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# Oral Abstracts

O1

## Adults with low CD4 cell counts that were not receiving antiretroviral therapy in England, Wales and Northern Ireland in 2004

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**Aims:** To investigate factors that were associated with the proportion of adults with low CD4 cell counts ( $CD4 < 200$  cells/ $\mu$ l) that were not receiving antiretroviral therapy (ART).

**Methods:** The annual Survey of Prevalent HIV Infections Diagnosed (SOPHID) provides an epidemiological profile of, and determines the prevalence of, individuals living with diagnosed HIV infections in England, Wales and Northern Ireland. Adults reported to the 2004 SOPHID survey with both CD4 and ART reported were included in the dataset.

**Results:** Individuals with  $CD4 < 200$  accounted for 14% (4934/35,242) of all reports in 2004, of which 19% (950) were not on ART. The proportion of individuals with  $CD4 < 200$  not on ART varied from 9% (Northern Ireland) to 36% (North East) across region of treatment. There was also variation across SHAs within regions. The proportion not on ART varied by most advanced clinical stage: 55% death with AIDS, 13% AIDS, 17% symptoms pre-AIDS and 29% asymptomatic. The proportion of individuals not on ART decreased with increasing age (26% at 15–24; 15% at 50+). There was little difference observed by ethnicity, exposure category or sex. Recent diagnoses accounted for 16% (84/514) of individuals not on ART with  $CD4 < 200$  in London.

**Conclusion:** One in five individuals with low CD4 cell counts were not on ART, of which relatively few were because they were recently diagnosed. Further work will be required to investigate regional and demographic differences in the proportion not on treatment and to consider reasons why people were not on ART according to BHIVA guidelines.

O2

## The demographic, clinical and virological characteristics of patients newly diagnosed with non-B HIV-1 subtypes in London

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**Objectives:** To characterise newly diagnosed persons infected with HIV-1 subtypes other than B.

**Methods:** HIV-1 subtype was determined by phylogenetic analysis of protease and RT. Drug resistance was assigned according to the IAS-USA list (2005) and Stanford interpretation algorithm when intermediate or high-level resistance. Serum samples were tested by a guanidine-based antibody avidity test to identify seroconversion within the previous 4–6 months (avidity index  $< 0.60$ ).

**Results:** From April 2004–November 2005, among 200 newly diagnosed persons, 112 (56%) were subtype B, including 106 (95%) males, 91 (81%) whites, 100 (89%) MSM; and 22 (25%) recent seroconverters. The median age was 34.5 years (19–57),  $CD4$  395 cells/ $\mu$ l (4–1.184), viral load 5.0  $\log_{10}$  copies/ml (4.3–6.9). Non-B subtypes comprised 36 C (41%), 14 A (16%), 10 CRF02 (11%), 7 D (8%), 5 G (6%), 4 CRF01 (5%), 4 CRF06 (5%), 1 CRF13 (1%), 1 CRF16 (1%), and five complex mosaic sequences (6%). Phylogenetic analysis identified seven clusters, each including two MSM. The non-B population comprised 34 males (39%), 61 (69%) black Africans, 72 (82%) heterosexuals, 5 (5%) MSM, and 9 (10%) recent seroconverters. The median age was 36,  $CD4$  387 cells/ $\mu$ l (46–803), viral load 4.7  $\log_{10}$  copies/ml (2.5–5.8). Among the non-B subtypes there were eight (9%) white European, four were from UK, one from Portugal, two from Poland, six were male and two female, and five were heterosexuals and three homosexuals: infected with subtype C (3), CRF06 (2), and one each with D, CRF01, and CRF02. Only one patient in this group was a recent seroconverter. Three MSM with CRF06 formed one phylogenetic cluster. Primary drug resistance was found in 14/200 (7%) by IAS and 9/200 (4.5%) by Stanford, including 12/112 (11%) MSM with subtype B, 1/12 heterosexual with subtype B and 1/12 heterosexual with complex mosaic sequence.

**Conclusion:** The genetic diversity of HIV-1 continues to increase in London. Although non-B subtypes are commonly associated with immigration from

Africa or Asia, they are no longer restricted to non-indigenous populations. Transmitted drug resistance is nearly entirely confined to MSM with subtype B at the present time.

O3

## Incident non-B clade HIV-1 infection in white gay men infected in UK between 2000 and 2005

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**Aims:** To investigate the distribution of HIV-1 subtypes among homosexual men with primary HIV infection.

**Methods:** Subjects attending a London HIV centre between 2000–2004 were recruited into a primary HIV infection (PHI) study where PHI is defined by one of the following criteria: previous HIV antibody negative within the previous 6 months followed by a subsequent positive result; a negative HIV antibody test in the presence of positive identification of virus by RNA/DNA PCR; an evolving HIV-specific antibody response. All subjects completed sexual behaviour questionnaires and had baseline viral sequencing performed in *pol*. Viral clade was determined comparing sequences in *pol* with the Stanford databases. Viral sequences were analysed by phylogenetic trees to determine viral clustering.

**Results:** 5/140 cases of PHI identified occurred in white gay men infected with non-B clade virus. Of these all had recombinant variants; one transmitting pair, confirmed by sexual history as well as phylogenetic analysis, were both infected with A/E<sup>PRO</sup>:D<sup>RT</sup>, one with C<sup>PRO</sup>:B<sup>RT</sup>, one D<sup>PRO</sup>:B<sup>RT</sup>, and one with CRF02-AG<sup>PRO</sup>:K<sup>RT</sup>. All reported sexually acquired infection with partners in the UK.

**Conclusion:** We report five cases of non-B clade HIV-1 infection amongst white gay men recently infected with HIV-1 in London between 2000 and 2005. There is current sexual transmission of multiple subtypes and recombination among white homosexual men in London.

O4

## Why are children still being infected with HIV? Experiences in prevention of mother-to-child transmission of HIV in a complex south London university hospital population

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**Aims:** Despite recent advances in efforts to reduce mother-to-child transmission (MTCT) of HIV, there are still children becoming infected. To understand this further, we report on the prevention of MTCT at this hospital between 1993 and 2004.

**Methods:** Prospective data collection on all HIV-infected women seen for antenatal care since 1993.

**Results:** 296 pregnancies to 274 women. 153/274 women (55.8%) were diagnosed from routine antenatal screening. 6/287 (2.1%) pregnancies with adequate follow-up resulted in HIV infection in the infant. We describe the six cases in more detail and highlight relevant points: case 1, illustrating prematurity; case 2, late presentation at 38 weeks gestation; case 3, a missed opportunity for a woman who did not attend follow up; case 4, co-infection with falciparum malaria and TB; case 5, early *in utero* infection, ART started at 27 weeks; case 6, acute seroconversion during pregnancy. 4/6 children were infected *in utero*.

**Conclusion:** The low transmission rate of 2% in the multicultural population served by this hospital attests to the efforts of a multidisciplinary care team dedicated to the care of this frequently hard-to-reach population. More importantly, *in utero* infection in these children may have been avoided by starting antiretroviral therapy at an earlier stage than is suggested by BHIVA guidelines.

O5

### Does zidovudine monotherapy (mZDV) in pregnancy predispose to the emergence of resistance?

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**Aims:** BHIVA guidelines recommend antenatal mZDV as an option in certain scenarios in pregnancy [baseline viral load (BVL) <20 000 copies/ml, 2001 guidelines; <10 000 copies/ml 2005 guidelines]. Concerns for evolution of resistance prompted this study to determine the incidence of resistance following mZDV exposure.

