the study was to assess how, if any, the screening has contributed to this rise and the impact it has made on local services.

**Method:** Case notes of all newly diagnosed female HIV-positive patients were retrospectively reviewed from January 2000 to December 2002. Data were collected on: ethnicity, presumed country of HIV acquisition, reason for HIV testing, time spent in the UK, stage of disease, co-infection, gestational stage (if pregnant at time of diagnosis) and mode of delivery.

**Results:** A total of 251 new cases were diagnosed during the study period, of which 129 (51%) were females; 31 (24%) were pregnant. Antenatal screening identified infection in 15 (12%). So far, 17 (55%) have delivered by Caesarean section. Of the 129 diagnosed, 115 (89%) had acquired their HIV infection outside the UK, 109 (95%) from sub-Saharan Africa; all HIV infection was acquired heterosexually. Sixty (55%) of these women are subsequently seeking asylum. At presentation, 67 (61%) had CD4 counts  $<350$  cells/ $\mu$ l and 55 (82%) are currently on highly active antiretroviral therapy (HAART). Syphilis serology was positive in seven (6%) and 5 (5%) were co-infected with hepatitis B co-infection. Details of measures taken and service networks established will be discussed.

**Conclusions:** Migrants dispersed to our area have contributed significantly to our cohort of HIV-positive individuals. A large number of these females are presenting with advanced disease and require HAART, either for themselves or to prevent vertical transmission. As this dispersal continues, more clinics will need to develop patient care pathways, with access to both healthcare and social-care professionals.

## 07

## Durability of efavirenz compared to nevirapine with long-term follow-up of an antiretroviral-naive patient cohort

G Matthews, Y Gillece, C Orkin, S Mandalia, MR Nelson, B Fisher, M Bower and BG Gazzard

*Chelsea and Westminster Hospital, London, UK*

**Background:** Few long-term data directly compare outcomes for efavirenz (EFV) versus nevirapine (NVP) regimens in antiretroviral-naive patients. We provide durability data on non-nucleoside reverse transcriptase inhibitors (NNRTIs) with up to 260 weeks' follow-up.

**Methods:** Antiretroviral-naive patients initiating EFV or NVP since 01/96 were identified from a prospective observational database. Virological failure [two viral load (VL) measurements  $>500$  copies/ml] or switch failure (discontinuation/switch) was identified. Multivariate analysis determining significant factors associated with failure and time to failure (TTVF) Kaplan–Meier (KM) curves was performed.

**Results:** 694 patients initiated NNRTI-based highly active antiretroviral therapy (HAART) (357 EFV, 337 NVP) since 01/96 with a total follow-up of 292 patient-years. No significant differences between EFV and NVP were found for sex, baseline VL or CD4, prior AIDS. EFV tended to be commenced in later years and with zidovudine/lamivudine (ZDV/3TC), NVP with stavudine/didanosine (d4T/ddI). In multivariate analysis, significant independent predictors of failure (virological and/or switch) were: prior AIDS illness [RH 1.48, 95% confidence interval (CI) 0.99–2.22], backbone d4T/ddI (RH 1.96, 95% CI 1.21–3.17) and NVP HAART (RH 1.60, 95% CI 1.07–2.40). Stratifying by year of therapy had no effect on outcome. 73 (10.5%) patients failed to achieve HIV VL  $<500$  copies/ml within 6 months of therapy. Of 621 patients achieving  $<500$ , 31 (5.0%) later developed virological failure and 45 (7.2%) had failure as defined by switch of therapy. KM curves showed an EFV benefit both in TTVF ( $P=0.0476$ ) and time to treatment failure (VF $\pm$ switch) ( $P=0.0324$ ).

**Conclusions:** This cohort provides the strongest evidence yet that durability of EFV over NVP continues with long-term follow-up.

## 08

## The success of tenofovir (TNF) and didanosine (ddI) when dosed together using low-dose didanosine 250 mg

M Tung, A Pathmanathan, J Chandra, M Bower, BG Gazzard and MR Nelson

*Chelsea and Westminster Hospital, London, UK*

**Aim:** Clinical trials have shown that TNF when co-administered with ddI at 400 mg increases ddI plasma concentrations  $>60\%$ , raising concerns over toxicity. To minimise this interaction, ddI at 250 mg co-administered with TNF and taken simultaneously has been suggested.

**Methods:** Retrospective study of all patients commenced on antiretroviral regimens containing TNF with either 400 or 250 mg ddI. Viral load at the start of the regimen and time to sustained undetectable HIV-1 RNA ( $<400$  copies/ml) were noted. All patients who had to switch regimens due to side effects or experienced virological failure were documented.

**Results:** Data are available on 24 patients who commenced regimens with TNF and 250 mg ddI, and 63 patients on tenofovir and 400 mg ddI. Four patients were treatment-naive. On-treatment analysis demonstrated virological suppression to  $<400$  copies/ml by 89% of patients on ddI 250, and 92% on ddI 400 at 3 months. At 6 months, 100% on ddI 250 and 91% on ddI 400 remain undetectable. By intention-to-treat analysis, virological suppression was achieved by 84% on ddI 250 and 92% on ddI 400 at 3 months, 67% on ddI 250 and 84% on ddI 400 at 6 months. In a second cohort of patients with a viral load  $<400$  copies/ml on, or switching to, TNF plus ddI 250 ( $n=78$ ) or ddI 400 ( $n=112$ ), time from below the level of detection to treatment failure between the two groups was not statistically different ( $P=0.40$ ), showing that ddI 250 is as efficacious as ddI 400.

**Conclusions:** Our clinical cohort has shown that TNF with ddI at 250 mg compares favourably with ddI at 400 mg. Thus low-dose ddI at 250 mg plus TNF is an effective combination.

## 09

## Efavirenz: what happens in the long-term?

L Swaden, CA Sabin, FC Lampe, MS Youle, MA Johnson and M Lipman  
Royal Free and University College Medical School, London, UK

**Background:** Non-nucleoside reverse transcriptase inhibitors (NNRTIs) have a known efficacy and side-effect profile. However, much of this is derived from either drug trial data or a relatively short-term follow-up.

**Methods:** We analysed an observational cohort of 483 subjects (78% male, 56% gay risk for HIV, 66% Caucasian origin) starting efavirenz (EFV) at our HIV centre from 1996 onwards and followed up for a median of 23.8 months.

**Results:** At the start of treatment, median CD4 count and HIV RNA viral load (VL) were 176 cells/ $\mu$ l and 5.21 log<sub>10</sub> copies/ml, respectively, with 38% being antiretroviral-naive. Of the 427 subjects with a baseline VL >500 copies/ml, 75% (Kaplan–Meier) achieved a VL <500 within the first 6 months; this occurred after a median of 92 days. Virological rebound (two consecutive VL >500 copies/ml) occurred in 16.7% by 1 year and was associated in multivariable analysis with younger age, starting EFV before 2000 and heavy prior use of NNRTIs or protease inhibitors (PIs). 201 (42%) of subjects stopped EFV; the proportions stopping by 3, 6, 12 and 24 months were 13%, 20%, 31% and 43% respectively (13%, 19%, 27% and 37% in those who were antiretroviral-naive). The most common causes of this were adverse events (AEs) ( $n=80$ ), patient choice ( $n=47$ ) and viral rebound ( $n=23$ ); 70% of AEs were neuropsychiatric in origin. The incidence of severe AEs did not decrease with prolonged follow-up. Risk factors for stopping due to AEs included concurrent use of PIs and Caucasian origin.

**Discussion:** EFV is a potent drug, though there is a high incidence of discontinuation due to AEs. These occur at a much later time (years rather than weeks) than reported previously.

## 010

## Optimising outcomes to antiretroviral therapy: a comprehensive multidisciplinary approach

HA Leake Date<sup>1</sup>, CA Sabin<sup>2</sup>, D Churchill<sup>1</sup>, G Dean<sup>1</sup>, D Williams<sup>1</sup> and M Fisher<sup>1</sup>

<sup>1</sup>Brighton and Sussex University Hospitals, Brighton, and <sup>2</sup>Royal Free and University College Medical School, London, UK

**Introduction:** A weekly multidisciplinary viral load meeting (VLm) identifies patients eligible for highly active antiretroviral therapy (HAART) and those on therapy with VL >50 copies/ml. Treatment decisions are aided by appropriate use and expert interpretation of resistance and drug-level assays. Concordance and adherence are promoted by multidisciplinary involvement before HAART initiation and ongoing support thereafter.

**Methods:** Observational cohort study of patients at an HIV centre on HAART (on-treatment analysis from weekly VLm), including those starting first HAART in 1999–2002 [intent to treat (ITT)].

**Results:** On-treatment analysis (all patients on HAART >6 months):

Year	Total no. clinic attenders (no. on HAART) on 31/12	% not on HAART at VLm, median (range)	% on HAART >6 months + VL <50, median (range)
2001	818 (494)	28 (16–48)	89 (80–100)
2002	895 (606)	25 (10–36)	92 (75–97)

An ITT analysis of antiretroviral-naive patients starting HAART at this centre from 1 August 1999 with over 6 months' follow-up will be presented, including data on clinical trial participation, treatment outcomes and reasons for stopping/switching.

**Discussion:** VL suppression rates (<50 copies/ml) of >90% can be achieved in routine clinical practice by the adoption of a structured multidisciplinary approach.

## 011

## Dose escalation or immediate full dose when switching from efavirenz- to nevirapine-based HAART?

A Winston, A Pozniak, N Smith, C Fletcher, S Mandalia, D Parmar, S Gibbons, D Back, BG Gazzard and MR Nelson  
Chelsea and Westminster Hospital, London, UK

**Background:** The NNRTIs nevirapine (NVP) and efavirenz (EFV) are both capable of inducing the metabolism of co-administered drugs. Not uncommonly, it is necessary to switch from one drug to another. When switching from EFV to NVP it is not known whether to dose-escalate or switch to full dose.

**Methods:** This is a pharmacokinetic observational study, powered to 80% for detection of average trough drug levels. Patients established on EFV, changing to NVP, were randomised to dose escalation [200 mg once daily for 2 weeks then 200 mg twice daily (bd)] or full dose (200 mg bd). Trough drug levels were checked on days 2, 8, 15, 22 and 29 as were liver function tests, CD4 and viral load (VL).

**Results:** Seven patients were randomised to dose escalation (group 1) and six to full-dose NVP (group 2). Average trough NVP levels to day 15 in group 1 were below the recommended level for virological success of 3000 ng/ml (Table 1). Average trough NVP levels in group 2 were above this threshold except for day 2 but were significantly higher than group 1 on this day. There was no increased incidence of raised alanine aminotransferase between either groups or VL changes.

**Conclusions:** When changing from EFV to NVP, patients should start on 200 mg bd initially, for therapeutic plasma drug levels without increased toxicity. Although virological failure was seen in those given lower-dose NVP, subtherapeutic plasma levels occurred for 3 weeks, which has potential for the development of drug-resistant virus.

Table 1: Average nevirapine plasma levels (ng/ml): \* $P<0.025$ .

	Day 2	Day 8	Day 15	Day 22	Day 29
Group 1	1187	2554	2881	4121	6724
Group 2	2544*	4358 <sup>NS</sup>	3426 <sup>NS</sup>	4490 <sup>NS</sup>	5306 <sup>NS</sup>

## 012

## Impact of archived NRTI resistance mutations on maintenance of virological control after switching from stavudine to tenofovir with an undetectable viral load

C McDonald<sup>1</sup>, S Kegg<sup>2</sup>, R Kulasegaram<sup>3</sup>, M Smith<sup>1</sup>, C Taylor<sup>1</sup>, P Easterbrook<sup>1</sup>, B Peters<sup>3</sup>, P Hay<sup>2</sup> and AM Geretti<sup>1</sup>

<sup>1</sup>King's College Hospital, <sup>2</sup>St Thomas's Hospital and <sup>3</sup>St George's Hospital, London, UK

**Objective:** To determine the impact of previously detected nucleoside reverse transcriptase inhibitor (NRTI) resistance on the maintenance of virological control in antiretroviral-experienced patients switching from stavudine to tenofovir with a viral load (VL) of <50 copies/ml.

**Methods:** Retrospective and prospective observational cohort study. Eligible patients ( $n=25$ ) had been on two or more previous antiretroviral regimens and had a stable viral load of <50 copies/ml at the time of switching. Genotypic resistance was determined in plasma samples by either the TruGene Assay (Visible Genetics) or in-house sequencing.

**Results:** The patients had a mean of 2.5 previous antiretroviral regimens and 5.1 years of NRTI therapy; 21/25 (84%) had one or more mutations at RT codons 41, 67, 70, 210, 215 and 219 (thymidine analogue mutations). None had K65R. Reasons for switching included lipotrophy in 18, peripheral neuropathy in two, hepatic steatosis in one and unstated in four patients. At week 24, 20/25 patients (80%) had VL <50 copies/ml, including 10 with previous M41L plus two other TAMs or L210W in any context; all 20 were on protease inhibitor (PI)-based therapy with nelfinavir, ritonavir/saquinavir or ritonavir/lopinavir. One was lost to follow-up. Four (16%) had a virological rebound >400 copies/ml (two on NNRTI- and two on PI-based therapy). At rebound, resistance testing showed re-emergence of mutations at codons 41, 70, 210, 215 and 219. Two patients had K65R.

**Conclusions:** In NRTI-experienced patients switching from stavudine to tenofovir with a PI-based regimen, virological control was maintained despite a history of resistance mutations known to affect tenofovir.

## 013

## CDE chemotherapy plus HAART for AIDS-related non-Hodgkin's lymphoma

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**Background:** Since 1999 the standard therapy in our unit for systemic AIDS-related lymphoma has been infusional cyclophosphamide/doxorubicin/etoposide (CDE), which has the potential for overcoming P-glycoprotein-mediated drug resistance, with highly active antiretroviral therapy (HAART).

**Methods:** C is given at 800 mg/m<sup>2</sup> IVI over 96 hours (200 mg/24 hours), D at 50 mg/m<sup>2</sup> IVI over 96 hours (12.5 mg/24 hours) and E at 240 mg/m<sup>2</sup> IVI over 96 hours (60 mg/24 hours). This is given monthly for up to six cycles with granulocyte colony-stimulating factor support, opportunistic infection prophylaxis and intrathecal chemoprophylaxis.

**Results:** 30 patients (27 male) (median age 46 years, range 27–60) were enrolled. The median interval between HIV-1 diagnosis and that of non-Hodgkins lymphoma (NHL) was 53 months (range 0–175) and all received HAART (nine a protease inhibitor-based combination, 20 a non-nucleoside reverse transcriptase inhibitor-based combination, one both). At presentation, the mean CD4 count was 142 cells/μl (range 4–636) and HIV-1 RNA viral load was undetectable in nine (30%) patients. International Prognostic Index (IPI) scores for aggressive lymphoma (based on age, LDH, stage, performance status and extranodal sites) were 0 in four patients, 1 in four patients, 2 in eight patients, 3 in seven patients and 4 in seven patients. The median overall survival (OS) was 1.2 years and 2-year OS was 50%. One patient died in remission 1.2 years after therapy of an HIV-related cause; the remaining 12 deaths were NHL- or therapy-related.

**Conclusions:** Treatment with CDE and HAART is associated with a median survival of over 1 year, comparing favourably with our previous regimens. The OS correlated with NHL-related factors (IPI index) rather than HIV-associated factors (CD4 count and viral load). This differs from prognostic indicators of the pre-HAART era.

## 014

## Pegylated interferon (PIFN) and ribavirin (RBV) in the treatment of acute hepatitis C in individuals co-infected with HIV

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**Aim:** To investigate the efficacy of treatment of acute hepatitis C (HCV) infection in individuals co-infected with HIV.

**Methods:** Prospective review of outcome of HIV-positive individuals diagnosed with acute HCV infection.

**Results:** 29 patients were diagnosed with acute HCV infection from December 1997 to January 2003. Three were HCV polymerase chain reaction (PCR) –ve at diagnosis. The patients were offered acute treatment for HCV at diagnosis; 16 were treated: nine (56%) became HCV PCR –ve and seven (44%) patients await follow-up PCRs. Eight (50%) patients received PIFN+RBV and became HCV PCR –ve (1–4 months). Five (31%) of these completed treatment early (2–5 months) and remain PCR –ve at 2–8 month follow-up. One (6%) patient received IFN+RBV for 9 months, became HCV PCR –ve at 5 months and remained so at the 15-month follow-up. One (6%) patient, treated with PIFN only, failed after 6 months of treatment. No patient discontinued PIFN. One patient discontinued RBV due to anaemia. Of nine who declined treatment for HCV, only one (11%) became HCV PCR –ve (follow-up range 1–32 months). 19 of the 29 patients were receiving antiretroviral therapy at the time HCV was diagnosed. Of those on HCV treatment, no patient lost virological control and the mean CD4 change was -14 cells/μl whereas three untreated patients failed with a high viral load and the mean CD4 change was -99 cells/μl.

**Conclusions:** Treatment of acute HCV results in higher rates of PCR negativity with no loss of HIV virological control. Tolerability of PIFN and RBV is problematic and our data suggest that shorter courses of HCV treatment should be assessed for efficacy.

