

8th ANNUAL CONFERENCE OF THE BRITISH HIV ASSOCIATION [BHIVA]

19-21 April 2002

**UNIVERSITY OF YORK
YORK**

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1 Mountview Court, 310 Friern Barnet Lane, London N20 0LD
 Telephone: 020 8446 8898 Facsimile: 020 8446 9194
 E-mail: bhiva@bhiva.org Website: <http://www.bhiva.org>
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CME approved

ABSTRACTS

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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 2002 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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Dr Martin Fisher
Prof Sebastian Lucas
Dr Anton Pozniak
Dr Mike Youle

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1 Mountview Court, 310 Friern Barnet Lane, London N20 0LD

Tel: 020 8446 8898

Fax: 020 8446 9194

E-mail: bhiva@bhiva.org

Website: <http://www.bhiva.org>

RESEARCH PRESENTATIONS

Friday 19 April 2002

1400–1500 Research Presentations: Session 1: Epidemiology and STIs

Chair: **Prof Abdel Babiker**,
MRC Clinical Trials Unit

1400–1410 Abstract O1

Current status of patients who started highly active antiretroviral therapy (HAART) during 1996: a descriptive analysis of EuroSIDA participants
LA Paddam, Royal Free and University College Medical School, London

1410–1420 Abstract O2

Changes in factors associated with HIV survival in a European cohort of seroconverters
K Bhaskaran, MRC Clinical Trials Unit, London

1420–1430 Abstract O3

Changing population cost of HIV service provision in England, 1996–2004
EJ Beck, Chelsea & Westminster Hospital, London

1430–1440 Abstract O4

Reaching proposed targets in the National Sexual Health Strategy? HIV testing in genitourinary medicine (GUM) services
G Arthur, Royal Free and University College Medical School, London

1440–1450 Abstract O5

Acute sexually transmitted infections (STIs) in HIV-positive gay men: a case for enhanced screening in HIV treatment centres
J McSorley, Royal Free and University College Medical School, London

1450–1500 Abstract O6

Will a syphilis outbreak result in a second HIV epidemic?
S Hopkins, St James's Hospital, Dublin

1600–1700 Research Presentations: Session 2: Virology

Chair: **Dr Anne-Marie Geretti**,
King's College Hospital, London

1600–1610 Abstract O7

Transmission of drug-resistant virus in primary HIV-1 infection (PHI)
M Brady, Imperial College School of Medicine, London

1610–1620 Abstract O8

Multidrug-resistant HIV-1 in the semen of men with acute sexually transmitted infections
ST Sadiq, Royal Free and University College Medical School, London

1620–1630 Abstract O9

Sequential transmission of HIV-1 containing drug resistance-associated mutations
S Taylor, University of Birmingham

1630–1640 Abstract O10

Reservoirs of persistent HIV replication are stable in patients with an undetectable viral load
J Morlese, Chelsea & Westminster Hospital, London

1640–1650 Abstract O11

Evidence of low-level viral replication (<50 copies/mL) predicts eventual virological failure
Y Mazer, Chelsea & Westminster Hospital, London

1650–1700 Abstract O12

The prevalence and determinants of the K65R mutation in HIV reverse transcriptase in tenofovir-naïve patients
A Winston, Chelsea & Westminster Hospital, London

RESEARCH PRESENTATIONS

Saturday 20 April 2002

1030–1140 Research Presentations: Session 3: HAART and its challenges

Chair: **Dr Fiona Mulcahy,**
St James's Hospital, Dublin

1030–1040 Abstract O13

Intradermal poly(lactic acid) (Newfill) for treatment of severe HIV-associated facial lipoatrophy
JN Day, North Manchester General Hospital

1040–1050 Abstract O14

The reproducibility of three-dimensional (3-D) laser surface scans for the assessment of facial lipoatrophy
P Benn, Royal Free and University College Medical School, London

1050–1100 Abstract O15

Perinatal antiretroviral therapy: mono- versus combination-therapy and neonatal anaemia
CJ Foster, St Mary's Hospital, London

1100–1110 Abstract O16

Management of maternal HIV diagnosed late in pregnancy
F Lyons, St James's Hospital, Dublin

1110–1120 Abstract O17

Efavirenz and nevirapine: possible candidates for therapeutic drug monitoring (TDM) in clinical practice?
SE Gibbons, University of Liverpool

1120–1130 Abstract O18

Who is lost to follow-up from an HIV clinic and why?
LJ Haddow, Royal Free and University College Medical School, London

1130–1140 Abstract O19

Predicting non-adherence to highly active antiretroviral therapy (HAART): the role of patients' doubts about personal need and concerns about potential adverse effects
R Horne, University of Brighton

1140–1230 Research Presentations: Session 4: Immunology

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

1140–1150 Abstract O20

Impact of antiretroviral therapy on hepatitis B virus (HBV)-specific immune responses in HIV/HBV co-infected patients
RM Lascar, Royal Free and University College Medical School, London

1150–1200 Abstract O21

Preservation of HIV-1 specific T-cell responses is restricted to a very small subset of true non-progressors
NA Qazi, Chelsea & Westminster Hospital, London

1200–1210 Abstract O22

Effect of HIV-1 viral load at the time of antiretroviral therapy interruption on the duration of HIV-1-specific T-cell responses
C Burton, Chelsea & Westminster Hospital, London

1210–1220 Abstract O23

The potential for immune reconstitution in HIV-infected individuals receiving highly active antiretroviral therapy (HAART) who achieve virological suppression
C Smith, Royal Free and University College Medical School, London

1220–1230 Abstract O24

A randomised, open label, phase 1 trial of highly active antiretroviral therapy (HAART) combined with interleukin-2 (IL-2) and/or an inactivated gp120 depleted HIV-1 immunogen (Remune)
G Hardy, Imperial College School of Medicine, London

1600–1700 Research Presentations: Session 5: Opportunistic Infections and Tumours

Chair: **Dr Ian Williams,**
Royal Free and University College Medical School, London

1600–1610 Abstract O25

Multicentre cohort study of testicular cancer in men with HIV
T Powles, Chelsea & Westminster Hospital, London

1610–1620 Abstract O26

Cytomegalovirus (CMV) viraemia is an independent predictor of disease progression and death in patients receiving highly active antiretroviral therapy (HAART)
JR Deayton, Royal Free Hospital, London

1620–1630 Abstract O27

New retinal infections in HIV-positive patients in the post-highly active antiretroviral therapy (HAART) era
AA Obi, Chelsea & Westminster Hospital, London

1630–1640 Abstract O28

A prospective multicentre study of discontinuing prophylaxis for opportunistic infections: the STOPIT study
P Hay, St George's Hospital Medical School, London

1640–1650 Abstract O29

Progression rate of liver fibrosis in HIV and hepatitis C virus (HCV) co-infected patients
AH Mohsen, King's College Hospital, London

1650–1700 Abstract O30

HIV/Hepatitis C virus (HCV) co-infected population: early outcomes with pegylated interferon and ribavirin
S Hopkins, St James's Hospital, Dublin

01

Current status of patients who started highly active antiretroviral therapy (HAART) during 1996: a descriptive analysis of EuroSIDA participants

LA Paddam¹, AN Phillips¹, JD Lundgren², on behalf of EuroSIDA

¹Royal Free and University College Medical School, London, UK, and ²CHIP, Hvidovre, Denmark

Objectives: To describe current (most recent data since July 2000) clinical, immune and viral status of patients in EuroSIDA who started HAART, including protease inhibitors (PIs) or nonnucleoside reverse transcriptase inhibitors, during 1996.

Methods: Current outcome was classified by recording whether a new AIDS event or death occurred since the start of HAART, the absolute CD4 cell count, change in the CD4 count and HIV RNA status since July 2000.

Results: 2287 patients [median age 38 years, interquartile range (IQR) 33–46; 85% men] were identified as starting a HAART regimen in 1996. Most ($n=2195$, 96%) were on PI-containing regimens, but only 261 (11.4%) were therapy-naïve. The median CD4 cell count at entry was 101 cells/ μ L (IQR 37–202) and the viral load was 4.7 log₁₀ copies/mL (3.9–5.3) in those with data available ($n=1358$ and 868, respectively). The median follow-up to the last clinic visit (up to April 2001) was 49 months (42–53). 287 (12.5%) patients died during follow-up. Of 1476 patients alive and followed after 1 July 2000, 267 (18.1%) had had an AIDS event. Of 1442 patients who had a CD4 cell count available after July 2000 (excluding those who died), 727 (50.5%) had >350 cells/ μ L. The median CD4 count change in 882 patients with baseline counts was +240 cells/ μ L (IQR 102–393). 1389 patients had a viral load reading after July 2000, of whom 910 (65.5%) were undetectable (<2.7 log₁₀ copies/mL). The median viral load change in 547 patients with baseline viral load was –2.35 log₁₀ copies/mL (IQR –1.01 to –3.35). Updated results will be presented.

Conclusion: EuroSIDA patients who started HAART in 1996 seem to be doing well more than 4 years later, despite most being nucleoside reverse transcriptase inhibitor-experienced at the start of HAART.

02

Changes in factors associated with HIV survival in a European cohort of seroconverters

K Bhaskaran on behalf of CASCADE collaboration

MRC Clinical Trials Unit, London, UK

Objectives: To investigate changes in survival following HIV seroconversion (SC) and factors associated with survival in three calendar periods.

Methods: We analysed CASCADE data pooled from 20 SC cohorts in Europe and Australia, using Cox models allowing for late entry. We estimated the effect of calendar year on survival, adjusting for age at SC; exposure category; sex; presentation during acute infection and stratified by cohort. These cofactors were then further investigated in each of three calendar periods (to 1996, 1997–1998, 1999–2001).

Results: Of 7154 seroconverters, 1880 (26%) died. Compared with pre-1997, the relative risk (95% confidence interval [CI]) of death fell to 0.42 (0.35–0.51), 0.29 (0.23–0.36), 0.19 (0.15–0.25) and 0.21 (0.14–0.31) in 1997, 1998, 1999 and 2000/2001 respectively. Compared with those aged 16–24 years at SC, the relative risk of death (95% CI) for persons aged 45 or more fell to 1.37 (0.56–3.34) in 1999–2001 compared with 3.00 (2.45–3.67) in the period before 1997. Despite no apparent difference in survival by exposure category in the period before 1997, injecting drug users (IDUs) appeared to have a higher risk of death in 1997–1998 and 2000–2001 compared with those exposed through sex between men (relative risk and 95% CI= 2.27, 1.64–3.15 and 3.27, 2.03–5.27 respectively).

Conclusions: The initial increase in survival expectations has continued. However, IDUs appear to have worse survival in later calendar periods compared to other exposure groups. Age at SC seems to have less prognostic importance in more recent periods.

03

Changing population cost of HIV service provision in England, 1996–2004

EJ Beck¹, A Miners¹, G Kinghorn², S Mandalia¹, D Parmar¹, M Youle¹, M Fisher², J Innes², MA Johnson², AL Pozniak², A Tang², IG Williams², BG Gazzard¹ for the NPMS-HHC Steering Group

¹NPMS-HHC CAC, Chelsea & Westminster Hospital, ²NPMS-HHC sites

Aim: To estimate population cost of HIV service provision in England for 1996–2004.

Methods: Costs by Communicable Disease Surveillance Centre (CDSC) stage of HIV infection were estimated for the years 1996–1999. Multiplied by those using NHS services, direct population costs for different highly active antiretroviral therapy (HAART) regimens (PI, protease inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor) were estimated. Patients using services in 2000–2004 were projected and the population cost estimated for these years (1999/2000 prices).

Results: People using HIV services increased by 25% from 13,400 in 1996 to 17,981 in 1999; if all were treated with 2NRTIs+1NNRTI, direct population costs increased by 29% from £209 million (m) (£176m–£253m) to £266m (£226m–£321m). Indirect costs added £53m–£133m in 1999. From a *public sector* perspective, estimates ranged from 28% to 34% of direct costs, assuming a 100% loss in production; with 50% loss of production, estimates varied between 20% and 25%. From a *societal* perspective, estimates varied between 22% and 27%, assuming a 100% loss of production, and 13–16% of direct costs for 50% production loss. People projected to be using HIV services increased by 92% from 13,400 in 1996 to 25,667 in 2004; total costs estimates increased by 76% from £316m (£283m–£360m) in 1996 to £556m (£498m–£634m) in 2004 managed with 2NRTIs+1NNRTI. Regimens with 2NRTIs + 1PI or 2PIs provided higher population cost estimates. **Conclusions:** Increased resources are required to maintain current standards of care. New configurations of HIV service delivery should be explored in conjunction with measures to reduce HIV transmission.

04

Reaching proposed targets in the National Sexual Health Strategy? HIV testing in genitourinary (GUM) services

G Arthur¹, F Burns¹, C Mercer², D Mercer²

¹Royal Free and University College Medical School and ²Department of Sexually Transmitted Diseases, Royal Free and University College Medical School, London

Objective: To understand current HIV testing practices at a central London GUM clinic in view of the proposed National Sexual Health Strategy targets.

Methods: All patients with a new problem attending routine GUM clinics between August 2000 and February 2001 were identified from the clinic database. Their basic demographics were then matched with HIV and sexually transmitted infection (STI) results. High-risk categories based on an African country of birth, ethnicity (black African), men who have sex with men (MSM) and concurrent STI were created. HIV prevalences (prev.) are based on those tested.

Results: 47% (3200/6787) of clients tested for HIV: 52% of men and 42% of women, $P<0.001$ (HIV prev. 3% and 1%, respectively). Clients from most 'high-risk' groups had a higher test uptake. Of MSM, 52% had HIV tests (HIV prev. 5%) versus 46% of heterosexuals (HIV prev. 1%), $P<0.001$. 52% of Africans (based on country of birth and ethnicity) (HIV prev. 9%) and 46% of non-Africans had tests (HIV prev. 2%), $P=0.04$. In contrast, there was no significant difference in test uptake for those with or without a concurrent STI (HIV prev. 2% for both). Overall, 49% of 'high risk' (HIV prev. 4%) and 45% of 'low risk' (HIV prev. 1%) clients had tests, $P=0.001$. Among 31 clinicians, test uptake rates ranged from 28 to 61% (mean 47.5%, 95% confidence interval 44.5–50.5%).

Conclusions: Overall HIV testing rates already exceed the proposed 40% national target for 2004. However, it is of concern that in those groups at higher risk, almost half remain untested. Clinician variation in test uptake suggests that training initiatives may improve test uptake.

05

Acute sexually transmitted infections (STIs) in HIV-positive gay men: a case for enhanced screening in HIV treatment centres

D Grover, J McSorley, SG Edwards, B George, S Smith, T Sadiq, P French, IG Williams

Department of Genitourinary Medicine, Camden and Islington CS NHS Trust, and Department of Sexually Transmitted Diseases, Royal Free and University College Medical School, London

Background: HIV treatment centres may play a key role in HIV prevention by providing improved screening and treatment of STIs. We provide a nurse-led STI screening and treatment service for patients attending for their routine HIV care.

Objectives: To describe the pattern of acute STIs and factors associated with diagnosis in HIV positive gay men attending a HIV treatment centre through January–December 2001.

Results: Of 1241 gay men attending for routine HIV care, 446 (36%) underwent at least one STI screen. Of these 143 (32%) had two or more (range 2–6) screens, a total of 677. 94/446 (21%) were diagnosed with 158 episodes of an acute STI (excluding syphilis): gonorrhoea 83 (52%), chlamydia 31 (20%), non-specific urethritis 44 (28%). The median CD4 count and plasma viral load (VL) of the 94 men were 495 cells/ μ L (range 80–1210) and 6500 copies/mL (range <50–3,413,800) respectively. 68/94 (72%) of the men with any STI and 24/34 (70%) with rectal gonorrhoea had detectable plasma VLs at the time of diagnosis. 42 episodes of infectious syphilis were also identified in 41 gay men attending for their routine HIV care.

Conclusions: More than 1/3 of all HIV-positive gay men attending for routine care underwent an STI screen. A high proportion (1/5) of those screened were diagnosed with an acute STI, of whom the majority had a detectable plasma viral load at the time of diagnosis. There is a need to develop and enhance targeted STI and sexual health services in HIV treatment centres.

06

Will a syphilis outbreak result in a second HIV epidemic?

S Hopkins, C Coleman, J Garvey, F Mulcahy, C Bergin
St James's Hospital, Dublin, Ireland

Introduction: Between January 2000 and December 2001, 227 cases of early syphilis were diagnosed and treated in our clinics. Many novel interventions have been initiated to control this outbreak.

Methods: Demographic details, sexual histories and full investigation for other sexually transmitted infections were performed in all cases. An outbreak control team, consisting of representatives from our clinic, Public Health, the National Disease Surveillance Centre and members of the gay community, was established.

Results: 27 cases of early syphilis were diagnosed in 2000 and 200 cases were diagnosed in 2001. 96 (42%) were primary; 92 (40%) were secondary; 39 (18%) were early latent. The male to female ratio was 215:12. 90% (203) of cases occurred in men who have sex with men (MSM). 85% (197) cases were Irish. The mean number of male partners and female partners in the previous 3 months was 5.86 (range 0–40) and 0.153 (range 0–4), respectively. The patients met their sexual partners in saunas (64%), clubs (74%), Internet (8%), outdoors/park (3%) and abroad (20%). 30 MSM with previously diagnosed HIV infection (range 6 months to 8 years) were diagnosed with early syphilis. 16 MSM were co-diagnosed with HIV and syphilis. 52% of patients were diagnosed as a direct result of novel interventions: designated contact tracing (26%); on-site serological testing for syphilis in gay venues (14%) or through education about the importance of a regular sexually transmitted infection screen (12%). Other interventions included advertisement and publicity campaigns (involving drag queens); designated syphilis clinics; and education forums with gay peer groups.

Discussion: Syphilis increases HIV viral load and is a known factor in HIV acquisition. Additionally, given the high rate of known HIV patients acquiring syphilis (approximately 10% of the clinic HIV MSM cohort), we can expect to see further co-diagnosis in this high-risk group.

07

Transmission of drug-resistant virus in primary HIV-1 infection (PHI)

M Brady, S Fidler, J Clarke, J Weber.

Faculty of Medicine, St Mary's Hospital, Imperial College, London

Objective: To measure the prevalence of resistant HIV-1 virus strains in a cohort of patients with PHI, all within 6 months of seroconversion.

Methods: PHI was defined as a negative HIV test in the previous 6 months, negative/evolving HIV antibody tests with positive HIV polymerase chain reaction (PCR) test and/or symptoms of HIV seroconversion. Genotypic resistance testing using ABI Viroseq version 2 was performed at baseline on all samples.

Results: 46 patients have been recruited (44 gay men, 1 heterosexual man and 1 heterosexual woman). The median age (range) is 30 years (21–77). The median (range) CD4 count and viral load at baseline were 465 cells/ μ L (90–1200) and 122,298 RNA copies/mL (179 to >500,000). All infections were sexually transmitted. Baseline resistance results are available on all 46 patients. 42/46 (91.3%) were subtype B. All non-B subtype infections were acquired in Africa. 44/46 (95.6%) were wild-type virus. Only two patients in the cohort (4.3%) had acquired a drug-resistant virus. Both are gay men, one infected in Australia and one in the UK. The first had mutations M184V, G196E, L63P, G73S, V77I and L90M, while the second had M41L, A98G, M184V, Y188L and T215Y mutations.

Conclusions: We report a much lower prevalence of drug-resistant virus in primary infection compared with previous studies. Transmission of drug-resistant virus appears to be an increasing problem and rapid genotypic resistant testing is essential in the context of treating primary HIV-1 infection.

08

Multidrug resistant HIV-1 in the semen of men with acute sexually transmitted infections

ST Sadiq¹, S Taylor^{2,3}, S Kaye², J Workman², P Cane², J Bennett¹, A Copas¹, S Drake³, I Weller¹, D Pillay

¹Royal Free and University College Medical School, ²Public Health Laboratory Service, University of Birmingham, and ³Birmingham Heartlands Hospital, Birmingham, UK

Objective: To investigate the effect of urethritis on seminal shedding of drug-resistant HIV-1 in patients receiving antiretroviral therapy.

Methods: Viral loads (VL) were measured on blood plasma (BP) and seminal plasma (SP) samples obtained from patients on antiretroviral therapy, with and without urethritis, and 1 and 2 weeks after treatment for urethritis. Samples were analysed for genotypic resistance by reverse transcriptase polymerase chain reaction and sequencing.