**Methods:** Retrospective review of women receiving mZDV in pregnancy with a BVL of <20 000 copies/ml in four hospitals. Demographic and clinical parameters were collected. Genotyping of samples nearest delivery was performed using population-based sequencing (Trugene HIV-1, Bayer and ViroSeq v2.6 Celera/ABI). A subgroup of samples was also examined for drug-resistant minority species using cloning technology (Zero Blunt TOPO, Invitrogen).

**Results:** Fifty-six women had samples available for analysis; 17 had <50 copies/ml off therapy and could not be genotyped; eight failed to amplify and 48 were sequenced successfully. Of these 48 women, median age was 30 years (19–40); 36 (75%) were Black Africans; 44 (92%) infected with non-B subtypes. Median pre-treatment HIV viral load (VL) and CD4 counts were 2101 copies/ml (285–14900) and  $410 \times 10^6/l$  (228–958) respectively. Median delivery VL was 1664 copies/ml (78–27930) and median duration of mZDV exposure was 11 weeks (3–21). No ZDV-associated mutations were detected by population-based sequencing ( $n=48$ ) and no drug-resistant minority species were detected by cloning ( $n=13$ ). There were no vertical transmissions in the cohort ( $n=73$ ).

**Conclusion:** Results to date from this cohort support the strategy of selective mZDV in preventing MTCT of HIV-1 without the development of significant resistance.

O6

### The reproducibility and clinical significance of HIV viral-load blips in patients on stable first-line HAART

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**Aims:** Assess frequency, reproducibility and long-term impact of viral-load (VL) blips, and determine whether blips are associated with emergence of resistance.

**Methods:** Reproducibility: two plasma aliquots were stored at 70°C. The second was tested under identical conditions if the first showed a blip (>50 and <400 copies/ml, preceded and followed by <50). Genotyping was done in six confirmed blips. In patients on first-line HAART with  $\geq 2$ NRTIs + PI/NNRTI ( $n=486$ ), univariable analysis was used to investigate whether having a blip was associated with subsequent VL rebound and CD4 changes over  $\leq 5$  years.

**Results:** Among patients on first-line HAART ( $n=486$ ), 367 (76%) were suppressers and 119 (24%) blippers during the first year after initial VL <50 copies/ml. Of the blippers, 35 (30%) had multiple blips (2–4). Over 938 PY of follow-up, the VL rebound rate per 100 PY was 3.36 (2.02–4.71) in suppressers (RR 1.25; CI: 0.51–3.07,  $P=0.62$ ) versus 2.70 (0.16–5.83) in blippers. The rate of mean CD4 increase per month in suppressers was 1.35 cells/ $\mu l$  greater than in blippers (95% CI: (1.35 to 4.05;  $P=0.32$ ). In 32 retested blips VL was >50 copies/ml in 11 (34%); detectable at <50 (10–42) copies/ml in 13 (41%); and undetectable in eight (25%). Genotyping showed wild-type virus in four blips, including two on first-line HAART and two from multi-drug experienced patients with previously documented resistance. The other two blips showed resistant virus; in both, the resistance profile was consistent with selection during previous therapy.

**Conclusion:** Blips occurred in 24% of patients on stable first-line HAART, but did not impact on long-term virological and CD4 responses. On repeat testing, 75% of blips showed detectable viraemia. Blips contained either wildtype or drug-resistant virus, but resistant mutants appeared to derive from previous drug failures.

O7

### SMART strategies for management of antiretroviral therapy

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The SMART study is a randomised international trial evaluating two antiretroviral strategies, the viral suppression (VS) and drug conservation (DC) strategies. Inclusion criteria were all patients with a CD4 count above 350 cells/ $\mu l$ . The VS arm was managed within current guidelines with continuous antiretroviral therapy (ART). The DC arm deferred or stopped ART until their CD4 count fell to less than 250. They then restarted ART until their CD4 count reached 350 when they stopped ART again. This approach was designed to preserve health whilst minimising drug exposure. The study was designed to recruit 6000 patients for follow up over 6–9 years. Patients were seen at 1, 2 and then every 2 months in the first year and every 4 months thereafter. CD4 counts and HIV viral load were checked at each visit and genotypic resistance testing done on all samples with a viral load >1000 copies/ml. Recruitment to the study was stopped on 11<sup>th</sup> January 2006 with 5472 patients enrolled. As of 10<sup>th</sup> December 2005, 93 patients in the DC arm had reached a primary endpoint (disease progression or death) versus 47 patients in the VS arm ( $P > 0.0001$ ). These differences remained significant for serious progression of disease, death and for major toxicities. This effect was assessed across groups defined by nadir and baseline CD4 count; all favoured the VS arm. Following the release of these data, patients on the DC arm of SMART were asked to contact their physicians to discuss restarting ART. Follow-up of all patients in SMART continues.

O8

### Older and wiser: continued improvements in clinical outcome and highly active antiretroviral therapy (HAART) response in HIV-infected children in the UK and Ireland, 1996–2005

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**Aims:** To describe changes over time in demographics, AIDS events and deaths, and exposure and response to HAART, in HIV-infected children in the UK and Ireland 1996–2005.

**Methods:** Analysis of prospective cohort data on HIV-infected children reported to the National Study of HIV in Pregnancy and Childhood, as well as HAART exposure and response for a subgroup (70%) in the Collaborative HIV Paediatric Study.

**Results:** Three hundred and fifty-four children with HIV were under care in 1996, rising to 614 in 2000 and 961 in 2004\*. 55% were born in the UK and Ireland, of whom only 20% were identified at delivery. 29% were aged  $\geq 5$  years at first presentation, and at last follow-up 26% were aged 10–14 years and 11% were  $\geq 15$  years. Rates of progression to AIDS (death) declined from 13.7 (8.4)/100 py pre-1997 to 4.0 (1.3) in 2000/2001 and 2.6 (0.5) in 2004/2005. HAART response in antiretroviral naive children improved over time: 34% suppressed viral load <50 copies/ml 6 months after HAART initiation in 2000/2001, rising to 64% in 2004/2005. Whilst the proportion of child-time spent on three-drug ART was stable at 63% from 1999 onwards, the proportion of time spent off all ART, having previously taken it, increased from 4.5% in 2000/2001 to 9.3% in 2004/2005. At last follow-up, 33% of 10–14 year olds and 41% aged  $\geq 15$  had experienced all three main classes of HAART.

**Conclusion:** Morbidity and mortality rates have continued to decline in HIV-infected children since the introduction of HAART in 1997. Short-term HAART response is improving but longer-term clinical management is complex. Provision of transitional services and continued monitoring will be essential as this treatment-experienced cohort progresses into adolescence and adulthood. \*2005 data are underestimated due to reporting delay.

O9

**Viral rebound in patients on antiretroviral therapy with viral suppression: association with extent of previous virological failure and time with viral suppression**

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**Background:** Few data are available on the association between use of antiretroviral regimens and rates of viral rebound in those attaining a viral load (VL) of <50 copies/ml while receiving highly active antiretroviral therapy (HAART). **Aims:** To determine whether the rate of viral rebound decreases with increasing duration of viral suppression in patients who have failed one or more antiretroviral regimens, and if so whether with sufficient time the rebound rate declines to as low as that observed in patients on first-line therapy.