## 015

## Co-infection with HIV-1 and hepatitis C does not ablate the allostimulatory function of dendritic cells

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**Objectives:** There is widespread recognition of the potential morbidity and mortality associated with HIV and hepatitis C (HCV) co-infection. To assess the feasibility of using autologous dendritic cells (DCs) in immunotherapy and to further elucidate this interaction, we examined the capacity of peripheral blood DCs recovered from co-infected individuals to stimulate naive T cells.

**Methods:** Monocyte-derived DCs were generated from HIV-1 seropositive patients with ( $n=10$ ) and without ( $n=10$ ) HCV infection. These individuals were matched for HIV-1 virological and immunological parameters. We performed mixed leucocyte reactions with cell division analyses, using carboxy fluorosuccinyl ester (CSFE), a fluorinated vital dye, in order to examine the allostimulatory potentials of DCs.

**Results:** Monocyte-derived DCs from co-infected individuals showed a similar allostimulatory capacity to *in vitro* generated DCs from HIV-1 infected individuals without HCV. This impairment was not reversed by increasing concentrations of either exogenous interleukin-2 or -12.

**Conclusions:** Monocyte-derived DCs from HIV-1 and HCV co-infected individuals have a similar allostimulatory capacity to DCs from patients with HIV-1. This has implications for immunotherapeutic approaches in co-infected individuals and is consistent with recent data showing that HCV and HIV-1 do not negatively affect one another.

## 016

## Increasing incidence of acute hepatitis C in HIV positive men secondary to sexual transmission: a new epidemic?

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**Background:** To evaluate changes in acute hepatitis C virus (HCV) seroconversion and risk factors for acquisition of HCV within a dedicated HIV/genitourinary medicine (GUM) clinic.

**Methods:** We identified acute seroconverters for HCV from our sexual health and HIV cohort between January 1997 and December 2002. Demographic, clinical and risk factor data were analysed.

**Results:** 28 patients were identified, 26 of whom were HIV-positive. There was a statistically significant increase in the incidence of documented HCV seroconversion, test for trend  $P<0.001$ . The only identifiable risk factor was unprotected sexual intercourse in 20 individuals. Four patients had a history of current intravenous drug use (IDU). Nine individuals were diagnosed with infectious syphilis in the year preceding HCV seroconversion, including three who were diagnosed with HCV and syphilis concurrently. 18 patients had asymptomatic seroconversion and the sole reason for HCV testing was to investigate abnormal liver function tests. There was a statistically significant increase in the number of patients testing positive for HCV in our clinical cohort but no increase in the total number of patients having HCV tests. This makes it unlikely that our observations are due to a lowered threshold for testing.

**Conclusions:** The high number of individuals reporting unsafe sex, low documented IDU and a high rate of concomitant syphilis infection suggests that sexual transmission is fuelling a significant increase in HCV seroconversion.

## 017

## Outcome of acute hepatitis C in HIV-positive homosexual men

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**Background:** An increasing number of HIV-positive patients are being diagnosed with acute hepatitis C. However, little is known about the requirement for and feasibility of interferon treatment in HIV-positive patients. Uncontrolled clinical trials of interferon treatment for acute HCV in HIV-negative patients suggest that most chronic infection can be prevented. Little is known about the outcome in HIV-positive patients. **Methods:** We present the results of a small observational study of HIV-positive patients diagnosed with acute hepatitis C during January 2000–January 2003. 15 patients were offered treatment with pegylated interferon- $\alpha$ 2b with the addition of ribavirin after 12 weeks if they were still HCV RNA-positive.

**Results:** Two patients presented with jaundice; others were asymptomatic but had elevated alanine aminotransferase levels. Five patients had concomitant syphilis and all had a history of unsafe sex; none had a history of intravenous drug use or iatrogenic risks for HCV exposure. Four patients had spontaneous seroconversion and became HCV RNA-negative within 3 months of the initial diagnosis, but all had HCV RNA resurgence on long-term follow-up. Eight patients started interferon therapy, and at 12 weeks, three patients were HCV RNA-negative; 24-week treatment data will be presented.

**Conclusions:** Some patients clear HCV RNA spontaneously after acute infection, but in this small series, reactivation occurred in all cases. Interferon treatment is feasible; however, larger prospective studies are needed, including study of the long-term outcome.

## 018

## Survival in HIV-infected individuals following liver transplantation is influenced by viral co-infection: the negative impact of HCV infection

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**Introduction:** Liver transplantation (LT) in HIV-positive individuals is still considered to be an experimental therapy with limited worldwide experience, and few long-term survival data. Published data suggest that the short-term outcome after LT is encouraging in selected patients. In the current study, we report our experience in 12 HIV-positive liver allograft recipients, and compare the outcomes of those co-infected with hepatitis C virus (HCV) to the non-HCV group.

**Methods:** 12 HIV-infected patients (10 male, two female, age range 26–59 years) underwent LT between January 1995 and March 2002. Indications for LT were HCV ( $n=5$ ), hepatitis B virus (HBV) ( $n=4$ ), ALD ( $n=2$ ), and non-A, non-B hepatitis ( $n=1$ ); three patients presented with acute liver failure. At LT, CD4 counts were 124–500 cells/ $\mu$ l (mean 267), and HIV viral loads from <50 to 197,000 copies/ml. Seven of 12 patients were exposed to highly active antiretroviral therapy (HAART) prior to LT.

**Results:** In the non-HCV group ( $n=7$ ), all patients are alive, with five surviving more than 365 days (range 4–67 months). No patient experienced HBV recurrence, and graft function is normal in all seven recipients. In contrast, all HCV-infected patients died after LT at 95–784 days (median 161). Four patients died of complications due to recurrent HCV infection and sepsis, despite antiviral therapy in three. Three patients experienced complications relating to HAART therapy.

**Conclusions:** The long-term outcome of LT in HIV-infected patients with HBV or other causes of chronic liver disease indicates that this is an acceptable therapeutic option for these patients. However, the long-term prognosis for HCV-HIV co-infected patients must remain guarded.

## 019

## Growth hormone and effective antiretroviral therapy augment immune function of HIV-1 infected individuals

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**Objectives:** To evaluate the effects of recombinant human growth hormone (rhGH) on the immune system of HIV-1-infected patients treated with highly active antiretroviral therapy (HAART).

**Methods:** Twelve chronic HIV-1-infected patients on HAART (4 years) received rhGH. Lymphocyte phenotype was assessed at baseline, 12 weeks after 4 mg/day of rhGH and a further 12 weeks after randomisation into three groups (placebo or alternate-day or twice-weekly rhGH). T-cell receptor rearrangement excision circles (TREC) analysis was performed for all time points.

**Results:** At week 12, a significant increase in memory/effector CD8+ T cells assessed by CD45RA and CCR7 expression, and increases in naive CD4+ and CD8+ T cells ( $P<0.01$ ) were observed. In addition, we observed an increase in HIV-1 antigen-specific CD4+ ( $P<0.005$ ) and CD8+ ( $P<0.05$ ) T-cell responses. Twelve weeks after initiation of the trial, randomisation into placebo, alternate-day dosing or twice-weekly dosing was instigated. The phenotype and function of the virus-specific effector CD8+ T cells seen at week 12 was maintained at week 24 regardless of randomisation, despite the disappearance of HIV-1-specific CD4+ T-cell responses in all patients. No changes were seen in TREC levels at any time point.

**Conclusions:** Concomitant administration of rhGH at 4 mg/day with HAART appears to attenuate the defects exerted on the immune system by HIV-1. This combination may be a valuable immunotherapeutic intervention for chronic HIV-1 infection.

## 020

## The heat shock protein receptor CD91 is up-regulated in monocytes of HIV-1-infected 'true' long term non-progressors

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**Background:** A small proportion of human immunodeficiency virus type 1 (HIV-1)-infected individuals remain asymptomatic for a long period after infection. It is thought that a vigorous immune response may contribute to long-term non-progression, although studies are confounded by heterogeneity among patients.

**Methods:** We studied the levels of HIV-1 receptors, co-stimulatory T-cell molecules and dendritic cell (DC) numbers in 18 individuals with long-term infection, a CD4 count >400 cells/ $\mu$ l and an HIV-1 viral load <50 copies/ml. These patients were further differentiated by the presence or absence of 2-long terminal repeat (LTR) DNA circles, a possible marker for residual ongoing HIV-1 replication.

**Results:** A statistically significant increase in levels of CD91, the heat-shock protein (HSP) receptor, was observed in therapy-naive individuals who had no evidence of ongoing viral replication ( $P=0.01$ ). This difference was most notable on their monocytes.

**Conclusions:** High levels of CD91 may be a host factor that contributes to maintenance of long-term non-progression. Its ability to internalise  $\alpha$ -defensins and cross-present exogenous antigen to cytotoxic T lymphocytes via major histocompatibility class I may maintain CD8+ responses in these individuals.

## 021

The impact of antiretroviral therapy and/or immunotherapy on the levels of circulating  $\beta$ -chemokines and IL-16 in HIV-1 infected individuals

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**Background:** A reduction in HIV-1 RNA in late-stage patients taking protease inhibitors (PIs) has been associated with increased macrophage inhibitory proteins (MIP)-1 $\alpha$ , MIP-1 $\beta$ , regulated-upon activation, normal T-cell expressed and secreted (RANTES), interleukin (IL)-16 and decreased monocyte chemoattractant protein (MCP)-1.

**Method:**  $\beta$ -chemokines and IL-16 were quantified in plasma by enzyme-linked immunosorbent assay (ELISA) in HIV-1+ patients, monthly, over the first 16 weeks of PI or non-nucleoside reverse transcriptase inhibitor (NNRTI)-based highly active antiretroviral therapy (HAART). MIP-1 $\beta$  was measured after randomisation to one of (a) IL-2, (b) Remune (therapeutic vaccine), (c) IL-2 and Remune or (d) HAART alone. Viral load and lymphocyte subsets were also measured.

**Results:** During the 16 weeks of HAART there were significant increases in levels of MIP-1 $\alpha$  and MIP-1 $\beta$  in the NNRTI group ( $P=0.0015$  and  $P=0.0006$ ), significant decreases in the PI group ( $P=0.0010$  and  $P=0.0352$ ), significant decreases in MCP-1 in the PI group ( $P=0.0003$ ), and no significant differences in RANTES and IL-16 levels. MIP-1 $\beta$  levels after randomisation showed little change; however, the IL-2 group had a significantly higher level at week 29 ( $P=0.0469$ ), possibly due to an increase in CD8+ T cells

**Conclusions:** Immunotherapy had little effect on plasma levels of MIP-1 $\beta$ . Patients treated with NNRTI-based HAART show a significantly higher level of MIP-1 $\alpha$  and MIP-1 $\beta$ . These higher levels may be beneficial, as high levels of  $\beta$ -chemokines have been associated with slower disease progression.

## 022

## Atorvastatin and pravastatin for hypercholesterolaemia in HIV-positive patients receiving HAART

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**Aim:** To study the effect of atorvastatin (A) and pravastatin (P) in reducing serum cholesterol in HIV-positive patients receiving highly active antiretroviral therapy (HAART).

**Methods:** A retrospective case-note review of patients attending the unit who had received 4 or more weeks of either A or P for hypercholesterolaemia associated with HAART. Mean serum cholesterol before and after starting or changing dose of therapy was recorded along with the number of patients whose cholesterol decreased to within normal parameters (3.5–6.5 mmol/l). The duration of therapy, demographic details and antiretroviral therapy were also recorded.

**Results:** 102 patients received A with 125 treatment episodes and 77 patients received P with 91 treatment episodes. Both groups were similar at baseline with respect to age, sex and risk category. In 56% of patients receiving A, cholesterol decreased to <6.6 mmol/l compared with 32% of patients receiving P ( $0.01 < P < 0.02$ , 95% confidence interval 0.141–0.339). Results are summarised below.

	Treatment episodes	Mean dose	Mean pre-treatment cholesterol	Mean post-treatment cholesterol	% with cholesterol <6.6 mmol/l
A	125	12.4 mg	7.8 mmol/l	6.4 mmol/l	56%
P	91	31.6 mg	8.2 mmol/l	6.8 mmol/l	32%

**Conclusions:** Both A and P decrease serum cholesterol in HIV-positive patients receiving HAART. Patients receiving A were significantly more likely to have a decrease in cholesterol to <6.6 mmol/l compared with those receiving P. We recommend that A be considered as first-line ahead of P for the treatment of hypercholesterolaemia in HIV-positive patients receiving HAART. There was no clear difference in the effect on protease inhibitor (PI)-containing regimens compared with non-PI regimens between treatment groups.

## 023

## Exocrine pancreatic insufficiency in HIV-positive patients

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**Background:** HIV+ patients on highly active antiretroviral therapy (HAART) may develop chronic diarrhoea. Microbiological, histological and endoscopic investigations are frequently negative and patients receive symptomatic treatment for presumed antiretroviral side effects. Low faecal elastase (<100  $\mu$ g/g) is a marker of exocrine pancreatic insufficiency (a cause of chronic diarrhoea).

**Method:** Retrospective case-note analysis of HIV+ patients on HAART with chronic diarrhoea and measurement of weight and faecal elastase.

**Results:** 7/22 HIV+ patients whose faecal elastase was measured had <100  $\mu$ g/g, indicative of severe exocrine pancreatic insufficiency. All seven had negative stool cultures and microscopy. All chronic diarrhoea patients with low faecal elastase had lost weight (2–10 kg). Patients with normal faecal elastase had not lost weight. 4/7 patients with low faecal elastase had symptoms of fat malabsorption compared with none in the normal faecal elastase group. 5/7 of the patients with diarrhoea were on a protease inhibitor, 4/7 on didanosine and 5/7 on stavudine. 1/7 also had giardiasis. 6/7 patients with low faecal elastase levels were started on pancreatic enzyme supplementation with marked improvement of symptoms. 1/7 died of endstage HIV disease.

**Conclusions:** HIV+ patients with chronic diarrhoea on HAART should have their pancreatic function assessed, particularly if associated with weight loss or symptoms of fat malabsorption and, if deficient, should be treated with pancreatic enzyme supplements.

## 024

## Changing mortality patterns in the HAART era

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**Aim:** To determine the changing incidence of cause of death with improvements in highly active antiretroviral therapy (HAART).

**Methods:** All deaths in three distinct time periods were recorded at two UK centres, period A (pre-HAART): May to November 1994, period B (early HAART): November 1996 to May 1998, period C June 2000 to September 2002.

**Results:** Deaths per month: 22, 8 and 5; median CD4 count: 20, 35 and 116 cells/ $\mu$ l ( $P < 0.0001$ ); viral load below detection: 0%, 8% and 39% ( $P < 0.0001$ ); previous AIDS: 93%, 77% and 44% ( $P < 0.0001$ ); heterosexual: 3%, 11% and 40% ( $P < 0.0001$ ) for periods A, B, C respectively

n (%)	KS	Lymphoma	PCL	Other cancer	Liver disease
A	17(13)	3(2)	8(6)	1(<1)	3(2)
B	9(7)	12(9)	7(5)	Nil	4(3)
C	3(2)	13(10)	2(2)	14(11)	16(12)
P	0.004	0.03	0.015	<0.001	0.002

n (%)	OIs	Sepsis	Suicide	OD	ART related	Other	Not known
A	35(26)	13(10)	1(<1)	0(0)	20(15)	32(24)	
B	24(18)	13(10)	5(4)	2(2)	22(17)	35(26)	
C	20(15)	24(18)	10(8)	4(3)	11(8)	14(11)	
P	0.059	0.056	0.018	0.13	0.11	0.002	

ART, antiretroviral therapy; OI, opportunistic infections.

**Conclusions:** Mortality has decreased with the advent of HAART. At the time of death individuals have a higher CD4 cell count and are less likely to have had a previous AIDS diagnosis. The spectrum of causation is changing with higher rates due to AIDS-defining cancers, systemic lymphomas, and liver disease and self-harm, while the proportion of deaths from Kaposi's sarcoma (KS) and primary cerebral lymphoma (PCL) has fallen.

## 025

## Is it time to rethink the roles of health professionals in the HIV outpatient setting?

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**Background:** Improved survival and continuing HIV incidence have led to significant changes in the needs of patients attending for routine HIV outpatient care. As the costs of antiretroviral treatment escalate, we decided to review the doctor-patient caseload.

**Methods:** Data were collected prospectively on all patients who booked appointments for routine HIV outpatient care between 24 June 2002 and 17 July 2002. Data collected included patient attendance, duration of appointment, CD4 count, HIV viral load, antiretroviral therapy, clinical status and grade of doctor seeing the patient.

**Results:** Data collection forms were completed for 431/433 consecutive appointments. The non-attendance rate was 18% (79/431). The median CD4 count and viral load were 350 cells/ $\mu$ l (range 10-1490) and 600 copies/ml (range <50 to 3 million), respectively. Consultant staff saw 66% of the patients. A quarter of consultations were used by patients requiring close monitoring of starting/changing antiretroviral therapy. Almost half (49%; 173/352) of the patients seen were defined by their physician as being asymptomatic with respect to HIV infection. These patients either had no new medical, psychological or social problems (63%; 108/173), had primary care-related problems (21%; 36/173) or had non-acute problems requiring discussion with an HIV-trained professional (e.g. lipodystrophy, high lipids, viral blips).