Results: 18/24 cases of urethritis and 13/26 controls had undetectable SP VL and BP VL at all visits. In 6/24 cases at presentation, median BP VL and SP VL were 42,457 copies/mL (range <500 to 98,882) and 11,091 copies/mL (1,512–100,000), respectively. In four of these cases, a genotypic analysis of SP was possible and detected primary drug resistance associated mutations to nucleoside reverse transcriptase inhibitors (NRTIs): $n=2$; NRTI+protease inhibitor (PI): $n=1$; NRTI+NNRTI: $n=1$. There was minimal discordance between mutations in blood and semen. Following treatment for urethritis, SP VL was significantly reduced in three cases.

Conclusions: In men with sexually transmitted infections, multidrug resistant HIV-1 and high viral loads were detected in the semen of those on suboptimal antiretroviral therapy but not in those on effective antiretroviral therapy. These findings may have important public health implications in both the developed and developing world.

09

Sequential transmission of HIV-1 containing drug resistance-associated mutations

S Taylor^{1,2}, P Cane¹, S. Hue¹, L Xu¹, T Win³, Y Lie³, N Hellman³, C Petropoulos³, J Workman¹, D Ratcliffe¹ and D Pillay¹

¹PHLS Antiviral Susceptibility Reference Unit, University of Birmingham, UK, ²Department of Sexual Medicine, Birmingham Heartlands Hospital, UK, and ³Virologic, South San Francisco, CA, USA

Objective: We have investigated a potential transmission chain of drug-resistant HIV-1 between three individuals over a 5-year period.

Methods: Sequencing of the *pol*, *env* and *gag* genes from these three individuals and 25 other geographically and temporally related samples was performed. Phylogenetic analysis was undertaken to provide molecular support for the transmission events. Genotypic and recombinant phenotypic analysis was performed to identify resistance-associated mutations, drug susceptibility and replicative capacity. Clonal analysis of *env* genes from blood and seminal plasma virus was undertaken to assess the impact of compartmentalization of virus at the time of sexual transmission.

Results: Viruses containing the reverse transcriptase drug resistance-associated mutations M41L, E44D, L210W, and T215D were transmitted sequentially between three homosexual men (A, B and C). They persisted in person B for at least 4 years, despite intermittent therapy and reduced viral replicative capacity, compared with wild-type strains. The likelihood of sequential transmission was supported by both epidemiological and phylogenetic evidence. Clonal analysis of the V3 loop of the *env* gene from semen and blood virus suggested that virus transmitted to patient C was of the syncytium-inducing phenotype and originated from the genital tract, rather than blood of person B.

Conclusions: Our data suggest that variants with drug-resistance associated mutations can persist within newly infected individuals, despite intervening antiretroviral therapy and can subsequently be sexually transmitted.

010

Reservoirs of persistent HIV replication are stable in patients with an undetectable viral load

J Morlese, I Teo, JW Choi, BG Gazzard, S Shaunak
Hammersmith Hospital and Chelsea & Westminster Hospital, London

Background: On-going viral replication in patients on antiretroviral therapy leads to treatment failure. We have shown that the 2-long terminal repeat (LTR) circle assay can be performed on peripheral blood mononuclear (PBMN) cells to monitor acute infection events throughout the body even when plasma HIV-1 RNA is <50 copies/mL. A new LightCycler (LC) based circle assay was used to prospectively monitor a cohort of HIV-1+ patients on antiretroviral therapy.

Methods: The circles in PBMN cells, plasma HIV RNA and CD4 count were prospectively measured at regular intervals over a 2-year period in 60 patients on antiretroviral therapy. Their plasma HIV-1 RNA was <50 copies/mL at all times. 2-LTR circles were extracted from PBMN cells by plasmid extraction and then quantified using the LC.

Results: All patients maintained a plasma HIV-1 RNA of <50 copies/mL for 31±2 months. The circles were monitored for 15±1 months of these months. The circle copy number ranged from <10 to 400 copies/10⁶ PBMN cells. 58% of the patients had no detectable circles (<10 copies/10⁶ PBMN cells). 42% had detectable circles (>10 copies/10⁶ PBMN cells). The two groups were mutually exclusive ($P<0.001$) and the circle copy number remained stable over the period of follow-up. A single circle-copy measurement was as reliable as multiple measurements to establish the presence of persistent viral replication. There was no correlation between circle-copy number and CD4+ or CD8+ T-cell count.

Conclusions: The circle assay is a simple method of identifying those patients with persistent viral replication despite an undetectable plasma HIV RNA. 42% of the patients with successful long-term suppression of plasma HIV RNA still had persistent viral replication. New drug combinations and therapeutic approaches are needed for these patients.

011

Evidence of low-level viral replication (<50 copies/mL) predicts eventual virological failure

Y Mazon, AL Pozniak, D Pillay, S Mandalia, A Wildfire, BG Gazzard
Chelsea and Westminster Hospital, London, UK

Introduction: A viral load between 50 and 400 copies/mL in patients previously undetectable (<50 copies/mL) on highly active antiretroviral therapy (HAART) may be due to laboratory factors, a true virological blip or the portent of imminent virological failure. We have examined whether low level viraemia (LLV) values are repeatable on the same sample and whether there is evidence of prior ongoing virological replication in those who subsequently fail virologically (viral load >400 copies/mL).

Methods: Patients on stable HAART who had at least two values of viral load <50 copies/mL (Chiron assay), then >50 but <400 copies/mL (LLV) and subsequently became undetectable (<50 copies/mL) had their viral loads remeasured on the same plasma sample. Those whose repeated value was still >50 but <400 copies/mL were called repeatable blips (RB), and those with a repeat <50 copies/mL were called non-repeatable blips (NRB). These were compared with a group who developed >400 copies/mL immediately after the LLV sample, called the viral failure (VF) group. The optical density normalized for background was measured in at least two samples of <50 copies/mL prior to LLV as an indirect measure of ongoing viral replication.

Results: Of 247 blip patients, 102 patients were RB (41%) and 145 were NRB (59%). 139 were in the VF group. At the time of LLV there was a significant difference in viral load between the VF group and both NRB and RB groups ($P<0.01$). There was evidence of greater ongoing viral replication at <50 copies/mL in the VF group from samples taken a median of 5.8 and 2.8 months before LLV. This was not seen in the NRBs, but in the RB group, the sample immediately prior to the LLV showed evidence of viral replication as well, but not in the previous sample taken at a median of 5.6 months.

Conclusion: 59% of all blips are non-repeatable on the same sample.

012

The prevalence and determinants of the K65R mutation in HIV reverse transcriptase in tenofovir-naive patients

A Winston, S Mandalia, D Pillay, B Gazzard, A Pozniak
Chelsea & Westminster Hospital, London

Background: The K65R mutation in HIV-1 reverse transcriptase is associated with reduced susceptibility to abacavir and tenofovir. We established its prevalence within a large clinical database, and investigated correlations with other resistance-associated mutations and antiretroviral history.

Methods: Genotypes from the Chelsea & Westminster Hospital resistance database (up to October 2001) were analysed. Data from patients who had received tenofovir were excluded.

Results: K65R was identified in viruses from 17 of 999 patients tested (1.70%). Nine of the 17 were receiving abacavir (group 1). In comparing group 1 with 177 patients failing treatment on abacavir without the K65R mutation (group 2), no differences were observed for time on abacavir, time on antiretrovirals or number of concurrent drugs. Current thymidine analogue treatment was more common in group 2 (68% versus 32%; $P<0.05$), as was the prevalence of two or more thymidine analogue-associated resistance mutations (48% versus 11%; $P<0.05$).

Conclusions: The presence of K65R is associated with prior abacavir use. Although rare, it is preferentially selected within non-thymidine analogue-containing regimens, compared with concurrent zidovudine or stavudine use, which is associated with emergence of thymidine analogue mutations. Both genetic routes taken may compromise both abacavir and tenofovir activity.

013

Intradermal poly(lactic acid) (Newfill) for treatment of severe HIV-associated facial lipoatrophy

JN Day, A Raabe, A M Shiner, EL Wilkins

Department of Infectious Diseases and Tropical Medicine, Monsall Unit, North Manchester General Hospital, Manchester

Background: The lipodystrophy syndrome (LDS) is increasingly prevalent in HIV-infected people. We present our experience in treating facial lipoatrophy with intradermal poly(lactic acid) (PLA) injections.

Methods: The patients received between two and five sets of intradermal injections of PLA over 3 months. Two-thirds of the patients were enrolled into a prospective open-label non-comparative trial. Results of treatment in all patients were assessed through a quality of life (QOL) instrument, subjective assessment and independent assessment of serial photography. Patients enrolled in the trial had also had ultrasonography of facial skin thickness.

Results: 27 patients received treatment. One patient had an adequate effect after two injections, nine patients have received three sets so far and 16 completed five sets of injections. All patients had subjective improvements in their appearance. There was a trend towards improvement in quality of life when treated patients were compared with untreated patients, but improvement in quality of life was not demonstrable in individual patients when assessed after 3 months of treatment. Treatment was well tolerated. All patients had swelling and discomfort for 48 hours after injection. One patient developed a pustule at an injection site: this did not require specific treatment.

Conclusions: PLA is a popular treatment among patients with facial lipoatrophy, all perceiving an improvement in their appearance. It is well tolerated, but objective improvement in quality of life has not yet been demonstrated.

014

The reproducibility of three-dimensional (3-D) laser surface scans for the assessment of facial lipoatrophy (LA)

P Benn¹, C Ruff², J Cartledge¹, V Sauret², A Copas³, A Linney², IG Williams³ SG Edwards¹

¹Department of Genitourinary Medicine, Camden and Islington CS NHS Trust, ²Medical Physics, University College London Hospital, and ³Sexually Transmitted Diseases, Royal Free and University College London Medical School, London

Aims: To evaluate the use and reproducibility of 3-D laser surface scans to assess facial LA.

Methods: 16 HIV+ men were recruited from the routine HIV clinic. Patients assessed themselves as having no ($n=2$), mild ($n=3$), moderate ($n=10$) or severe ($n=1$) facial LA. Details of height, weight, CD4 count, viral load and antiretroviral therapy were recorded. Three blinded clinicians also assessed the severity of facial LA. Two 3-D laser surface scans were taken a week apart by the same technician in a standardized way. The two 3-D digital images were superimposed using bony landmarks. Corresponding points in regions overlying five areas of the face, the forehead, right and left temporal and cheek areas were compared. The mean variability between 50% of corresponding areas was measured.

Results: Overall, the variability between 50% of corresponding points for all five areas was <0.55 mm (forehead = 0.22 ± 0.09 mm; right and left temporal area = 0.4 ± 0.26 mm and 0.35 ± 0.14 mm; right and left cheek areas = 0.55 ± 0.25 mm and 0.55 ± 0.29 mm). Scan reproducibility was not affected by the degree of LA as reported by patient or physician.

Discussion: 3-D laser surface scans of the face are reproducible in patients with and without LA. They may provide an objective means of monitoring facial LA. Further longitudinal studies are needed.

015

Perinatal antiretroviral therapy: mono- versus combination therapy and neonatal anaemia

CJ Foster¹, I Roberts², EGH Lyall¹ and GP Taylor^{1,2}

¹Family HIV Clinic, St Mary's Hospital, and ²Imperial College, London

Aim: To compare the effect of monotherapy versus combination antiretroviral therapy on neonatal haemoglobin (Hb) in non-HIV-infected infants.

Methods: Retrospective review of infants born at St Mary's to HIV-infected women between October 1998 and September 2001.

Patients: Of the 53 women identified, 74% were of black African origin and 25% were diagnosed on antenatal screening; 24 conceived on combination therapy, and 13 received third-trimester zidovudine (ZDV) alone. At delivery, the median maternal CD4 count was 360 cells/ μ L (23%), and 72% had an undetectable viral load. Of the 54 live infants, 31 received ZDV monotherapy, 21 other antiretroviral and 32 received zidovudine. All infants were HIV polymerase chain reaction (PCR)-negative.

Results: Mean Hb at birth was 14.1 g/dl, which is more than 2 standard deviations below the age-adjusted mean of 18.5 g/dl. No significant difference in Hb was observed between those infants exposed to antiretroviral therapy from conception compared with those only exposed from second/third trimester, Student's *t*-test, $P=0.54$. However, a significant reduction in Hb was observed in those infants exposed *in utero* to antiretroviral therapy that included ZDV (mean 13.6 g/dl) compared with antiretroviral therapy without ZDV (mean 16.3 g/dl), Student's *t*-test, $P=0.049$. One infant required transfusion and four received iron/folic acid supplementation. Two infants did not receive postnatal antiretroviral therapy due to anaemia. The anaemia had resolved by 3 months of age.

Conclusions: Perinatal antiretroviral therapy is highly effective in preventing the vertical transmission of HIV-1 but causes significant reduction in neonatal Hb that, in this cohort, was independent of length of antiretroviral exposure but most marked with ZDV-containing regimens.

016

Management of maternal HIV diagnosed late in pregnancy

F Lyons, S Hopkins, K Butler, C Bergin, K Butler, F Mulcahy

GUIDE Clinic, St James's Hospital, Dublin, Ireland

Background: Late diagnosis of maternal HIV-1 in pregnancy presents multiple challenges. This clinic has witnessed a dramatic rise in the numbers of pregnant women presenting, particularly late in pregnancy. The mean gestation at diagnosis from January to December 2001 was 26 weeks. A protocol for managing late presenters is presented.

Methods: Since 1998 a database of HIV-1 infected pregnant women has been maintained. Classification is according to time of diagnosis 'pre-conception', 'early' $\leq 28/40$ weeks, 'late' $\leq 28-36/40$, 'very late' $\geq 36/40$, 'in labour', 'postnatal' and 'refuses therapy'. Group, virological and immunological markers determine specific management.

Results: Of 180 deliveries between January 1998–December 2001, there have been two transmissions, with all other infants having at least one negative HIV polymerase chain reaction (PCR) test at ≥ 3 months of age. From January to December 2001 there were 51 pregnancies, 19 (37%) in women previously known to be HIV-1 infected and 32 (63%) diagnosed antenatally. Of the 32 diagnosed antenatally, 15 (47%) were diagnosed early, eight (25%) were diagnosed late and nine (28%) were diagnosed very late. All women with a CD4 count of ≤ 300 cells/ μ L are commenced on three-drug antiretroviral therapy regardless of gestational age (after the first trimester) and viral load. The management of women with CD4 count of >300 cells/ μ L, presenting at $>28/40$ weeks, will be outlined. All women are offered intrapartum/peri-operative intravenous zidovudine as per paediatric AIDS Clinical Trials Group (PACTG) 076. All infants receive antiretroviral therapy for 4 weeks post partum. All antiretroviral therapy is started as soon as possible in the various eligible groups. All women are advised not to breast-feed.

Conclusions: Effective management of HIV-1 infection diagnosed late in pregnancy requires detailed guidelines based on different scenarios.

017

Efavirenz and nevirapine: possible candidates for therapeutic drug monitoring (TDM) in clinical practice?

SE Gibbons, HE Reynolds, J Lloyd, JF Tjia, SH Khoo, DJ Back
Department of Pharmacology and Therapeutics, University of Liverpool

Introduction: Recent studies have put forward putative target concentrations for the nonnucleoside reverse transcriptase inhibitors (NNRTIs) efavirenz (EFV) and nevirapine (NVP), attempting to correlate plasma concentrations with virological response or the development of toxicity. However, the case for TDM of NNRTIs is currently not as strong as for protease inhibitors.

Methods: EFV and NVP requests received by the Liverpool TDM service since 1999 were categorized according to virological status at the time of TDM or (in the case of EFV) reported toxicity. Only adult patients receiving EFV at 600 mg once daily or NVP at 200 mg twice daily were included in the analysis. Target concentrations for viral suppression were 1200 ng/mL for EFV and 3000 ng/mL for NVP. EFV concentrations >4000 ng/mL have been reported to be associated with increased toxicity.

Results: For EFV, viral load (VL) data were available from 113 patients, with 50 being virally suppressed (VL <50 copies/mL). There was no apparent difference in EFV trough concentrations between the two groups: 25% of patients with VL >50 copies/mL had concentrations <1200 ng/mL compared with 20% of virally suppressed patients. Only 31% of patients with suspected EFV toxicity had trough concentrations >4000 ng/mL. For NVP, VL data were available from 102 patients, with 33 being virally suppressed. 41% of patients with VL >50 copies/mL had NVP trough concentrations <3000 ng/mL, compared with 24% of virally suppressed patients.

Conclusions: The results from our selective TDM data set suggest that for NVP and EFV, plasma concentrations alone are insufficient to account for viral response or the development of toxicity. Full clinical and virological data are essential to interpret TDM results.

018

Who is lost to follow up from an HIV clinic and why?

LJ Haddow¹, SG Edwards¹, K Sinka², DE Mercey¹
¹Royal Free and University College Medical School and ²Communicable Disease Surveillance Centre, Colindale, London

Background: The majority of HIV+ patients are young and some may engage in ongoing high-risk sexual activity. Regular follow-up allows prevention and treatment of HIV complications and may be an opportunity for risk reduction.

Aim: To determine which patients were lost to follow up (LFU) and describe the characteristics of this group.

Methods: Patients who had not attended during 2001 but had done so in the previous 15 months were defined as LFU. Case notes were reviewed. Data collected included demographics, CD4, viral load (VL), Centers for Disease Control and Prevention (CDC) stage, antiretroviral treatment, co-morbidity and reason for LFU.

Results: Out of 1522 patients, we identified 174 LFU. 69 had documented reasons for LFU (28 transferred to other centres, 24 had their main HIV care elsewhere, 17 died). 11 case notes were not obtained. Of the remaining 94, the median age was 33 years (range 22-56); 80% were male, 62% white and 21% black African. The main risk behaviour was men having sex with men (65%). Demographic data were not statistically different from those of patients attending for regular follow-up. At the time of last attendance, the median CD4 count was 420 cells/ μ L (range: 10-1561; 14% CD4 <200). Median VL=12,200 (range: 300-619,300). 61% were CDC A. 28% were taking antiretroviral therapy at last visit. A range of psychological and social issues was identified. Data will be presented on whether they later accessed care at another UK centre (CDSC Colindale).

Conclusion: While most patients LFU were at no immediate health risk to themselves, it is of concern that some patients had started antiretroviral therapy, some had advanced disease, and opportunities for health promotion were lost. Patient groups of special concern will be discussed.

019

Predicting non-adherence to highly active antiretroviral therapy (HAART): the role of patients' doubts about personal need and concerns about potential adverse effects

R Horne¹, V Cooper¹, M Fisher²
¹University of Brighton and ²Brighton and Sussex University Hospitals NHS Trust

Background: We present the preliminary findings of a study to test whether patients' perceptions of HAART prior to starting treatment predict subsequent adherence.

Methods: A prospective, longitudinal study in which consecutive patients ($n=46$; response rate = 81.5%) accepting an offer of HAART (made according to BHIVA Guidelines) completed a validated questionnaire assessing perceptions of personal need for HAART and concerns about potential adverse effects. These patients were separated into high- and low-adherence groups (reporting taking <90% HAART over previous month or stopping HAART without consulting a doctor). The effect of baseline beliefs on subsequent adherence was assessed.

Results: Patients' perceptions of HAART before starting treating predicted subsequent adherence. Low adherence at $t_1 = 1$ month and $t_2 = 3$ months was predicted by baseline concerns ($t_1 = 2.1$; $P < 0.05$ and $t_2 = 3.07$; $P < 0.005$) and by the degree to which individuals rated concerns relative to perceived needs (NCD $t_1 = -2.49$; $P < 0.05$; NCD $t_2 = -2.52$; $P < 0.01$).

Conclusions: This ongoing study shows that beliefs about HAART predict adherence. It suggests that interventions to support adherence will be more effective if they take account of patients' beliefs about HAART as well as the practicalities of taking it.

020

Impact of antiretroviral therapy on hepatitis B virus (HBV)-specific immune responses in HIV/HBV co-infected patients

RM Lascar¹, R Johnstone¹, A Bertoletti², RJC Gilson¹, MK Maini²
¹Royal Free and University College Medical School and ²Institute of Hepatology, University College London

Objectives: To assess the impact of highly active antiretroviral therapy (HAART) on reconstitution of HBV-specific CD4 and CD8 responses in HIV-positive patients with natural immunity to HBV and in a group of HBV chronic carriers.