**Method:** Patients achieving a VL <50 copies/ml for the first time while receiving HAART were followed until viral rebound (two consecutive VLs >400 copies/ml). **Results:** 10,243 patients from the UK Collaborative HIV Cohort (UK CHIC) achieved a VL <50 copies/ml whilst on HAART. Virological rebound rates per 100 person-years (p-years).

Number of regimens previously failed	Duration of viral suppression to ≤50 copies/ml (p-years)				
	<1	1-2	2-3	3-4	>4 years
0	8.4	5.2	4.1	3.1	3.0
1	18.0	11.1	7.1	4.4	2.3
2	22.2	13.1	10.7	4.7	4.3
3	27.7	12.8	8.9	5.3	4.6
4	29.7	9.9	6.5	11.4	-
>5	41.9	19.3	5.5	11.3	8.1

**Conclusion:** The rate of viral rebound diminishes markedly with increasing time with viral suppression, especially in those who have failed previous regimens.

O10

**Pharmacokinetics (PK) and antiretroviral (ARV) response to TMC114/r and TMC125 combination in patients with high-level viral resistance**

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**Background:** In patients with three-class HIV resistance, combinations of investigational ARVs may represent the only therapeutic option. TMC114 and TMC125 are potent investigational ARVs with activity in naive and experienced patients. However, the drug interaction between these agents has not been characterised in HIV patients.

**Methods:** Multi-class-experienced HIV patients with documented three-class resistance were enrolled into a study to investigate the PK, safety and efficacy of TMC114/r 600/100 mg bid and TMC125 200 mg bid (new formulation) plus NRTIs with or without enfuvirtide (ENF). TMC114/r/TMC125 steady-state PK was assessed over 12 h. HIV resistance, safety and efficacy were assessed. PK parameters were compared to historical data; associations with virological response were assessed by linear regression analysis.

**Results:** 10/11 patients completed both PK phases; median (range) baseline characteristics included age 43 (38-56) year; CD4 75 (3-490) cells/μl; log<sub>10</sub> viral load (VL) 4.6 (3.9-5.5); N of mutations (IAS, October 2005) for PI, primary 4 (0-5) and resistance associated 11 (2-13), for NRTI 7 (2-9), and for NNRTI 2 (0-6). PK parameters measured on day 28 reflected unchanged exposure to TMC114 and modestly reduced (30%) exposure to TMC125 when compared to historical controls. At week 12, all patients had achieved at least a 2 log<sub>10</sub> decrease in HIV-RNA with a median of (2.76; all had VL < 400 (8 < 40). Median CD4 increase was 87 cells/μl. No serious adverse events or changes in laboratory safety were reported.

**Conclusion:** No clinically significant PK interaction between TMC114 and TMC125 was observed. The combination was well-tolerated and showed

impressive short-term efficacy against three-class-resistant HIV. Studies of this combination are warranted.

O11

**A randomised immediate versus delayed replacement study of Trizivir as a substitute for two NRTIs plus efavirenz in persons experiencing CNS symptoms**

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**Background:** Efavirenz (EFV) is associated with CNS disturbances, such as sleep disturbances and mood changes, which may persist in some patients.

**Methods:** Individuals with HIV RNA <50 copies/ml on initial therapy with two NRTIs plus EFV and reporting persistent CNS disturbances replaced the NRTIs with Trizivir and were randomised to either continue efavirenz or matching placebo for 4 weeks. After week 4 all patients remained on Trizivir alone. Evaluations through week 24 included hospital anxiety and depression (HADS) score, 10 sleep dimensions by VA scale, biochemical and lipid parameters and HIV disease markers.

**Results:** 18 individuals were screened and 16 randomised. No abacavir hypersensitivity (HSR) or HIV-1 RNA rebounds were observed. One individual modified zidovudine to atazanavir. Switching therapy was associated with significant improvements in HADS scores from baseline to week 24 (P=0.01 both groups combined) with both anxiety (P=0.008) and depression (P=0.022) scores improving. Differences were not observed between groups at any time point. Combined sleep VA assessments did not significantly change although scores for sleep restfulness, dream vividness and morning sluggishness all improved. Total cholesterol (0.7 mmol/l), LDL (0.5 mmol/l) and HDL (0.16 mmol/l) decreased significantly through week 24.

**Conclusion:** Switching from 2NRTI + EFV to Trizivir is effective and well tolerated in initial therapy patients. HADS scores and some sleep characteristics improve gradually with switching. Total, LDL and HDL cholesterol levels decline following switching.

O12

**Pharmacokinetic interactions between rifabutin and lopinavir/ritonavir in HIV-infected patients with mycobacterial co-infection**

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**Objectives:** Current British HIV Association (BHIVA) and Centres for Disease Control and Prevention (CDC) guidelines suggest that when using a lopinavir/ritonavir (Kaletra)-based antiretroviral regimen, the rifamycin drug of choice is rifabutin. The dose of rifabutin should be reduced from 300 mg daily to 150 mg three times a week. We investigate current guidelines to ensure they result in therapeutic rifabutin levels.

**Methods:** Therapeutic drug monitoring (TDM) of Kaletra and rifabutin was performed on five patients on concurrent treatment (>2 weeks) at currently recommended doses.

**Results:** Rifabutin levels for all five patients were found to be sub-therapeutic, with one patient deteriorating clinically.

Patient	Rifabutin 4 h post- level (mg/l)	Kaletra trough level (ng/ml)
1	0.16	9352*
2	0.33	1030*
3	0.17	18 035*
4	<0.10	1549*
5	0.16	7910*

Rifabutin post-dose: 0.50-1.0 mg/l

Kaletra trough level: for wildtype virus: 1000 ng/l

\*Experienced patients: 8000 ng/l

**Conclusion:** Our data suggests current BHIVA and CDC guidelines result in sub-therapeutic rifabutin levels. In our study one in five patients clinically deteriorated. Further formal investigations are required to establish the clinical significance of this, and determine the optimum dosing regimes for Kaletra and rifabutin in co-infected patients. Further formal investigations are required to establish the clinical significance of this, and determine the pharmacokinetic impact of changing the rifabutin dose.

O13

### The epidemiology of HIV-Associated Nephropathy (HIVAN): the London HIV-Nephropathy study cohort

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**Introduction:** There are limited data on the epidemiology of HIVAN in the HAART era. Our objective was to assess the impact of viral suppression with HAART on renal outcome and progression to end-stage renal disease (ESRD).

**Methods:** Retrospective study of all HIVAN cases diagnosed between 01/1998 and 12/2004 in London. HIVAN was defined using histological or clinical criteria (proteinuria >1.5 g/d in absence of other medical diagnoses).

**Results:** The prevalence of HIVAN among black African/black Caribbean patients with newly diagnosed HIV infection was 1.3%, and the incidence among those with established infection was 0.4/1000 py. At HIVAN diagnosis, median age was 36 years; CD4 count 68 cells/ $\mu$ l (IQR = 28–187); viral load 90 875 copies/ml (IQR = 31 500–250 611); serum creatinine 228  $\mu$ mol/l (IQR = 151–434); and proteinuria 4000 mg/d (IQR = 2340–7800). No patients were HBV/HCV co-infected, and 68% had biopsy-proven HIVAN. HAART was initiated in 36 patients, with a median follow-up of 780 days. Kaplan-Meier survival analyses showed 94% and 80% survival at 1 and 3 years. The proportion of patients who progressed to ESRD at 1 and 3 years was 25% and 33% respectively. There was a statistically significant association between progression to ESRD and incomplete viral suppression on HAART (OR = 6.14, 95% CI = 1.1–34.2,  $P=0.04$ ), but no association with age, baseline CD4 count, creatinine or level of proteinuria. Conversely, attainment of an undetectable VL versus persistent viraemia was strongly associated with stable or improving renal function ( $P=0.0011$ ).