**Conclusions:** A high proportion of patients attending routine HIV outpatient clinics have needs that could be met by other healthcare professionals. With an ever-increasing demand on services, there is a need to develop cost-effective models of care that match the patient caseload with appropriate professional expertise without reducing the quality of care.

## 026

## Missed opportunities to diagnose HIV infection

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**Background:** Early diagnosis and intervention is important to reduce the morbidity and mortality of HIV infection and BHIVA guidelines recommend that antiretroviral therapy is initiated before the CD4 count falls below 200 cells/ $\mu$ l. Patients with symptomatic HIV may present to a variety of clinical services providing a diagnostic opportunity. We performed an audit to identify whether such opportunities may be missed and to determine clinical outcome where delay has occurred.

**Methods:** Retrospective review of 50 new HIV diagnoses in 2002. Data included CD4 count at diagnosis, previous medical care, time from first HIV-related symptoms to diagnosis and clinical outcome.

**Results:** 31/50 patients presented with symptomatic disease with the other 19 being tested as part of antenatal or genitourinary medicine clinic screening. Of these symptomatic patients, 16/31 had a CD4 count of <50 cells/ $\mu$ l and 29/31 had <200 cells/ $\mu$ l. In contrast, of those detected through screening only, 4/19 had a CD4 count <200. 12 (24%) patients had previously presented to a variety of clinical services at different hospitals or primary care with symptoms suggestive of HIV. In six cases, the potential diagnostic delay exceeded 12 months. Five of these 12 patients presented with serious opportunistic infections requiring prolonged hospitalisation, two suffered permanent neurological damage and one died.

**Conclusions:** Clinicians still fail to recognise HIV-related symptoms, resulting in unnecessary morbidity and mortality. There is a continuing need to raise HIV awareness, particularly in areas of high local prevalence.

## 027

## National strategy does not ensure PCT-level priority or national equity for HIV services

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**Background:** Clinicians across England report a lack of attention to sexual health and HIV at primary care trust (PCT) level, and delayed response to the National Strategy due to National Health Service (NHS) reorganisation.

**Methods:** The Terrence Higgins Trust (THT), with BHIVA and PACT, undertook short postal surveys of English PCTs and BHIVA members in August 2002. In all, 66 PCTs and 80 clinicians returned questionnaires. Returns were collated and presented to Parliament in early 2003.

**Results:** The returns showed highly variable levels of response to the National Strategy and a growing gap between resources and need. 54% of PCTs had no agreed process yet for implementing the Strategy; 18% had no sexual health lead or multi-agency planning team. Regions varied widely in response; for example, 100% of London PCTs had sexual health leads but only 50% of Eastern Regions had. 59% of clinicians said their ability to provide services had worsened while 3% felt it had been improved by the Strategy and NHS changes. 69% expected overspends on their drugs budget while 27% did not know who their PCT lead was. West Midlands clinicians reported least problems and those in Trent and the South-West the most. London clinicians provided the most critical additional comment.

**Conclusions:** Simultaneous introduction of the National Strategy alongside NHS reorganisation has had a damaging effect upon coordination and prioritisation of HIV services and has failed, so far, to improve national access or tackle the rising rates of sexual ill-health and HIV.

## 028

## CD4 cell counts in HIV-infected adults at HIV diagnosis in England and Wales, 1990 to 2001

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**Aims:** To describe differences and trends in CD4 cell counts of HIV infected adults in England and Wales.

**Methods:** Adults, reported to the CD4 Surveillance Scheme from 60 laboratories, were matched to the UK database of diagnosed HIV infections and AIDS cases. This confirmed their HIV-positive status and provided a date of HIV diagnosis, ethnicity and probable HIV-risk group.

**Results:** 15,284 individuals had a CD4 count within 6 months of the date of HIV diagnosis and one of these exposure categories: men who have sex with men (MSM), injecting drug users (IDU), heterosexual sex. Over a third of HIV-positive individuals were diagnosed with CD4 counts <200 cells/ $\mu$ l. Heterosexuals were diagnosed at lower CD4 counts (median 230 cells/ $\mu$ l, 95% confidence interval 220-231) than MSM (310, 307-320) and IDUs (300, 280-320). The median CD4 counts of black African heterosexuals at diagnosis were also lower than in white heterosexuals. Median CD4 counts at diagnosis in MSM averaged 308 cells/ $\mu$ l between 1990 and 1996 but increased to 370 in 2001. Updated results will be presented including 2002 data.

**Conclusions:** Many adults are still diagnosed with CD4 levels at which the initiation of HAART is associated with reduced survival. Monitoring CD4 counts will help to assess the goals of the Sexual Health Strategy.

## O29

## South Asians with HIV infection in London: a growing epidemic?

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**Background:** The South Asian (SA) HIV pandemic is one of the most rapidly growing worldwide. Currently, there are no data describing HIV+ SAs in the UK.

**Methods:** Retrospective case-note review using a standardised proforma of all SAs presenting to four London HIV treatment centres between January 1985 and December 2002. Data on demographics, reasons for HIV test, CD4, viral load (VL) and CDC stage at diagnosis were collected on those defining their ethnicity as Indian, Pakistani, Bangladeshi or Sri Lankan.

**Results:** 116 patients were identified, 22 diagnosed in 1989–1995 and 87 in 1996–2002, 88 male, 28 female. Regions of origin included: Africa (39%), the Indian subcontinent (35%) and the UK (16%). 81% were of Indian ethnicity. Risk factors included heterosexual 61 (53%), homosexual 36 (31%), unknown 13 (11%), injecting drug users (IDUs) two (2%), blood transfusion four (3%). At diagnosis, the median age was 34 years and the median CD4 count was 289 cells/ $\mu$ l, with 41% having symptomatic HIV or AIDS. Heterosexuals compared with gay men were: more likely to present at a lower median CD4 count (214 versus 390,  $P=0.03$ ); have an AIDS-defining illness (ADI) (17/74; 23% versus 5/36; 14%:  $P=0.3$ ); and were significantly less likely to be diagnosed in a genitourinary medicine (GUM) clinic (2/74; 3% versus 17/36; 47%  $P<0.001$ ). *Pneumocystis jiroveci* pneumonia (PCP) ( $n=8$ ; 35%) and tuberculosis ( $n=8$ ; 35%) were the commonest ADIs.

**Conclusions:** In order to respond appropriately to the evolving epidemic among SAs, it is critical to understand the socio-cultural differences that may lead to non-attendance at GUM clinics and late presentation.

## O30

## HIV and black Caribbeans in the UK

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**Background:** The impact of HIV in the Caribbean has been marked, with prevalence rates in several countries surpassed only by those of sub-Saharan Africa. With an estimated black Caribbean population of 612,000, frequent travel to the Caribbean and continuing immigration, it is no surprise that the numbers of black Caribbeans with HIV in the UK are increasing.

**Methods:** Data on new diagnoses were obtained from reports received at CDSC by 30 September 2002, and on diagnosed prevalent infections from the Survey Of Prevalent Diagnosed HIV Infections (SOPHID).

**Results:** In the UK, 759 black Caribbeans have been diagnosed with HIV since the beginning of the epidemic, the majority since 1998. In 1991 there were 14 new HIV diagnoses, by 2001, 165, and this figure will increase as further reports are received. Of the black Caribbeans newly diagnosed with HIV, 531 (70%) were male and 228 female. Median ages at diagnosis were 33.7 and 32.9 years, respectively. 297 (39%) were probably infected through sex between men and 407 (53%) through heterosexual sex, of whom 195 (48%) were male. Region of infection was recorded for 530 individuals: 270 (51%) were probably infected in Latin America/the Caribbean (including 142 in Jamaica); and 194 (37%) were probably infected in the UK. SOPHID 2001 recorded 705 black Caribbeans seen for HIV-related treatment and care in England, Wales and Northern Ireland, a 57% increase since 1999. In 2001, 538 (76%) of the black Caribbeans resided in London.

**Conclusions:** New HIV diagnoses among black Caribbeans in the UK are increasing, against a background of a high incidence of bacterial sexually transmitted infections in this community. Targeted and culturally sensitive prevention methods are required to address this issue.

## P1

### The impact of NRTI resistance mutations on responses to tenofovir as part of salvage therapy in an ethnically diverse population of drug-experienced patients in South London

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**Objective:** To assess 48-week virological and immunological responses to salvage highly active antiretroviral therapy (HAART) in ethnically diverse highly drug-experienced patients with nucleoside reverse transcriptase inhibitor (NRTI) mutations affecting tenofovir susceptibility.

**Methods:** In a prospective study of patients failing HAART and starting tenofovir-based salvage therapy, genotypic resistance was assayed in plasma samples collected at the last failure and all available previous failures [TruGene Assay (Visible Genetics) or in-house sequencing].

**Results:** 45 subjects (28 males and 17 females), 58% Caucasian, 38% black African and 4% black Caribbean, had a baseline median viral load (VL) of 4.2 log<sub>10</sub> copies/ml (mean 5), median CD4 count 224 cells/μl (mean 263), mean 47 months of antiretroviral (ARV) therapy, mean eight ARV drugs, mean four failures and mean two NRTI resistance mutations with thymidine analogue mutations (TAMs) (41L, 67N, 70R, 210W, 215Y/F, 215Q) or 65R; 17 (38%) had 41L plus two other TAMs; 13 (29%) had 210W in any context; three (6%) had 65R. 32 patients reached 48 weeks, five of whom (16%) were lost to follow-up; six (19%) stopped therapy due to severe side effects in two (acquired Fanconi's; grade 3 hyperlipidaemia), intolerance in three and pregnancy in one. 14 (44%) had VL <400 and 12 (37.5%) <50 copies/ml. Virological failure occurred in six (19%). Mean CD4 count rise 84 cells/μl.

**Conclusions:** Among highly treatment-experienced patients with NRTI resistance mutations known to affect tenofovir susceptibility, 44% showed a sustained virological response to salvage therapy containing tenofovir and 53% a significant immunological response.

## P2

### Audit of adherence to BHIVA resistance testing guidelines

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**Background:** BHIVA resistance testing guidelines were published in 2001.

**Objectives:** To examine compliance within our unit to BHIVA guidelines by determining (a) whether eligible patients were offered resistance testing and (b) whether resistance tests when performed were appropriate.

**Methods:** (a) Retrospective audit of all patients with a viral load (VL) >50 copies/ml on highly active antiretroviral therapy (HAART) during January 2002; (b) retrospective audit of genotypic resistance tests performed January–May 2002.

**Results:** (a) 112 patients had VL >50 copies/ml on HAART, most being persistently above this level. In five patients, this was the first or second detectable VL measurement following suppression to <50 copies/ml and resistance testing was performed in all. (b) 112 resistance tests were performed in 109 patients. 94 case notes were reviewed, identifying 10 seroconverters, six pregnant women and 75 treatment-experienced patients (three having duplicate tests). In the treatment-experienced group, 24 (32%) were on first-line therapy, 34 (45%) were on second-line therapy and the remaining 17 (23%) were heavily treatment-experienced. No chronically infected drug-naive patients underwent resistance testing over the study period.

**Conclusions:** The use of resistance testing at St Mary's closely follows the BHIVA recommendations. The development of a local protocol will help ensure good practice continues.

## P3

### Factors influencing nevirapine plasma concentrations

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**Background:** Nevirapine (NVP) is extensively metabolised by the liver and there is concern about the development of hepatotoxicity in subjects receiving NVP. It has been suggested that high plasma NVP concentrations may predispose patients to the development of toxicity; recent data from the 2NN study comparing once and twice daily NVP possibly lends support to the role of drug concentrations in driving toxicity. In addition to dose regimen, factors such as body weight, sex and HCV co-infection need to be considered.

**Methods:** (1) A retrospective analysis was performed on peak (1–4 h) and trough (10–14 hours post dose) samples received by the Liverpool Therapeutic Drug Monitoring (TDM) Service for NVP quantification from adults receiving NVP at 200 mg twice a day. The relationship between plasma NVP and sex, weight and body mass index was investigated. (2) NVP concentrations in a heterogenous cohort of HIV+ patients were related to markers of hepatotoxicity, hepatitis C (HCV) co-infection, sex and weight.

**Results:** (1) TDM samples from females had a greater percentage of NVP trough concentrations 2× or 3× the target concentration of 3000 ng/ml (45% versus 25% and 21% versus 11%, females versus males). There was a correlation between peak NVP and weight ( $n=92$ ;  $P=0.009$ ). (2) Cohort patients showed a weak association between higher NVP concentrations and laboratory abnormalities. Subjects with  $\gamma$ -glutamyl transferase and/or alanine aminotransferase over the upper limit of normal had significantly higher NVP concentrations. HCV co-infection was significantly associated with higher NVP levels.

**Conclusions:** These data highlight some of the potential factors influencing NVP plasma concentrations.

## P4

### The UK HIV Drug Resistance Database

D Dunn, R Matthias and T Hill on behalf of the UK Collaborative Group on HIV Drug Resistance

**Background:** The UK HIV Drug Resistance Database is a collaboration between public-sector laboratories performing HIV resistance testing on patients, which aims to centralise the results of all tests performed as part of routine clinical care. Clinical data linked to the resistance test results are also collected.

**Methods:** Both resistance and clinical data are obtained from local databases where available; otherwise resistance data are manually entered from (anonymised) photocopies of the reports and clinical centres are asked to complete a standard proforma.

**Results:** By the end of January 2003, results on 5333 tests from over 30 centres had been entered into the database. The main reasons for testing, where this was recorded, were treatment failure (59%), starting antiretroviral therapy (ART) for first time (20%), re-starting ART after an interruption (11%) and seroconversion (7%). Of 5015 samples that were successfully sequenced, 1885 (38%) had no primary drug mutations, 2746 (55%) had at least one primary nucleoside reverse transcriptase inhibitor mutation, 1218 (24%) had at least one primary protease inhibitor mutation and 1762 (35%) had at least one primary non-nucleoside reverse transcriptase inhibitor mutation; 475 (9%) showed resistance to all three drug classes.

**Conclusions:** The UK HIV Drug Resistance Database is a rich resource that will enable: (1) insights into HIV drug resistance *in vivo*; (2) analysis of use/impact of resistance testing in clinical management; (3) surveillance for transmitted and secondary drug resistance; and (4) feedback of electronic data to participating centres for local analyses and audit.

## P5

## Lopinavir/ritonavir combined with indinavir at 400 mg twice a day: pharmacokinetics and pharmacodynamics in blood, cerebrospinal fluid (CSF) and semen

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**Background:** We hypothesised that adding indinavir (IDV) at 400 mg twice a day to lopinavir/ritonavir (LPV/RTV) would give therapeutic concentrations of both drugs in plasma and of IDV in CSF and semen. **Methods:** 10 HIV-1 +ve men on LPV/RTV participated in a prospective pharmacokinetic (PK) and pharmacodynamic study. Sampling was performed prior to and 2 weeks after adding IDV to stable regimens. Blood plasma (BP) was drawn at 0 hours and 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 10, 12 hours after drug. CSF and semen (SP) at 10-12 hours after drug. **Results:** 10 men provided BP for 0-12 hours PK determination. Six patients provided CSF and five SP samples. Baseline BP LPV PK parameters were within previously described ranges. All men had LPV CSF below the limit of detection (BLD), i.e. <10 ng/ml. Eight provided BP for the second 0-12 hours study. When co-dosed with IDV, the change in PK parameters for LPV from baseline were +9% (range -23% to +78%), +46% (-68%, +130%) and +20% (-36%, +102%) for maximum ( $C_{max}$ ), minimum ( $C_{min}$ ) concentrations and area under the curve ( $AUC_{0-12}$ ), respectively ( $P=0.32$ , 0.32 and 0.2; Wilcoxon signed rank). At visit 2, median IDV  $C_{max}$  was 3365 ng/ml (range 2130-5194),  $C_{min}$  293 ng/ml (14-766),  $T_{max}$  2.25 hours (1-3),  $AUC_{0-12}$  22,452 ng/ml per hour (11,243-33,661), half-life 2.8 hours (1.4-3.7); median CSF IDV 39 ng/ml (21-86); median SP IDV 592 ng/ml (96-983). 2/8 men with detectable VL in BP became BLD (<50 copies/ml) after IDV and 2/4 with low-level viraemia in SP (BPVL BLD) became BLD (<400 copies/ml) post IDV. All subjects had CSF VL BLD (<400 copies/ml) before and after IDV. **Conclusions:** IDV did not significantly alter median LPV PK parameters. IDV in BP ( $C_{min}$ ), CSF and semen was > $IC_{90}$  for wild-type in most samples.

## P6

## Phenotypic changes induced by antiretroviral therapy intervention during recent HIV-1 infection

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**Objectives:** To evaluate the effects of highly active antiretroviral therapy on the phenotype of T cells in recently infected patients.

**Methods:** 17 subjects with recent HIV-1 infection (RI) (viral exposure >180 days but less than 1 year) were recruited. Lymphocyte phenotype was assessed at baseline and weeks 4, 12, 24, 36 and 52 after antiretroviral therapy (ART). We assessed for naive/memory/effector (CD45RO/RA and CD27) changes, activation markers [CD38 and human leucocyte antigen (HLA)-DR], interleukin (IL)-2 receptors (CD25 and CD122) and co-stimulatory molecules (CD28 and CTLA-4), using four-colour flow cytometry. Lymphocyte counts and plasma viral load were also assessed.