Background: HBV-specific cytotoxic T lymphocyte (CTL) responses have a crucial role in controlling HBV replication. Our previous data suggested attrition of HBV-specific CTL responses associated with HIV infection in patients with natural immunity to HBV.

Methods: HBV-specific immune responses were studied in a group of human leucocyte antigen (HLA) A2+ HBV immune and HBV carriers co-infected with HIV. Patients were sampled prospectively for a period of 6 months after starting HAART. HLA tetramers and intracellular cytokine staining *ex vivo* and 10 days after *in vitro* stimulation were used to analyse the HBV-specific CD8 responses. CD4 responses to HBV core antigen were measured by intracellular cytokine staining directly *ex vivo*.

Results: All patients had an increase in the CD4 count and a good virological response to HAART. In the HBV-immune group we demonstrated reconstitution of functionally active HBV-specific CD8 responses, correlating with a recovery of HBV core-specific CD4 responses. In the HBV/HIV co-infected group we show that treating HBV in the context of HAART may overcome the HBV-specific CTL hyporesponsiveness usually seen in this chronic carrier group.

Conclusion: Preliminary results suggest that HBV-specific CTL responses can be restored by HAART in the HBV-immune group. Data will be presented for the HBV chronic carrier group.

021

Preservation of HIV-1 specific T-cell responses is restricted to a very small subset of true non-progressors

NA Qazi¹, BG Gazzard¹, N Imami²¹St Stephen's Centre, Chelsea & Westminster Hospital, and²Department of Immunology, Imperial College

Background: Recently much attention has been shifted towards the development of therapeutic vaccines in an attempt to boost the immune system's control of HIV-1. However, this has been hampered by the inability to identify conserved antigenic determinants to which responses should be directed and because in chronic HIV-1 infection antiviral immune responses remain poor. Long-term non-progressors (LTNPs) represent a group of HIV-1-infected patients who have very slow (or no) disease progression with high CD4 T-cell counts and very low or undetectable viral loads after many years of infection. Clearly these patients represent a group in whom the immune response to HIV-1 appears to be preserved. Therefore, analysis of altered viro-immunopathology in these patients becomes imperative.

Methods: Prospective study of 41 LTNPs originally identified in 1996. Patients who were naive to underwent analysis of CD4 T-cell proliferative responses. Comparison was made with those who progressed.

Results: Of the 41 patients defined in the 1996 cohort, 35 had progressed, with 29 now receiving antiretroviral therapy. Of these 29, 23 were started on highly active antiretroviral therapy (HAART) as they fulfilled the BHIVA guidelines of CD4 T-cell count <330 cells/ μ L and/or viral load >30,000 copies/mL. The remaining six patients developed recurrent infections and were recommended HAART by their regular clinic doctors. The six patients not currently on HAART have been regularly reviewed and show signs of falling CD4 T-cell counts, and are likely to need therapy in due course. By comparison, the six true LTNPs have maintained good HIV-1 specific CD4 T-cell proliferative responses to nef, tat p24 and gp120.

022

Effect of HIV-1 viral load at the time of antiretroviral therapy interruption on the duration of HIV-1-specific T-cell responses

C Burton¹, M Nelson², P Hay³, BG Gazzard², F Gotch¹ and N Imami¹Departments of ¹Immunology and ²HIV/Genitourinary Medicine, Chelsea & Westminster Hospital, and ³Genitourinary Medicine, St George's Hospital, London

Objective: To measure the duration of HIV-1-specific T-cell responses, during interruption of antiretroviral therapy in chronic HIV-1 disease.

Methods: 14 patients stopped antiretroviral therapy temporarily, due to adverse side effects caused by one or more components, adherence problems, drug resistance or drug toxicity. Responses to HIV-1 antigens were assessed by lymphocyte proliferation and ELISpot assays. Viral load, CD4 and CD8 T-cell counts were also monitored.

Results: Eight patients had an undetectable viral load at the time of the interruption (group A), six had persistent HIV-1 viraemia (mean 13,964 copies/mL, range 158–62,294) preceding the cessation (group B). CD4 T-cell numbers did not differ significantly between the two groups over the study period. CD8 T-cell numbers were significantly different between the two groups 5 weeks after cessation of antiretroviral therapy ($P=0.045$) being higher in group A. Of the eight patients in group A, one generated a significant response to HIV-1 p24 at week 5 after cessation, and two showed responses to HIV-1 gp160 at week 5. In group B, one of the six patients demonstrated a response to both HIV-1 p24 and gp160 at week 10 after cessation. Responses were transient and disappeared 5 weeks after generation. There was a statistical difference in gp160-specific responses between the two groups at week 5 ($P=0.044$)

Conclusion: We have previously reported that during interruption of antiretroviral therapy, transient HIV-1-specific responses can be generated in patients with chronic HIV-1 infection, with low-level viral rebounds. Here we report that viral load preceding the interruption has little effect on the generation or duration of HIV-1-specific responses. All responses seen are transient and ablated by the re-emerging virus.

023

The potential for immune reconstitution in HIV-infected individuals receiving highly active antiretroviral therapy (HAART) who achieve virological suppression

C Smith, C Sabin, F Lampe, S Madge, M Youle, A Cozzi-Lepri,

H Gumley, M Johnson, A Phillips

Royal Free and University College Medical School, London

Objectives: To study the long-term immune response to HAART in previously therapy-naive patients whose viral load levels remain below 500 copies/mL for prolonged periods of time.

Methods: Patients whose viral load level reached and remained <500 copies/mL after starting HAART were included. Changes in CD4 counts were analysed using mixed-effects models, with the slope allowed to change at 1, 12 and 24 months after HAART. The correlation between changes in CD4, CD4% and CD8 was assessed.

Results: 187 patients were followed for a median of 2.23 (0.82-4.47) years. After an initial rapid increase in the first month after HAART [78 cells/ μ L per month, 95% confidence interval (65.4, 87.2)], increases in CD4 counts continued but at a less rapid rate (rate of increase 11.9). This increase slowed non-significantly at 1 year after HAART and again at 2 years [change in slope 5.0 (2.2, 7.8), $P=0.0005$], but CD4 counts continued to increase overall (slope at 2 years 5.1/month). The percentages of patients with an increase in CD4 count in the first, second and third years after HAART were 92%, 84% and 61% respectively. By the end of follow-up, CD4 counts had risen by a median of 285 (range -210, 990) cells/ μ L and were above 500 cells/ μ L in 51% of patients. CD4% and CD8 counts had increased by 11% (-15%, 31%) and 11 (-2839, 2596) cells/mL. Changes in CD4 count at 3 years were correlated with changes in CD4% ($r=0.53$), but not with changes in CD8 counts ($r=0.13$).

Conclusions: Although the rate of immune recovery starts to slow after 2 years, CD4 counts continue to rise in most patients and CD4 counts begin to return to levels seen in HIV-negative individuals.

024

A randomised, open-label, phase I trial of highly active antiretroviral therapy (HAART) combined with interleukin-2 (IL-2) and/or an inactivated gp120 depleted HIV-1 immunogen (Remune)

G Hardy¹, N Imami¹, A Sullivan¹, M Nelson¹, C Burton¹, J Pido-Lopez¹, R Moss², BG Gazzard¹ and F Gotch¹¹Imperial College School of Medicine, Chelsea and WestminsterHospital, London, UK, and ²Immune Response Corporation, San Diego, CA, USA

Objective: To enhance HIV-1-specific CD8 cytotoxic T-lymphocyte (CTL) and CD4 helper T-lymphocyte (HTL) responses following cessation of HIV-1 activity by HAART using combination immunotherapy.

Methods: A randomized, phase I study of HAART in combination with IL-2 and/or Remune in advanced chronically infected patients (mean baseline CD4 T-cell count 303 cells/ μ L blood) was conducted. 36 patients were treated with HAART for 16 weeks before randomization to: (A) HAART alone ($n=9$); (B) HAART + IL-2 ($n=11$); (C) HAART + IL-2 + Remune ($n=7$); (D) HAART + Remune ($n=9$).

Results: While HAART is insufficient to allow regeneration of HIV-1-specific responses, specific factors allow transient regeneration of these responses. Most significantly, therapeutic failure leading to virological breakthrough induced strong CD4 HTL and CD8 CTL T-cell responses to HIV-1 in the context of immunotherapy. Recall CD4 HTL responses improved upon therapy with IL-2. IL-2 substantially increased CD4 T-cell counts. IL-2 induced transient viraemia that was seen predominantly in group B, but less in group C patients. No changes in plasma macrophage inflammatory protein (MIP)-1 α levels were seen for any patients in the study. T-cell receptor excision circle levels were significantly reduced in patients receiving IL-2 ($P<0.05$).

Conclusion: Overall, no differences were seen in the induction of HIV-1 CD4 HTL or CD8 CTL responses between those receiving IL-2 and/or Remune, despite an apparent protective effect against virological events by their combination.

025

Multicentre cohort study of testicular cancer in men with HIV

T Powles¹, G Daugaard², MR Nelson¹, T Oliver³, M Fisher⁴, J Stebbing⁵, J Anderson³, M Johnson⁵, BG Gazzard¹ and M Bower¹

¹Chelsea & Westminster Hospital, London, UK, ²Rigshospitalet, Copenhagen, Denmark, and ³St Bartholomew's, ⁴Royal Sussex County and ⁵Royal Free Hospitals, London, UK

Introduction: We present a large multicentre series addressing the clinical presentation, therapy and prognosis of HIV-related germ-cell tumours (GCT) and their treatment.

Methods: During 1984–1999, 31 HIV-positive men presented with GCT to four UK and one Danish HIV treatment centres. The median age was 33.7 years (range 23–61) and CD4 count 275 cells/μL (90–922) at diagnosis. The median duration of HIV infection prior to diagnosis of GCT was 42 months (0–108).

Results: 78% were diagnosed with seminoma and 22% with mixed GCT. Treatment comprised surveillance or adjuvant therapy for stage I disease, chemotherapy (CT) or radiotherapy (RT) for stage II and CT for stage III. Ten patients received CT, five RT and one had both, without excessive adverse effects. Treatment caused a fall in the median CD4 count (283–200 cells/μL). Four patients received highly active antiretroviral therapy before GCT diagnosis, and 14 started subsequently.

Stage	n	Prior AIDS	CD4 count (cells/μL)*	Follow-up (months [range])	HIV deaths	GCT deaths
I	21	38%	275	52 (90–118)	28%	4%
II	6	16%	190	54 (6–96)	33%	16%
III	4	0%	320	68 (12–115)	25%	0%

*At diagnosis of GCT

Discussion: The excess of seminoma supports the findings of large US cohort studies; other series from Europe have suggested an excess of mixed GCT and teratomas. The GCTs in this series present and should be treated as in the HIV-negative population. Chemotherapy and radiotherapy are well tolerated, but adversely affect the CD4 count.

026

Cytomegalovirus (CMV) viraemia is an independent predictor of disease progression and death in patients receiving highly active antiretroviral therapy (HAART)

JR Deayton, CA Sabin, MA Johnson, VC Emery, PD Griffiths
Royal Free and University College School of Medicine,
Royal Free Campus, London

Objective: To investigate whether CMV viraemia remains independently associated with disease progression and survival in the era of HAART.

Methods: All patients whose CD4 count had ever been below 100 cells/μL were prospectively monitored for CMV viraemia by qualitative polymerase chain reaction (PCR): this was continued even if CD4 levels increased after HAART. End points were progression to a new AIDS event, new CMV disease and death.

Results: 390 patients were studied for a median of 36 months. Progression to a new AIDS event was significantly associated with CD4 count [relative hazard (RH) 1.08] and HIV load (RH 1.28) but more strongly associated with CMV viraemia (RH 2.34). CMV viraemia was strongly associated with progression to CMV disease (RH 32.01). CMV viraemia was associated with an increased risk of death with a progression rate of 20.4% in viraemic patients compared with 8.2% in non-viraemic individuals ($P=0.003$). The RH of death associated with CMV viraemia was 4.23, and 1.18 for the CD4 count. HIV load was not associated with CMV disease or death in time-updated models.

Conclusions: CMV viraemia is independently associated with disease progression and death in the era of HAART and is more strongly correlated with risk of death than CD4 count or HIV load. CMV viraemia appears to be a more sensitive predictor of prognosis than other markers and may thus provide a marker for sustained immune function after HAART. Short-term changes in CMV PCR status are important for prognosis, suggesting that treatment of CMV viraemia should be evaluated in a placebo-controlled trial.

027

New retinal infections in HIV-positive patients in the post-highly active antiretroviral therapy (HAART) era

AA Oji, BG Gazzard, SM Mitchell
St Stephen's Centre, Chelsea & Westminster Hospital, London

Objective: To describe the risk factors and response to treatment of HIV-1-infected patients developing new retinal infections in the post-HAART era.

Methods: Review of HIV-1-infected patients developing new retinal infections between 1998 and 2002 to determine their risk factors and response to treatment.

Results: 37 patients (24 men, 13 women) developed a new retinal or choroidal infection over the study period. The majority of patients were Caucasian (57%) although 41% were black (mainly African): 51% of patients were homosexual and 46% were heterosexual; 49% had a new or recent HIV diagnosis, while 38% had failed to respond to HAART. Infection was due to cytomegalovirus in 28 (76%) patients, varicella-zoster virus in six (16%), cryptococcus in two, with one case each being due to toxoplasmosis and miliary tuberculosis; 11 patients died within 17 months of diagnosis (mean 7.1 months). The median CD4 count and HIV viral load at ocular diagnosis were 17 cells/μL (range 1–245) and 5.17 log₁₀ copies/mL (range 1.00 –5.70), respectively. Discontinuation of treatment was possible in seven patients following immune reconstitution on HAART.

Conclusions: Despite the increasing availability of HAART, retinal infections continue to occur, with the majority of patients having a new or recent HIV diagnosis.

028

A prospective multicentre study of discontinuing prophylaxis for opportunistic infections: the STOPIT study

P Hay¹, H Green², D Dunn², A Babiker² on behalf of STOPIT
¹St George's Hospital and ²Medical Research Council Clinical Trials Unit, London

Objective: To assess whether it is safe to discontinue prophylaxis (primary or secondary) for opportunistic infections (OIs) following a good immunological/virological response to highly active antiretroviral therapy (HAART).

Methods: Participating clinical sites ($n=37$) prospectively identified patients in whom the discontinuation of prophylaxis for any OI was considered to be clinically indicated, due to a sufficiently high CD4 count or sufficiently low viral load, although levels were not predefined. A follow-up report was subsequently sent every 6 months.

Results: Prophylaxis for *Pneumocystis carinii* pneumonia (PCP) was withdrawn in 500 patients (410 primary, 90 secondary prophylaxis), for *Mycobacterium avium* complex (MAC) in 30 (15, 15), and for CMV in 13 (1, 12). The median CD4 count at discontinuation of PCP prophylaxis was 350 cells/μL (only 5% had <200). Values for MAC (median 180) and CMV (median 220) were lower. CD4 counts were generally maintained above accepted prophylaxis threshold levels during the follow-up period. Total follow-up to last report or re-continuation of prophylaxis was 791, 67 and 28 person-years for PCP, MAC and CMV, respectively. No cases of PCP were reported but one patient had a recurrence of MAC and one a recurrence of CMV retinitis. Corresponding incidence rates are 0.0 (upper 95% confidence limit 0.4), 1.5 (7.2), 3.6 (16.9) per 100 person-years.

Conclusions: The risk of developing OIs in the absence of prophylaxis is very low provided adequate CD4 count levels are maintained. This study lends support to recommendations that prophylaxis or maintenance for PCP, MAC and CMV is not necessary in the context of HAART.

029

Progression rate of liver fibrosis in HIV and hepatitis C virus (HCV) co-infected patients

AH Mohsen, S Norris, C Taylor, R Kulasegaram, B Portmann, S Lucas, P Easterbrook, GKT HIV-HCV Collaborative Group
King's College Hospital, London

Introduction: There are limited comparative histological data on the relative rate of HCV progression in HIV-1/HCV and HCV-infected patients.

Aim: To compare the rate of fibrosis progression in HIV/HCV co-infected and HCV mono-infected patients.

Methods: Patients were included only if the duration of HCV infection were known. Detailed epidemiological data were collected. Liver biopsies were Ishak-scored by a single experienced observer.

Results: 38 HCV/HIV co-infected cases and 95 infected with HCV alone were analysed. Most were male (73%) and had received highly active antiretroviral therapy (HAART) (82%). Risk factors included intravenous drug use in 81% and blood products/transfusion in 19%. The average progression rate in co-infected patients was 0.182 fibrosis units/year compared with 0.128 in HCV-only patients ($P=0.002$). The estimated time from infection to established cirrhosis in co-infected patients was 21.97 years compared with 31.25 in HCV alone. The rate of HCV progression in five patients who had repeat liver biopsies was 0.29 fibrosis units/year, equating estimate time to cirrhosis of 13.8 years. There were no significant differences in sex distribution ($P=0.72$), fibrosis stage ($P=0.2$), alanine aminotransferase ($P=0.83$), age at infection ($P=0.98$) and duration of HCV ($P=0.6$) between the two groups. Co-infected patients had significantly higher inflammatory grade ($P=0.003$) despite a lower alcohol intake ($P=0.003$). By multivariable analysis, HIV was significantly associated with faster fibrosis progression ($P=0.01$) and higher inflammatory grade ($P=0.05$).

Conclusion: HIV/HCV co-infected patients have a more rapid rate of fibrosis progression and higher inflammatory grades than patients infected with HCV only.

030

HIV/hepatitis C virus (HCV) co-infected population: early outcomes with pegylated interferon and ribavirin

S Hopkins, F Lyons, F Mulcahy, C Bergin
St James's Hospital, Dublin, Ireland

Background: With the advent of highly active antiretroviral therapy, the prognosis of HIV+ patients has altered. End-stage liver disease is an increasing cause of morbidity and mortality in those patients co-infected with HCV.

Methods: All co-infected patients are followed at a designated treatment clinic. All patients are eligible if virologically suppressed with a CD4 count >200 cells/ μ L, or do not currently need HAART by current international guidelines and fulfil treatment criteria for HCV.

Results: 16 patients (12 males, four females) have commenced therapy (mean age 37.9 years, range 28–49); 87.5% contracted HIV and HCV through intravenous drug use (IDU). Eight patients are currently on methadone maintenance therapy. 10 are genotype 3 and six are genotype 1. The mean biopsy score is 3.7/6. Side effects to date are flu-like symptoms (100%), diarrhoea (8%), headache (64%), itchy/dry skin (32%) and alopecia (8%). The mean weight loss was 4.5 kg (range 2–10) over the first 4 weeks. Haematological side effects have occurred in all patients though only three required dose modification (thrombocytopenia, severe haemolytic anaemia). The mean haemoglobin (Hb) at baseline was 14.6 g/dL and fell to mean 11 g/dL at 4 weeks; the mean absolute neutrophil count fell from 2.67 to 1.8×10^9 /L. One patient suffered severe haemolytic anaemia with a drop in Hb from 14.3 to 7.8×10^6 /L. One patient discontinued therapy secondary to severe depression at week 10. 11 patients have >12 weeks on therapy. At week 12, five are HCV RNA– (all genotype 3); six are HCV RNA+ (three genotype 1; three genotype 3).

Conclusion: Any patient with Hb <10 g/dL is given erythropoietin (4000 IU subcutaneously weekly). Early response rates are low, primarily due to advanced HIV disease and prolonged HCV infection.

P1

Calculated 10-year cardiovascular risk in HIV-infected patients receiving protease inhibitors

J Whetham, AM Smith, IG Williams

Royal Free and University College Medical School, London

Background: Coronary heart disease (CHD) has been reported in HIV-positive patients treated with antiretroviral therapy. Hyperlipidaemia, diabetes mellitus (DM) and hypertension (HT) are associated with protease inhibitor (PI) treatment. These complications may increase the future incidence of CHD in this patient population. Risk calculation formulae are available to calculate 10-year risks for individuals.

Methods: Data on patients receiving a PI-containing regimen were obtained from notes and a case report form. Data were collected on age, blood pressure (BP), cigarette smoking, plasma lipids, DM, previous CHD and family history of CHD. The Joint British Societies Cardiac Risk Assessor (*Heart* 1998; 80: s1–s29) was used to calculate the estimated 10-year risk of fatal and non-fatal myocardial infarction for each individual.