**Conclusion:** In this large black African/Caribbean HIVAN cohort, the use of HAART and sustained viral suppression was associated with an improved renal outcome.

O14

### Hepatitis C virus (HCV) co-infection in HIV-infected patients in the UK Collaborative HIV Cohort (CHIC) Study

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**Aims:** To describe trends in HCV testing and prevalence of HCV co-infection in the UK CHIC Study.

**Methods:** Data from all centres in the UK CHIC study that contributed HCV antibody test data were included in the analysis (six of seven centres).

**Results:** 11357/18630 (61.0%) patients had had at least one HCV antibody test. 9386 (86.6%) of these patients were male, 7770 (68.74%) white, 427 (3.8%) were injection-drug users (IDUs) and 7806 (68.7%) were homosexual; the median age of those tested was 36.3 (IQR: 31.4, 42.1) years. The proportion of patients tested increased over time, with 369/5204 (7.1%) patients undergoing follow-up in 1995 having been tested at some time, 2861/8233 (34.8%) in 2000 and 8033/10219 (78.6%) in 2004. 1045/11357 (9.2%, 95% CI: 8.7–9.7) of the patients tested for HCV antibody had at least one positive result with the proportion of positive results falling over time – 94/369 (25.5%) in 1995, 369/2861 (12.9%) in 2000 and 648/8033 (8.1%) in 2004. Among those with a test result, factors independently associated with detectable HCV antibody were earlier calendar year of test, younger age, female gender, injection-drug use and black African ethnicity. **Conclusion:** As there has been a move towards testing all individuals for HCV, rather than only those felt to be at high risk, the proportion of patients testing positive for HCV antibody has decreased. Further analyses will determine the incidence of HCV infection and the impact of HCV-HIV co-infection on response to HAART.

O15

### The effect of hepatitis C virus (HCV) on HIV progression in a late salvage population: results from the OPTIMA (OPTions In Management with Antiretrovirals) Study

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**Aims:** Studies on the effect of co-infection with HCV on HIV progression have yielded conflicting results. We aimed to investigate this effect in a late salvage population.

**Methods:** Using data from OPTIMA, the effect of HCV on survival and progression to a new AIDS event or death was evaluated using Cox models controlling for treatment and baseline CD4.

**Results:** Of the 311 patients for whom HCV status and follow-up data were available, 72 (23%) were HCV+. The median (range) follow-up time was 21 (0.7, 47) and 23 (0.3, 47) months for HCV+ and HCV– patients respectively. 25% of HCV+ patients died compared to 16% of HCV– patients. Injecting-drug use was reported as a possible mode of HIV transmission by 74% of HCV+ patients compared with only 26% of HCV– patients. There was evidence to suggest that HCV is associated with impaired survival [HR = 1.79, 95% CI (1.01–3.16),  $P=0.045$ ]. The effect size was similar after adjusting for mode of transmission [HR = 1.70 (0.86–3.36),  $P=0.13$ ], but after further controlling for (time-dependent) number of ART drugs the effect was much attenuated [HR = 1.37 (0.67, 2.80),  $P=0.39$ ]. The median (range) time to first switch/stop of on-study ART was 3.8 (0.03, 36) and 6.5 (0.03, 46) months in HCV+ and HCV– patients, respectively. HCV+ patients were no more likely than HCV– patients to experience an AIDS event during follow-up (23% versus 25%). We found no statistically significant effect of HCV on time to a new AIDS event or death [HR = 1.32 (0.84, 2.08),  $P=0.23$ ].

**Conclusion:** Co-infection with HCV appears to increase the risk of mortality, but this effect might be partly explained by a shorter time to switching/stopping ART. One possible reason may be that HCV+ patients are less able to tolerate ART.

O16

### A 48-week-study of tenofovir (TDF) or lamivudine (3TC) or a combination of TDF and 3TC for the treatment of chronic hepatitis B in HIV/hepatitis B virus (HBV) co-infected individuals

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**Background:** Optimal therapy of HBV in HIV-infected individuals remains unclear.

**Methods:** Multicentre open-label randomised study of TDF versus 3TC versus TDF+3TC as part of HAART in individuals with active HBV either without previous 3TC-experience or in the presence of 3TC. Primary endpoint was HBV DNA reduction via DAVG analysis at 24 weeks. In the 3TC arms, TDF was added at 24 weeks for naive subjects and could be added at 24 weeks in experienced subjects.

**Results:** 59 of 78 subjects were randomised prior to alterations in the BHIVA guidelines.

ARM (n)	3TC- experienced			3TC naive		
	TDF (12)	3TC (9)	TDF/3TC (11)	TDF (10)	3TC (11)	TDF/3 TC (6)
Median baseline HBV DNA(log copies/ml)	7.7	8.2	7.7	8.2	7.5	8.2
Median ALT IU/l (range)	48	61	62	77	66	35
Median change in HBV DNA(24 weeks)	-3.41	-0.82	-3.93 $P < 0.001$	-4.66	-3.31	-5.03 $P=0.045$
Median change in HBV DNA (48 weeks)	-3.07	-2.50	-4.50	-5.41	-4.55	-6.23
HBV DNA <400 copies/ml(24 weeks)	2	0	4	4	4	3
HBV DNA <400 copies/ml (48 weeks)	4	1	6	3	7	2
Normalisation ALT (<37 IU/l) (48 weeks)	7	5	8	7	9	5
HbeAg negative (48 weeks)	2	0	3	3	5	2

**Conclusion:** At 24 weeks in 3TC-naive subjects, combination therapy with TDF was superior. There was no statistical difference between TDF alone and 3TC. In 3TC-experienced subjects, there was no benefit in continuing with 3TC alone; adding or switching to TDF was superior. This study supports current guidelines of combination therapy in 3TC-naive subjects. 3TC-experienced subjects should add TDF or switch to TDF depending on 3TC activity against HIV.

O17

### A prognostic index for AIDS-associated Kaposi sarcoma in the era of HAART

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**Background:** We wished to develop a simple model for predicting outcome in individuals affected with AIDS-KS in the era of HAART.

**Methods:** We performed univariate and multivariate Cox regression analyses to identify covariates predictive of overall survival on a cohort of 326 HIV-positive patients who developed KS since 1996.

**Results:** In these individuals, a prognostic score from 0 to 15 can be calculated commencing at the number 10, incorporating S stage (the presence of another HIV-associated illness, +3 if the S stage is 1), age (+2 if age >50 years old at diagnosis), KS as a first ADI (3 if KS is the ADI) and CD4 cell count (1 for each increase of 100 cells/ $\mu$ l at diagnosis). Individuals with a prognostic score of 0, 5, 10 and 15 had 1-year survivals of 99.4%, 96.7%, 83.4% and 37.8% and 5-year survivals of 98.4%, 91.8%, 63.1% and 8.4%. Increasing the prognostic score by 1 increases the risk of death by 40% (HR 1.4, 95% confidence interval (CI) 1.28–1.53, bootstrapped [HR 1.39, 95% CI 1.25–1.51]) and the index has a concordance of 76.8% (95% CI 71.7–82.3%). The prognostic index, validated internally using a bootstrap procedure with resampled data, applied to individuals on and off HAART at KS diagnosis.