**Results:** There was an increase in absolute CD4+ T-cell counts which was evident just 4 weeks post ART ( $P<0.01$ ). A decline was seen in the CD8+ T-cell subset ( $P<0.05$ ). No significant changes were seen in the CD45RA+CD27+ (naive) CD4+ and CD8+ T-cell compartments. There was a decrease in CD45RO+CD8+ memory T-cell subset ( $P<0.02$ ); however, this was paralleled by an increase in effector CD45RA+CD27-CD8+ T cells ( $P<0.005$ ). T-cell activation assessed by CD38 and HLA-DR expression was significantly reduced on both CD4+ and CD8+ T-cell subsets ( $P<0.02$  and  $P<0.005$ , respectively), which reflected the efficient arrest in viral replication seen by week 4 ( $P<0.01$ ). Co-stimulatory molecules CD28 and CTLA-4 expression did not change significantly and IL-2 receptors remained low throughout the study.

**Conclusion:** Initiation of ART during recent infection significantly reduces T-cell activation and induces effector CD8+CD45RA+CD27- T-cell formation. CD4+ and CD8+ T-cell numbers appeared to change towards values closer to normality.

## P7

## Surveillance of HIV drug resistance in the UK: a sentinel site study

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**Methods:** We established a surveillance programme for HIV drug resistance within the UK between the years 1998 and 2000, representing the years immediately following the introduction of triple combination antiretroviral therapy. Sentinel sites included large, medium-sized and small clinical centres.

**Results:** Of nearly 300 samples tested, from patients receiving HIV therapy with a viral load >2000 copies/ml, the majority had viruses with some degree of drug resistance. Overall resistance increased between 1998 and 1999, and fell again in 2000 (69% versus 88% versus 55%). However, major differences were observed between drug class, such that non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance rose dramatically over the period, in association with the introduction of this drug class in clinical practice. Further, an overall increase in prevalence of viruses with resistance to drugs within all three available classes of drugs was observed. Higher prevalences of drug resistance were observed in patients from smaller clinical centres. **Conclusions:** This is the first such sentinel surveillance dataset from the UK and is relevant to the increased transmission of HIV drug resistance observed over this period.

## P8

## The prevalence of the K65R mutation in HIV-1 reverse transcriptase in patients receiving tenofovir

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**Background:** *In vitro* data have shown that the K65R mutation in HIV-1 reverse transcriptase occurs rarely in the presence of tenofovir. We established its prevalence within patients receiving tenofovir and investigated the associated antiretroviral drug therapy.

**Methods:** Genotypes from the Chelsea and Westminster Hospital resistance database from October 2000 to October 2002 were analysed.

**Results:** K65R was identified in viruses from 20 of 1136 patients tested (1.76%). This is unchanged from the previously reported prevalence of K65R in tenofovir-naive individuals. 15 cases of K65R were seen out of 106 individuals failing tenofovir. Of these 15 cases, nine were receiving the same antiretroviral combination of abacavir/didanosine/tenofovir. A total of only 23 patients in the department had been given this combination during the same time period, making the prevalence of K65R in this group 39%.

**Conclusion:** The prevalence of K65R is unchanged with the advent of the use of tenofovir over a 2-year period. However, the specific combination of abacavir/didanosine/tenofovir was associated with a high prevalence of K65R, which may be due to all components of this regimen selecting for the development of this mutation.

## P9

## The impact of reducing didanosine dosage from 400 mg to 250 mg when combined with tenofovir

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**Background:** The co-administration of didanosine (DDI), and tenofovir may increase ddl concentrations by up to 60%, increasing the risk of toxicity. The aim of this study was to describe virological outcomes in patients in whom the dose of ddl was reduced from 400 mg to 250 mg following awareness of these findings.

**Methods:** 40 patients at the Royal Free Hospital have received both ddl and tenofovir. Of these, 22 have reduced their dose from 400 to 250 mg. Four additional patients started ddl at the reduced dose. HIV viral load has been measured at regular intervals before and after the dose reduction and the maximum viral load in the first 6 months after the dose reduction was considered as an outcome.

**Results:** Viral loads prior to the dose switch ranged from <50 to 750,000 (median 51) copies/ml. Viral loads in the first 6 months after the dose change were available for 20/22 patients and ranged from 50 to 750,000 (median 400) copies/ml. Eleven patients (55%) maintained levels <400 copies/ml, two (10%) experienced a decrease in viral load and the remaining seven (35%) experienced increases. In 6/7 of these cases, the patients were known to have stopped treatment totally. Viral load responses in the four patients who started ddl at the lower dose were generally good; all four experienced large decreases in viral load over the first few months of therapy.

**Conclusions:** Although a minority of patients experienced increases in the viral load after a reduction in ddl dose, many of these were known to have taken treatment breaks at the time. In the other patients, a reduction in the ddl dose from 400 to 250 mg did not appear to have a detrimental effect on virological control.

## P10

## The prevalence of hypophosphataemia in patients taking tenofovir

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**Background and methods:** Tenofovir (TDF), a nucleotide analogue, is structurally similar to adefovir, which can cause hypophosphataemia (HP). Although not a significantly reported adverse event in TDF trials, anecdotal cases of HP and Fanconi's syndrome have been described recently. Pending evaluation of this issue, all patients receiving TDF at this treatment centre are now routinely screened for serum phosphate (SP) levels and proteinuria/glycosuria.

**Results:** (at 14 February 2003)

No. on TDF	Time on TDF (months) range (median)	SP: no. ever abnormal (no. tested)
105	0-38 (8)	12 (45)

One patient developed symptomatic HP that resolved on discontinuation of TDF, and one patient who developed HP shortly after initiation of TDF had previously discontinued adefovir due to renal toxicity. Further data on the relationship of HP to time on TDF, outcome of HP, urinalysis and comparison with HIV +ve controls (both on and off highly active antiretroviral therapy) will be presented.

**Conclusions:** The excellent short-term tolerability of TDF has resulted in its widespread use, but as with all new agents, vigilance is required to identify longer-term and/or infrequent toxicities. While there appears to be a significant minority of TDF recipients who develop HP, the clinical value of routine monitoring of SP and urinalysis requires further evaluation.

## P11

## The association between nevirapine and abnormal liver function tests in a cohort setting

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**Aims:** Nevirapine (NVP) is known to cause hepatotoxicity in a proportion of patients who initiate highly active antiretroviral therapy (HAART). However, there have been suggestions that the association between abnormal liver function tests (LFTs) and NVP is often over-estimated. We investigated this relationship within a large cohort of non-nucleoside reverse transcriptase inhibitor (NNRTI)-treated patients.

**Methods:** All patients initiating an NVP-containing regimen since 1/99 were included. Those developing alanine aminotransferase (ALT) of >100 IU/ml or >2.5-fold change from baseline were identified. Patient records were used to identify the cause of abnormal LFTs. Statistical analysis of all antiretroviral-naïve patients starting HAART was done to identify the relative risks of NVP and other factors in the raised LFTs.

**Results:** 126/710 (18%) of patients who initiated an NVP-containing regimen had at least one ALT >100 IU/ml or 2.5x baseline. 30 (29.1%) had NVP-related toxicity and stopped the drug. Of these, 13 had hypersensitivity with rash and/or acute hepatitis and 17 had slowly rising LFTs on NVP. 21.4% stopped NVP for other reasons and 49.5% remain on NVP. The commonest reasons identified for abnormal LFTs other than NVP were other non-ARV medication (12.6%), intercurrent illness including metabolic syndrome (12.6%), chronic hepatitis B (9.7%), chronic hepatitis C (8.7%) and alcohol (8.7%). There were no significant differences between those with and without NVP toxicity in hepatitis B or C or antiretroviral-naïve status. There were no fatalities as a result of NVP.

**Conclusions:** Despite a high incidence (18%) of patients on NVP with an ALT >100 IU/ml or 2.5x baseline, only 29% of these were directly related to NVP and led to drug cessation. Most abnormal transaminases on NVP (71%) were due to other causes or were isolated readings.

Caution s

## P12

## Gout and HIV: a new facet of the fat redistribution syndrome?

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**Background:** Since 1996 there has been one case report of gout in an HIV+ patient. Over a 2-year period, 18 cases of gout were seen at a single HIV centre.

**Methods:** All cases of hyperuricaemia attending the Mortimer Market Centre between 1 February 2000 and 1 February 2002 were identified from the hospital database. Notes were scrutinised using a standardised proforma, to identify predisposing factors for gout, HIV clinical history, lipodystrophy and laboratory markers.

**Results:** All 18 cases had clinical manifestations of gout and elevated serum urate (mean 686, range 428-1552). 12 had stage C disease and six stage B. Mean CD4 was 356 cells/μl (range 50-1100) and mean viral load (VL) 13,559 copies/ml (range below detection to 83,000). 16/18 were receiving highly active antiretroviral therapy (HAART) and had been on it for an average of 41 months (range 3-48). Eight had predisposing risk factors for gout (e.g. pyrazinamide therapy, haematological malignancy). 7/10 of the remainder were receiving a boosted protease inhibitor [ritonavir (RTV)/saquinavir (SQV) n=5, RTV/indinavir n=1, RTV/amprenavir n=1], had dyslipidaemia (mean triglycerides 6.1 mmol/l, range 4.2-8.8) and proven features of lipodystrophy. Patients with gout were significantly more likely to be taking boosted SQV than the remainder of the clinic attenders (50% versus 10%, P<0.00001).

**Conclusions:** We report a high level of gout in our HIV population from 2000 onwards, especially in patients receiving boosted protease inhibitors. Most of these patients had dyslipidaemia and clinical features of lipodystrophy. As gout is known to be associated with insulin resistance, atherosclerosis and visceral fat accumulation in the HIV-negative population, this suggests that gout may be another metabolic complication of HAART.

## P13

## Audit of adherence services provided by a specialist HIV clinic

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**Background:** The BHIVA/Medical Society for the Study of Venereal Diseases (MSSVD) guidelines on provision of adherence support to patients receiving antiretroviral therapy (ART) form the standard of care for adherence services in the UK. We audited the adherence services provided by a specialist HIV clinic in a large district general hospital against these guidelines.

**Methods:** A retrospective case-note review of HIV+ patients who attended the Mayday Hospital Genitourinary Medicine clinic was performed. Data recorded on an Excel spreadsheet included: which healthcare professional last reviewed the patient, whether adherence was raised as an issue, how adherence was measured, whether the pharmacist saw the patient on starting ART and whether the patient had had an adherence review with the pharmacist in the last 6 months.

**Results:** In 22% of patients adherence was raised as an issue and of these, 15% of patients had adherence measured. In 78% of patients adherence was not recorded as being raised by the doctor. 98% of measured adherence was by a mixture of patient self-report and provider estimates and 2% was by therapeutic drug monitoring. 55% of patients were referred to the pharmacist on initiation of ART and 29% of the patients had an adherence review with the pharmacist.

**Conclusions:** Although the BHIVA/MSSVD guidelines have not made any quantitative recommendations, adherence raised in 22% of cases would be considered low. Doctors were less likely to record or measure adherence than the pharmacist. The development of local adherence guidelines using a standardised tool for measuring and documenting adherence would further improve this.

## P14

## Clinical relevance of a programme to sustain adherence

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**Background:** Adherence is one of the most important factors in effective antiretroviral therapy. In March 2000 we started a project called SOS Therapy, to support adherence in HIV+ patients. Here we report an evaluation of the clinical effectiveness of this intervention.

**Methods:** A multidisciplinary team-based approach was used, focused on a trained tutor-nurse. From 3/2000 to 1/2003, 34 patients with a history or a high risk of insufficient adherence were recruited. 30 patients (group 1) were followed for at least 6 months. A control group of 30 was selected (group 2), with the same CDC disease stage, adherence level, follow-up period and risk factors. Group 2 received standard care, including genotyping, but not the support intervention. Viral load was used as the biological marker of improved adherence and to distinguish responders from non-responders.

**Results:** Two patients in group 1 and 10 in group 2 were progressors (opportunistic infections and other clinical manifestations of AIDS); 28 in group 1 and 20 in group 2 were non-progressors [relative risk (RR) =0.20; 0.05<RR<0.84]. All 12 progressors were non-responders (no viral load reduction or a reduction <1 log<sub>10</sub> copies/ml). 22/48 non-progressors were non-responders (five in group 1 and 17 in group 2) and 26 responders (reduction in viral load ≥1 log<sub>10</sub> copies/ml; 23 in group 1 and three in group 2; P=0.02).

**Conclusions:** This intervention to improve and sustain adherence in non-adherent patients may achieve a clinical benefit through a reduction in the viral load, which would probably be even more evident with a longer follow-up.

## P15

## Changes in symptom experience and interpretation over time: effects on adherence

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**Aim:** To examine changes in symptom experiences over time in relation to adherence.

**Methods:** As part of a prospective study, consecutive patients (n=65) completed validated questionnaires assessing the type and severity of symptoms they attributed to HIV and highly active antiretroviral therapy (HAART), perceptions of HIV and HAART, depression, anxiety and adherence. Assessments were completed before starting HAART (T0), after 1 month (T1) and after 6 months (T2).

**Results:** The number of people reporting low adherence (taking <95% of doses as prescribed) increased from 15.4% at T1 to 29.2% at T2 (P<0.01). There was an improvement in HIV-related symptoms over time. At T0, 86.2% of participants reported one or more moderate-severe symptom attributed to HIV, compared with 60% at T2, while the mean number of moderate-severe HIV-related symptoms decreased from 5.3 at T0 to 3.3 at T2 (P<0.01). Those whose symptoms improved between T0 and T2 reported higher adherence at T2 (P<0.05). The number of people reporting moderate to severe HAART side effects also decreased from 1 month (71.9%) to 6 months (56.9%), while the mean number of HAART-related side effects decreased from 4.0 at T1 to 3.2 at T2 (P<0.05). However, a quarter of participants indicated that their side effects had worsened and this was related to lower adherence at T2 (P<0.05). Perceiving a lack of improvement in HIV-related symptoms or worsening of HAART side effects was associated with more negative views of HIV and HAART and a poorer psychological profile at T2.

**Conclusions:** These findings have implications for the continued monitoring of symptoms attributed to HIV and aggressive treatment of HAART side effects to ensure that adherence is optimised and maintained over time.

## P16

## What is the future of HIV prevention?

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**Background:** Rising HIV infection rates both in the UK and internationally point to the ongoing critical challenge of HIV prevention: how to reduce the rate of new infections in target populations? The National AIDS Trust (NAT) has been analysing new HIV-prevention options on the horizon, in light of existing HIV-prevention methodologies.

**Methods:** HIV prevention is best understood in its widest context. NAT positions new HIV-prevention options as part of its list of nine essential features of an effective national HIV-prevention plan. It considers how behaviour change and condom models fit into that picture, as what is required to have the nine essential features in place. The breadth of the UK's HIV prevention response will be examined, particularly as it relates to gay men and the UK's African communities, and this will be compared and contrasted with global HIV-prevention challenges.

**Results:** This paper will explore what needs to be in place, both now and into the future, for an effective and robust national HIV prevention plan. Fundamental prevention methodologies like condom-oriented interventions will be critiqued. The impact and the meaning of new HIV-prevention technologies will be discussed, alongside the expansion of existing HIV-prevention methodologies. Is the HIV-prevention workforce in the UK ready to grapple with debates about HIV vaccines and microbicides? What will it take to get an effective vaccine or microbicide in place and accessible both here in the UK and globally?

**Conclusion:** Through examining the nine essential feature of effective HIV prevention, gaps in the UK response will be identified, and an advocacy agenda for the future of HIV prevention in the UK will be proposed.

## P17

## HIV-1 infection among black Caribbeans in southeast London

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**Background:** The high rates of sexually transmitted infections among black Caribbeans (BCs) in the UK has raised concerns about the potential for increasing HIV transmission. The number of new HIV diagnoses among BCs in the UK has increased almost sixfold since 1995. To date, no studies have focused on HIV in this population.

**Methods:** Demographic, clinical and laboratory data were collected on 169 HIV-1-infected BC patients registered at King's College Hospital. 42 were subtyped using an in-house enzyme immunoassay, of whom 29 have had *env* sequencing.

**Results:** 121 BCs (72%) were male, 56 of whom (46%) were homosexual. 41/48 (85%) women had heterosexually acquired infection. Of 137 with known country of birth, 73 (53%) were born in Jamaica, 53 (39%) in the UK and 11 (8%) elsewhere in the Caribbean. The median age at HIV diagnosis was 31.5 years (IQR 25.9–37.5), and the median CD4 count and viral load at presentation were 316 cells/ $\mu$ l (IQR 161–472) and 14,463 copies/ml (IQR 2,565–55,232), respectively. 18 (11%) had an AIDS diagnosis at presentation. The CD4 count at presentation among BCs was similar to that among our white patients (312 cells/ $\mu$ l,  $P=0.7$ ) but higher than that among our black African patients (227 cells/ $\mu$ l,  $P<0.05$ ). 57.5% were infected with subtype B, and this was strongly associated with homosexually acquired infection (60% versus 23%,  $P<0.05$ ). The non-B subtypes include five subtype C (four born UK, one born Jamaica), 2 A (one UK, one Jamaica), two D (one UK, one Jamaica), one F (Jamaica), one H (Trinidad and Tobago), one CRF02\_AG (UK) and two B/C mosaics (UK).