Results: Data were available in 204 patients, median age 41 years (range 17–65), median CD4 count 390 cells/ μ L (range 10–1180); 85% ($n=174$) had undergone PI treatment for over 6 months. Calculations were validated for 170 patients (excluding seven with CHD, 10 on cholesterol/BP treatment and 17 aged <32 years). The estimated proportion with a 10-year CHD risk of 15–30% was 14% ($n=24$), and >30% had 2% ($n=3$).

Conclusions: 16% of our patient population on a PI-containing regimen had a high 10-year risk of CHD. The contribution of PI-associated metabolic abnormalities to CHD risk is uncertain, as is the impact it has on the incidence of CHD over time compared with a general adult population of the same age range. Clinicians should be aware that national guidelines suggest that individuals with a 10-year risk >15% should be targeted for risk modification.

P2

Prevalence of cardiovascular disease (CVD) risk factors in an ethnically diverse HIV-positive population

C Hodgson¹, L Hodgson², S Murad¹, J Herman¹, C Taylor¹, D Macallan², P Easterbrook¹¹King's College Hospital and ²St George's Hospital, London

Objective: To determine the prevalence of CVD risk factors in an ethnically diverse and antiretroviral-naive population.

Methods: Eligible patients were treatment-naive HIV-1-positive individuals attending King's College and St George's Hospitals about to commence highly active antiretroviral therapy (HAART). A standardized questionnaire was used to collect data on demographic, lifestyle and CVD risk factors. An anthropometric and dietary assessment was also performed, with selected laboratory measures including cholesterol (CHL), high-density and low-density lipoprotein subfractions and triglycerides. A CVD risk factor score was generated using a British CVD risk model.

Results: 64 patients have been enrolled to date; 60.9% were men, 42.2% were black African, 34.4% were white and 15.6% were black Caribbean. The median age at evaluation was 35.4 years, and the median CD4 count and viral load were 177 cells/ μ L and 78,522 copies/mL, respectively. The overall prevalence of CVD risk factors was: ever smoked (59.4%); current smoking (35.9%); heavy alcohol intake (>28 units for men and >21 units for women; 32.8%); family history of CVD risk factors (95.3%); body mass index ≥ 30 kg/m² (6.3%) and waist circumference >88 cm (men) or >102 cm (women) (21.9%). Mean blood pressure and plasma lipids were within the normal range. There were significant differences in CVD risk factors according to sex and ethnicity. However, the overall 10-year risk of CHD over the next 10 years was <15%, based on the CVD risk model.

Conclusions: A high proportion of our patients have at least one modifiable CVD risk factor. This highlights the importance of identifying those who may benefit from lifestyle changes.

P3

No evidence of hyperlipidaemia or lipodystrophy with nonnucleoside reverse transcriptase inhibitor (NNRTI)- or nucleoside reverse transcriptase inhibitor (NRTI)-based regimens in an ethnically diverse population

L Hodgson¹, C Hodgson², S Murad², J Herman², C Taylor², P Easterbrook², D Macallan¹¹St George's Hospital and ²King's College Hospital, London

Objective: To determine the incidence of hyperlipidaemia and lipodystrophy in an ethnically diverse population of antiretroviral-naive patients who received NNRTI- or NRTI-based regimens.

Methods: Eligible patients were treatment-naive HIV-positive individuals attending King's College and St George's Hospitals and about to commence highly active antiretroviral therapy (HAART). A standardized questionnaire was used to collect data on demographic, lifestyle and cardiovascular risk factors. An anthropometric and dietary assessment was also performed, with selected laboratory measures including cholesterol, triglycerides, high- and low-density lipoprotein cholesterol at baseline and 3, 6, 9 and 12 months after starting HAART.

Results: 64 patients have been enrolled to date. 60.9% were men, 42.2% were black African, 34.4% were white, and 15.6% were black Caribbean. The median age at evaluation was 35.4 years and the CD4 count and viral load were 177 cells/ μ L and 78,522 copies/mL, respectively; 65.6%, 13.5% and 18.7% of patients began efavirenz-, nevirapine- or triple NRTI-based regimens, respectively. We analysed patients with anthropometric and lipid data at baseline and at least one follow-up visit (≥ 3 months). Although there was an overall significant gain in weight ($P=0.006$) the change in anthropometric indices (upper arm, waist and hip circumferences; triceps, biceps and supra-iliac skinfold thicknesses) were not consistent with lipodystrophy during follow-up.

Conclusions: We confirmed an absence, over the short-term, of lipid or body habitus changes in this ethnically diverse population with non-PI-containing regimens.

P4

Identifying patient groups at risk of developing a nevirapine rash

BM Clark, A Alonso, FJ Vilar, EGL Wilkins

Department of Infectious Diseases and Tropical Medicine, North Manchester General Hospital, Manchester

Background: The nonnucleoside reverse transcriptase inhibitor nevirapine is an important component of many HIV antiretroviral drug combinations. Between 10% and 40% of patients develop a hypersensitivity rash within 8 weeks of commencement. The use of steroids and antihistamines has not conclusively been shown to prevent this. We hypothesized that this side effect may be predictable in certain patient groups.

Methods: 203 patients were identified as having received nevirapine. A retrospective case note analysis was performed.

Results: 31 patients (15%) developed a hypersensitivity rash following nevirapine within 6 weeks. There was a significant association between a high HIV plasma viral load (>100,000 copies) at commencement of nevirapine and the development of a hypersensitivity rash [odds ratio 3.9 (1.74–8.89), $P<0.01$]. There was no association with concurrent illness, treatment-naive versus -experienced patients, smoking history, sex, race or age.

Conclusions: Our study suggests that patients with high viral loads are more likely to develop a rash. In this patient group, therefore, the physician may have to consider alternatives to nevirapine.

P5

Septrin hypersensitivity (SHS): another immune reconstitution phenomenon?

Z Warwick, C Timaeus, GL Dean, DR Churchill, M Fisher
Brighton and Sussex University Hospitals NHS Trust, Brighton

Introduction: HIV-positive individuals have a higher incidence of adverse drug reactions (ADRs) than those who are HIV-negative. Several mechanisms have been suggested to explain this phenomenon, one of which is immune-mediated hypersensitivity. We describe five cases of severe SHS with features consistent with previously described immune reconstitution syndromes.

Case studies: The five patients commenced septrin a median of 24 days (range 7–72) before starting highly active antiretroviral therapy (HAART) without any ADR and received HAART for a median of 14 days (range 10–29) before developing SHS. SHS presented as: fever ($n=2$), erythema nodosum ($n=1$) and widespread maculopapular rash ($n=3$). All cases had shown a marked drop in viral load upon starting HAART (median 2.2 log₁₀ drop; range -1.46 to -3.7 at 2 weeks) and a CD4 count rise of median 41 cells/μL (range -57 to +874). In all cases there was resolution of SHS symptoms upon discontinuation of septrin.

Discussion: We postulate that the timing alongside HAART introduction, association with virological/immunological response to HAART and atypical/severe ADR features suggest that SHS may represent an immune reconstitution phenomenon. In addition to providing insights into the pathogenesis of ADRs in HIV, this hypothesis requires consideration by clinicians. There is considerable overlap between the SHS features described and those well described with antiretroviral agents (such as abacavir and nonnucleoside reverse transcriptase inhibitors) which, if missed, may result in unnecessary discontinuation of HAART.

P6

Hepatic steatosis and lactic acidosis in an HIV/hepatitis C (HCV) co-infected patient following liver transplantation (LTX)

R Parkes¹, C McDonald, M Foxton², B Drejovic³, MR Nelson³, A Knisely², B Portmann², N Heaton², S Norris², C Taylor¹

¹Department of HIV/Sexual Health, ²Institute of Liver Studies, King's College Hospital, and ³Kobler Centre, Chelsea & Westminster Hospital, London

Background: Between 1995 and October 2001, King's College Hospital performed 11 orthotopic liver transplants in 10 known HIV-infected patients. Hepatic steatosis is a complication of nucleoside reverse transcriptase inhibitor therapy, the mechanism being gamma polymerase inhibition leading to mitochondrial toxicity. We report a patient infected with HIV and HCV who developed lactic acidosis and hepatic steatosis after LTX.

Case report: A 41-year-old man tested HIV-positive in 1993. In 1998 highly active antiretroviral therapy (HAART) was started and he also tested positive for HCV RNA. In January 2001 he developed ascites and jaundice. He underwent LTX in August 2001 at which time he was on didanosine, stavudine, efavirenz and tenofovir. Immunosuppression consisted of tacrolimus and mycophenolate. Pegylated interferon was added on day 45. At day 128 the patient presented with nausea and abdominal pain. His lactate was 8.3, bilirubin 63, aspartate aminotransferase 186, gamma-glutamyl transferase 1444. Liver biopsy showed 60% microvacuolar steatosis and electron microscopy demonstrated mitochondrial abnormalities. HAART was stopped and L-carnitine, riboflavin, ubiquinone and pabrinex commenced. He improved clinically and biochemically.

Conclusion: Hepatic steatosis is a complication of HCV infection. However, in view of lactic acidosis and microvacuolar steatosis in this patient, morbidity cannot be ascribed to HCV disease alone, but also to the effects of HAART. Antiretroviral and immunosuppressive therapy must be selected to minimize liver dysfunction.

P7

Short-course antiretroviral therapy in primary HIV infection (PHI)

M Brady¹, S Fidler¹, A Oxenius², D Price², T Zhang², R Phillips², J Weber¹

¹St Mary's Hospital, Imperial College, London, and ²Nuffield Department of Medicine, John Radcliffe Hospital, Oxford

Objective: To evaluate whether a short course of antiretroviral therapy in PHI preserves HIV-specific CD4 T-helper responses.

Background: National guidelines call for treatment of PHI. The nature, optimal timing and duration of this therapy remain unclear. HIV specific T-cell responses are thought to play a key role in viral load decline during PHI and determining the subsequent viral set point. These responses are usually lost after PHI in the absence of therapeutic intervention.

Methods: 46 subjects identified with PHI were recruited and offered a choice of a short course of therapy or no therapy. HIV-specific CD4 T-cell responses were analysed using ELISPOT technology.

Results: All subjects receiving therapy achieved a plasma viral load (pVL) of <50 copies RNA/mL by a median of 12 weeks (range 4–32 weeks). Two of the 46 had evidence of genotypic HIV drug resistance at baseline, and none developed *de novo* drug resistance mutations following therapy. Patients who chose short-course therapy showed preservation of HIV-specific CD4 T-helper responses. The average pVL after >24 weeks off therapy was significantly lower than baseline (mean drop 0.5 log₁₀ HIV-1 RNA copies/mL, $P=0.05$). The median CD4 count after >24 weeks off treatment was 160 cells/μL higher than at baseline.

Conclusions: Short-course antiretroviral therapy was safe and associated with preserved HIV-specific immune responses. PHI is highly heterogeneous, and a large randomized trial of antiretroviral therapy at PHI is now needed.

P8

Durability and tolerability of nevirapine (NVP)-containing regimens in a cohort of antiretroviral-naïve HIV-positive patients

N Mackie¹, CA Sabin², R Weston¹, J Weber¹

¹St Mary's Hospital, Imperial College School of Medicine, and ²Department of Primary Care and Population Sciences, Royal Free and University College Medical School, London

Background: Many clinicians favour a regimen of two nucleoside reverse transcriptase inhibitors (NRTIs) and one nonnucleoside reverse transcriptase inhibitor (NNRTI) in highly active antiretroviral therapy (HAART)-naïve patients. We performed a retrospective cohort analysis of HAART-naïve patients starting an NVP-containing regimen.

Method: Case notes were reviewed. Kaplan-Meier methods were used to assess time to virological failure (viral loads >500 copies/mL on two consecutive occasions). Patients who stopped NVP were considered as failures but not those who switched an NRTI backbone for toxicity.

Results: 287 patients were eligible for analysis: 74% were male, 61% Caucasian and 30% black African. Risk factors for infection were: homosexuality (58%), heterosexuality (38%) and intravenous drug use (4%); 8% had co-infection with hepatitis B (HBV) or C (HCV) and 14% had a previous AIDS-defining illness. The median (range) baseline CD4 count and HIV-1 RNA were 200 (0–821) cells/μL and 54,494 (202–500,000) copies/mL. The median (range) follow-up was 18 (0–57) months. Over this time, 16% of patients required a change to the NRTI backbone, and 67/287 (23%) failed therapy for virological (29/67, 43%), toxic (24/67, 36%), death (2/67, 3%) and other (4/67, 18%) reasons. 22/67 (33%) stopped NVP in ≤3 months, due to toxicity, mainly rash ($n=16$). Only three (one HBV+, one HCV+) experienced hepatotoxicity resulting in cessation of NVP. All significant hepatotoxicity occurred in the first 6 weeks and there were no further discontinuations because of liver problems after this period, even in co-infected patients. No patient stopped NVP for lipodystrophy. The median change in the CD4 count from baseline was 190 (-50 to +940).

P9

Virological response and safety of amprenavir plus lopinavir/ritonavir in heavily pretreated patients

R Shah, S McCormick, R Kulasegaram, W Tong, B Peters
St Thomas's Hospital, London

Background: Pharmacoenhancement of two protease inhibitors (PIs) with ritonavir might offer increased potency over single-PI enhancement in heavily experienced patients. Potential disadvantages of this approach (increased pill burden/complexity of regimen, and possibly increased incidence of short- and long-term adverse events) must be weighed against the benefits of an improved viral load response and improved clinical outcome.

Methods: Patients with multiple treatment regimen failure were assessed for suitability for amprenavir plus lopinavir/ritonavir. Genotypic analyses, when available, were used to inform the treatment choice. Treatment history, virological and immunological responses plus any liver function and lipid changes were collected retrospectively for the interim 24-week analysis.

Results: 18 patients' data were available for analysis. Prior exposure to nucleoside reverse transcriptase inhibitors ranged over 2-6 months (mean 4.9), PIs 1-6 months (2.9) and nonnucleoside reverse transcriptase inhibitors 1-2 months (one patient unexposed). The mean baseline viral load was 92,943 copies/mL (676 to >500,000) and the mean baseline CD4 count 200 cells/ μ L (3-444). 11/18 achieved <50 copies/mL at 24 weeks, and 13/18 <400 copies. The mean CD4 count rise was 132 cells/ μ L (10-717). No significant trends in liver function, lipids or adverse events were noted. Intent-to-treat and genotypic analysis of patients reaching 24 and 48 weeks will be presented.

Conclusions: In heavily pretreated patients with limited antiretroviral options, an effective, tolerable and safe regimen is required. In our cohort the use of a pharmacoenhanced amprenavir/lopinavir combination met these requirements in the majority of our patients, and might be an alternative option to mega-highly active antiretroviral therapy or strategic therapeutic interruptions.

P10

Antiretroviral therapy in severely immunocompromised patients

S Creighton, SG Edwards, A Copas, CB Taylor
Caldecot Centre, Department of Genito-Urinary Medicine,
King's College Hospital, London

Background: Highly active antiretroviral therapy (HAART) reduces morbidity from AIDS, but the majority of trials are initiated in patients with a CD4 count >200 cells/ μ L. Longitudinal prognostic data is not available in these patients. Individuals with CD4 <50 cells/ μ L have a prognosis of 6 months without therapy, and so improvements in life expectancy are seen more quickly.

Objectives: To compare the response to different antiretroviral regimens in individuals with CD4 <50 cells/ μ L.

Methods: Retrospective cohort study of all clients attending King's College Hospital with CD4 <50 cells/ μ L between 1 January 1996 and 31 December 1999. Endpoints included changes in the CD4 count and viral load and progression to AIDS or death.

Results: 74 males and 25 females were seen, with a baseline CD4 of 27.8 cells/ μ L (range 20-50) and baseline viral load 272,847 HIV-1 RNA copies/mL (range 400-4,822,000). The average duration of follow-up was 6.2 months in those receiving no therapy and 16.2 months in those on triple therapy. 14/46 (29%) receiving no antiretroviral therapy died in this time, compared with 2/104 (2%) receiving triple therapy ($P < 0.0000$). Triple therapy reduced the risk of a detectable load (odds ratio 0.03, 95% confidence interval 0.01-0.1) and increased the CD4 count by 35 cells/ μ L compared with no therapy. There was no significant difference between regimens containing a protease inhibitor versus a nonnucleoside reverse transcriptase inhibitor (NNRTI).

Conclusions: Triple therapy reduced death rates 15-fold, doubled the duration of follow-up and significantly improved viral load and CD4. PI-based regimens were as effective as those containing an NNRTI.

P11

Assessment of patients' attitudes towards taking Trizivir versus Combivir plus abacavir in their highly active antiretroviral therapy (HAART) regimen

E Davies, K McCormick, SE Barton
Department of HIV/Genito-Urinary Medicine, Chelsea & Westminster Hospital, London

Objective: To assess attitudes and the uptake of Trizivir by patients previously prescribed Combivir and abacavir.

Methods: In a prospective clinical audit of patients attending the HIV Unit at the Chelsea & Westminster Hospital, two groups of patients were studied. Group 1 had previously been established on Trizivir but switched to Combivir and abacavir due to unavailability of Trizivir. Group 2 had only ever taken Combivir and abacavir. After a 3-month period on Combivir/abacavir the patients were asked to complete a questionnaire before being offered Trizivir as an alternative. The questionnaire was designed to ascertain patient preferences between the two drug regimens.

Results: 60 questionnaires were completed, 42 in group 1 and 18 in group 2. 41/42 patients in group 1 expressed a preference for Trizivir and requested to switch back; one patient preferred to remain on Combivir/abacavir, stating that Trizivir tablets are 'too large'. Five of 42 felt that having Combivir/abacavir for the 3-month period had reduced their adherence. Four of these patients gave reasons, which included 'less easy to take', 'confusion due to similar-looking pills' and 'increased nausea'. In group 2, all 18 patients wished to try Trizivir as an alternative to Combivir/abacavir.

Conclusion: There is a lack of adherence data to support the intuitive belief that Trizivir is superior to Combivir/abacavir because of a reduced pill burden. However, this small study demonstrates that the majority of patients preferred Trizivir when given the option. In addition, the use of Combivir/abacavir in a small number of patients previously treated with Trizivir resulted in a reduction in self-reported adherence.

P12

Once daily dosing of highly active antiretroviral therapy (HAART) in Edinburgh

C Leen, S Morris, A Chiswick, R Brettie
Western General Hospital, Edinburgh

Introduction: Poor adherence remains the most important barrier to successful HAART. Many patients are incapable of or unwilling to take HAART twice daily. Good results from once daily dosing have previously been reported.

Objective: To examine the efficacy and durability of once daily dosing in a predominantly intravenous drug user (IDU) population.

Methods: Patients incapable or unwilling to take HAART twice a day were identified. They gave informed consent to be treated with a once daily HAART regimen. The components of the regimen depended on previous HAART use and patient acceptability. Changes in viral load (VL) and discontinuations were recorded.

Results: 26 patients (13 males; 13 females; 19 IDUs, five heterosexuals, two homosexuals) received 27 once daily regimens [27 on nucleoside reverse transcriptase inhibitors; 11 on nonnucleoside reverse transcriptase inhibitors (NNRTIs); 10 on protease inhibitors (PIs); six on NNRTIs + PI]. 16 patients had already received three or more previous HAART regimens. 11/26 patients had an initial VL of >100,000 copies/mL. Eight of 16 patients (50%) who were on opiate maintenance required dose modification. 21 patients had been followed up for more than 6 months. At 6 months, five patients had discontinued HAART, and 14 of 17 patients remaining on HAART had a VL of <400 copies/mL. Five patients maintained a VL of <50 copies/mL for >1 year. At one year, only two of 10 patients who discontinued their regimen did so because of viral rebound.

Conclusions: Once daily dosing of HAART is effective for some patients. A low rate of discontinuation due to viral rebound was noted. Tolerability remains an issue for patients taking a PI as part of their HAART regimen. New tolerable once daily dosing agents might improve these results further.

P13

Virological and CD4 cell response to tenofovir-based regimens in heavily experienced patients

BM Clark, EL Wilkins

Department of Infectious diseases, North Manchester General Hospital

Aims: To analyse the clinical, virological and immunological responses of patients prescribed tenofovir-containing antiretroviral regimens.

Methods: Patients prescribed tenofovir in Manchester from July 2001 onwards were identified. A retrospective case note analysis was performed, focusing particularly on previous antiretroviral experience, resistance testing results, and response to treatment at 6, 12 and 24 weeks.