**Conclusion:** An accurate prognostic index can be obtained for individuals with AIDS-KS in the HAART era by combining age, S stage, KS as an ADI and CD4 count. This can be used to guide therapeutic options.

O18

### Metabolic syndrome and its associations in HIV patients

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**Objectives:** To estimate the prevalence and associations of metabolic syndrome (MS) in an HIV cohort.

**Methods:** Prospective longitudinal cohort study. Observations thus far obtained from 200 patients include demographics, disease stage, details of HAART and incidence of MS. The national Cholesterol Education Program definition of MS was used. This requires the presence of three or more of the following: high blood pressure, high fasting glucose, low HDL cholesterol, high fasting triglycerides and abdominal obesity. Data was analysed on Excel spreadsheet and *P*-value was obtained using Mann-Whitney/Wilcoxon Two sample test.

**Results:** Complete data on MS was available on 128/200 patients. Median age 39.5, 76.6% were male, 23.4% female, 51.6% Caucasian, 49.4% non-Caucasian (32% African). The prevalence of MS was 9.4% (12/128). For those who had MS, 75% were male, 58.3% Caucasian, 41.7% non-Caucasian (33.3% African), 58.3% were on HAART, 28.6% on Protease Inhibitors (PI) and 16.7% had AIDS. Regarding those who did not have MS, 76.6% were male, 50.9% Caucasian, 49.1% non-Caucasian (31.9% African), 19.1% had AIDS, 73.3% on HAART, 45.2% on PI. The median age for the patients with MS was 46.5, compared to 39.0 in non-metabolic syndrome arm (*P*-value 0.0037).

**Conclusion:** The patients with MS tend to be male and of a higher age group. There seems to be no effect of stage of disease or, surprisingly, the type of HAART on the incidence of MS. Our data showed that prevalence of MS among HIV patients is less than what has been reported previously, but this might be partly because of an under-reporting bias which will be corrected as missing data are retrieved.

O19

### Clinical utility of HLA-B\*5701 testing in a UK clinic cohort

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**Aims:** To determine whether pre-treatment genotyping for HLA-B\*5701 reduces the frequency of hypersensitivity reactions (HSRs) in patients commencing abacavir (ABC).

**Methods:** A prospective study of B\*5701 testing in patients starting or switching HAART. ABC was avoided in those testing positive for B\*5701 and HSR rates monitored. The proportion experiencing an HSR was compared with that in patients starting ABC prior to B\*5701 testing (Fisher's exact test).

**Results:** A total of 271 patients was tested and 26 (10%) were positive. Gender/ethnicity were as follows: males = 249 (92%), females = 22 (8%); black = 42 (15%), white = 215 (79%), other ethnicity = 11 (4%), not known = 3 (1%). The carriage rate was 23/215 = 11% in whites and 3/42 = 7% in blacks. 106 patients were treatment-naïve or on a treatment interruption; 165 were considering switching (135 of the latter were on a thymidine analogue). 81 patients subsequently started abacavir with an HSR rate of 0 (95% CI 0–4.6%) compared to 20/322 = 6% (95% CI 4.1–9.4%) HSR rate prior to B\*5701 testing (*P*=0.01).

**Conclusion:** This is one of the first studies to report on B\*5701 carriage rate in a UK-based clinical cohort. Testing for B\*5701 significantly reduced the frequency of HSR. Incorporating this strategy into routine clinical practice is likely to lead to significant improvements in patient safety and counter the long-term toxicity of HAART.

O20

### Application of an interferon-gamma release assay to investigate transmission of *Mycobacterium tuberculosis* to HIV-infected people

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**Background:** The control of tuberculosis (TB) requires an accurate diagnostic test for latent infection. The tuberculin skin test (TST) lacks specificity and sensitivity in an HIV-infected population. Assays that measure interferon- $\gamma$  (IFN- $\gamma$ ) production in response to the RD1-encoded *M. tuberculosis* antigens such as culture filtrate protein 10 (CFP-10) show evidence of improved specificity and sensitivity in HIV-uninfected people, but have rarely been evaluated in the setting of HIV.

**Methods:** We aimed to assess the diagnostic value of the IFN- $\gamma$  assay in the detection of latent tuberculosis among 16 HIV-infected individuals exposed to an index case of smear-positive pulmonary tuberculosis and 18 non-exposed HIV-infected controls. IFN- $\gamma$  production in response to T-cell stimulation with CyaA-CFP10 (CFP-10 presented as a toxoid antigen within the inactivated adenylate cyclase of *Bordetella pertussis*) and PPD was measured using an ELISA. The results were correlated with the degree of exposure to the index case and results of the TST.

**Results:** Four patients in the exposed group produced IFN- $\gamma$  in response to CyaA-CFP10. This correlated with an increased duration of exposure and a strongly positive TST in one patient. In the control group, 3/5 patients with positive responses to CyaA-CFP10 may have been latently infected as they were born in high-incidence areas. Two exposed patients responded to PPD *in vitro*; there was no correlation with duration of exposure. A trend towards a higher CD4 count in responders was observed.

**Conclusion:** IFN- $\gamma$  production in response to CyaA-CFP10 correlates with the degree of exposure to *M. tuberculosis* in an HIV-infected cohort.

O21

### Marginal zone B cells are depleted in HIV-1 infection and are not restored by antiretroviral therapy

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**Aims:** Invasive pneumococcal disease is an important cause of morbidity and mortality in HIV-1 infection. High affinity IgM anti-pneumococcal antibodies secreted by marginal zone B (MZB) cells play an important role in host immunity against invasive pneumococcal infection. The aim of this study was to determine the concentration of MZB cells and pneumococcal antibodies in drug-naïve and antiretroviral-treated (ART) HIV-1 patients.

**Methods:** B-cell subsets were determined using a whole blood-flow cytometric method and pneumococcal serology was evaluated by standard ELISA technology in 15 healthy controls (HC), 25 drug-naïve and 30 ART HIV-1 patients.

**Results:** The percentage of MZB cells was significantly reduced in drug-naïve and ART patients compared with healthy controls (HC). Drug-naïve HIV-1-infected patients with a CD4 cell count >350 cells/μl had a significant increase in MZB cell percentage compared with patients who have more advanced disease. There was no difference between the percentage of germinal centre memory B-cells between the HIV patient groups and HC. Serum levels of pneumococcal IgM levels were significantly depressed in both HIV-1 patient groups compared with HC.

**Conclusion:** Our data suggest a possible reason for the increased risk of invasive pneumococcal disease in HIV-1 infection. Further functional studies of immune responses to pneumococcal immunisation are in progress and will be reported.

O22

### Natural killer cell NKG2A expression is unaffected by short-term increases in HIV-1 viraemia during treatment interruption

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**Aims:** NKG2A is an inhibitory C-type lectin receptor whose expression is dysregulated in natural killer (NK) cells and T cells during HIV-1 infection. This longitudinal study analysed whether changes in the number and phenotype of NK cells occurred after an interruption in HAART and whether increases in HIV-1 viraemia during treatment interruption (TI) affected the expression of the inhibitory C-type lectin receptor NKG2A on NK cells and T cells.