**Conclusions:** Non-B subtypes were common among our population. In-depth studies to gain insights into the emerging HIV epidemic among black Caribbeans in the UK are urgently needed.

## P18

## HIV resource use in secondary care: a model designed to support NHS resource planning

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**Aims:** Recent NHS changes have resulted in devolution of the commissioning and funding of HIV treatment and care to Primary Care Trusts. This pilot aimed to assist HIV commissioning using a planning model to forecast secondary care resources required by the local population over 3 years.

**Methods:** An Excel model was constructed, with advice from primary and secondary care focus groups. The model was designed to assess the requirement for clinician and nurse visits, diagnostic and monitoring tests. Drug budget data were not covered. The model was populated with national level data from literature, national audits and BHIVA guidelines as the standard of care. Local data can be input to reflect more accurately the local population, its growth and the resultant impact on resource use. Scenario-based sensitivity analyses were carried out to highlight key drivers of resource use. The model was piloted in 10 locations in the UK to HIV healthcare professionals and commissioners.

**Results:** Key drivers of total resource use were resources used per patient, population size and proportion of new versus current patients. In areas with rapid growth the model highlighted future resource requirements, for example, for consultant and adherence support to continue delivering the local standard care. The model will be developed during 2003 to include more detailed analyses of resource and population requirements.

**Conclusions:** The model was most useful in areas with limited data sources or rapid population growth. It can be used as a tool to identify resources required for current and future populations.

## P19

## Emerging patterns of HIV transmission associated with experiences of torture and trauma in African women in East London

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**Background:** Newham has one of the highest populations of people with HIV in the UK. Nationally, there are now almost twice as many women diagnosed with HIV than men, a pattern, which is reflected in Newham. The majority are asylum-seekers and refugees from sub-Saharan Africa. Approximately 80% of refugees worldwide are women and children and 50% of these women have experienced rape by soldiers and police officers. As a result of this, many asylum-seekers arrive in the UK with experiences of loss, persecution and torture (involving violence/rape).

**Case reports:** We will present medical and psychology case reports that illustrate the emerging pattern of HIV transmission associated with histories of torture (involving rape) and trauma in African women in East London. We will describe the problems encountered when caring for such women and the model of care developed to meet these challenges.

**Discussion:** Women who have undisclosed histories of torture and trauma associated with an HIV-positive diagnosis have reported feeling re-traumatised at the point of diagnosis of HIV because of this association. Language barriers coupled with the distressing nature of these experiences often result in non-disclosure to medical professionals and necessitate referral to the clinical psychologist. For those with language difficulties, the Health Advocacy service offers invaluable support.

**Conclusions:** Clinical management of patients presenting with high levels of distress (where the underlying factors are unclear) presents challenges and can impact on care provided, not only in terms of the process of engagement with the medical care system, but also with regard to adherence, disclosure, sexual and mental health.

## P20

## Risk behaviour and the meaning of 'resistance' in a sample of HIV positive Africans accessing services in central London: clinicians be aware

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**Background:** The Padare project aimed to assess risk knowledge, attitudes and behaviour in a sample of HIV-positive people from London's migrant African communities.

**Methods:** A self-report questionnaire was distributed within two HIV clinics and seven HIV support agencies in central London; domains of questions covered demographics, HIV knowledge and attitudes, risk behaviour, service use, disclosure, sexually transmitted infections, reproduction and sexual dysfunction.

**Results:** 214 HIV-positive participants returned questionnaires. Of the 74% who reported penetrative sex in the previous month, 40% reported either occasional or no condom use. 61% reported having had unprotected sex with one or more partners in the previous year. Only 18% were sure that they knew what was meant by 'drug resistance'. 20% believed that or were unsure whether 'resistance' meant that they could not transmit HIV to their sexual partners. 16% claimed they had been told they had developed resistance, with another 8% unsure whether they had been told this. 45% of the sexually active participants who had been told they had resistance reported inconsistent or no condom use in the previous month.

**Conclusions:** This sample of HIV-positive African migrants report significant levels of risk behaviour and misinformation regarding HIV and 'resistance'. Clinicians and other service providers must take care when discussing 'resistance' with these patients.

## P21

## Bridging the gap between paediatric and adult HIV services

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**Background:** HIV-associated stigma, issues surrounding new sexual opportunities and the potential or actual loss of lifetime carers add to the complicating factors faced by HIV-positive adolescents transferring care. Neither a simple transfer to adult services nor allowing adolescents to 'drop out' of medical care is considered acceptable care for young people with HIV. This poster discusses the transition of care from paediatric to adult services and the need to develop adolescent-specific services.

**Methods:** Semi-structured interviews explored the experiences of seven adolescents who had undergone the transition between paediatric and adult HIV outpatient care services.

**Results:** The involvement of adult service providers early on in the preparation for transition was considered beneficial. Some participants found the transition 'easy' whereas others had concerns, such as co-ordination of haemophiliac and HIV care, which possibly delayed their transition. Some were not prepared for the adult and predominantly gay population. The benefits of transition included the sense of independence, the shift in responsibility to the adolescent and satisfaction in being treated as an adult. For those with a strong paediatric staff rapport, a sense of loss was expressed.

**Conclusions:** This study supports the need for effective transition policies and the development of adolescent-specific models of care that facilitate continuity between paediatric and adult services.

## P22

## HIV prevalence in pregnant women in North Thames: 1998–2001

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**Objective:** To describe trends in the prevalence of HIV in an ethnically diverse population of pregnant women.

**Methods:** Data on parental country of birth from national birth registration records were linked to neonatal dried blood spot samples routinely collected for neonatal screening in the North Thames region between 1998 and 2001. Identifiers were subsequently irreversibly deleted prior to establishing maternal HIV status by testing the neonatal samples.

**Results:** The prevalence of maternal HIV infection in pregnant women was estimated on the basis of 394,862 newborn dried blood spots; 771 (0.19%) were seropositive. There were 149, 159, 204 and 259 positive samples each year, an overall significant increasing trend. The highest prevalence of HIV (1.96%) was in women born in sub-Saharan Africa (SSA) and the lowest (0.03%) in women born in the UK.

**Conclusions:** There was no significant rise in HIV prevalence in women born outside SSA. Over 90% of children at risk of vertical transmission of HIV had at least one parent born abroad.

## P23

## Uptake of HIV testing in patients with a confirmed sexually transmitted infection

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**Background:** Sexually transmitted infections (STIs) other than HIV have been shown to facilitate transmission of HIV by acting as cofactors. Hence, patients confirmed with a STI should be targeted to test for HIV. **Methods:** After introducing clinic changes following an audit in 1999, a re-audit of patients attending for a sexual health screen in July 2002 compared the uptake of HIV testing in those confirmed with an STI (case group) to those with a negative STI screen (control group). The changes comprised nurse-led asymptomatic screening, routine HIV testing in place of an opt in policy, discontinuing pre-HIV-test counselling in low-risk patients and the ability to access HIV test results by post. Age, diagnosis, sex, ethnicity, sexuality and HIV testing data were collected on 574 patients (286 cases and 288 controls).

**Results:** Uptake of HIV testing overall and in the case and control groups was 57%, 45% and 68%, respectively, showing significant statistical improvements since the 1999 audit (18.6%, 14% and 33%, respectively).

**Conclusions:** The clinic interventions increased HIV testing in patients attending the genitourinary clinic, including those confirmed with an STI. These figures are in keeping with sexual health strategy targets.

## P24

## Sexual functioning in HIV+ women

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**Background:** Few studies have examined sexual functioning in women living with HIV. This study investigated: (1) current levels of sexual activity and enjoyment; (2) safer sex; (3) other factors that may affect sexual behaviour and satisfaction.

**Methods:** 82 HIV+ women completed questionnaire packs including demographics, information about relationships, sexual behaviour, safer sex, the Hospital Anxiety and Depression Scale (HADS) and the Golombok Rust Inventory of Sexual Satisfaction (GRISS).

**Results:** 28% of women reported no sexual partners since diagnosis (mean time diagnosed 69 months, range 4–191). Time since diagnosis was not associated with having had a sexual partner. Of the 59% who had a current sexual partner, 75% reported intercourse in the past month. Of these, 70% reported always or usually using condoms. The most prevalent GRISS subscales were infrequency of sex (84%), avoidance (84%), non-communication (69%) and dysfunction (60%). Endorsement of HIV-impaired sexual enjoyment was associated with reduced sexual frequency ( $P=0.006$ ) and sexual dysfunction ( $P=0.042$ ). Sexual dissatisfaction was associated with infrequency of sex ( $P=0.037$ ), avoidance ( $P=0.02$ ) and non-communication ( $P=0.032$ ). Overall, 54% and 35% of women reported clinically significant levels of anxiety and depression, respectively. Among the sexually active, depression was associated with avoidance of sex and higher total GRISS scores ( $P=0.006$  and  $P=0.042$ ). There was a trend between reduced condom use and higher levels of depression and anxiety ( $P=0.09$  and  $P=0.06$ , respectively).

**Conclusions:** Sexual difficulties, including abstinence, were prevalent in this sample, indicating the potential for interventions addressing the psychosexual needs of HIV+ women and their partners.

## P25

## Improving sexual health care access in the HIV outpatient setting: a multipractitioner approach

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**Background:** In 1997, the Bloomsbury HIV clinic improved the standard doctor-led screening for sexually transmitted infections (STIs) by introducing a nurse-led walk-in STI screening service. However, this service was mainly used by those who perceived they had an acute infection. To encourage asymptomatic patients to be more pro-active about their sexual health and to cope with the increasing demand for screening, a further appointment clinic was introduced in July 2002, led by a nurse consultant.

**Methods:** Data were collected prospectively on all HIV-positive patients attending sexual health services between 1 July 2002 and 31 January 2003.

**Results:**

	Doctor led (%)	Nurse led (%)	Nurse consultant led (%)
Total screened 1/7/02-1/1/03	196 (28)	265 (38)	244 (35)
Symptomatic at presentation	99 (51)	101 (38)	86 (35)
Diagnosis: Gonorrhoea	8 (4)	30 (11)	15 (6)
Chlamydia	4 (2)	15 (6)	14 (6)
NGU	21 (11)	25 (9)	25 (10)
Syphilis	12 (6)	4 (2)	5 (2)

NGU, non-gonococcal urethritis.

**Conclusions:** Offering a multitiered sexual health service within HIV outpatient clinic allows a high level of patient access, retains essential sexual health skills for all staff and distributes the ever-increasing workload among all practitioners.

## P26

## Increasing syphilis surveillance in an HIV clinic in response to the current outbreak in Manchester

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**Introduction:** During the recent syphilis outbreak in Manchester, North Manchester General Hospital (NMGH) introduced serological tests for syphilis (STS) into the HIV outpatient clinics. We evaluated the uptake of such tests, the number of new cases detected and the outcome in each case.

**Methods:** Details of the STSs from October 2001 to October 2002 were analysed. The case notes of those with positive results were reviewed to establish the diagnosis and the management. The number of HIV viral load tests requested by the department during the same period was a surrogate for the number of routine blood tests performed in the clinic.

**Results:** There were 3127 HIV viral load tests performed and 1338 STS, a 43% uptake rate. 77 patients had positive STSs and in 75 cases the notes were available for review. There were 31 cases of early syphilis (primary, secondary or early latent), six of late latent disease, 37 old treated infections and one false-positive. Of the 74 patients with positive STSs, 33 (45%) were referred to genitourinary medicine (GUM). Of the 41 not referred to GUM, 20 had early infection and were treated, 16 had old treated infection and five were untreated.

**Conclusions:** The introduction of routine STSs to the HIV clinics has resulted in the new diagnosis of a significant number of syphilis infections and has proved a worthwhile intervention. The increased uptake of STSs from the current 45% would result in the detection of additional cases and we recommend that patients with syphilis should be referred to GUM for further management.

## P27

## Sex and relationships for HIV+ women

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**Background:** There is little available research on sexual relationships in HIV+ women other than within risk behaviour paradigms. Increased life expectancy with the advent of HIV combination therapy may increase the opportunity for women to develop sexual relationships.

**Method:** In this study, we investigated sexual functioning in HIV+ women. As part of a two-armed study collecting quantitative ( $n=82$ ) and qualitative data, 21 semi-structured interviews were carried out with HIV+ heterosexual women attending two London clinics. Verbatim transcripts were analysed using interpretative phenomenological analysis (Smith 1995).

**Results:** Dominant themes identified included: (1) difficulties with sexual functioning, in particular lowered libido and enjoyment, and reduced intimacy; (2) barriers to forming new relationships: fears of HIV disclosure, fears of infecting partners; (3) coping strategies included: relationship avoidance, having casual partners to avoid disclosure, seeking seroconcordant partners; (4) safer sex: personal dislike of condoms, lack of control, lack of suitable alternatives; (5) highly active antiretroviral therapy (HAART): no apparent impact on sexual activity and satisfaction; (6) reproductive choices: having fewer children, fear of infection, guilt, but more likely to continue unplanned pregnancies because of HAART; and (7) personal resources, strengths and accessing support.

**Conclusion:** Women are experiencing a range of sexual and relationship difficulties that appear to be relatively unchanged despite the advent of HAART. Focused psychosexual and couples work should be more readily available for HIV+ women and their partners.

## P28

## Cost of HIV treatment and CD4 counts in UK antiretroviral-naïve HIV-infected patients on highly active antiretroviral therapy (HAART), 1996–2000

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**Objective:** To assess the correlation between direct hospital and community HIV care costs and CD4 count for antiretroviral-naïve patients managed between 1 January 1996 and 31 December 2000.

**Method:** At 10 NPMS-HHC sites, 2-monthly mean CD4 counts were calculated and corresponding costs estimated by multiplying mean use of services by standard unit costs. Weighted drug costs were calculated for two nucleoside reverse transcriptase inhibitors (NRTIs) plus one non-nucleoside reverse transcriptase inhibitor (NNRTI), two NRTIs + one protease inhibitor (PI) and three NRTIs. Analyses were stratified by CDC stage and year of follow-up.

**Results:** 2076 patients started HAART, 52% with two NRTIs + one NNRTI, 39% two NRTIs + one PI, 5% a PI-boosted HAART regimen and the remainder with three NRTIs. Baseline median CD4 count was 170 cells/ $\mu$ l (IQR: 72–262). Median time from HIV-positive test to start of therapy was 741 days (IQR: 65–2295) and decreased significantly over time. The strongest correlation was observed between the mean CD4 count and average cost, independent of stage of HIV infection ( $r=-0.79$ ,  $P<0.0001$ ). The average cost of hospital care was £16,041 in HAART year 1 (range £11,691–£22,638), falling to £13,335 (£10,250–£17,978) by year 5. With community care, annual costs were £19,649 (£14,235–£27,563) in year 1 and £16,943 (£12,794–£22,904) in year 5.

**Conclusions:** Strong linear relationship were observed between the CD4 count and treatment costs. For those staying on first-line therapy, annual costs decreased. These data can be used to assess drug cost-efficacy or to assess resource requirements for new or existing services.

## P29

## HIV/AIDS related knowledge, attitude and practice among high school students in Eastern Nepal

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**Aims:** A study was conducted among 210 class 9 and 10 students in Eastern Nepal to assess their knowledge, attitude and practice regarding HIV/AIDS and to determine whether a school education programme would bring about statistically significant positive changes in knowledge of and attitudes to HIV/AIDS.

**Methods:** The tool for assessment was a closed-end questionnaire administered confidentially both before and after the education programme by graduate doctors.

**Results:** Knowledge of some aspects of the disease was quite low in the study group. 20.5% had prior knowledge of sexually transmitted disease and 6.7% knew that it was curable. 47.1% knew that infected blood could transmit HIV/AIDS and the causative agent was known to 23.8%. Similarly, 27.6% knew that sex with one reliable person could prevent the disease and 31.9% knew that there was no vaccine for the disease. The pre-education level of knowledge/positive attitude was >90% for five of the 27 questions tested.

**Conclusions:** This education programme brought about statistically significant positive changes in the knowledge of and attitudes to (16 of 27 questions tested) HIV/AIDS. There was a great sense of unwillingness to discuss information about sexual practices (31% response). 2.4% had had sexual intercourse.

## P30

## Abacavir hypersensitivity in HIV-positive patients: demonstration of the presence of drug-specific lymphocyte proliferation in vitro

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**Background:** Abacavir (ABC) is associated with hypersensitivity reactions in 5% of patients. This is thought to be immune-mediated. We used a lymphocyte proliferation assay to investigate the cellular basis of ABC hypersensitivity.

**Methods:** Peripheral blood monocytes (PBMCs) from 30 HIV-positive ABC hypersensitivity patients and 15 HIV-positive controls on ABC without hypersensitivity were incubated with ABC and some metabolites (aldehyde). Co-incubations with interleukin (IL)-2, IL-12, anti-IL-10 antibody, brefeldin A (BA) and concanamycin A (CMA) were also performed. A stimulation index (SI)  $\geq 2$  is taken as evidence of lymphocyte proliferation.

**Results:** Nine out of 30 of the ABC-hypersensitive patients showed PBMC proliferation in response to 2.5  $\mu\text{mol/l}$  ABC (median SI 3.4, range 2–56), while none of the control patients had an SI  $\geq 2$  ( $2P=0.007$ ; Fisher's exact test). One of the ABC-hypersensitive patients responded to both ABC and its reactive aldehyde generated *in situ* (SI 2.6), while another patient responded only to the aldehyde intermediate (SI 2.3).