Results: 51 patients were included (92% men), with a mean age of 40 years. 50 patients had a median of 68 months of previous highly active antiretroviral therapy (range 19–131). Lopinavir was used in over 75% of combinations; one patient received IL-2. There was an increase of 98 cells/ μ L in the CD4 count at 6 weeks compared with baseline, though this was not sustained at 12 and 24 weeks. A viral load fall of 1.6 \log_{10} at 6 weeks, 2.1 \log_{10} at 12 weeks and 2.7 \log_{10} at 24 weeks was recorded (median values).

Conclusions: Tenofovir is a valuable drug for use in the treatment of heavily pretreated patients, producing significant falls in the viral load when used with other agents, in particular lopinavir/ritonavir. It is also very well tolerated.

P15

HIV-related lung cancer in the pre- and post-highly active antiretroviral therapy (HAART) era

T Powles, MR Nelson, S Mandalia, BG Gazzard, M Bower

Chelsea & Westminster Hospital, London

Background: Lung cancer is commoner in HIV patients than in age-matched HIV-negative people. Before the introduction of HAART, data from large cohort studies calculated a relative risk of 2.8 (95% confidence interval 2.4–3.1). HAART has led to a decrease in the incidence of both Kaposi's sarcoma and non-Hodgkin lymphoma, but little is known about its impact on lung cancer. Since 1986, clinical data on 8,636 HIV-positive patients, representing 36,158 patient-years of follow-up, has been prospectively collected in our unit, including 10 patients with HIV-related lung cancer.

Results:

	Pre-HAART (1986–1996)	Post-HAART (1996–2001)	HIV negative
Patient follow-up (years)	22,694	13,464	
Lung cancer (no.)	3	7	
Median age (years)	48 (41–61)	45 (31–58)	68
Histology (% NSCLC)	100%	83%	71%
Cancer rate (95% CI)	1.3 (0.3–0.9)	5.2 (2.1–10.7)	1.5*
Stage IV disease	66%	100%	48%
Years of smoking	40	30	
CD4 at diagnosis cells/ μ L (range)	70 (50–320)	342 (117–995)	
Median survival (range)	2 months (1–8)	2 months (1–14+)	7 months (stage IV)

*Age-matched data. NSCLC=non-small-cell lung cancer.

Conclusions: Patients with HIV and lung cancer present with advanced disease and have a poor outcome. This study suggests that the incidence of the disease may be rising in the HAART era, despite improved immune function. Larger, more powerful studies are required to investigate this further.

P14

Nonnucleoside reverse transcriptase inhibitor (NNRTI)-based therapy for the treatment of acute and early HIV-1 infection: clinical issues and immunological studies

S Portsmouth¹, N Imami², A Pires², J Hand¹, F Gotch², MR Nelson¹, BG Gazzard¹¹Chelsea & Westminster Hospital and ²Imperial College School of Medicine, London

Background: Treatment of acute and early HIV-1 infection may have immunological and prognostic benefits.

Methods: 21 patients were prospectively followed during treatment of acute and early HIV-1 infection with Combivir and efavirenz.

Results: 18 patients attended following an illness that had features recognizable as acute HIV-1 seroconversion and were HIV-1-antibody positive by enzyme-linked immunosorbent assay (ELISA); three were ELISA-negative but had a positive p24 antigen and HIV-1 RNA viral load. The median baseline CD4 count was 493 cells/ μ L and viral load 200,000 copies/mL. Three of 21 patients showed baseline CD4 T-cell virus-specific proliferative responses to HIV-1 or virus-specific intracellular interferon- γ responses. All patients began with Combivir and efavirenz. Treatment was started a median of 40 days (range 9–120) after the illness thought to be seroconversion. 20 patients are still on antiretroviral therapy. 50% of patients described symptoms related to efavirenz, one discontinued therapy and two were switched to alternative regimens. At 52 weeks, all patients on therapy had a viral load of <50 copies/mL and a median CD4 count of 634 cells/ μ L. Transient T-cell responses to at least one HIV-1 antigen were observed during 24 weeks of follow-up in 30% of patients.

Conclusions: Identifying patients with acute HIV-1 infection is difficult; most start therapy >40 days after infection. The median CD4 change from baseline was 190 (–50, +940) cells/ μ L. Nonnucleoside reverse transcriptase inhibitor-based combination therapy for early HIV-1 infection is tolerated and effective at controlling HIV-1 viraemia and there is little restoration of HIV-1-specific immunity.

P16

Duodenal HIV-1 RNA load is increased in HIV patients with an opportunistic intestinal pathogen or pathogen-negative diarrhoea

P Hayes, D Datta, Y Miao, BG Gazzard

St Stephen's Centre, Chelsea & Westminster Hospital, London

Background: Symptomatic gastrointestinal pathology is common in HIV-1 infection and is primarily due to infection with opportunistic intestinal pathogens. However, such pathogens are undetectable in some HIV patients presenting with diarrhoea, with intestinal HIV replication proposed as the cause of the pathology. The aim of this study was to assess the effect of opportunistic intestinal pathogens, diarrhoea and highly active antiretroviral therapy (HAART) on duodenal HIV RNA load.

Methods: Duodenal biopsies were obtained from 15 HIV-1-positive patients, eight with diarrhoea and intestinal pathogens (D+P+), three with diarrhoea but no intestinal pathogen (D+P-) and four with neither (D-P-). HIV-1 RNA copies/g total RNA were subsequently determined. Frozen biopsy samples were homogenized in Trizol followed by a chloroform extraction of the RNA. Typically, a yield of 20–30 μ g total RNA was obtained from a single biopsy. HIV-specific long terminal repeat (LTR)-RNA was reverse-transcribed and quantified by real time polymerase chain reaction amplification using appropriate controls.

Results: Before HAART, D+ patients had significantly higher duodenal HIV loads than D- patients ($P=0.006$), as did P+ versus P- patients ($P=0.008$). D+P+ and D+P- patients had similar duodenal HIV loads ($P=0.54$), significantly higher than D-P- patients ($P=0.01$ and 0.034). Duodenal HIV loads decreased with HAART with no significant differences between the groups. However, duodenal HIV RNA was detectable at 1 month on HAART in four of five patients and at 6 months in none of 11 patients with undetectable plasma viral loads.

Conclusion: The higher duodenal HIV loads observed in this study in patients with an opportunistic intestinal pathogen may be due to inflammation and immune activation associated with these infections. The intestine may be an important reservoir of HIV during HAART.

P17

The incidence of Kaposi's sarcoma (KS) since the introduction of highly active antiretroviral therapy (HAART): nonnucleoside reverse transcriptase inhibitor (NNRTI)-based regimens prevent KS

S Portsmouth, M Bower, S Mandalia, MR Nelson, BG Gazzard
Chelsea & Westminster Hospital, London

Objectives: To determine the incidence of KS in HIV-1-infected patients from 1985 through to 2001.

Methods: From the database of 8640 patients followed up at the Chelsea & Westminster Hospital since 1985, all cases of KS were identified. KS incidence was calculated. Evidence of virological or immunological treatment failure was sought from the case notes of those with KS. Nadir CD4 cell counts were identified for both pre-1996 and post-1996 KS patients.

Results: From the total cohort of 8640 patients, 1204 cases of KS were identified. 198 cases of KS were diagnosed between 1996 and 2001. The incidence of KS was constant at about 30 cases/1000 patient-years before 1995. In 1995 and 1996 the incidence was 7.6/1000 patient-years, co-incident with dual therapy, and since 1996 the incidence has fallen dramatically to 0.03/1000 patient-years in 2001. Of the 198 cases of KS diagnosed since 1996, only 35 patients were on HAART at the time of diagnosis, and of these, 30 were HAART-experienced (mean 6.6 regimens) and were experiencing treatment failure. The median nadir CD4 count in the pre-HAART era and in the post-HAART era of those developing KS was similar. The incidence of KS was significantly lower in patients on regimens containing NNRTIs compared with protease inhibitors (PIs).

Conclusions: Since the introduction of HAART in 1996, the incidence of KS has dropped sharply. Most KS occurs in antiretroviral-naive patients. Patients developing KS while on HAART are usually experiencing treatment failure. NNRTIs are as effective at preventing KS as PIs are.

P18

High prevalence of herpes simplex virus (HSV)-2 infection in HIV-seropositive patients in South London

M Ramaswamy¹, M Smith¹, C Taylor², M Zuckerman¹, D Brown³, AM Geretti^{1,4}

¹Department of Infection and Public Health Laboratory (PHL),

²Department of HIV/Genito-Urinary Medicine (GUM), ³Central PHL, Colindale, and ⁴Academic Department of HIV/GUM, King's College Hospital and GKT School of Medicine, London

Background: Recent data indicate that HSV-2 seropositivity increases the risk of HIV transmission, independently of a diagnosis of genital herpes. These data are a cause for concern, as they indicate that HSV-2 acts as a cofactor for HIV transmission, and suggest a possible synergism between the two viruses.

Objective: To determine HSV-2 seroprevalence in an ethnically diverse cohort of HIV-infected patients.

Methods: 541 sera collected at the time of HIV diagnosis were tested for HSV type-specific antibodies by EIA (Focus Technologies, USA).

Results: The study group comprised 340 (65%) males and 201 (35%) females, including 42% black African, 41% white and 7% black Caribbean patients. HSV-1 and HSV-2 seroprevalence was 87% and 70%, respectively. Among females, seroprevalence was 91% for HSV-1 and 83% for HSV-2. Among males, seroprevalence was 86% for HSV-1 and 63% for HSV-2. HSV-1 seroprevalence was 94% in Black African, 84% in black Caribbean and 82% in white patients. HSV-2 seroprevalence was 88% in black African, 63% in black Caribbean and 54% in white patients.

Conclusions: HSV-2 seroprevalence is high among HIV-infected individuals in South London, and appears to be influenced by both gender and ethnicity. In the face of increasing risk-taking behaviour among HIV-infected individuals, consideration should be given to screening patients for HSV-2 antibodies, and counselling co-infected patients about HSV-2 ability to increase HIV transmission.

P19

Co-infection of HIV and hepatitis C virus (HCV): response to antiretroviral therapy in treatment-naive patients

J Atkinson, RP Brettle, A Wilson
Western General Hospital, Edinburgh

Objective: To compare the CD4 cell response to antiretroviral therapy in treatment-naive patients with and without HIV/HCV co-infection.

Methods: A retrospective analysis of prospectively collected data in 103 individuals commencing antiretroviral therapy.

Results: 36 (35.0%) of patients were co-infected with HCV, of whom 31 (86.1%) had acquired HIV by injecting drugs. In regression analysis there was no significant difference in the baseline, peak or rate of CD4 cell response, with respect to HCV serostatus. There was, not surprisingly, a strong correlation between HCV infection and intravenous drug use. The rate of the CD4 cell response was inversely correlated with age at start of therapy (-0.152) and time to reach peak (-0.361), but there was no difference with regard to HCV serostatus. For those with a CD4 count of <200 cells/ μ L the likelihood of their having a CD4 count >200cells/ μ L at 1 year was 51%.

Conclusions: Our experience (unlike the Swiss cohort) was that HCV co-infection had no effect on CD4 response in antiretroviral-naive patients during the first year of therapy.

P20

Cancers of the head and neck (HNC): a new HIV-related tumour?

T Powles¹, J Powles², MR Nelson³, BG Gazzard³, M Bower¹
Departments of ¹HIV Medicine, ²Ear, Nose and Throat Surgery, and ³Medical Oncology, Chelsea & Westminster Hospital, London

Background: Highly active antiretroviral therapy (HAART) has led to an increased life expectancy in people with HIV. Several solid tumours occur more frequently in HIV. The Epstein-Barr virus and the human papilloma virus have both been implicated in the pathogenesis of HNC, and therefore could be expected to occur at an increased frequency in HIV disease. We examined the Chelsea & Westminster Hospital database for 1987-2001 and found seven HNC patients.

Results: The median age at presentation was 48 years (range 32-53). All seven were homosexual males and two had an AIDS-defining diagnosis before HNC. Six smoked cigarettes. The incidence of HNC was 1.7 (95% confidence interval 0.7-3.6) new cases per 10,000 patient-years, versus 0.6 for the HIV-negative males. Treatment with radiotherapy or chemotherapy was poorly tolerated, with marked mucositis (grade 3-4) and a median fall in the median CD4 cell count from 131 to 77 cells/ μ L. The median progression-free survival was 7 months (range 3-96+) and the overall median survival was 27 months. Five of the seven died from progressive malignancy and one of HIV.

Site of cancer	Histopathology	Stage	Nadir CD4* (cells/ μ L)	Treat-ment	Survival (months)
NP	Anaplastic	T3N0M0	280	RT	17
NP	Undif	T2N2M0	347	RT	12
Laryngeal	Squamous	T1N0M0	90	Surgery	48
Laryngeal	Squamous	T3N0M0	124	RT	27
OC	Squamous	T2N0M0	250	Surgery/RT	96+
OC	Squamous	T1N0M0	183	Surgery	35
OC	Squamous	T2N0M0	10	S	11

*Before head and neck cancer diagnosis. NP=nasopharyngeal; OC=oral cavity; RT= radiotherapy; undif=undifferentiated.

P21

Occult hepatitis B (HBV) infection in HIV-infected patients with hepatitis

JN Day, A Bonington

Department of Infectious Diseases and Tropical Medicine, Monsall Unit, North Manchester General Hospital

Background: HIV patients are commonly infected with hepatotropic viruses, and screening for these is part of routine care. Two patients with biochemical evidence of hepatitis, negative hepatitis B surface antigen but high HBV viral loads are described.

Description: Both patients were severely immunosuppressed with CD4 counts of 6 and 12 cells/ μ L. Each had evidence of hepatitis with elevated transaminases, and one patient had liver biopsy consistent with mild to moderate hepatitis. Both patients were hepatitis A immunoglobulin G negative and hepatitis C polymerase chain reaction negative. Both patients were HBV core antibody positive, surface antigen negative, and had HBV viral loads of $>200\,000$ copies/mL.

Conclusion: So-called 'occult' HBV infection is well described in HIV-negative patients. However, the viral load is usually <1000 copies/mL. The implication of these high HBV viral loads in HIV-positive patients is unclear. Routine antibody/antigen tests may not be sufficient to exclude chronic active hepatitis of viral origin in severely immunosuppressed patients.

P22

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

MR Nelson¹, A Barr¹, M Fisher², BG Gazzard¹¹Chelsea & Westminster Hospital, London, and ²Royal Sussex Hospital, Brighton

Aim: To investigate the activity of tenofovir for the treatment of HBV in individuals co-infected with HIV.

Methods: Prospective review of patients treated with tenofovir as part of their HIV antiviral regimen who are co-infected with chronic HBV and HIV.

Results: 14 patients received tenofovir at a standard dose of 300 mg once a day as part of their HIV antiviral regimen. 11 patients had an undetectable HIV viral load at the time of commencement of tenofovir. 13 had previously received lamivudine (3TC) with evidence of continuing HBV replication. All but one patient continued 3TC as part of their antiviral regimen. The median alanine aminotransferase (ALT) at commencement of therapy was 59 IU (range 20–286) and median hepatitis B DNA was 1.3×10^9 genome equivalents (GE) per mL (range 9.4×10^4 to 2.7×10^9). Undetectability was defined as HBV DNA $<1 \times 10^4$ GE/mL.

	Week 4	Week 12	Week 24
<i>n</i>	10	7	4
Normal ALT	1	2	2
Mean log ₁₀ decrease HBV DNA	2.48	2.47	3.15
HBV DNA $<1 \times 10^4$ GE/mL	4 (40%)	4 (57%)	3 (75%)

No patient converted to e antibody positive during the study period. No patient lost HIV virological control as a result of switching or adding tenofovir. All individuals continue on tenofovir at the present time.

Conclusions: Tenofovir has activity against HBV when used in HIV-positive patients. Those who reach criteria for initiation of HIV antiviral therapy with evidence of HBV replication should consider tenofovir as part of their antiviral regimen. The role of dual therapy with tenofovir and 3TC remains unclear.

P23

The treatment of lung cancer in the era of highly active antiretroviral therapy (HAART)

T Powles, R Hawkin, P Shah, S Cox, D Sarker, MR Nelson, BG Gazzard, MR Bower

Chelsea & Westminster Hospital, London

Patients and methods: 197 patients with lung cancer have been managed at Chelsea & Westminster Hospital between 1999 and 2001, including six (five males, one female) HIV-seropositive patients. All six patients had advanced (stage IV) disease. The mean age was 44.2 years (range 313–58). The median CD4 cell count at lung cancer diagnosis was 342 cells/ μ L (range 117–995) and median viral load 283 copies/mL (range <50 to 30,020) and five patients were on HAART (see table).

Sex	Histology	Stage	Smokers	Survival
Male	Squamous	IV	60 PY	0.7 years
Male	Adenoma	IV	40 PY	0.5+ years
Female	SCLC	Ext	30 PY	0.1 years
Male	Squamous	IV	30 PY	0.2 years
Male	NSCLC*	IV	40 PY	0.2 years
Male	Broncho-alveolar	IV	No	1.2+ years

PY=pack-years, Ext=extensive; SCLC, small-cell lung cancer; *NSCLC=non-small-cell lung cancer unclassified.

Results and discussion: All six patients were treated with platinum-based combination chemotherapy using the same protocols that are employed in immunocompetent patients. The actuarial 1-year overall survival is 25% and there is no significant difference in overall survival compared with the non-HIV patients with lung cancer (log rank $P=0.43$). Lung cancer in HIV-positive patients is not associated with advanced immunosuppression and may be treated in the same fashion as in the general population with similar survival outcomes.

P24

New respiratory pathogens in HIV/hepatitis C (HCV) co-infected patients

C De Gascun, J Garvey, S Hopkins, F Lyons, F Mulcahy, C Bergin
St James's Hospital, Dublin, Ireland

Background: *Candida* spp. in HIV-positive patients usually occurs on mucous membranes and infection has been reported to result in endocarditis, myocarditis and meningoencephalitis. A Medline literature search revealed no cases of invasive *Candida* spp. pneumonia in HIV-positive patients.

Methods/Results: A 36-year-old intravenous (IV) drug user with advanced HIV and HCV infection presented to the Accident and Emergency Department with a productive cough. He had a significant past history of recurrent *Pneumocystis carinii* pneumonia (PCP) infection and progressive multifocal encephalopathy. He had recently self-discontinued lamivudine/stavudine/nevirapine. His viral load was 99 copies/mL and CD4 count 24 cells/ μ L before admission. On initial assessment, he was found to be drowsy, icteric, tachycardic and tachypnoeic. Respiratory exam revealed coarse crepitations and dullness in his right lung field. ABG showed type 1 respiratory failure. Complete blood count and renal profile were normal. Liver function tests showed a mixed cholestatic and hepatitic abnormalities; INR was 2.3. Provisional diagnosis was of community-acquired pneumonia with hepatic decompensation. He was commenced on IV co-amoxiclav. IV co-trimoxazole was added. Sputum culture yielded a resistant *Pseudomonas* sp. and *Candida* spp. Antibacterial therapy was altered to piptazobactam; co-trimoxazole continued. 72 hours after admission he desaturated and became hypotensive. He had an asystolic arrest and CPR was unsuccessful. A postmortem revealed invasive *C. albicans* pneumonia with no evidence of disseminated disease; consistent with primary invasive *Candida* sp. pneumonia. Prolonged incubation of antemortem blood cultures did not yield a fungal organism.

Conclusions: Many HIV-positive patients have *Candida* spp. isolated on sputum culture, usually regarded as a colonizer or a pharyngeal pathogen. Invasive *Candida* is more frequent in decompensated liver disease.

P25

Candida glabrata arthritis in a HIV-1 infected former intravenous drug user (IDU)

P Coakley, A Holmes, S Hopkins, F Lyons, F Mulcahy, C Bergin
St James's Hospital, Dublin, Ireland

Background: *Candida glabrata* has been reported as an emerging significant nosocomial pathogen.

Methods: Detailed case description and Medline literature search.