**Methods:** Expression of NKG2A on NK cells and T cells was investigated in two groups of HIV-1-positive patients, either with or without viraemia prior to TI. Cell phenotype was analysed by flow cytometry before TI, during early TI (0.5–2 months) and within 1 month of resuming HAART after patient-directed TI.

**Results:** Patients with baseline undetectable viral loads had a significantly greater proportion of NK cells expressing NKG2A (mean 33.7 ± SD 11.2%) compared to those with viraemia (20.7 ± 10.9%,  $P < 0.005$ ). In healthy controls 58.6 ± 12.6% of NK cells expressed NKG2A. Despite similar viraemia during TI in both groups, no significant changes occurred in the absolute numbers or percentages of NK cells in either group. There was no change in the proportion of NK cells expressing NKG2A during or after the period of TI. In contrast, the proportion of T cells expressing NKG2A increased, on average from 2.7 ± 1.4% to 3.8 ± 2.3% ( $P < 0.005$ ), in both groups over the course of TI and no significant differences were observed between the two groups.

**Conclusion:** Patients with long-standing viral suppression have a greater percentage of NKG2A-expressing NK cells than those with chronic viraemia. Reduced proportions of NKG2A<sup>+</sup> NK cells are not determined by short-term changes in viraemia; in contrast, NKG2A<sup>+</sup> T cells are more sensitive to virus.

O23

### Switch in C-type lectin receptor phenotype from NKG2A to NKG2C in HIV-1 infection

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**Aims:** HIV-1 infection is characterised by an increase in inhibitory receptors and loss of activating receptors on natural killer (NK) cells, resulting in loss of NK cell activity. Paradoxically, the proportion of NK cells bearing inhibitory NKG2A decreases during infection but CD94 co-receptor remains constant. Here we test whether another receptor, NKG2C, is preferentially expressed in HIV-1 infection and if this corresponds to dysregulation of other NK receptors.

**Methods:** We have studied HIV-1-positive treatment-naïve (TN) individuals ( $n=13$ ), HIV-1-positive individuals receiving successful antiretroviral therapy (ART) for a minimum of 1 year without interruption ( $n=10$ ) and a group of 10 age-matched healthy control (HC) individuals. Flow cytometry was used to study the expression of killer immunoglobulin-like receptors (KIRs), natural cytotoxicity receptors (NCRs) and C-type lectin receptors to define expanded populations of NK cells. *In vitro* assays of secretory functions and cytotoxicity were performed. Mann-Whitney *U*-test and Wilcoxon signed rank test were used for analyses.

**Results:** We have shown highly significant differences in the expression of NKG2C between HC (5% of CD94<sup>+</sup> NK cells) and HIV-1-positive TN individuals (37% of CD94<sup>+</sup> NK cells) ( $P < 0.0001$ ). We also observe significantly altered expression of KIR and NCR between these subsets of NK cells. These NK cells from HIV-1-positive individuals express perforin and exhibit cytotoxicity and so are potentially functional.

**Conclusion:** We demonstrate a dramatic switch from NKG2A (inhibitory) to functional NKG2C (activatory) receptor-expressing NK cells in HIV-1-infected individuals with concurrent redistribution of NCR and KIR. This emergence of NKG2C<sup>+</sup> NK cells may have consequences for the recognition and survival of infected CD4<sup>+</sup> T cells in HIV-1-positive individuals.

O24

### A polymorphism reducing RANTES expression is associated with protection from death in HIV-positive Ugandans

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**Background:** HIV-1 utilises two key co-receptors to gain entry to CD4 cells. One of these receptors, CCR5, is a target for a new class of antiviral drugs. A number of endogenous ligands for this receptor exist, including RANTES (CCL5). A single genetic variant (INT1.1C), apparently upregulating RANTES activity, has been associated with accelerated disease progression in American cohorts and, it has been suggested, accounts for 37% of disease progression in Africans. We investigated the role of this variant in a Ugandan cohort.

**Methods:** Seven hundred and ninety-four HIV-positive individuals were recruited from a cohort in Uganda between 1995 and 1998. Data were available for follow-up until 2001. Polymorphisms within the RANTES gene were typed in these populations.

**Results:** HIV-positive individuals homozygous for the INT1.1C polymorphism, previously associated with low RANTES expression, were less likely to die when compared to other genotypes (HR 0.53 = 95%, CI 0.33–0.83,  $P=0.007$ ).

**Conclusion:** This first report of a non-HLA genetic association with HIV-1/AIDS disease progression in an African population reveals a genetic effect different to that reported for African-Americans. The variant previously associated with disease progression is here associated with disease protection. These findings may impact therapeutic strategies targeting the RANTES pathway in HIV infection.

O25

### Sexual behaviour among HIV-positive black Caribbeans in south London: the LIVITY study

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**Background:** The increasing rates of new HIV diagnoses among the black Caribbean community (BCC) in the UK are of major public health concern. However, there remains a paucity of research in this area.

**Objectives:** The LIVITY study is an in-depth epidemiological and behavioural study to determine the current status and potential future impact of HIV in the BCC.

**Methods:** Eligible patients were HIV-positive black Caribbeans (BC) registered at ten clinics in south London. Participants completed an 11-part self-administered questionnaire, including sexual behaviour before and after HIV diagnosis, sexually transmitted infections (STIs) and sex in, or with people from, the Caribbean.

**Results:** As of January 2006, 206 patients were enrolled. Median age was 38 years (IQR = 31–43), 36.9% were born in the UK, and 43.2% in Jamaica. 31.5% were female and 61.6% of men were homo/bisexual (HoM/BM). 51% reported HIV acquisition in the UK and 61.2% reported sex either in the Caribbean in the last 5 years (36.4%) or with recent arrivals from the Caribbean (24.8%). Median number of lifetime sexual partners was 6.5 (IQR = 4–10) for heterosexual women (HW); 40 (IQR = 10–100) for heterosexual men and 95 (IQR = 23–400) for HoM. Before HIV diagnosis, patients reported always using condoms with 25.6% of their partners versus 63.8% post-diagnosis. Patients reporting an STI after HIV diagnosis ranged from 12.7% in HW to 31% in HoM/BM.

**Conclusion:** The LIVITY study is the first comprehensive study in HIV among BCs in south London. These findings highlight ongoing risk behaviour in a proportion of patients, in particular BC HM/BM, and an important overlap with the epidemic in the Caribbean.

O26

### Knowledge of HIV post-exposure prophylaxis in HIV-positive and HIV-negative men in an urban clinic population

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**Introduction:** HIV post-exposure prophylaxis (PEP) is increasingly used following possible sexual exposure. It is unclear how aware patients are of PEP as this is not routinely discussed in genitourinary (GU) or HIV clinics.

**Methods:** A prospective questionnaire survey was carried out at a central London clinic in December 2004. Respondents were 100 men attending a walk-in GU clinic and 100 men attending the HIV clinic.