**Conclusion:** PBMCs from a subset of ABC-hypersensitive patients proliferated following *in vitro* drug antigen stimulation. This provides the first direct laboratory evidence that ABC hypersensitivity is T-cell mediated. The support of GSK is acknowledged.

## P31

## Delayed-type immune restoration disease (IRD) after effective antiretroviral therapy (ART) is associated with lack of specific T-cell responses

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**Objectives:** To evaluate specific CD4 T-cell responses of HIV-1+ patients with delayed type IRD and compared these with asymptomatic clinical progressors (CPs) on therapy and uninfected controls (UCs). **Methods:** T-cell responses were assessed in nine HIV-1+ patients who presented with immune reconstitution-related illnesses and were subdivided into those receiving ART alone ( $n=5$ ) or ART and interleukin (IL)-2 plus granulocyte-macrophage colony-stimulating factor (GM-CSF;  $n=4$ ), and 10 successfully treated CPs who had no evidence of opportunistic infections.

**Results:** IRD patients presented with median nadir CD4 T-cell counts of 45 cells/ $\mu\text{l}$  (2–280) before ART initiation, which rose to 109 cells/ $\mu\text{l}$  (72.5–220) at admission with IRD, after initiation of ART. An undetectable viral load was seen in eight of nine patients during the same period. Weak CD4 T-cell responses were observed in 60% of IRD patients. This contrasts with CPs, with a median CD4 T-cell count of 76 cells/ $\mu\text{l}$  (25.5–90) at baseline, which rose to 249 cells/ $\mu\text{l}$  (187.5–303)  $\geq 6$  months post ART, when vigorous T-cell responses were seen in >80% of patients. Such responses were comparable to those observed in seronegative controls. Immunotherapy with IL-2 and GM-CSF induced strong pathogen-specific responses, which were paralleled by clinical remission of opportunistic infection.

**Conclusions:** IRD is associated with inadequate immune reconstitution rather than a vigorous specific T-cell response. Furthermore, concomitant administration of immunotherapy with effective ART may be associated with a more rapid immune recovery.

## P32

## Initiation of antiretroviral therapy (ART) during recent HIV-1 infection results in lower residual viral reservoirs and weak HIV-1 specific responses

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**Objective:** To assess the effects of ART in residual viral reservoirs and HIV-1 specific T-cell responses at different stages of infection.

**Methods:** We recruited 15 subjects with recent HIV-1 infection (RI) (viral exposure >180 days but <1 year), 10 with chronic infection (CI) (>1 year) and seven long-term non-progressors (LTNPs) (infected >5 years, therapy-naive and controlled viraemia). Cellular proviral (p) DNA was assessed with the Amplicor Monitor test (Roche Diagnostics, New Jersey, USA). Virus-specific responses were evaluated using intracellular interferon (IFN)- $\gamma$  staining and <sup>3</sup>H-thymidine incorporation.

**Results:** At baseline, the median HIV-1-pDNA was 297.4 (IQR 165–618) and 248 (IQR 144–470) HIV-1 copies/ $\mu\text{g}$  total DNA in RIs and CIs, respectively. Eight months post ART there was a decrease in pDNA in the RI group to 33 (IQR 21.4–104.7) HIV-1 copies/ $\mu\text{g}$  total DNA ( $P<0.05$ ), which was comparable to the pDNA levels seen in the LTNPs of 16 (IQR 7.4–99) HIV-1 copies/ $\mu\text{g}$  total DNA. Equal periods of ART in the CI group did not reduce the HIV-1 pDNA reservoir, which remained higher [152 (IQR 76–157)] than those seen in RIs and LTNPs ( $P<0.02$  for both). HIV-1-specific T-cell responses were absent in >85% of RI patients at baseline; however, 8 months after the initiation of ART, HIV-1-specific T-cell responses were seen in >40% of patients. CIs showed an even lower frequency and magnitude of HIV-1-specific T-cell responses. In contrast, LTNPs showed vigorous HIV-1-specific responses.

**Conclusions:** A reduction of HIV-1 pDNA to levels comparable to those seen in LTNPs is only apparent if therapy is initiated during the early stages of disease. The timing appears to be more sensitive for preserving HIV-1-specific T-cell responses.

## P33

## Effect of interleukin (IL)-2 therapy on T-cell phenotype, activation and IL-2 receptor expression

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**Background:** IL-2 causes sustained increases in CD4 T-cell counts in HIV-1-infected patients. Its effect on T-cell activation and IL-2 receptor expression is less well described.

**Methods:** HIV-1-infected patients were enrolled in a prospective, randomised, controlled trial in which, after 16 weeks of highly active antiretroviral therapy, they were randomised to receive IL-2 at 5 MU subcutaneously twice a day for 5 days for three 4-weekly cycles (group 1) or no IL-2 (group 2). Samples were taken for CD4 T-cell counts and viral load. Three-colour flow cytometry was performed on CD4 and CD8 T-cell subsets for naive (CD45RA) and memory cells (CD45RO), activation markers [human leucocyte antigen (HLA)-DR, CD38], co-stimulatory molecule (CD28) and the  $\alpha$ - and  $\beta$ -chain IL-2 receptors (CD25 and CD122, respectively). Receptor expression intensity was also measured. **Results:** Of 41 patients, 37 were randomised (19 to group 1) and 15 received 46 cycles of IL-2. At 65 weeks, the mean viral load was undetectable ( $P < 0.001$ ) and the mean CD4 T-cell count had risen significantly, but more in group 1 ( $P = 0.002$ ). Naive and memory CD4 and CD8 T cells increased further in the IL-2-treated group. The percentage CD8+/45RO+ cells increased further acutely in relation to IL-2 therapy. Percentage CD8+/HLA-DR+ and /CD38+ cells decreased over the study period. IL-2 cycle-related increases did not differ between groups at study end. The percentage of CD4+/CD25+ cells rose acutely with each IL-2 cycle and the intergroup difference was sustained ( $P = 0.04$ ). The percentage of CD4+/CD122+ and CD8+/CD122+ cells rose acutely in response to IL-2, but was not sustained. **Conclusions:** These data support the current approach to IL-2 therapy, with a prolonged lag between IL-2 induction and maintenance therapy.

## P34

## Kaposi's sarcoma (KS)-specific dendritic cells (DCs) respond to KS-associated antigens through CD91, the heat-shock protein (HSP) receptor

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**Background:** The diverse families of HSPs bind antigenic peptides and play major roles in immune responses via their receptor, CD91. We investigated the role of this pathway in HIV-1 seropositive patients with and without KS.

**Methods:** 12 patients with KS were matched for CD4 count and HIV-1 viral load to patients without KS. We compared the potentials of KS-DCs for stimulating allogeneic T cells and investigated the pathways used by tumour lysates, viral lysates and viral particles in their activation. In particular, we observed immune activation following HSP receptor blockade.

**Results:** Despite an impaired allostimulatory capacity, these DCs can prime the adaptive arm of the immune system in a saturable fashion following exposure to a wide and diverse variety of antigens. Such priming with disease-associated antigens is shown to occur through CD91, the HSP receptor, leading to phenotypic activation and stimulation of tetramer-positive CD8+ cytotoxic T cells. Additionally, we show that interferon-producing plasmacytoid DCs are significantly reduced in number in KS-positive compared with matched KS-negative HIV-1-infected subjects.

**Conclusions:** Infected and functionally impaired DCs can cross prime immune responses via CD91. These results have important implications for the aetiopathogenesis of KS and for the development and design of any compounds including antitumour and antiviral vaccines that are derived from cellular lysates.

## P35

## Limited thymic contribution to initial CD4 T-cell restoration during supplementation of HAART with interleukin (IL)-2 and/or Remune

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**Objective:** The thymus is proposed to play a role in CD4 reconstitution during HIV therapy. We determined the thymic function of HIV-1-infected patients during highly active antiretroviral therapy (HAART) alone or in conjunction with IL-2 and/or HIV-1 immunogen (Remune). **Method:** A T-cell receptor excision circles (TRECs) assay was used to quantify thymic output, as it is the best way of quantifying human thymic function. Patients were treated with HAART alone (group A), HAART+IL-2 (group B), HAART+IL-2+Remune (group C) or HAART+Remune (group D) over 70 weeks. Viral loads, CD4 and CD8 T-cell numbers were also assessed.

**Result:** TREC levels declined progressively in the first 35 weeks in patients receiving HAART+IL-2 and/or Remune then increased from week 50. Patients on HAART and HAART+Remune failed to show notable TREC changes throughout. Viral loads remained constant, while CD4 T-cell counts increased for the first 15 weeks of therapy in groups B and C. CD4 counts in groups A and D remained uniform throughout. CD8 T-cell numbers remained generally constant throughout in all groups.

**Conclusions:** Despite early increases in CD4 in the first 20 weeks of therapy in patients given IL-2, TREC levels declined. These results indicate little thymic contribution to CD4 restoration and suggest proliferation and/or redistribution as the mechanism responsible for CD4 rises as well as the TREC decline. Increases in CD4 and total T-cell numbers accompanied by rises in TRECs beginning at week 50 suggests a late contribution by the thymus to cell restoration.

## P36

Evaluation of interferon (IFN)- $\gamma$  T-cell responses during antiretroviral therapy (ART) in comparison with those of long-term non-progressors (LTNPs)

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**Background:** CD8 T-cell responses to HIV-1 are pivotal in the control of viral activity and disease. ART results in a loss of these responses, likely due to clearance of viral antigen. The extent of this loss and the factors that influence it are poorly known.

**Methods:** We evaluated the magnitude of IFN- $\gamma$  T-cell responses in LTNPs and in patients receiving ART with a wide range of viral loads and CD4 counts by ELISpot assay.

**Results:** Significant correlations were found between IFN- $\gamma$  T-cell responses and CD4 count when the viral load was detectable, for *pol* ( $P = 0.005$ ), *gag* ( $P = 0.061$ ) and *nef* ( $P = 0.085$ ). This relationship with the CD4 count existed exclusively for those with positive viral loads. No direct relationship was found between any response and viral load. LTNPs responded robustly to *gag*, *nef* or *pol* peptides. LTNPs also broadly responded to recombinant HIV-1 antigens.

**Conclusions:** LTNPs make high IFN- $\gamma$  responses to HIV-1 peptides and antigens. In contrast, ART-treated patients with undetectable viral loads demonstrate disparate IFN- $\gamma$  T-cell responses. When viraemia is positive, the magnitude of response appears to relate to that of the CD4 count.

## P37

Reduced interferon (IFN)- $\gamma$  production in HAART treated HIV-1+ individuals: partial recovery on growth hormone therapy

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**Background:** Natural killer (NK) cell numbers, proliferation and cytolytic activity are restored during highly active antiretroviral therapy (HAART). However, NK cell IFN- $\gamma$  production in response to interleukin (IL)-2 + IL-12 remains impaired. Our study was designed to determine whether IFN- $\gamma$  production could be recovered using IL-15, and also whether an increase in NK cell numbers in patients receiving human growth hormone + HAART would be reflected in additional recovery of function.

**Methods:** Peripheral blood mononuclear cells (PBMCs) were prepared from seven healthy controls, 12 HIV-1+ patients receiving HAART only and 12 receiving HAART before and after treatment with recombinant human growth hormone (rhGH, Serono). NK cells were tested for CD69 expression and IFN- $\gamma$  production in response to either IL-2 + IL-12 or IL-15 + IL-12, using flow cytometry.

**Results:** Stimulation with either IL-2 + IL-12 or IL-15 + IL-12 led to a comparable increase in CD69 expression in HAART-treated patients and controls. IL-15 + IL-12 stimulation did not lead to a recovery in NK cell IFN- $\gamma$  production in HAART-treated patients. rhGH therapy resulted in further increases in CD69 expression and IFN- $\gamma$  production compared with baseline.

**Conclusions:** NK cells from HAART-treated subjects may be defective in common pathways leading to IFN- $\gamma$  production. Human growth hormone therapy results in partial recovery of NK-cell function.

## P38

## Development of autologous neutralising antibodies following primary HIV infection

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**Background:** Early studies suggest that neutralising antibodies (NAbs) do not appear until several months after primary HIV infection (PHI), when the set-point viral load (VL) has been established. These studies mainly used laboratory expanded virus isolates, which may only measure cross-reactive antibodies (Abs).

**Objective:** To determine the role that antibodies play in the control of viraemia following PHI.

**Methods:** Serial serum samples collected from four homosexual men, participating in an ongoing study of PHI, were analysed for the presence of NAbs from the time of presentation up to 2.5 years post diagnosis. NAb detection was determined using recombinant virus containing patient-derived (autologous) envelopes (Envs). For comparative purposes, neutralising activity was also assayed against the laboratory strain IIIB. The level of Env-binding Abs was assessed by enzyme-linked immunosorbent assay (ELISA).

**Results:** The reactivity of patient serum to the autologous Envs was not substantially higher than the reactivity to control HIV IIIB Env. Low levels of anti-Env Abs were detected in the first month and continued to rise up to 7–12 months post PHI. Although early sera (1–3 months) were occasionally weakly neutralising, sustained and strong autologous neutralising activity was not observed until after 7–10 months in three out of the four subjects. In contrast, neutralisation of heterologous strains, with some sequence homology to autologous virus, remained weak but detectable up to 2.5 years post PHI.

**Conclusions:** We conclude that the presence of NAbs alone does not play a major role in determining the viral load set-point after PHI.

## P39

## Recent HIV infections in heterosexuals: Is STARHS applicable?

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**Background:** The use of the Serological Testing Algorithm for Recent HIV Seroconversion (STARHS) in determining HIV incidence in an HIV-1 subtype B-infected population has been well documented. However, its use in populations infected with non-B subtypes is incompletely validated. We describe a method that allows trends in recently acquired infections to be determined using the STARHS assay in a population largely infected with non-B subtypes, and where subtype is known.

**Methods:** Between 1997 and 2000, a total of 839 specimens from heterosexuals attending 15 sexually transmitted infection (STI) clinics were identified as anti-HIV-positive as part of the Unlinked Anonymous Prevalence Monitoring Programme. Of these, 797 were available for STARHS testing, and for 551 an HIV subtype was assigned. Regardless of subtype, a standardised optical density cut-off of 0.75 was used for determining an incident infection for STARHS.

**Results:** The proportion of recent infections among those infected with HIV subtype B fell from over 22% in 1997 to 3% in 2000, but remained relatively stable in those infected with a non-B subtype. There was an increase in recent infections among those classified as infected with a circulating recombinant form.

**Conclusions:** These results indicate continuing transmission of HIV in heterosexuals. Although an annual incidence cannot be calculated, the measurement of proportions of recent infection among those infected with non-B subtypes provides a means of monitoring current transmission patterns.

## P40

## HIV incidence remains constant in men who have sex with men (MSM) despite widespread use of effective antiretroviral therapy

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**Background:** The Serological Testing Algorithm for Recent HIV Seroconversion (STARHS) was applied to left-over anti-HIV-1 positive serum specimens from MSM attending 15 sexually transmitted infection (STI) clinics collaborating in an unlinked anonymous serosurvey (UAS).

**Methods:** STARHS was performed on anti-HIV-1-positive specimens as previously described, and HIV incidence rates were determined. Specimens from those with previously diagnosed HIV infection or AIDS were excluded. National data on the uptake of antiretroviral therapy, AIDS mortality and diagnoses of gonorrhoea in MSM were used to aid interpretation of the HIV incidence findings.

**Results:** Of 43,100 specimens from MSM, 3,565 were anti-HIV-1-positive; 1645 serum specimens were eligible and available for STARHS testing, and 317 were determined as coming from recently acquired infections. The overall estimated annual incidence ranged from 3.3% (1996) to 1.5% (1999), and was 2.45% in 2001, with a 3.1% incidence in London and 1.0% elsewhere.

**Conclusions:** Despite the increasingly effective use of antiretroviral therapy, we found no evidence of a significant decline in HIV incidence. Individuals whose HIV infection has been diagnosed should be less infectious, but 22% of infections in MSM remain undiagnosed, many with acute STIs, and this may be an important driver of the ongoing epidemic. Initiatives to diagnose and treat a greater proportion of HIV infections, including those with a suspected seroconversion illness, may be key to reducing the HIV incidence in MSM.

## P41

## Deaths in seroconverters without AIDS since the introduction of highly active antiretroviral therapy (HAART) in the UK

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**Objectives:** To describe characteristics, causes of death and antiretroviral exposure of HIV-infected persons who died since HAART became available in 1996.

**Methods:** We used data from a cohort of persons with well-estimated dates of HIV seroconversion (seroconverters): antibody-negative test results were available within 3 years of the antibody-positive dates, or else with laboratory evidence of acute infection. All persons were followed up annually through the clinic and records of those lost to follow-up were cross-matched with records of deaths in England and Wales (through ONS) and Scotland (through GRO) using soundex code and date of birth. Information on cause(s) of death were obtained from the clinic, where available, or else from ONS and GRO (only since 1 January 2001).