Results: A 36-year-old, HIV-1-positive former IDU presented with a 4-month history of intermittent right knee swelling and pain. He was diagnosed HIV-positive 2 years previously (no IDU since diagnosis). There was no history of cannulation/trauma. At presentation his CD4 count was 257 cells/ μ L (22%) and viral load 13,483 copies/mL (not on highly active antiretroviral therapy). His peripheral leucocyte count was 6×10^9 /L and he had normal biochemistry. The erythrocyte sedimentation rate (ESR) was 28 mm/hour and C-reactive protein (CRP) 39.2 mg/dL. X-ray showed a small knee effusion with no bone destruction. Knee aspirate was performed. Microscopy was negative. *C. glabrata* was cultured. Progression of symptoms led to admission, with ESR and CRP then 97 mm/hour and 58 mg/dL, respectively. Magnetic resonance imaging revealed significant synovial inflammation and ruptured anserine bursa. Knee arthroscopy revealed grade III destructive changes to the medial and lateral tibial plateau. Gram stain of synovial fluid identified pus cells but no organisms. Synovial tissue histology demonstrated hyperplastic synovium and chronic inflammation. *C. glabrata* grew from the synovial tissue. Intravenous amphotericin B (1 mg/kg) was begun. Deterioration in renal function necessitated a switch to liposomal amphotericin (3 mg/kg) after 10 days. Clinical response to therapy was rapid. After 21 days of daily amphotericin, current maintenance is amphotericin three times a week.

Discussion: A Medline search showed two cases of *C. glabrata* arthritis and one of a prosthetic hip infection. All cases were HIV-negative and had hospital exposure. The only identifiable risk infections in the present case are HIV infection and former IDU.

P26

Diagnostic yield of stool analysis and endoscopy in HIV population presenting with diarrhoea

D Datta, BG Gazzard

St Stephen's Centre, Chelsea & Westminster Hospital, London

Background: HIV patients commonly attend with history of diarrhoea. The use of highly active antiretroviral therapy (HAART) has led to a change in the epidemiology of diarrhoea in HIV patients. The patients with negative stool studies are frequently referred for endoscopic evaluation. We aimed to determine the diagnostic yield of stool analysis and endoscopy in HIV patients presenting with diarrhoea.

Methods: We reviewed 525 HIV-positive patients who presented with diarrhoea from 1 January 2000 to 31 August 2001 at Chelsea & Westminster Hospital. These patients were divided into three groups: (group 1: CD4 count ≥ 200 cells/ μ L; group 2: >200 but <350 cells/ μ L; group 3: ≥ 350 cells/ μ L). Patients with two or more stool examinations were included. We also reviewed the endoscopy and biopsy findings of the patients who had negative stool studies.

Results: Of 86 group 1 patients, the stool examination was diagnostic in 30 (34.8%), the commonest diagnosis being cryptosporidiosis (10 patients, 11.6%); other causes were *E histolytica*, giardiasis, campylobacter, salmonella, C diff toxin, microsporidia, isospora and rotavirus. Of 30 patients, 12 (40%) were on HAART, but only two (20%) presenting with cryptosporidiosis were on HAART. In groups 2 and 3, a stool examination was diagnostic in 37 (24.34%) and 74 patients (25.78%), respectively. The most frequent cause in these two groups was giardiasis (14 patients, 9.2%) and campylobacter (20, 6.96%), respectively. In 64 patients (16.6%) with negative stool studies, upper and lower gastrointestinal (GI) endoscopy with biopsies was diagnostic in 12 (30%) and 19 (50%), patients respectively.

Conclusion: In our population, stool analysis in HIV patients with higher CD4 count has a low diagnostic yield. With HAART, infectious causes of diarrhoea are probably less important. Upper and lower GI endoscopies with biopsies were useful diagnostic investigations.

P27

The clinical utility of therapeutic drug monitoring (TDM) in the management of patients receiving indinavir (IDV) and ritonavir (RTV)

SE Gibbons, HE Reynolds, J Lloyd, JF Tjia, SH Khoo, DJ Back

Department of Pharmacology and Therapeutics, University of Liverpool

Introduction: The co-administration of low-dose RTV with IDV allows twice daily dosing of IDV without food restrictions. Various dosing regimens are being used in clinical practice and TDM may have an important role in optimizing a regimen for the individual patient.

Methods: TDM for IDV has been offered by the Liverpool TDM Service since 1999. The data set has been analysed to determine the IDV plasma concentrations in patients with suspected toxicity receiving IDV/RTV regimens and physicians' management of those patients with high concentrations.

Results: Suspected toxicity was indicated on the TDM request form for 103 patients receiving IDV/RTV. Nine IDV/RTV regimens were being prescribed to these patients, the most common being 800/100 mg twice a day (55%), followed by 600/200 mg twice a day (27%). For all regimens, peak IDV concentrations (1–3 hours post dose) ranged from 272 to 21205 ng/mL and trough IDV concentrations (10–14 hours post dose) from 106 to 7728 ng/mL. Follow-up data were available on 46 patients; 10 stopped IDV, 11 had no immediate dose modification but had repeat TDM and 25 had dose modification of IDV and/or RTV. For those on IDV/RTV 800/100 mg, the most frequent dose modifications were to 600/100 mg ($n=7$), 600/200 mg ($n=5$) or 400/100 mg ($n=4$).

Conclusions: From the wide range of IDV/RTV regimens in clinical use in the UK, there is great variability in the resulting plasma concentrations. TDM has a role in identifying those patients with high concentrations and individualizing IDV/RTV regimens.

P28

The pharmacokinetic (PK) interaction of lopinavir/ritonavir (LPV/r) and amprenavir (APV) in clinical practice

SE Gibbons, HE Reynolds, JF Tjia, J Lloyd, SH Khoo, DJ Back

Department of Pharmacology and Therapeutics, University of Liverpool

Introduction: APV in combination with LPV/r is becoming increasingly used in clinical practice and there have been conflicting reports of a PK interaction with these drugs. At least two studies have demonstrated a 50% reduction in APV when used with LPV/r compared with APV/r, leading to a recommendation to increase the dose of APV to 750 mg twice a day (bd) when given with LPV/r. However, other studies have indicated that APV was not apparently reduced when given with LPV/r and a nonnucleoside reverse transcriptase inhibitor (NNRTI). In addition, lower LPV concentrations have been reported in the presence of APV, both in the absence and presence of an NNRTI.

Methods: The Liverpool TDM Service has offered TDM for APV and LPV since early 2001. The data set has been analysed to determine the nature of this PK interaction in adult patients. Statistical analysis was performed using the Mann-Whitney U-test.

Results: The median APV trough concentration for APV/r (600/100 mg bd) was 1724 ng/mL ($n=10$). For APV/LPV/r (750/400/100 mg bd), the median APV trough concentration was significantly lower (1122 ng/mL, $n=16$; $P=0.05$) despite an increase in the APV dose. The presence of an NNRTI with APV/LPV/r further reduced the median APV concentration (678 ng/mL, $n=6$; $P=0.06$). For LPV/r (400/100 mg bd), the LPV median trough concentration was 6375 ng/mL ($n=34$). Adding APV (600-1200 mg bd) resulted in a significant decrease in the median LPV concentration (3464 ng/mL, $n=13$; $P=0.03$); however, addition of an NNRTI had a lesser effect (4683 ng/mL, $n=8$; $P=0.4$).

Conclusions: This is a complex PK interaction and the marked interpatient variability highlights the potential importance of TDM.

P29

Pharmacological Optimization of PIs and NNRTIs (POPIN): the implementation of a nurse-led therapeutic drug monitoring (TDM)/adherence package for patients receiving highly active antiretroviral therapy (HAART)

J Lloyd¹, J Sweeney², P Flegg², A Bonington³, E Wilkins³, S Gibbons¹, DJ Back¹, SH Khoo¹

¹Department of Pharmacology and Therapeutics, University of Liverpool, ²Department of Genito-Urinary Medicine and Infectious Diseases, Victoria Hospital, Blackpool, and ³Department of Infectious Diseases, North Manchester General Hospital

Introduction: The use of TDM to optimize therapy is increasing. There are many factors to be considered in the TDM process to ensure accurate and clinically meaningful drug concentrations. Adherence is a major determinant of treatment outcome and its relationship to drug levels needs further evaluation.

Methods: A retrospective analysis of 2123 assays received by Liverpool HIV Pharmacology Group between October 2000 and December 2001 inclusive was performed.

Results: Requests were the responsibility of nurses (40%), doctors (43%) and pharmacists (10%). Information necessary for interpretation varied between doctors (76%), nurses (95%) and pharmacists (92%). Trough-sample timing was classified inaccurate ($\pm 12.5\%$ of trough target time) in 18% of cases.

Conclusions: The collection of clinical data and timing of samples is frequently suboptimal and varies according to healthcare professional. Adherence should be assessed in all patients receiving TDM. Dedicated personnel are required to provide the level of intervention necessary for TDM. Nurses are well placed to provide such an intervention. The POPIN clinic has been introduced in three centres in the UK to provide a best-practice model for TDM.

P30

Experience of voluntary named testing for HIV for antenatal patients in a North West London Hospitals NHS Trust

OJ Braithwaite¹, E O'Sullivan¹, A Phil-Ebosie², M Costello¹

¹Northwick Park Hospital and ²Central Middlesex Hospital, London

Objective: To review the demographic details and pregnancy outcome, of known HIV-positive women in two northwest London hospitals where screening uptake rate has been over 90%.

Methods: Prospectively recorded data of women invited for testing from May 1999 to December 2001 were reviewed to determine the rate of uptake of testing and the outcome of pregnancies of women testing positive.

Results: 15,594 women were booked during the study period and the mean screening uptake was 94.25%; 45 of these were HIV-positive, including 19 who knew their HIV status prior to pregnancy and 25 were diagnosed through antenatal voluntary screening. Of the 19 who knew their status before pregnancy, four opted for termination of the pregnancy, there was one early miscarriage and one patient was lost to follow-up. 10 patients were delivered by elective Caesarean section at term and two had preterm deliveries; there was one normal vaginal delivery. In the group of patients who were first diagnosed antenatally, 21 had elective Caesarean sections. Three patients had vaginal deliveries, one of which was for a Trisomy 18 baby. One patient transferred her care to another hospital and the outcome is unknown. 44 of 46 babies of all the HIV-positive mothers who delivered in the study period have all had three negative polymerase chain reaction tests and there was one case of seroconversion.

Conclusions: Testing has been successful in identifying HIV-positive women in the Brent and Harrow area. A proportion of the patients with known HIV disease now feel confident about either starting a family or having more children, knowing that expert care is available. None of the patients diagnosed antenatally opted for termination of pregnancy.

P31

Leptomeningeal involvement in AIDS-related non-Hodgkin's Lymphoma

D Sarker, J Lukawska, J Nathan, MR Nelson, BG Gazzard, M Bower
Chelsea & Westminster Hospital, London

Background: Leptomeningeal involvement is frequent in AIDS-related lymphoma (ARL) and is associated with bone marrow involvement, Burkitt's histology and paraspinous and paranasal space disease.

Methods: The ARL database includes 176 patients with systemic ARL. Patients with meningeal disease at presentation are treated with intrathecal chemotherapy and craniospinal irradiation in addition to systemic chemotherapy. Patients identified at high risk of meningeal relapse (criteria above) receive prophylactic intrathecal chemotherapy. **Results:** 18 (10%) patients had meningeal disease at presentation. These patients had similar CD4 cell counts, age, performance status and B symptoms to those of patients without meningeal disease. However, more (28%) had bone marrow ARL (χ^2 -test, $P=0.08$) and Burkitt's histology (33%) (χ^2 -test, $P=0.018$). There was no significant difference in overall survival durations: 1-year survivals, 25% (95% confidence interval 3.4-46.6) for meningeal disease versus 33.1% (25.5-40.7) (log rank $P=0.35$). Of 158 patients without meningeal disease, 26 high-risk patients received intrathecal chemoprophylaxis and three (12%) subsequently relapsed in the meninges. In addition, there were three (2%) meningeal relapses in the 132 low-risk patients (χ^2 -test, $P=0.24$).

Conclusions: Meningeal disease correlates with established risk factors, and prophylaxis in these high-risk groups prevents meningeal relapse in >80%.

P32

Drug interaction between nevirapine (NVP) and warfarin

M Ghanem, PS Allan, A Wade

Coventry Sexual Health Services, Department of Genito-Urinary Medicine, Coventry and Warwickshire Hospital, Coventry

Background: Patients with HIV are administered multiple drug regimens and adverse drug interactions may compromise efficacy and/or enhance toxicity. NVP may reduce warfarin levels; however, this is based on data from ketoconazole drug interaction. There were no reports of interactions between NVP and warfarin until recently, when D Dionisio *et al.* reported three cases. We report two cases to highlight the clinical importance and expand information on this interaction.

Case 1: A 40-year-old male was commenced on Combivir and NVP, with a CD4 count of 353 cells/ μ L. Right deep vein thrombosis (DVT) was diagnosed and was treated with low-molecular-weight heparin (LMWH) and 18 mg warfarin (INR 2.3). A thrombophilia screen was negative. Warfarin was discontinued after 6 months, but 18 months later, he had extensive DVT involving the right popliteal and femoral veins, requiring heparin and 18 mg warfarin a day for an INR of 2.4.

Case 2: A 43-year-old man developed pulmonary embolism while on lamivudine, abacavir and NVP (CD4 552 cells/ μ L). Initially, he was treated with LMWH and warfarin up to 16 mg a day. Subsequently, 12 mg warfarin per day was required to maintain INR therapeutic range.

Discussion: Warfarin is the oral anticoagulant of choice in the UK and many other countries. Cytochrome (CY)P450 2C9 is the main enzyme to catalyse S-warfarin and CYP1A2 and CYP3A4 are the principal enzymes to catalyse R-warfarin. NVP is primarily an inducer of CYP3A4 enzyme and therefore would be expected to interact with warfarin. In view of the current evidence, clinicians should be aware of that interaction. In managing patients, a higher dose of warfarin than usual might be necessary. Changing NVP to other antiretroviral drugs, if possible, might be considered, especially when an INR higher than 2-3 is recommended.

P33

HIV and pregnancy: experience in an inner city District General Hospital

S Limb¹, D Aleksin², R Edwards², K Erskine², J Anderson³

¹St Bartholomew's Hospital and the London NHS Trust, ²Homerton University Hospital NHS Trust, ³St Bartholomew's Hospital and The London School of Medicine and Dentistry

Objective: Growth of HIV testing for women in antenatal clinics, a rise in HIV infection in the UK and improvements in antiretroviral therapy have increased the numbers of HIV-positive pregnant women cared for at the Homerton University Hospital. This study reviews the patterns of referral and management of women seen since 1998.

Method: A retrospective case note review was carried out on all HIV-positive pregnant women seen at Homerton University Hospital between January 1998 and January 2002.

Results: The notes of 64 women were reviewed; 39 were newly diagnosed in the antenatal clinic and 25 had been aware of their HIV status prior to pregnancy. Numbers of HIV-positive women presenting via the antenatal clinic rose over the 4-year period, representing 2% (2/90) of total new HIV diagnoses at the hospital in 1998, rising to 10% (29/208) in 2001; 55 women (86%) were of African origin; 12 of the 29 women diagnosed in 2001 have not yet delivered. Of the remaining 52 women, five had a miscarriage. The obstetric/neonatal details of a further four are unknown. Of 43 patients for whom full information is available, 26 had an elective Caesarean section, eight had an emergency Caesarean section and nine had spontaneous vaginal delivery. There was one neonatal death. Five of these 43 women were not on antiretrovirals at the time of delivery and six had detectable virus (>50 HIV-1 RNA copies/mL) in plasma. No children in this cohort have been found to be HIV-infected to date.

Conclusion: Pregnant women account for an increasing proportion of new HIV diagnoses. The antenatal clinic provides an important front door to HIV services with complex resource and service implications.

P34

Antenatal HIV testing in England: review of policy, African women's experiences, Africans' denial of access to medical care and implications for HIV prevention

L Kawonza

Terrence Higgins Trust, London Health Promotion Services, London

Objective: To describe the Department of Health (DoH) current antenatal HIV-testing policy, its impact on HIV-positive pregnant African women who are visitors, students with less than a year's residency in the UK and over-stayers and to suggest how the situation could be improved.

Method: A brief overview will be given of the DoH antenatal HIV-testing policy aimed at reducing the incidence of mother-to-baby HIV transmission and launched in September 1999. The policy's success depends on HIV-positive pregnant women having access to medical care. Three case studies will be used to demonstrate the impact on and outcome for HIV-positive pregnant women who did not qualify for medical care. The possible impact on vertical transmission of HIV will be highlighted. The policy, although well intended, does not address issues relating to immigration, asylum, responsibility for children living in the UK and better understanding and support of HIV-positive women. Stop-gap measures that were taken to deal with the relevant cases will be explained. There is concern regarding women who may refuse the test for fear.

Conclusions: There is a need for longer-term solutions and clarity of policy in order to achieve effective mother-to-child HIV prevention. There needs to be a clear decision to ensure women are told that they will not be able to access care so that they could decide to take a test or not, knowing those facts. BHIVA as an organization could influence future policies to help improve the situation.

P35

Subsequent HIV testing in children of HIV-positive mothers

S Vergnano, J Railton, M Sharland
St George's Hospital, London

Aims: To establish what proportion of children of HIV-positive mothers attending a South London department of genito-urinary medicine have been tested and are under the care of a paediatrician.

Methods: A prospective study was conducted over 3 months (April–July 2001) in St George's Hospital. Female patients attending the HIV clinic were informed about the study and asked to complete a questionnaire, with a health adviser.

Results: During the study period, 158 women attended the clinic; 69 (43%) questionnaires were completed and one woman declined. The sample included 133 children; 59% of women were black, African and Afro-Caribbean, 33% were white and 8% Asian. Of the 102 children living in the UK, 82 (81%) had been tested. The children tested and living in the UK were mainly tested at birth (25%) or within a year from maternal diagnosis (37%). Seven children (9%) were tested before any other family members. Of these, one was diagnosed in 1999, and all the others prior to 1998. All the 13 children (17%) tested more than a year after their mothers were tested before 1998. All the HIV-positive children were under the care of a paediatrician.

Conclusions: The results are encouraging, as 81% of children living in the UK had been tested. In more recent years, the number of children diagnosed late (more than a year from their mothers) have decreased. Children not tested are clustered in a small number of families. To further reduce late diagnosis in children, we proposed to formalize guidelines for the health advisers to ensure that the issue of testing children is raised routinely after maternal diagnosis.

P36

HIV diagnosis in the year 2000: attitudes to HIV and testing.

S Madge¹, A Cozzi-Lepri¹, T Fernandez¹, MA Johnson¹, A Johnson²

¹Royal Free Centre for HIV Medicine and ²Department of Primary Care, Royal Free Hospital, London

Objectives: To investigate circumstances of HIV diagnosis and HIV testing history; to evaluate access to medical care prior to HIV diagnosis; to assess attitudes to HIV testing and HIV itself; and to identify factors that might contribute to late presentation

Methods: A semi-structured questionnaire was completed with SM at routine clinic visits. It was offered to all those diagnosed in 2000.

Results: Data are available on 56 patients, 41 men and 15 women; 15 (27%) had AIDS at diagnosis; 50% were Caucasians; 43% were infected by homosexual sex; 45% stated they made a sole decision to test; 35% of all patients stated that they were expecting a positive result or felt they had been at risk; 39% knew about highly active antiretroviral therapy (HAART) when testing. Many were concerned about coping with HIV (50%), stigma (37%) and disclosure (42%). Overall, 83% felt those at risk should seek testing, and 35% felt counselling before the test was not always necessary; others felt testing could be offered in non-medical settings (59%) or via home-testing kits (43%); 64% felt they tested at the right time, 28% too late; 57% had never previously tested; 91% were registered with a general practitioner (GP) and 84% had visited the GP in the 3 years before the test. Three patients were diagnosed by a GP. 72% had attended clinics as outpatients (mostly genito-urinary medicine and accident and emergency); 41% were inpatients in the 3 years before diagnosis. Those with AIDS were more likely to have been asked to test by a doctor and be diagnosed as inpatients and 'too late' ($P=0.001$ for all). People with AIDS were, however, more optimistic, with a greater proportion disagreeing that HIV is a fatal disease ($P=0.003$).

Conclusions: These patients were from high-risk groups but many had not previously tested, despite good access to medical care. Many expressed strong views. Few differences were seen in late presenters.

P37

Limited lives: experiences of black African women with HIV living in London

J Anderson¹, L Doyal²

¹St Bartholomew's and the Royal London School of Medicine and Dentistry, London and ²School for Policy Studies, University of Bristol, Bristol

Objective: Black Africans, more than 50% of whom are women, form the second largest group of HIV/AIDS service users in London. We document the circumstances of HIV-positive women from African backgrounds in London and their experiences of health and social care.