**Results:** Of HIV-positive patients, 52% were aware of PEP; only 19% had discussed PEP with a doctor, although 47% had been screened for sexually transmitted infections. 84% of those aware were MSM. 57% had recent unprotected anal intercourse (UAI). (Of these, 17% had UAI with >5 partners and 23% thought it probable that they had sex with a person of discordant HIV status, but none had discussed PEP.) Another 19% had discussed PEP with a partner; all were using condoms. 54% of HIV-positive men unaware of PEP had had recent UAI with >1 partner. 19% of GU patients were aware of PEP; 56% of which were MSM. 63% had a previous negative HIV test. Of the 82% not aware of PEP, 18% were MSM and 0.08% heterosexual with endemic risk of HIV acquisition. 76% would consider using PEP. However, of 17% reporting UAI (1/2 with >1 partner), only 1/8 would consider PEP, despite 1/4 estimating probable HIV exposure. No men had been sexually assaulted.

**Conclusion:** This study demonstrates that most men attending this centre are unaware of PEP as an intervention to reduce HIV transmission. This includes those at highest risk of acquiring HIV and HIV-positive men having UAI with multiple partners.

O27

### Intentional and unintentional UAI among gay men who HIV test in the UK: qualitative results from an investigation into risk factors for seroconversion among gay men who HIV test (INSIGHT)

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**Objectives:** Recently acquired HIV infections among gay men continue to be diagnosed in the UK whilst behavioural studies show increases in risk behaviour. INSIGHT combines qualitative and quantitative methods to understand risk factors for recently acquired infections in men who are tested for HIV.

**Methods:** In-depth interviews exploring the context of sero-conversion were conducted among 48 respondents to the case-control survey (CCS) of men who had recently tested positive (cases) or negative (controls), having previously tested negative. Purposive selection ensured diversity in socio-economic and behavioural characteristics. Analysis was conducted with the aid of Framework.

**Results:** Results from the CCS show that unprotected anal intercourse (UAI) remains the predominant mode of HIV acquisition. Narratives of sexual behaviour demonstrate that among cases and controls, UAI with a partner of sero-discordant (sd) or unknown HIV status can be an intentional decision in sexual relationships or encounters, made as a result of trade-offs between the perceived impact of HIV infection compared to the effect of not having UAI on the quality of men's emotional and sexual life. Unintended UAI with casual partners occurred among men who identified periods of depression, anxiety and bereavement that were coterminous with sexual compulsivity, increased use of drugs and alcohol or feeling 'out of control' in sexual encounters. Unplanned sdUAI occurred among men in relationships who believed their long-term partners were HIV negative.

**Conclusion:** Consistent condom use in casual and sero-discordant sexual encounters presents a challenge for some groups of men. Interventions are required that are responsive to these men's circumstances and wider needs.

O28

### Barriers to voluntary confidential HIV testing among African men and women in England: results from the Mayisha II community-based survey of sexual attitudes and lifestyles among Africans in England

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**Objectives:** In response to rising diagnoses of HIV infection in Africans in the UK, Mayisha II aimed to measure diagnosed and undiagnosed HIV infection among African communities and explore the socio-demographic and behavioural associations with HIV infection.

**Methods:** A community-based survey was conducted among 1359 Africans in London, Luton and the West Midlands with in-depth follow-up interviews among 44 selected survey respondents during 2004–2005. Oral fluid samples were provided by 75% of respondents using an Orasure device for anonymous testing for HIV antibodies. Respondents were recruited from venues and social gatherings by community fieldworkers who also administered the Orasure tests.

**Results:** Despite high levels of HIV testing in the survey sample, half of females and 43% of males reported never having a voluntary confidential HIV test (VCT); fear of reprisals following an HIV diagnosis continue to deter others from VCT and contribute to undiagnosed HIV in the sample. Analysis of narrative accounts indicates that HIV infection is associated with sexual 'misbehaviour' and 'immorality'. Consequently, there are expectations of retribution and rejection by partners and family members following diagnosis. However, respondents' accounts of outreach work and the uptake of the Orasure test during the survey suggest that interventions can have an impact on such beliefs.

**Conclusion:** Findings from Mayisha II confirm that the impact of discrimination and stigma is widespread within the lives of Africans in the UK and contributes to decisions to HIV test. Outreach work is having an impact on the acceptability of VCT in the community, but more action is needed to reduce HIV-related stigma and discrimination.

O29

**Could primary care be doing more?**

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**Introduction:** In the UK, Africans present to HIV services with significantly more advanced HIV disease than non-Africans, denying themselves the full benefit of available treatment. Little is known about healthcare utilisation prior to diagnosis for this population.

**Objectives:** To identify opportunities for earlier diagnosis of HIV amongst Africans in London.

**Methods:** A survey of newly diagnosed HIV-positive Africans attending 14 HIV treatment centres across London between April 2004 and February 2006 using a self-completed questionnaire linked to clinical records.

**Results:** 236 questionnaires were completed, representing an 82% response rate. 66% of respondents were women, 72.3% came from countries with an HIV prevalence of over 15%, 78.3% were aged between 25 and 44, and 54.2% had advanced HIV (CD4 <200 cells/ $\mu$ l or an AIDS-defining illness) at the time of diagnosis. 84.7% of respondents were registered with a GP for a medium time of 3 years, and 75% saw their GP within the 2 years prior to diagnosis, most commonly for flu or chest infection. In the year prior to diagnosis 69.3% saw their GP for a medium of two visits (range 1–18). HIV testing was raised by the GP for 16.3% of participants.

**Discussion:** These preliminary data show that primary care services are well accessed by this population. The demography alone should alert clinicians to considering HIV irrespective of health status. However, for over 80% of respondents who attended their GP, the issue of HIV testing was not broached. Work with primary care services is required to understand and overcome the barriers to discussing HIV infection for this, and all, populations.

O30

**Point-of care testing for HIV antibody as a new model of care**

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**Aims:** Validate and implement the Abbott Determine assay for nurse-led delivery of point-of-care (POCT) HIV antibody testing.

**Methods:** Validation: 210 sera tested by Determine and lab-based Vitros, including: (a) HIV-infected patients with subtype B (25) or non-B (25; A, C, D, F, G); (b) 84 patients seeking HIV testing; (c) 40 patients with hepatitis C or B; (d) 36 patients with equivocal Vitros reactivity but negative confirmatory tests, including patients seeking HIV testing, pregnant women and renal dialysis patients; (e) 27 samples taken from acute seroconverters over 28 days. Implementation: policy document, standard operative procedure, recorded training and certification, health and safety, risk management, and internal/external quality control programmes set up to ensure compliance with clinical governance and accreditation requirements.

**Results:** Validation (a) 25/25 B and 25/25 non-B patients positive by both assays; (b) 5/84 patients positive by both assays, confirmed HIV-positive; (c) 40/40 patients negative by both assays; (d) 36/36 samples negative by Determine. In acute seroconverters, Vitros and Determine became positive at days 7–23 and 14–28 after presentation, respectively. On average, Determine became positive 5–7 days later than Vitros. Implementation: the POCT service started in January 2006 to be run twice weekly and open to all patients seeking HIV testing. For reactive Determine results, service provision includes lab-based confirmatory antibody test (1 h turn-around), followed by two additional confirmatory antibody tests and viral load (48 h turnaround).

**Conclusion:** Determine showed excellent agreement with the lab-based assay. With quality assurance in place, implementation is feasible in routine clinical settings. Caution is required in the interpretation of negative Determine results in patients with symptoms suggestive of acute seroconversion.