**Results:** Between 1 January 1996 and 31 December 2002, 166 of 1494 persons under follow-up died. For 145, information on AIDS status was available from their clinic within 6 months of death, 39 of whom had not received antiretroviral therapy. Of these 145, 90 had been diagnosed with AIDS. Causes of death for persons without AIDS (27 gay men, 19 injecting drug users, eight sex between men and women, one needlestick) were as follows: 12 suicide, overdose or accidental death, six hepatitis B or C infection, five non-AIDS defining cancers, four liver failure or alcoholism, three cardiovascular disease and three from other causes. For 20, the cause of death is not currently available. The last median CD4 count for 55 persons without an AIDS diagnosis was 282 cells/ $\mu$ l (IQR=143–440).

**Conclusions:** The role of hepatitis infection and non-AIDS-defining cancers as causes of death merits further research, particularly given the high CD4 levels at which deaths occur.

## P42

## Post-exposure prophylaxis (PEP) for HIV after sexual exposure: South Thames HIV Physicians survey

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**Background:** There are no UK guidelines on the use of PEP after possible sexual exposure to HIV (PEPSI). We surveyed HIV physicians in South London to assess their practice and opinion regarding PEPSI.

**Methods:** Questionnaires were sent to the 95 clinicians who manage HIV patients in 23 centres across the South Thames region.

**Results:** Responses were received from 22/95 (23%) of physicians but this represented 17 of the 23 centres in South Thames (74%). 41% of centres had developed their own guidelines for PEPSI. 94% of physicians would prescribe a regimen recommended in the UK Health Department's guidelines for occupational PEP. There was a wide variation in the length of time after the potential exposure to HIV that physicians were willing to offer PEPSI, and only three out of 19 physicians were willing to give PEP after 72 hours. Access for PEPSI was via Accident and Emergency Departments in 68%. Following a sexual assault, 81% of physicians would be willing to prescribe PEPSI to a male victim and 72% to a female victim. Data on willingness to prescribe PEPSI after consensual sex will be presented.

**Discussion:** The majority of physicians in South Thames were willing to prescribe PEPSI after high-risk sexual exposure to HIV but there was a wide variation in willingness to prescribe PEPSI in lower-risk situations or when the HIV status of the partner was unknown. In the absence of specific UK guidelines on sexual exposure, the majority would prescribe drugs recommended in 2000 by the UK Department of Health for occupational exposure to HIV. This questionnaire highlights the need for UK guidelines on PEPSI to guide management of these cases.

## P43

## Gender difference in HIV viral load levels: North American and European women have consistently lower viral loads

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**Background:** Meta-analysis has demonstrated that women have lower HIV RNA levels than men. We undertook an analysis to investigate the consistency of this effect by year and country.

**Methods:** Plasma HIV RNA and CD4 count data were analysed for patients attending HIV clinics in the USA (HIV Insight™ database) and the Netherlands [AIDS Therapy Evaluation Netherlands (ATHENA) database]. Generalised linear models were used to test for an effect of gender on viral load while adjusting for age, risk group, year of HIV diagnosis, year of measurement, use of highly active antiretroviral therapy (HAART) and CD4 count. Undetectable viral loads were assumed to equal the lower limit of detection (LLOD) or half the LLOD, to test the sensitivity of results.

**Results:** Viral load and CD4 counts from 13,258 patients were analysed (8681 from HIV Insight; 4577 from ATHENA; 16% women overall). Women were found to have significantly lower HIV RNA levels than men (HIV Insight™: 0.066 log<sub>10</sub> copies/ml difference,  $P < 0.001$ ; ATHENA: 0.092 log<sub>10</sub> copies/ml difference,  $P < 0.001$ ). The viral load difference did not differ by country ( $P = 0.283$ ). Results were not affected by assumptions regarding undetectable measurements and were consistent with previous findings from Canada, Italy and Switzerland.

**Conclusions:** Given antiretroviral treatment decisions may depend on the viral load, the finding that differences between men and women are consistent in different countries should provide a solid scientific basis for the development of gender-specific treatment guidelines, if appropriate.

## P44

## Gender differences in the rate of stopping highly active antiretroviral therapy (HAART)

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**Introduction:** With a continuing rise in HIV-infected women, gender differences in stopping HAART are becoming more important.

**Methods:** Gender differences in the rates of and reasons for stopping HAART in treatment-naïve, HIV-positive subjects starting a regimen with a protease inhibitor (PI) or non-nucleoside reverse transcriptase inhibitor (NNRTI) between 1996 and 2002 were examined. Comparisons were made between gender and within different treatment groups (one PI, one NNRTI, two PIs, >one NNRTI and one PI + one NNRTI).

**Results:** 785 patients met the inclusion criteria. 24% were female. They were primarily black African (63%), heterosexual (90%) and had a median age of 32 years, while men were mainly white (79%) and homosexual (75%) with a median age of 35 years. Men started HAART 8 months before women from first diagnosis ( $P = 0.05$ ) and at higher CD4 counts ( $P = 0.003$ ). Women were more likely to start on a single NNRTI-containing regime (47% versus 39%,  $P = 0.05$ ), and men with a single PI (50% versus 42%,  $P = 0.09$ ). The overall median time to stopping was 422 days [95% confidence interval (CI) = 308–695] in women and 675 days (549–776) in men ( $P = 0.2$ ). However, the median time to stopping a single or dual PI regimen was about half that of a single NNRTI. Women were 22%, 40% and 700% more likely to stop a single PI, a single NNRTI and dual PI regimen than men, respectively (95% CI = 0.7–2.1, 0.8–2.5, 1.5–42.8, respectively). There was no significant gender difference in the reasons for stopping, although differences were noted for men between treatment groups. Men on a PI were more likely to stop due to virological/immunological failure and gastrointestinal upset, and those on an NNRTI for central nervous system toxicity.

**Conclusions:** Median times to stopping/switching a first HAART regimen were quite long. Rates of stopping may be higher in women.

## P45

## Acute Hepatitis C (HCV) in a cohort of HIV-positive homosexual men: patient characteristics, risk factors and outcomes

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**Background:** Sexual transmission of HCV is low risk. We sought to determine sexual risk factors for the transmission of recently acquired HCV in a cohort of HIV positive homosexual men, and their treatment outcomes.

**Methods:** Acute HCV was defined by a documented negative hepatitis C antibody in the last 6 months together with a positive antibody test currently or a positive HCV RNA by reverse-transcriptase polymerase chain reaction (RT-PCR). Patients were treated as soon as possible (within 6 months of documented seroconversion) with pegylated interferon and ribavirin.

**Results:** 19 patients were identified with sexual transmission being the only risk factor. Nine patients had a history of a sexually transmitted infection (STD). Six patients spontaneously seroconverted (HCV RNA negative). Eight patients were commenced on HCV therapy, of which two discontinued (family illness). Five patients are awaiting HCV treatment. Preliminary results show that HCV treatment in acute infection is a viable option.

**Conclusions:** Unprotected anal intercourse, fisting, oral sex and a recent history of a STD were identified as sexual risk factors. We continue to monitor outcome to therapy.

## P46

## Prevalence of hepatitis C (HCV) in an ethnically diverse HIV infected cohort in South London

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**Background:** To determine the prevalence of HCV infection among an ethnically diverse cohort of HIV-infected patients in South London.

**Methods:** 1019 HIV infected patients who attended the King's College Hospital HIV clinic at least once between September 2000 and August 2002 were screened for HCV infection using an enzyme-linked immunosorbent assay (ELISA; Abbott HCV version 3.0). HCV-positive results were confirmed by polymerase chain reaction (PCR) or recombinant immunoblot assay. Demographic data were abstracted from the local HIV database. UK-wide estimate of total co-infected patients was calculated using sex and risk-factor distribution of current HIV-positive patients.

**Results:** The overall prevalence of HCV infection was 8.9%. A higher HCV prevalence was found among the 73 injecting drug users (82%) and 22 blood transfusion recipients (32%) than among 376 homosexual men (3.7%) or the patients with heterosexually acquired infection (2%). Patients born in southern Europe (14.4%) had a higher prevalence than those born in sub-Saharan Africa (2.3%), the Caribbean (2%) and elsewhere in the world (4.5%). Multivariable logistic regression analysis identified a history of injecting drug use [odds ratio (OR) =139.6, 95% confidence interval (CI) 48.7–400.2] and having received blood/blood products (OR=17.5, 95% CI 5.4–56.5) to be independently associated with increased prevalence of HCV co-infection. Gender, ethnic origin, sexual orientation and place of birth were not independently associated with an increased risk of HCV infection.

**Conclusions:** A moderate prevalence of HCV infection was observed in our HIV-1-infected cohort. This is likely to be much higher in cohorts with a greater representation of injecting drug users.

## P47

Pneumonia due to antibiotic-resistant *Streptococcus pneumoniae* (SP) and *Pseudomonas aeruginosa* (PA) is associated with advanced HIV infection in individuals receiving highly active antiretroviral therapy

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**Aims:** Highly active antiretroviral therapy (HAART) has revolutionised the prognosis of those with HIV. Studies comparing the impact on the incidence of pneumonia differ. We determined the incidence of antimicrobial resistance in SP- and PA-associated pneumonia in 5000 HIV-infected patients, with symptoms and clinical and/or radiological signs of pneumonia between May 1996 and May 2002, and from whom at least one positive isolate of SP or of PA was obtained.

**Results:** There was no significant difference in CD4 count or viral load in those with positive isolates of SP or of PA. There were no significant differences in CD4 count or viral load between fully sensitive isolates of SP compared with resistant isolates. There was a sustained rise in the number of drug-resistant isolates of SP. No significant differences were observed in the incidence of susceptible versus resistant SP in those on HAART and the HAART-naive. Acquisition of antibiotic-resistant strains of PA was associated with a low CD4 and higher viral load ( $P<0.05$ , Mann-Whitney U-test). Patients with advanced disease were more likely to acquire antibiotic-resistant strains of SP or PA. HAART did not confer added protection against resistant strains of SP if the patient had advanced HIV disease. There was a small, non-significant trend towards protection against resistant isolates of PA if the patient was on HAART. There was a crude incidence of 675/100,000 for SP, of which 24% had resistant isolates. The crude incidence for PA was 350/100,000; 18% had resistant isolates.

**Conclusions:** These findings have implications for the treatment of patients with serious infections given blind antibiotic treatment.

## P48

## Paradoxical reactions in TB patients with and without HIV co-infection

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**Background:** Transient worsening or new diagnoses of HIV-related tuberculosis (TB) have been reported following the introduction of highly active antiretroviral therapy (HAART) and have been likened to the paradoxical reactions (PRs) seen in HIV-negative subjects. We sought to describe the frequency of PRs in both HIV+ and HIV- subjects.

**Methods:** Patients diagnosed with TB/HIV from February 1997 to February 2002 (group 1) were compared with a TB+ HIV- population (group 2), excluding patients if the follow-up was <6 months. PR was defined as a worsening of TB symptoms or signs.

	HIV+ (n=54)	HIV- (n=51)
Median age	36 (24–62)	32 (16–69)
Median CD4 (cells/ $\mu$ l)	119 (2–831)	No values
Paradoxical reaction	28%	10%
Median time to PR (days)	See text	87 (23–157)

In patients on TB treatment, a PR was more common in those starting HAART within 6 weeks of TB diagnosis (five of 13 versus two of 18 at >6 weeks). In those who started HAART and then developed TB ( $n=13$ ), six developed PRs. Nine of 15 patients with a PR received steroids, with improvement at a median of 3 days (35 days if no steroids given). Three relapsed after stopping steroids. PRs were associated with disseminated disease in groups 1 and 2 (10 of 20 and four of five subjects, respectively).

**Conclusions:** Our data confirm that a PR is common in HIV/TB patients but is related to several distinct clinical scenarios.

## P49

## Occult hepatitis B virus infection in HIV-infected patients

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**Background:** Occult hepatitis B infection has been described by several authors in immunocompetent patients. However, there is very little information on its prevalence or significance in HIV-infected patients.

**Methods:** In order to determine the prevalence of occult hepatitis B virus (HBV) infection in an HIV-infected population and to identify any associations between occult HBV and immunosuppression, we retrospectively performed quantitative HBV polymerase chain reaction (PCR) on 50 plasma samples from hepatitis B surface antigen (HBsAg)-negative, hepatitis B core antibody (HBcAb)-positive, HIV antibody-positive patients. Patients treated with lamivudine or tenofovir in the previous 3 months were excluded.

**Results:** HBV DNA was detected in six of 50 patients (12%), with an HBV viral load ranging between 200 and >200,000 copies/ml. No significant relationships were found between the quantity of HBV detected and HIV viral load or CD4 count.

**Conclusions:** Occult HBV infection does occur in HIV-infected patients but does not seem to be related to the level of immunosuppression. It is hypothesised that this reflects HBV reactivation in this sample population. The significance of occult HBV in HIV-infected subjects remains uncertain and further study is required.

## P50

## Chemo-irradiation for anal squamous cell carcinoma in the era of highly active antiretroviral therapy (HAART)

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**Background:** Chemo-irradiation is the gold standard treatment for anal squamous cell carcinoma (SCC) in the immunocompetent. However, many clinicians have been wary of adopting this approach in HIV-seropositive people on account of the considerable toxicity described in the pre-HAART era.

**Methods:** In a retrospective study, we collected data on HIV-infected patients developing SCC in the post-HAART era (after 1995) and treated by chemo-irradiation in six UK oncology centres.

**Results:** Eighteen HIV-positive patients (17 homosexual males and one female) were treated with chemo-irradiation for anal SCC. At the time of anal SCC diagnosis, the mean age was 42.4 years (range 28–59), median CD4 cell count 240/μl (range 52–626), median HIV viral load 50 copies/ml (range 0–130,000), and 78% (14/18) were receiving HAART. The remainder had not required HAART. Chemo-irradiation was discontinued in one patient because of toxicity. There were six deaths (three due to recurrent/progressive anal SCC, two HIV-related, one pulmonary embolus) during a median follow-up of 504.4 days (range 205–2399). Overall survival was 100% 1 year from diagnosis and 47% after 2 years. There were no relapses more than 1 year after anal SCC diagnosis.

**Conclusions:** The toxicity and treatment outcome of chemo-irradiation for anal SCC in patients with concomitant HAART is similar to that of the non-HIV population. The stoma-sparing justification for chemo-irradiation applies to these patients.

## P51

## Incidence and outcome of HIV-related lung cancer in the era of highly active antiretroviral therapy (HAART)

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**Objectives:** Published series from the era before HAART suggests that people with HIV are at increased risk of developing lung cancer and have a worse outcome compared with HIV-negative controls. This study aimed to address the impact of HAART on the incidence and outcome of patients with HIV-related lung cancer (HL).

**Methods:** Patients with HL were identified from a prospective database of 8400 HIV-seropositive people. The incidence of HL in the pre- and post-HAART cohorts were compared with the age- and sex-matched population of southeast England. The treatment and outcome of the patients in the post-HAART era were each compared with two age- and stage-matched HIV-negative controls treated for lung cancer at the same hospital.

**Results:** The incidence of HL increased from 0.8 [95% confidence interval (CI) 0.2–3.2] /10,000 patient-years' follow-up in the pre-HAART era, to 6.7 (95% CI 3.1–13.9) /10,000 patient-years' follow-up in the post-HAART era. The age- and sex-matched incidence of lung cancer in southeast England was 0.75 (95% CI 0.63–0.87), suggesting that HL only occurred more frequently in the post-HAART era (relative risk 8.93, 95%CI 4.92–19.98). Patient characteristics were similar in the pre- and post-HAART eras, although the time interval between an HIV-positive test and developing HL was longer for post-HAART patients. The median survivals of the HIV-positive and HIV-negative groups were identical (4 months). Kaplan-Meier analysis found no difference in overall survival between cases and controls.

**Conclusions:** In this study, HL occurred more frequently in the post-HAART era compared with the general population. The outcome of this disease may have improved since the introduction of HAART.

## P52

## Natural history of high-grade anal intraepithelial neoplasia (HGAIN) in HIV-positive homosexual men

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**Background:** The progression rate of HGAIN to anal carcinoma (Ca) in this group is unknown. Screening has been recommended on the basis of unproven assumptions about progression and treatment efficacy.

**Method:** A prospective observational study of 26 subjects with HGAIN on biopsy (Bx). The subjects were monitored every 6 months with cytology and anoscopy for a total of 140 patient-years of observation. All but two were enrolled before beginning highly active antiretroviral therapy (HAART) and started HAART during the study.

**Results:** All had oncogenic human papillomavirus (HPV) and showed an average CD4 rise of 70 cells/μl. No cases of anal Ca were observed. Sequential smears showed a trend suggesting regression in 13/21 who had severe dyskaryosis at enrolment. Validation by repeat Bx in 16 patients (average follow-up 5 years, Bx results: 10 HGAIN, six negative/low-grade AIN) showed smears to have good specificity (100%) but poor sensitivity (60%) for HGAIN (smear series undercalled persistent HGAIN in four of the 10 cases).

**Conclusions:** The rate of progression to Ca is low over 5 years, but malignant change may take longer. Regression is not a rare event. Cytology is a specific but relatively insensitive tool to screen for HGAIN. More data about the progression rate and the evaluation of effective treatments are needed before the introduction of screening.

## P53

## Angiogenic correlates in the treatment of AIDS-related Kaposi's sarcoma (KS)

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**Purpose:** Angiogenesis is central to the aetiopathogenesis of KS. We measured angiogenic cytokines and growth factors in patients with KS during treatment with both antiretrovirals and second-line paclitaxel chemotherapy.