Method: A qualitative investigation was conducted using a sample of women drawn from four London hospitals. The women completed a demographic questionnaire and participated in a semi-structured interviews, which were audio-taped, transcribed and analysed.

Results: 62 women from 11 different countries receiving care in four London hospitals took part. There was a wide range of socio-economic and educational backgrounds. The majority had dependent children. HIV imposed a variety of limitations on their lives, in particular limitations imposed by poverty and isolation, the tensions involved in managing relationships with the African community both in London and back home and the complexity of making decisions about disclosure. Many women were reluctant to look for support to organizations concerned with the welfare of people living with HIV/AIDS.

Conclusions: The policy implications for the future delivery of primary and secondary HIV care and prevention for this group of patients raised by these findings are discussed.

P38

Trends and determinants of HIV testing in genito-urinary (GUM) clinics and primary care in England, 1990–2000

T Chadborn, C McGarrigle, K Fenton

Public Health Laboratory Service Communicable Disease Surveillance Centre, London

Aims: To describe the trends and determinants of HIV testing at GUM clinics and in primary care in England.

Methods: Data on all first HIV tests were obtained from seven sentinel laboratories. Age, sex, exposure category, reasons for testing and symptoms at the time of test and HIV test result were collected.

Results: 90% of the 208,125 first HIV tests reported were requested from GUM clinics. This number has increased over time. Overall, 12% of HIV tests carried out at GUM clinics were in men who have sex with men (MSM), and 3% were in injecting drug users (IDUs). In contrast, 3% of tests at general practitioners (GPs) were from MSM and 12% from IDUs. The proportion of tests from MSM decreased from 5% in 1990 to 1% in 2000, while the proportion of tests from IDUs increased from 4% to 20%. HIV prevalence at GUM clinics was 6.9% in MSM, 2.8% in IDUs, 0.9% in heterosexuals and 0.2% in others compared with 6.0% in MSM, 0.9% in IDU, 0.9% in heterosexuals and 0.3% in others at GPs.

Conclusions: HIV testing in GUM clinics has increased without a decline in overall prevalence. If there is a shift to increasing HIV testing in primary care, services should be prepared for an increased need for counselling and referral to specialist services, including drug treatment agencies.

P39

Evaluation of an HIV testing awareness media campaign

PJ Easterbrook¹, T Chadborn², A Boyd¹, P Salami³, M Akello⁴, M Kizairwe⁵, I Steen¹, S Shafi⁶, AM Murrin-Geretti¹, T Leung¹, J Mortimer²

¹King's College Hospital, ²Communicable Diseases Surveillance Centre, ³Blackliners, ⁴ACIA, ⁵UAAF and ⁶Central Middlesex NHS Trust, London

Objective: To develop a media campaign to promote the benefits of early diagnosis and treatment of HIV infection, and to evaluate the impact of the campaign on HIV testing patterns.

Methods: The campaign was launched in December 2000: 6000 copies of four different posters and 55,000 leaflets were distributed to over 2000 sites in South London, in addition to a series of television and radio interviews promoting the message of the campaign, 'HIV can be treated: take control – take the test'. The impact was evaluated by the number of first HIV tests and HIV-positive rates in the years before and after (2001) the campaign, at two laboratory sites in London.

Results: At the south London laboratory site, there was a 20% increase (1695 additional tests) in the total number of HIV tests during 2001 compared with 2000 against a progressive background rise in the number of HIV tests since 1997. The greatest increases were in tests performed in sexually transmitted disease (STD) clinics (35% increase) and by general practitioners (GPs; 55% increase); among heterosexuals (22% increase); and among those worried about HIV (75% increase). The HIV-positive rate increased from an average of 3.32% to 4.09% in the last quarter of 2001. Similar though less marked trends were seen in the north London laboratory site.

Conclusions: There was an increase in the number of HIV tests performed, particularly in heterosexual attendees of STD clinics and GPs in South London following the campaign. Further details of the organization and conduct of the campaign will be presented.

P40

Comparison of HIV-positive nationals versus non-nationals in Ireland

N Boyle, O Lesens, F Lyons, F Mulcahy

GUIDE Clinic, St James's Hospital, Dublin

Background: 10,325 asylum seekers arrived in Ireland in 2001, 60% coming from sub-Saharan Africa, causing a significant change in the profile of HIV-positive patients attending the Department of Genito-Urinary Medicine and Infectious Diseases, Dublin. This study examines differences in baseline characteristics between Irish and non-Irish HIV patients diagnosed from January 2000 to September 2001.

Methods: Demographic data, including country of origin, age at diagnosis, sex, risk category and HIV testing site, were collated for all patients. Centers for Disease Control and Prevention (CDC) classification, concomitant diagnoses, stage of HIV-1 disease at time of presentation and number of pregnancies were also recorded.

Results: 266 people were diagnosed with HIV-1 infection in the study period, 138 (52%) Irish and 128 (48%) non-Irish; 97 (76%) of the non-Irish were of African origin: South Africa, 42 (33%), and Nigeria, 22 (17%). The Irish group had 106 (77%) males and 32 (23%) females versus 47 (37%) males and 81 (63%) females in the non-Irish group. There have been significantly more pregnancies in the non-Irish versus the Irish group: 52 (64%) and 6 (19%), respectively. The commonest place of diagnosis in the non-Irish group was the antenatal clinic at 36 (28%), followed by the voluntary screening services at point of entry to the country at 32 (25%). The non-Irish group mainly acquired HIV heterosexually at 103 (80%) versus 17 (12%) for the Irish group. The seroprevalence of hepatitis B s-antigen and hepatitis C antibodies was 3%/3% and 8%/30% in the non-Irish and Irish, respectively. There were eight (5.8%) AIDS-defining illnesses at the time of HIV-1 diagnosis in the Irish group and three (2.3%) in the non-Irish group.

Conclusion: HIV infection in non-nationals accounted for 48% of all new diagnoses in the study period. Most were females, with 28% diagnosed via antenatal testing, indicating a potentially larger pool of hitherto undiagnosed cases in men.

P41

Perceptions of highly active antiretroviral therapy (HAART) among HIV-positive men who have been recommended treatment

V Cooper¹, R Horne¹, G Gellaitry¹, N Lambert¹, M Fisher²

¹University of Brighton and ²Brighton and Sussex University Hospitals NHS Trust, Brighton

Background: Patients' beliefs about HAART and HIV have been shown to predict uptake of HAART. In this study, we explored the way in which HAART is perceived by those who accept and those who decline a treatment offer.

Methods: In-depth interviews were conducted with consecutive patients offered HAART in Brighton. The interview transcripts were subjected to a thematic analysis and checked for inter-rater reliability. **Results:** Declining HAART ($n=20$) was characterized by six themes: doubting personal need for HAART; having concerns about taking HAART; having previous negative experience of HAART; holding negative beliefs about medicines in general; and requiring autonomy in the treatment decision. Accepting HAART ($n=35$) was also characterized by six themes: recognizing personal need for HAART; expecting benefits from taking HAART; having addressed concerns about taking HAART; believing personal circumstances to be conducive to starting treatment; being influenced by other people's experiences; and being in accordance with medical recommendations.

Conclusion: This study has improved our understanding of how HAART is perceived by people faced with difficult treatment decisions. It provides an insight into patients' perspectives of HAART, with implications for the development of interventions to provide decision support.

P42

Is the L90M mutation selected more frequently in non-B subtype HIV-1-infected patients failing nelfinavir (NFV)-containing highly active antiretroviral therapy (HAART)?

L Navaratne, W Tong, J Mullen, S O'Shea, G duMont, A de Ruiter, R Kulasegeram

St Thomas's Hospital, London

Objective: To analyse a group of HIV-1-infected patients failing on an NFV-containing regimen with known genetic sequences containing D30N and/or L90M.

Methods: A retrospective review of 48 patients who had a genotypic resistance test containing D30N and/or L90M over a 2-year period. Data were collected on HIV-1 subtype and current and previous NFV-containing HAART.

Results: 29 (63%) patients had been exposed to protease inhibitor therapy containing NFV. 17 (37%) had only been exposed to NFV prior to genotypic analysis and the results of this group are shown in the following table:

Subtype	D30N (%)	L90M (%)	D30N + L90M (%)	Total (n)
B	4 (100)	0 (0)	0 (0)	4
Non-B	5 (38)	7 (54)	1 (8)	13
Total	9	7	1	17

Non-B subtypes: A=6, C=2, D=3, A/G=1, A/E=1.

Conclusions: In this small observational study of patients failing after NFV therapy alone, L90M was selected at least as frequently as D30N in non-B subtypes. The clinical significance of developing this mutation could result in cross-class resistance to other PIs not previously thought to be associated with the use of NFV as a first-line protease inhibitor. Larger samples are needed to confirm the significance of this important observation.

P43

Serological testing algorithm for recent HIV seroconversion (STARHS) identifies a high proportion of newly diagnosed HIV infections as incident

GL Dean¹, JV Parry², G Murphy², M Fisher¹

¹Brighton and Sussex University Hospital NHS Trust, Brighton, and ²Central Public Health Laboratories, London

Introduction: The identification of primary HIV infection (PHI) is essential for the effective management of early HIV disease, contact tracing, monitoring resistance patterns and local epidemiology. Newer diagnostic techniques (e.g. STARHS) identify cases with PHI within the last 4–6 months. This study aimed to evaluate the role of STARHS in identifying incident infections that may otherwise have been missed.

Methods: Clinical data were collected on all newly diagnosed HIV infections from 1 January 2000 to 31 July 2001. In addition to conventional antibody testing, we performed STARHS on all samples.

Results: 225 individuals were anti-HIV-1-positive for the first time at this centre. 119 gave a history of previous positive results elsewhere. Of the 106 for whom this was their first positive result:

	No new infection	Previous HIV+, last 18 months	Incident infection in STARHS (%)	Total incident infection
2000	67	8 (12%)	18 (27%)	20 (30%)
2001*	39	8 (18%)	16 (41%)	17 (44%)
Total	106	15 (14%)	34 (32%)	37 (35%)

* to end July 2001, but full 2001 data will be presented.

12 (not included above) were initially identified as incident by STARHS but re-designated as prevalent based on clinical data: eight were known HIV-positives on HAART; four had advanced HIV disease.

Conclusions: STARHS, as a routine adjunct to HIV antibody testing, assists in the identification of incident infections. It is, however, essential that appropriate clinical information is matched to the STARHS results as reduced antibody levels (secondary to advanced HIV or HAART) may be interpreted incorrectly.

P44

Patient and clinician variability in assessing the severity of facial lipoatrophy (LA)

P Benn¹, S Edwards¹, J Cartledge¹, A Copas², C Ruff³, A Linney³, IG Williams²

¹Departments of ¹Genito-Urinary Medicine, ²Sexually Transmitted Diseases and ³Medical Physics, Royal Free and University College Medical School, London

Aims: To evaluate patient and doctor variability in assessing the severity of facial lipoatrophy (LA).

Methods: 23 HIV-positive men were recruited from the routine HIV clinic; 18 had received combination antiretroviral therapy (CART) for at least 6 months. 15 of the 23 had facial LA and three did not; five of the 23 were CART-naïve without facial LA. Details of height, weight, CD4 count, viral load and CART were recorded. Each patient and three clinicians evaluated the whole face, temporal and cheek areas for the presence and severity of facial LA, using a 4-point scale. Changes in body habitus were recorded using a 7-point scale. All were blinded. All anthropometric measurements were taken by one clinician. Correlations between patient, doctor and intra-doctor evaluations were measured by the Wilson matched-pair significant rank test.

Results: Dr A reported lower scores for overall facial LA than the patients ($P<0.005$). Patients and doctors reported no significant differences in LA between temporal and cheek areas. Dr A reported lower scores for overall facial LA compared with Drs B and C ($P<0.005$) and for the temporal area than Dr B ($P=0.01$). Dr B also reported lower scores for overall facial LA than Dr C ($P<0.05$). Less than 50% of patient/Dr B pairs reported identical scores for arms, abdomen and buttocks.

Discussion: There is significant patient/doctor and intra-doctor variability in evaluating the severity of facial LA. An objective reproducible method of assessing facial LA is needed.

P45

Retrospective audit of use of viral load (VL) test

S Dundas, CLS Leen

RIDU, Western General Hospital, Edinburgh

Background: Our VL budget allows four tests per patient per annum. In 2001 we were grossly over budget.

Objectives: To determine the number of episodes where patients had VL tests repeated within 3 months; to identify indications for a VL repeat test within 3 months; to quantify the inappropriate premature VL test repeats; and to develop a protocol for the use of the VL test.

Methods: A retrospective audit over the 18-month period ending June 2001, with linkage of laboratory VL database and clinical database. Inappropriate premature VL repeat tests were defined as (1) two preceding VLs <50 copies/mL, CD4 >200 cells/ μ L and therapy unchanged; or (2) two preceding VLs >100,000 copies/mL and not on therapy.

Results: 342 patients were identified, with 1816 VL requests and 1264 (70%) VLs repeated within 3 months. (1) 302 premature VL repeat tests were done when two preceding VLs <50 copies/mL. The commonest reasons were CD4 failure (21%) and a change in therapy (11%). 138 VL tests were repeated prematurely without reason. (2) 15 premature VL repeat tests were done when two VLs were >100,000 copies/mL without reason.

Conclusions: A high proportion (70%) of VL tests were repeated within 90 days. Only 153/1264 were without reason. £91,000 was spent on VL testing, of which £7600 was used inappropriately. Complex management dictates that many patients need more than four VL tests per year. The budget needs to be redressed.

P46

The creation of a large UK-based cohort of HIV infected individuals: the Seven Centre HIV Database Project

C. Sabin, T Hill, for the UK Seven Centre HIV Database Project Steering Committee

Royal Free and University College Medical School, London

Objective: To describe the development of the UK Seven Centre HIV Database, a collaboration of seven clinical centres in London and southeast England, which aims to pool clinical and laboratory information on all HIV-positive patients seen at the centres since 1 January 1996.

Methods: Centres provided data on demographics, laboratory measures, clinical events and antiretroviral therapy. Data sets were checked for logical errors and inconsistencies, which were resolved in collaboration with the centres. Information from patients thought to have attended more than one centre has been linked and the information contained in the data set is currently being audited, with information on data quality fed back to each centre.

Results: Currently, the database contains information on 13,825 individuals attending six of the seven centres. The cohort is 82% male and risk factors for HIV infection are: homo-/bisexual sex (61%); heterosexual sex (22%); intravenous drug use (4%); other/unknown (12%). Ethnicity data are available for 11,350 patients (67% Caucasian, 19% black African). Of the patients under follow-up at the start of 2000 and 2001, 69% and 73%, respectively, have received antiretroviral therapy.

Conclusion: Once the audit is complete and all data queries resolved, this database will provide a unique opportunity to address many key questions relating to changes in HIV disease, survival and uptake over time in a large UK-based cohort. Correlates of clinical, immunological and virological response to therapy will be assessed. Downloads of data are planned every 6–9 months to ensure that the data set provides timely information on any changes in disease progression.

P47

Epidemiology of HIV-1 subtypes among different ethnic groups in southeast London

I Aggarwal, AM Geretti, M Smith, M Zuckerman, S Murad, PJ Easterbrook

King's College Hospital, London

Objective: To determine factors associated with B subtype infection among black Africans and non-B subtype infection among white UK and black Caribbean patients.

Methods: 359 patients with HIV-1 infection were subtyped using an in-house enzyme immunoassay. A standardized proforma was used to collect demographic, clinical and laboratory data from medical records. Information on sexual behaviour, networks and travel history was obtained via a questionnaire.

Results: 17.3% of black Africans were infected with B subtypes; 14.6% of white UK and 31.4% of black Caribbean patients were infected with non-B subtypes. Black Africans were predominantly female (67%) and heterosexual (86%). Those with B subtypes were significantly more likely to be Ugandan in origin than those with non-B (69.6% versus 17.3%, $P < 0.001$). White UK patients were predominantly male (93.2%) and homosexual (74%). The majority of black Caribbean patients were male (62.9%), and all those with homosexually acquired infection had B subtype. No other significant differences between B and non-B subtype in the three ethnic groups were observed. Additional data from the analysis of sexual behaviour and networks will be presented. *Env* sequencing is ongoing to confirm HIV-1 subtype.

Conclusions: This preliminary analysis suggests that country of origin and risk group are important in determining local transmission patterns of HIV subtypes among different ethnic groups.

P48

HIV surveillance in the UK: trends over time

K Sinka, Z Shaheem, A McHenry, J Mortimer, T Chadborn

Public Health Laboratory Service AIDS and Sexually Transmitted Diseases Centre at the Communicable Disease Surveillance Centre, London

Objective: To describe important changes in the UK epidemic, using trends seen in national surveillance data over time.

Background: Surveillance of AIDS cases began in 1982, and of HIV diagnoses in 1985 following the development of antibody tests. Since then, other surveillance schemes have come into existence. Together, these provide a comprehensive measure of HIV in the UK. The systems have all been in place for several years and show important changes in the epidemic over time.

Methods: Descriptive methods are used: (1) to illustrate the changes that the widespread use of highly active antiretroviral therapy (HAART) have made in the epidemiology of HIV disease in the UK and in immune suppression at the population level; (2) to follow the changing pattern of new diagnoses and the increasing impact of the global epidemic in the UK. Finally, the size of the UK epidemic is projected to 2005, based on adjusted prevalent diagnosed infections data.

Results: A marked fall in cases of AIDS and HIV-related deaths followed the widespread use of HAART after 1996. A concurrent steady increase in the number of new diagnoses, with increasing numbers of heterosexually acquired infections from sub-Saharan Africa, means that prevalence has continued to rise. Forecasts anticipate a 47% rise in numbers attending HIV services between 2000 and 2005.

P49

Emergence of cytotoxic T-lymphocyte (CTL) escape viral variants during early HIV-1 infection

NA Jones¹, X Wei², M Wong¹, P Newton³, D Cornforth³, IG Williams³, GM Shaw², P Borrow¹

¹Viral Immunology Group, The Edward Jenner Institute For Vaccine Research, Compton, Berkshire, UK, ²Howard Hughes Medical Institute, University of Alabama at Birmingham, USA, and ³Department of Sexually Transmitted Diseases, Royal Free and University College Medical School, London, UK

Background: Virus-specific CD8 CTL responses occur very early after infection with HIV-1 and are thought to play an important role in the containment of virus replication. Broad, strong CD8 T-cell responses were seen from very early after infection in patients who naturally established low persisting viral loads. The primary HIV-specific CD8 T-cell response in subjects who establish high persisting viral loads is much more limited. A consequence of mounting a narrowly directed, primary HIV-specific CD8 T-cell response might be increased selection for viral variants with mutations that prevent recognition by epitope-specific CD8 T cells. We investigated this in depth.

Results: In one patient with a high persisting viral load, the HIV-specific CD8 T-cell response was initially mainly directed against immunodominant epitopes in gp160 and gag, then subsequently broadened to recognize epitopes in other viral proteins. Rapid and sequential selection for viral variants able to escape recognition by the initially immunodominant responses. A subdominant response to an epitope in tat was also seen. In a second patient, with a much lower persisting viral load, a broad CD8 response against >30 epitopes in multiple proteins was seen in acute infection. The strongest responses were to epitopes in gp160 and tat. Escape-conferring mutations were selected only in a group of overlapping epitopes in tat. In these patients, sequential selection of CTL escape viral variants was associated with a primary HIV-specific CD8 T-cell response focused on a limited number of viral epitopes and poor control of early virus replication.

P50

Varied autoimmune thyroid disease phenotypes in a cohort of immune reconstituted HIV patients

F Chen, S Day, G Sethi, W Tong, R Metcalfe, J Welch, S Edwards, D Lewis, G Scullard, A Weetman, S Robinson, M Kapembwa, A de Ruiter

St Mary's Hospital and St Thomas's Hospital, London

Objective: Autoimmune thyroid disease (AITD) has been observed in HIV-positive patients taking highly active antiretroviral therapy (HAART), suggesting that immune reconstitution (IR) may promote organ-specific autoimmunity. Hence, a case collection of patients with AITD was performed to analyse the spectrum of disease observed, its temporal relation to HAART and temporal changes in thyroid antibody (tAb) titres.

Methods: All cases of AITD in six HIV treatment centres were identified. Data were collected on clinical features, thyroid function, CD4 count (cells/ μ L), serum HIV RNA viral load (VL), tAbs and technetium scans. tAbs were measured during thyrotoxicosis and in archived samples, retrospectively.