**Methods:** Cytokine levels were measured by enzyme-linked immunosorbent assay (ELISA) in 17 patients with KS who had progressed within 6 months of receiving liposomal anthracyclines and were treated with paclitaxel. Measurements were taken before progression and during and after completion of paclitaxel treatment.

**Results:** Plasma cytokine levels showed marked heterogeneity. Patients with AIDS Clinical Trials Group (ACTG) stage T1 disease had higher plasma vascular endothelial growth factor (VEGF) ( $P=0.05$ ) and lower plasma tumour necrosis factor (TNF)- $\alpha$  levels ( $P=0.05$ ) than patients with earlier-stage T0 KS. There was no correlation between plasma cytokines [basic fibroblast growth factor, VEGF, TNF- $\alpha$ , interleukin (IL)-2, IL-6, IL-12] and CD4, CD8 counts or HIV-1 viral load. There were no differences in cytokine levels in patients receiving protease inhibitors (PIs) compared with those on PI-sparing regimens. The objective response rate to paclitaxel was 71% (95% confidence interval 60–81) and response was associated with a fall in plasma IL-6 levels ( $P=0.04$ ) but no change in other cytokines. There were no significant changes in CD4, CD8, CD16/56, CD19 cell counts and HIV-1 viral loads during chemotherapy.

**Conclusions:** Angiogenic cytokines may correlate with KS disease extent. The response to paclitaxel therapy was correlated with a fall in plasma IL-6 levels, and data suggest that this correlates with KS herpesvirus viral load. The overall clinical response in KS was correlated poorly with known angiogenic cytokines.

## P54

## Histopathological correlates in Kaposi's sarcoma (KS)

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**Background:** Three histopathological stages of HIV-associated KS have been described: patch stage is the earliest; with subtle vascular changes, plaque stage demonstrates increased vascularity and spindle cell proliferation; and, finally, nodular stage comprises a tumour mass with increased pleomorphism of spindle cells.

**Methods:** Since the start of 2000, 70 patients have presented with newly diagnosed KS, including 41 with biopsy-proven disease. For 35 patients, biopsies were reviewed by a single histopathologist and categorised in one of the three histopathological stages.

**Results:** 14 (40%) patients had patch-stage, 14 (40%) plaque-stage and seven (20%) nodular-stage KS. The histopathological stage correlated with visceral involvement; three of seven patients with nodular KS had visceral disease compared with none of 14 with plaque and one of 14 with patch stage ( $\chi^2$ -test:  $P=0.012$ ). Patients with nodular-stage KS were also significantly less likely to be on highly active antiretroviral therapy (HAART) at the time of KS diagnosis: none of seven nodular, seven of 14 plaque and three of 14 patch stage ( $\chi^2$ -test:  $P=0.049$ ). In contrast, the histopathological stage did not correlate with CD4 cell count or racial group. The histopathological subtype was not a prognostic factor for overall survival, although this may reflect the small numbers and short follow-up.

**Conclusions:** Although the nodular subtype of KS is associated with visceral involvement, it is not correlated with lower CD4 cell counts. This suggests that factors other than host-cell-mediated immunity (e.g. inflammatory cytokines in the tumour microenvironment and human herpesvirus-8 strain variants) are associated with visceral dissemination of KS.

## P55

## A study comparing disease characteristics and treatment outcomes in HIV-positive and HIV-negative populations with anal human papillomavirus (HPV) disease attending an anoscopy clinic

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**Background:** An anoscopy service has been established since 1996, to diagnose and treat anal canal HPV disease. Previous data have suggested that HIV+ patients have more aggressive disease that responds less well to treatment.

**Methods:** Retrospective case-control study of HIV+ and HIV- subjects among those presenting with anal HPV disease.

**Results:** 108 patients attended the service. 47 were HIV+ (39 men, eight women; average age 33.5 years), 38 were HIV- (33 men, five women; average age 28.7 years) and 23 were untested. Men who had sex with men accounted for 36 HIV+ patients and 30 HIV- patients. 38 (80.9%) of the HIV+ cohort and 25 (65.8%) of the HIV- cohort had extensive perianal HPV disease involving three or more quadrants of the anal canal. 24 (51.1%) of the HIV+ cohort and 13 (34.2%) of the HIV- cohort had high-grade disease [anal intraepithelial neoplasia (AIN) 2 or AIN 3]. 20 (46.6%) of the HIV+ cohort and 22 (57.9%) of the HIV- cohort have become disease-free.

**Conclusions:** The presentation characteristics of anal HPV disease were similar in both the HIV+ and HIV- cohorts. Cure rates from anal HPV disease were similar in both HIV+ and HIV- cohorts. No significant differences were noted in disease presentation or cure rates in either cohort.

## P56

## Kaposi's sarcoma (KS) in the third millennium

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**Background:** With the introduction of highly active antiretroviral therapy (HAART) there has been a decline in the incidence and an improvement in outcome of HIV-associated KS.

**Methods:** The clinicopathological details and treatments for all patients with newly diagnosed KS were reviewed.

**Results:** 70 patients (67 male) have been diagnosed over 2 years since January 2000. The mean age at KS diagnosis was 42 years (range: 23–66) and the median interval between HIV diagnosis and developing KS was 1.3 years (range 0–17). Nine patients had visceral KS at presentation and the AIDS Clinical Trials Group (ACTG) stages were T0I0 42%, T1I0 30%, T0I1 12% and T1I1 15%. At the time of KS diagnosis, the median CD4 cell count was 212/ $\mu$ l (range 5–638) and 20 patients were on HAART, of whom 11 had undetectable HIV-1 viral loads. Of the 50 patients not on HAART at the time of KS diagnosis, 35 were treated with HAART alone. For these patients, the 1-year (additional) treatment-free survival was 91% and only five required systemic chemotherapy or radiotherapy for KS. Overall for the whole cohort, four patients died [two from *Pneumocystis jirovecii* pneumonia (PCP) and two from Castleman's disease]. The 2-year overall survival was 93% (95% confidence interval 86–100%).

**Conclusions:** The majority of patients who present with KS in the third millennium are either HAART-naïve or are failing HAART therapy. The mortality associated with KS is low, and even when visceral disease is present, this is not an adverse prognostic variable for survival. The high frequency of fatal Castleman's disease in this cohort reflects the well-known association with human herpesvirus-8 and the lack of effective therapies for HIV-associated Castleman's disease.

## P57

## Factors associated with virological rebound in those who initially control viraemia with antiretroviral therapy (ART)

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**Aim:** To investigate the factors associated with virological failure in a cohort of virologically suppressed HIV-positive patients receiving ART.

**Methods:** 618 patients at the Royal Free Hospital who achieved two consecutive viral loads <50 copies/ml while on ART were followed until the time of virological rebound (first of two consecutive viral loads >50 copies/ml). Possible factors associated with time to virological failure were assessed using survival methods.

**Results:** 22/618 (4%) and 65/618 (11%) of patients had experienced virological rebound by the end of the first and second year of follow-up, respectively. In a multivariable Cox model, every 100 cell/μl increase in the CD4 count from baseline resulted in a decrease in the hazard of having a virological rebound 4 weeks later of 26% [relative hazard (RH) 0.74; 95% confidence interval (CI) 0.62, 0.88]. Independently, for every 100 cell/μl increase in the CD8 count from baseline, the hazard of rebound increased by 7% (95% CI 1.03, 1.11). Also independently associated with time to virological failure were treatment history (first-line highly active ART regimen versus other, RH 0.50; 95% CI 0.29, 0.86) and the addition or switching of a protease inhibitor (PI), a non-nucleoside reverse transcriptase inhibitor (NNRTI) or abacavir (ABC) to the ART regimen (time-updated covariate, RH 1.66; 95% CI 0.99, 2.81).

**Discussion:** The change in CD4 count from the time of virological suppression could be used to predict when virological failure is likely to occur. Further information can be gained from the current CD8 count. Switching or adding a PI, an NNRTI or ABC increases the risk of virological failure and may be related to the reasons why patients switch.

## P58

## First-line highly active antiretroviral therapy (HAART) experiences at the Royal Free Hospital

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**Aim:** To describe antiretrovirals used in first-line HAART regimens and the reasons for drug discontinuations at the Royal Free Hospital

**Methods:** We studied antiretroviral-naïve patients who started HAART [three or more antiretrovirals including a protease inhibitor (PI), a non-nucleoside reverse transcriptase inhibitor (NNRTI) or abacavir (ABC)] from January 1996 onwards.

**Results:** Of 788 patients, 343 (44%) started with one PI + two nucleoside reverse transcriptase inhibitors (NRTIs); 303 (39%) with one NNRTI + two NRTIs; 61 (8%) with two PIs + two NRTIs and 81 (10%) with other regimens. The most common PIs and NNRTIs used were indinavir (17%), nelfinavir (20%), nevirapine (21%) and efavirenz (23%). The most common NRTI backbones used were stavudine (d4T) + lamivudine (3TC) (35%), and Combivir (33%). The median time to stopping the HAART 'anchor' (PI, NNRTI or ABC) for toxicity was 2.7 (95% confidence interval 2.1, 3.2) years. The median time to stopping at least one NRTI was 2.1 (1.8, 2.3) years. 22% of those on 3TC stopped for lipodystrophy, 12% on d4T stopped for peripheral neuropathy, 16% on efavirenz for central nervous system effects, and 8% on indinavir stopped due to raised liver function tests. Compared with one PI + two NRTIs, the relative hazard (RH) of stopping the anchor of those on one NNRTI + two NRTIs was 0.68 (0.51, 0.91), of those on two PIs + two NRTIs was 1.54 (1.01, 2.32) and for other regimens, 1.39 (0.92, 2.09). For every 100 CD4 cells/μl higher at the time of starting HAART, the RH of stopping the anchor increased by 6% (1.00, 1.23). Baseline viral load and demographic factors were not associated with time to discontinuation. **Conclusions:** Both patients and clinicians must evaluate likely toxicities as well as clinical efficacy when deciding on first-line HAART.

## P59

## Relationship between HIV-1 viral subtype, disease progression and response to antiretroviral therapy

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**Background:** To compare the rate of immunological progression prior to antiretroviral therapy (ART) and both the initial response to highly active antiretroviral therapy (HAART) and the virological rebound in patients infected with B compared with A, C and D non-B HIV-1 subtypes in an ethnically diverse population of HIV-infected patients in south London.

**Methods:** 867 HIV-1-infected patients from King's and St Thomas's Hospital HIV clinics were subtyped using an in-house enzyme immunoassay (EIA) based on the CDC peptide antigens to discriminate between B (47.5%) and non-B (34.5%) subtypes. 48 (5.5%) were of mixed reactivity and 108 (12.5%) were either non-reactive or below detectable limits. *env* gene sequencing was used to confirm the precise distribution of non-B subtypes and various mosaic strains. The rate of disease progression was determined using the rate of CD4 cell decline (first 3 years after diagnosis) after adjustment for initial CD4 count; response to ART was assessed on time to a viral load ≤50 copies/ml and time to virological rebound (≥250 copies/ml).

**Results:** 86.5% of non-B subtypes identified on EIA were confirmed on *env* sequencing. Analyses were based on 867 patients with complete data. 457 were B, and 317 were non-B subtype, of which 60 (19%) were A, 114 (36%) were C, 30 (9%) were D and 14 (4.4%) were infected with recombinant strains: the most common was CRF02\_AG (*n*=8). Most (85.2%) non-B and recombinant strains were in black Africans from sub-Saharan Africa (mostly Uganda, Zimbabwe, Nigeria, Ivory Coast and Ghana). There was a similar rate of pretreatment CD4 decline and similar time to viral undetectability for B, A, C and D subtypes.

## P60

## Exposure to antiretroviral therapy (ART) and its relationship to virological status: results from the UK CHIC Study

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**Background:** While the prognosis of HIV-infected individuals has improved since the introduction of highly active ART, there is concern that some patients may gradually exhaust all treatment options and subsequently experience virological failure.

**Methods:** We assessed the relationship between ART exposure and virological status in the UK Collaborative HIV Cohort (CHIC), a multicentre cohort containing data on 13,833 HIV+ve patients (82% male, 56% white, 63% homosexual) from six UK centres.

**Results:** By the end of 1996, 41% of the 7294 patients under follow-up had been exposed to ART [13% to protease inhibitors (PIs), 4% to non-nucleoside reverse transcriptase inhibitors (NNRTIs)], the patients had been exposed to up to nine drugs and <1% had been exposed to all three classes. By the end of 2001, 70% of the 9231 patients under follow-up had been exposed to ART (42% PIs, 50% NNRTIs), up to 15 drugs had been used and 26% had been exposed to all three classes (37% of those who had received ART). Median HIV-1 RNA levels decreased from 4.4 to 2.9 log<sub>10</sub> copies/ml over the same period. Median RNA levels remained constant in those who had not been treated but decreased from 4.3 to 2.0 log<sub>10</sub> in those who had received ART, and from 4.6 to 1.0 log<sub>10</sub> in those exposed to all three classes. Among this group, the proportion with >500 copies/ml decreased from 87% in 1996 to 32% in 2001.

**Conclusions:** This patient population has become increasingly treatment-experienced over time. While those exposed to all three classes of drugs show little evidence of failing treatment, a number of them do have detectable viral loads, highlighting the urgent need to develop new classes of drugs and drugs with limited cross-resistance.

## P61

### Trizivir and tenofovir as a simple salvage regimen

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**Objective:** To assess the use of the combination of trizivir and tenofovir in antiretroviral-experienced patients.

**Background:** Tenofovir shows significant activity against HIV when added to a stable background of highly active antiretroviral therapy, and treatment simplification to Trizivir maintains viral suppression in patients with viral loads below 400 copies/ml. Treatment simplification may improve adherence in patients who have failed successive regimens where compliance is thought to be an issue.

**Methods:** A retrospective analysis of Trizivir and tenofovir as salvage therapy in 50 patients having virologically failed at least one previous antiretroviral combination, identified via the clinic database. Viral load and CD4 counts were recorded at baseline and after 1, 3 and 6 months.

**Results:** The patients had a mean of four previous antiretroviral regimens, a median CD4 count of 152 cells/ $\mu$ l and viral load of 25,796 copies/ml at baseline. 88% had previously received lamivudine (mean duration 25 months), 64% zidovudine (ZDV; mean 20 months), 50% abacavir (ABC; mean 17 months) and 18% tenofovir (mean 6 months). After 6 months, 12 dropped out (eight lost to follow-up, one ABC reaction, one ZDV anaemia, two patient requests) and the mean CD4 increase (on treatment) was 120 cells/ $\mu$ l. 82% of patients (on treatment) achieved a 1  $\log_{10}$  drop in viral load and 73% had <50 copies/ml, at 6 months. The presence of the 184 mutation had no significant impact on viral load outcomes, but three or more thymidine analogue mutations (TAMs) were associated with a drop in the number of patients reaching viral load targets (80% versus 50% <50 copies/ml at 6 months). A raised mean corpuscular volume (MCV) (from ZDV) was taken as a crude measure of adherence to the regimen. More patients with a raised MCV (>100 fl) achieved an undetectable viral load than those with a 'normal' MCV (<100 fl) at each time point.

**Conclusions:** Salvage therapy with Trizivir/tenofovir is associated with an improved outcome in heavily pretreated patients with a resistance history of less than three TAMs. Compliance is still a problem.

## P62

### Factors associated with long-term CD4 cell rises among those receiving highly active antiretroviral therapy (HAART)

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**Aim:** To investigate the factors associated with rises in the CD4 cell count in a cohort of HIV-positive patients starting HAART.

**Methods:** 596 previously antiretroviral-naive patients starting HAART (at least three antiretrovirals) were followed for a median (IQR) of 2.5 (1.0, 4.0) years. Factors associated with changes in CD4 counts were analysed using generalised linear models.

**Results:** Of the 596 patients included in analyses, 75% were male, 56% were homosexual, 63% were white and the median (IQR) age on starting HAART was 25 (31, 41) years. The median baseline CD4 count and viral load (VL) were 194 (75, 314) cells/ $\mu$ l and 5.3 (4.8, 5.7)  $\log_{10}$  copies/ml. After 6, 12 and 24 months of HAART, the median increase in the CD4 count was 114, 181 and 248 cells/ $\mu$ l, respectively; 84%, 84% and 79% of the cohort had a VL of <400 copies/ml in the same time periods. On average, those who had a VL <400 copies/ml had an increase of 149 [95% confidence interval (CI) 125, 172] cells/ $\mu$ l greater than those who did not ( $P<0.0001$ ). For every 100 cells/ $\mu$ l higher baseline CD4 count, the increase in CD4 count while on HAART was 17 (6, 28) cells/ $\mu$ l lower ( $P=0.005$ ). Those of a white ethnicity were found to have greater changes in CD4 counts (average change 27 cells/ $\mu$ l; 95% CI 1, 54;  $P=0.04$ ). There is some evidence of a relationship between hepatitis C virus (HCV) status and change in CD4 count. Sex, risk group, age, HAART regimen and calendar year were not found to be associated with CD4 cell increases.

**Conclusions:** These findings emphasise the importance of maintaining virological suppression, and suggest other factors that also influence the long-term CD4 cell response.

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