Results: 10 patients (nine females, one male), of median age 37 years, were diagnosed with thyrotoxicosis. All were on HAART, with a median pre-HAART nadir CD4 count of 50 cells/ μ L. The median time from first VL <50 to diagnosis of AITD was 14 months, and the mean increase in the CD4 count was 311 cells/ μ L. Grave's Disease (GD) was diagnosed in nine patients (eight females, one male): one had profound secondary hypoadrenalism, a rare observation; two developed GD 8–12 months after childbirth; one had Hashi-toxicosis; eight showed a sequential rise in tAb titres and two had very high TSHR-blocking tAb titres.

Conclusions: Although data on AITD in HAART-naive patients are needed, our observations of varied and rare AITD phenotypes, in temporal relation to HAART, appear unlikely to be chance observations. These phenotypes are observed during the phase of naive CD4 cell expansion, making IR-AITD a plausible phenomenon.

P51

Two-long terminal repeat (2-LTR) circles are a reliable and reproducible measure of recent infection events in HIV-1-infected patients

J Morlese, I Teo, JW Choi, BG Gazzard, S Shaunak
Hammersmith Hospital and Chelsea & Westminster Hospital, London

Background: On-going viral replication in patients on antiretroviral therapy leads to treatment failure. We have shown that the 2-LTR circle assay can be performed on peripheral blood mononuclear (PBMC) cells to monitor acute infection events throughout the body, even when the plasma HIV-1 RNA is <50 copies/mL. Controversy still exists on the half-life of circles *in vivo* and *in vitro*. We have established a quantitative LightCycler polymerase chain reaction assay to measure the circle copy number in infected cells. The assay was used to determine the circle half-life in patient PBMC cells *in vivo* and in monocyte-derived macrophages (MDMs), PBMCs and C8166 cells *in vitro*.

Methods: (1) In 10 patients, the 2-LTR circle copy number was monitored weekly before and after starting antiretroviral therapy. (2) MDMs, PBMC cells and C8166 cells were infected with primary isolates of HIV-1 *in vitro*. A combination of zidovudine, lamivudine and indinavir was then added to suppress new rounds of infection and the circle half-life determined. The circles were extracted from cells by a plasmid extraction method and quantified using a LightCycler.

Results: The circle copy number in 10 patients before antiretroviral therapy was 288 (127 copies/ 10^6 cells with a baseline CD4 lymphocyte count of 117 \pm 22 cells/ μ L). In seven of these patients, the *in vivo* circle half-life was 5.7 days. In two, there was no change in the circle copy number and the tenth patient had an undetectable circle copy number at all times. In these *in vitro* studies, the circle half-life was 19 hours in MDMs, 10 hours in PBMC cells and 11 hours in C8166 cells.

Conclusions: The median *in vivo* half-life of 2-LTR circles is 5.7 days versus an *in vitro* mean half-life of <12 hours. 2-LTR circles may be a measure of persistent viral replication, being labile *in vitro* and *in vivo*.

P52

Recombinant human growth hormone (rhGH) with highly active antiretroviral therapy (HAART) for the treatment of HIV-1 has beneficial effects on the immune system

A Pires¹, J Pido-Lopez¹, GJ Moyle², BG Gazzard², F Gotch¹ and N Imami¹

¹Department of Immunology and ²Department of HIV/Genito-Urinary Medicine, Chelsea & Westminster Hospital, London

Objectives: To evaluate the effects of rhGH on the immune system of HIV-1 infected patients on HAART.

Methods: 12 chronic HIV-1-infected patients on HAART received rhGH. The lymphocyte phenotype was assessed at baseline, 12 weeks after 4 mg/day of rhGH and 24 weeks after randomization into three groups (placebo or alternate day or twice weekly dosing of rhGH). T-cell receptor rearrangement excision circles (TREC) analysis was performed for all time points.

Results: At baseline, four patients showed a second, activated subset of lymphocytes, and 12 weeks after administration of rhGH this was seen in 11 patients. This subset comprised mainly CD8 memory/effector T cells, as assessed by CD45RA and CCR7 expression. There was an increase in the naive compartment in the smaller subset, from 24.9% to 37% ($P<0.01$) and from 23.6% to 32% ($P<0.01$) in CD4 and CD8 T cells, respectively. Changes in TREC levels correlated with phenotype in five patients. By week 24, all patients had undetectable TREC levels, which may be due to dilution by proliferative effector cells. The larger lymphocyte subset was sustained in 11 patients, the majority of these cells comprising CD8 T cells. A significant increase was seen in the expression of CD38 on both CD4 and CD8 T cells to 68.9% and 71%, respectively, from baseline to week 12 ($P<0.01$ for both).

Conclusion: The use of rhGH appears to have a direct effect on thymic function, promotes thymocyte development, resulting in an increase in naive T cells, and induces differentiation into functional memory effector T cells.

P53

The immunological effects of liposomal anthracycline chemotherapy and concomitant highly active antiretroviral therapy (HAART) during and after treatment of HIV-1-related Kaposi's sarcoma (KS)

B Esdale, M Davies, S Portsmouth, D Sarker, MR Nelson, BG Gazzard, M Bower

Departments of Oncology and HIV Medicine, Chelsea & Westminster Hospital, London

Background: Liposomal anthracycline chemotherapy for HIV-1-associated KS in the pre-HAART era was associated with a fall in CD4 cell counts and an increased risk of opportunistic infections.

Objectives: We aimed to measure the effects of combining HAART with liposomal anthracycline chemotherapy on immune cell counts and HIV-1 viral load during and up to 1 year after the chemotherapy.

Methods: CD4, CD8, CD19 and HIV-1 viral load were assayed at the initiation of chemotherapy, at the completion of chemotherapy and up to 1 year following chemotherapy in 50 HIV-1-infected KS patients.

Results: At the start of chemotherapy, the median CD4 count was 219 cells/ μ L (range 3–1165), CD8 count 886 cells/ μ L (range 86–924) and the CD19 (B-cell) count 126 cells/ μ L. The median HIV-1 viral load was 229 copies/mL and 64% of patients had a viral load <50 copies/mL. There were no significant changes in T-cell subsets or HIV-1 viral load throughout the study period. There was a significant drop in CD19 cells from baseline during chemotherapy, but this had recovered by 6 months.

Conclusions: Liposomal anthracycline chemotherapy, given to patients on HAART, does not adversely affect T-lymphocyte subsets or lead to virological failure.

P54

HIV-specific CD4 T-helper responses in patients with long-term non-progression in HIV infection

M Boaz¹, E Sefia¹, A Waters², P Easterbrook², A Vyakarnam¹

¹Immunology and ²Department of HIV Medicine, King's College School of Medicine, London

Objective: To assess HIV-specific immune responses in a cohort of patients with slow and long-term non-progression.

Method: A study of HIV gag p24-specific T-helper responses was performed in 16 long-term non-progressors (LTNP) and 15 patients who had progressed to disease; both groups were antiretroviral-naïve and had median durations of infection of more than 14 years. Intracellular cytokine staining by four-colour flow cytometry was used to determine frequencies of blood CD4 T cells that were CD69+ interferon (IFN)- γ + and IFN- γ + interleukin (IL-2)+.

Results: CD4+IFN- γ positive responses were detected widely in both LTNP and subjects who progressed at similar frequencies (0.11% and 0.07%, respectively). Conversely, levels of memory effector CD4 T cells, as indicated by dual IL-2 and IFN- γ production at the single-cell level, were significantly higher in LTNP versus slow progressors ($P=0.01$). Frequencies of p24 CD4 T-cell IFN- γ responses were augmented in three LTNP from 0.03%, 0.11% and 0.11% to 1.29%, 6.79% and 1.32% following second-round *in vitro* antigen stimulation.

Conclusions: HIV-specific CD4 T-cell responses determined by IFN- γ production do not correlate with control of infection. However, levels of HIV-specific CD4 T cells determined by both IFN- γ and IL-2 production, likely memory effector T-cells, do appear to be correlates of long-term non-progression.

P55

Impact of highly active antiretroviral therapy (HAART) on opportunistic illnesses (OIs) and individual costs of HIV service provision, England, 1996–1999

EJ Beck¹, S Mandalia¹, D Parmar¹, A Miners¹, M Youle¹, BG Gazzard¹, M Fisher², J Innes², MA Johnson², G Kinghorn², A Pozniak², A Tang², IG Williams², for the NPMS-HHC Steering Group

¹NPMS-HHC CAC, Chelsea & Westminster Hospital, London, and ²NPMS-HHC sites, England

Objective: To describe the impact of HAART on OIs and the individual cost of HIV service provision in England.

Method: Data were collected from seven NPMS-HHC sites. Weighted mean per patient-year (wPPY) indices of service use and cost were calculated per semester by Communicable Diseases Surveillance Centre stage of HIV infection, 1 January 1996 to 31 December 1999.

Results: Of 9931 patients, 84% were men. Increased prescribing of HAART coincided with a reduction in mono- or dual antiretroviral therapy. OIs decreased from a mean 363.1/1000 patient-years [95% confidence intervals (CIs) 334.8 to 393.1] in 1996 to 185.2 (95% CIs 161.9 to 211.0) in 1999. Mean inpatient days for AIDS patients decreased from 11.8 (95% CI 10.3–13.3) to 7.5 (6.58–8.32) wPPY. Estimated costs of managing AIDS patients decreased from £25,170 (£19,981–£32,285) to £23,263 (£18,074–£30,378) for two nucleoside reverse transcriptase inhibitors (NRTIs) + one nonnucleoside reverse transcriptase inhibitor (NNRTI) or from £30,669 (£25,480–£37,784) to £27,762 (£23,573–£35,877) wPPY for two NRTIs + two protease inhibitors (PIs). Significant inverse correlations were observed between uptake of HAART, new OIs and cost of managing AIDS patients.

Conclusions: Increased uptake of HAART reduced AIDS-defining OIs and costs of managing AIDS. By reducing HIV associated morbidity and mortality, HAART reduced the need for inpatient services and the cost of treating people with AIDS. Increasing the number of people alive with HIV infection may increase the population costs for HIV care.

P56

Clinical governance and the autopsy in HIV disease

SB Lucas

Department of Histopathology, Guy's and St Thomas's Hospital, London

Objective: To review how organ/tissue retention problems affect pathologists' ability provide information for clinical governance.

Methods: Examination of adult HIV-positive Coronial and consented autopsies in London and southeast England in 2000–2001.

Results: 61 autopsies were performed, of which 43 (70%) were Coronial; 33 (54%) were African and 28 (46%) Caucasians; ages ranged from 13 to 66 years (five were >60 years). Seven (11%) were first diagnosed HIV-positive at autopsy, and another seven during final admission to hospital. 18 (30%) were deaths in the community, and 45 in hospital. Significant clinical pathologies included:

Sudden unexpected deaths ($n=20$): six were illicit drug overdose-related, two pulmonary embolism/deep vein thrombosis, two coronary artery disease, two meningococcaemia, one suicide, one tuberculosis (TB) and one central nervous system toxoplasmosis.

Unexplained respiratory failure ($n=11$): three TB, two *Pneumocystis carinii* pneumonia (PCP), two adult respiratory disease syndrome, two aspergillosis and one CD8+ lymphocytosis.

Probable highly active antiretroviral therapy (HAART)-associated deaths ($n=9$): three coronary artery disease, two steatosis/lactic acidosis, one liver necrosis and three immune reconstitution inflammatory syndrome (TB, PCP, cryptococcus).

Observation: Coroners tend to relax their Rule 9 interpretation on tissue retention in HIV cases. Of 10 families approached for consent for organ retention, or clarification of consent, all readily agreed and were content to be involved.

Conclusion: Much unexpected pathology emerged for feedback to clinicians, often needing extensive histological and other tests. Most HIV-positive autopsies are Coronial, with little limitation on investigations, and families co-operate when approached for permission to study material further.

P57

Correlation between CD4 response and cost of hospital treatment in antiretroviral-naïve HIV-infected patients on triple antiretroviral therapy

S Mandalia¹, D Parmar¹, M Fisher², A Pozniak², A Tang², M Youle¹, BG Gazzard¹, EJ Beck¹ on behalf of the NPMS-HHC Steering Group
¹NPMS-HHC CAC, Chelsea & Westminster Hospital, London, and
²NPMS-HHC sites, England

Objective: To investigate the correlation of CD4 response to antiretroviral therapy and costs of HIV service provision for English HIV-infected populations managed between 1 January 1998 and 31 December 1999.

Method: This multicentre prospective open cohort study was part of the NPMS-HHC. Two monthly mean CD4 counts were calculated, corresponding costs were estimated by multiplying mean inpatient days, outpatient and dayward visits by standard unit costs since commencing first-line triple antiretroviral therapy. Cost estimates were combined with average costs for two nucleoside reverse transcriptase inhibitors (NRTIs) and one nonnucleoside reverse transcriptase inhibitor (NNRTI) and two NRTIs and one protease inhibitor (PI). Analyses were stratified by Centers for Disease Control and Prevention (CDC) stage of HIV infection for a 24-month period of follow-up.

Results: 585 patients were treated with two NRTIs + one NNRTI or two NRTIs + one PI. The correlation between mean CD4 count and average costs across all three stages of HIV infection was strongest: $r = -0.85$, $P < 0.001$. The annual cost of treating patients with triple therapy and CD4 0–50 cells/ μ L ranged from £19,086 to £18,390; for a CD4 count of 50–200 cells/ μ L, the cost ranged £18,390 to 16,298; for a CD4 count of 200–500 cells/ μ L, the cost ranged £16,298 to £12,117; for patients with CD4 >500 cells/ μ L, the cost was £12,117 or less for a year of treatment.

Conclusions: A strong linear relationship was observed between the CD4 count and the cost of hospital treatment. Cost-efficacy of drugs and requirements for existing or developing new services can be assessed.

P58

Role of positron emission tomography (PET) scans in the investigation of people with HIV

C Watson, I Ho Shon, A de Ruiter, M O'Doherty
 St Thomas's Hospital, London

Objective: To review the role of fluorodeoxyglucose positron emission tomography (PET) in the investigation of complications of HIV infection.

Methods: The outpatient notes of HIV-positive patients with PET scans between 1 January 1994 and 31 July 2001 were reviewed.

Results: PET scans were performed on 81 patients; 69 case notes have been reviewed to date; 50/73 PET scans were performed prior to diagnosis; 31/50 patients had a supportive diagnosis made on PET scan, eight had scans in which the diagnosis was less likely but possible and 11 PET results did not correspond with the final diagnosis. Of these 11 patients, two had proven cerebral lymphoma (CL), two presumed CL, two Kaposi's sarcoma (KS), one presumed lymphoma recurrence, one *Mycobacterium avium* complex (MAC), one nodular prurigo, one respiratory tract infection (RTI) and one no obvious disease. Five of six mycobacterial infections were supported by a PET scan before diagnosis and two of four diagnoses of KS. Two of two diagnoses of nodal or disseminated lymphoma were supported by a PET scan prior and a further 11 had PET supporting a diagnosis of lymphoma after the diagnosis was made. 23 patients presented with fever; 11 had a PET scan prior to the diagnosis; in seven of these, the scan supported the final diagnosis. Four PET scans did not correlate with the diagnosis (one KS, one MAC, one CL and one RTI). Of the 12 patients with fever who had a PET scan after the diagnosis, five had lymphoma and three *Mycobacterium avium intracellulare*. In all of these cases the PET scan supported the diagnosis.

Conclusion: 62% of PET scans resulted in correct or supportive information. In this small group of patients with probable cerebral lymphoma, the results were unhelpful in half. It is possible that the earlier use of PET in patients with fever may point to a site for biopsy and confirm extent of disease.

P59

Behind the pharmacy door: dispensary-based contributions to HIV patient care

HA Leake Date¹, D Godfrey², on behalf of the HIV Pharmacy Association³

¹Brighton and Sussex University Hospitals NHS Trust, ²Mayday University Hospital and ³HIV Pharmacy Association (HIVPA)

Introduction: A recent Audit Commission report, *A Spoonful of Sugar*, highlighted the frequency of drug-related adverse events/errors (ADEs) and the role pharmacy teams can play in minimizing them. The role of specialist clinical pharmacists is increasingly well-recognized, but this survey aimed to assess the contribution of dispensary-based pharmacy staff to the care of HIV-positive individuals (PWH), highlighting prescription errors or patient counselling, for example.

Methods: A data collection form was designed and distributed to all HIVPA members in December 2001. Centres that wished to participate were asked to record all dispensary-based contributions to the care of PWH ('interventions') for one week in January 2002. Interventions made outside the dispensary (e.g. ward/clinic) were not collected. Data were analysed using Microsoft Excel.

Results: Preliminary data from 17 participating hospitals showed a total of 592 interventions on 412 prescriptions (one intervention per nine items dispensed, a mean of 1.4 interventions per treatment). 25% were judged to be of moderate–major clinical significance. Further data (including types of staff involved, nature of contribution, outcomes, demographics of participating centres) will be presented.

Discussion: Dispensary-based pharmacy staff have a key role to play as part of the multidisciplinary team in promoting adherence and minimizing ADEs in PWH. The results of this survey can be used to highlight training needs for healthcare professionals and to identify ways of preventing ADEs. They can also help in the planning of future pharmacy services for HIV teams.

P60

Pain management in HIV-positive patients

DA Aldington¹, E Foley², RJH Baylis¹, D Rowen³

¹Department of Pain Medicine and ²Department of Genito-Urinary Medicine, Portsmouth Hospitals NHS Trust, and ³Department of Genito-Urinary Medicine, RSH Hospital, Southampton

Objective: To establish the incidence of pain as a significant complaint in HIV-positive patients attending a UK clinic.

Methods: The records of HIV-positive patients regularly attending a single clinic during 2001 were studied. Any mention of pain, and its treatment, was recorded.

Results: 111 sets of hospital records were studied; 70% were males, aged 3–66 years; 64% of patients had complained of pain in the study period. There was no statistical significant difference between the sexes with regard to reporting pain. Abdominal and lower limb pains were most common (18%), often related to the side effects of highly active antiretroviral therapy. There was no significant difference in CD4 count. No formal assessment of pain had been made, and in most cases, simple analgesics had been prescribed. Although some patients had been referred to the local pain clinic, they were still waiting to be seen.

Conclusions: Pain appears to be a common and significant symptom in HIV-positive patients but is poorly managed. Protocols to assess and manage pain should be implemented and joint clinics with a pain management team should be considered.

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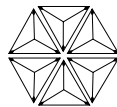
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ABSTRACTS OF THE 8th ANNUAL CONFERENCE OF THE BRITISH HIV ASSOCIATION [BHIVA]

ERRATUM

The abstract shown on page 16 as P32 is the wrong abstract. The correct abstract for P32 is shown below.

P32

Impact of a notes proforma on the management of HIV+ women

KP Prime¹, J Lloyd², AJ Robinson¹, SG Edwards¹

¹Royal Free and University College Medical School and ²Archway Sexual Health Centre, London

Objective: To assess the impact of using a casenotes proforma on the discussion and documentation of issues specific to women's sexual health.

Methods: Retrospective casenote review of 141 female attendees at our HIV clinics 6 months before and after the introduction of a notes proforma. Issues pertinent to women's sexual health were assessed: cervical smear outcomes, sexual activity, contraceptive use, pregnancy plans and screening for sexually transmitted infections (STIs).

Results: The annual cervical smear targets increased from 93/141 to 117/141 after the introduction of a proforma. Of the 24 smear targets not met, reasons included DNAd appointments ($n=5$), declined smears ($n=2$), pregnancy ($n=3$), awaiting colposcopy ($n=3$) and smears not offered ($n=11$). With the proforma, documentation of sexual activity improved by 100% (62 versus 125/141). Among sexually active women, documentation of contraceptive use and pregnancy plans increased from 38% (51/134) to 82% (72/88) and from 26% (35/136) to 75% (70/93), respectively. Discussion about STI screening and uptake of screens also increased by 62% (38/141 versus 61/141) and by over 100% (23/141 versus 47/141), respectively. Changes were documented in the women's lifestyle during the study period, in sexual activity (32/141), contraceptive use (7/141) and pregnancy plans (12/141).

Conclusions: Consultation covers a wide range of issues, each of which may take up a large proportion of a routine clinical visit. Clients also attend a clinic over a long period of time and women may change partners, contraceptive method and pregnancy plans, highlighting the need for repeated documentation. This study shows that the introduction of a notes proforma improved discussion and documentation of specific areas of management of women's sexual health.