O31

**Missed opportunities for diagnosing acute seroconversion illness**

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**Aims:** To investigate whether individuals with primary HIV infection (PHI) presented to a healthcare facility with symptoms of the acute seroconversion illness (ASI) prior to their diagnosis being made.

**Methods:** All individuals diagnosed with PHI between 2003 and 2005 were identified (based on an evolving antibody response, negative HIV test within 18 months or the serological testing algorithm for recent HIV seroconversion). Symptoms of ASI (recorded prospectively) and previous presentation to other healthcare providers were ascertained from genito-urinary medicine (GUM) clinic notes and laboratory records (a single laboratory performing all of the HIV tests in the area).

**Results:** 119 individuals were diagnosed with PHI. Clinic notes were accessible for 102 (96 male, 88 homosexual). A history of ASI was elicited in 71 (70%). Of these, 37 (52%) did not present to a healthcare provider during the symptomatic period. Of the 38 (48%) who did, 22 were diagnosed with PHI at first presentation (14 GUM, eight non-GUM). In 15 patients a diagnosis of PHI was not entertained at first presentation (all non-GUM). In one patient (GUM), with recent high-risk and early ASI, a fourth-generation HIV test was negative and diagnosis was only made after the three-month window period.

**Conclusion:** Even though the majority of patients with PHI had symptoms, a significant proportion did not access healthcare. Of those who presented to non-GUM specialities, the opportunity to identify ASI was often missed. In order to reduce onward transmission, the diagnosis of PHI needs to be improved by increasing awareness of ASI within both at-risk groups and primary healthcare providers.

O32

**Meeting the needs and service development for the longer term follow-up of young people with perinatally acquired HIV infection**

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**Objectives:** Children with perinatally acquired HIV-1 infection are surviving into adult life, transferring to adult services and presenting complex medical and multi-disciplinary problems for adult physicians. Despite careful transition, 4/5 young people initially transferring from our paediatric to adult services failed to attend for regular care. Identifying specific needs of these young people may improve service provision and uptake.

**Methods:** Retrospective case-note audit of young people aged 12+ years attending a paediatric HIV clinic.

**Results:** Two hundred and ten infected children, 74 (35%) aged 12+, of whom 25 (33%) are 16 or older. Of the 74 young people, 13 (18%) are antiretroviral therapy (ART) naive: median CD4 count  $530 \times 10^9/l$  (range 240–890), median viral load 8466 copies/ml (range 315–120629). Of those currently on ART, 34 (69%) have viral loads of <50 copies/ml, eleven >1000 copies/ml. Median CD4 count for those on ART  $560 \times 10^9/l$  (IQR = 330–710). Six (8%) have CD4 counts below  $200 \times 10^9/l$ , four of whom have no peripheral CD4 cells and multidrug-resistant virus. Two young people are in the terminal-care phase of their illness. Of those on ART, 35 (71%) have received all three major classes; two have failed on the fusion inhibitor T20. Of the 74, 9% have abnormal neurology, most commonly hypertonic diplegia, 11% have significant visual/hearing impairment and 47% have a statement of educational need or additional support in school.

**Conclusion:** A proportion of young people transitioning towards adult services are highly ART-experienced with significant neurodevelopmental concerns. A dedicated long-term follow-up clinic for adults with perinatally acquired HIV infection has been established to try to meet the needs of this complex cohort.

O33

### Cause and time to treatment failure of HAART and cost of care in UK NPMS-HHC Clinics, 1996–2002

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**Aims:** To estimate time to treatment failure for first-, second- and third-line HAART, identify factors predicting treatment failure and the cost of service provision.

**Method:** Cox's PH regression models were used to estimate likelihood of treatment failure after starting first-, second- or third-line HAART. Analyses were adjusted for other factors. Reasons for treatment failure were investigated and treatment failure time estimated using survival analysis. Unit costs for use of hospital services were estimated.

**Results:** 3647 on first-line HAART had an estimated time to failure of 6.7 years (IQR = 3.2 to 10.3 years). For second-line this was 4.3 years (IQR = 2.0 to 6.7 years) and for third-line 4.2 years (IQR = 2.0 to 6.5 years). Likelihood of treatment failure increased if started on a PI regimen, starting with CD4 count of below 170 cells/ $\mu$ l for first- and 190 cells/ $\mu$ l for second-line HAART and starting at CDC non-AIDS stage (first-line). Of those who failed first-line treatment, 42% were due to virological failure, immunological failure or clinical progression. The average cost of hospital services until first-line treatment failure was £112 158 (IQR = £53 568 – £172 422), £71 212 (IQR = £33 122–£110 959).

**Conclusion:** Median time to treatment failure for people on second- or third-line HAART was less than that of first-line, but time to treatment failure has improved dramatically over time. Around 50% of people failed because of reasons other than virological failure, immunological failure or clinical progression, and are most likely related to the occurrence of adverse events. Average hospital costs for those on first-line therapy were greater compared with second- or third-line therapy, reflecting shorter duration for onset of treatment failure for second- and third-line therapy.

# Poster abstracts

## Large

P1

### Relative antiviral efficacy of TMC114/r and tipranavir/r versus control PI in the POWER and RESIST trials

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**Aims:** To compare the relative antiviral efficacy of TMC114 with low-dose ritonavir (TMC114/r) and tipranavir (TPV/r) versus control PI (CPI) in treatment-experienced patients, using data from POWER 1/2 and RESIST 1/2 trials. The four trials all recruited antiretroviral (ARV)-experienced patients with HIV RNA >1000 copies/ml and at least one primary PI mutation, used optimised RTIs with or without enfuvirtide (ENF), plus investigator-selected CPI in the control arms, and had the same primary efficacy endpoint.

**Methods:** Summary statistics were obtained from published presentations and drug labels. For the POWER trials, data from the 600/100 mg bid dose and CPI arms was included, while all data from the RESIST trials (TPV/r 500/200 mg bid and CPI) were included. The difference in week 24 efficacy for the new PI versus CPI was compared between the trials. All analyses used intent-to-treat TLOVR methods.

**Results:** Overall baseline characteristics (age, gender, race, HIV RNA, IAS-USA PI mutations) were well matched across the trials. At week 24, 72% of TMC114/r patients achieved a  $\geq 1$  log<sub>10</sub> reduction in HIV RNA compared to 40% of TPV/r patients (CPI patients 21% and 18%, respectively). The treatment benefit of TMC114/r over CPI in the POWER trials was greater (outside the 95% confidence intervals) than the benefit of TPV/r over CPI in the RESIST trials, for the 24-week HIV RNA endpoints of 1 log reduction, <400 copies and <50 copies/ml, plus for mean rise in CD4 count. This effect was also found for the subgroups of ENF-naïve patients and patients not using ENF.

**Conclusion:** Given the caveats of cross-study analysis, the efficacy benefits of TMC114/r versus CPI in the POWER trials appear to be greater than the benefits of TPV/r versus CPI in the RESIST trials for HIV RNA suppression and CD4 rises.

P2

### 48-Week durable efficacy and safety results of TMC125 in HIV patients with NNRTI and PI resistance: study TMC125-C223

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**Methods:** TMC125-C223 is a randomised, controlled, partially-blinded study of TMC125 in 199 patients with documented NNRTI resistance and  $\geq 3$  primary PI mutations (median 4). Patients received TMC125 (400 mg or 800 mg bid) with an investigator-selected background, or a standard-of-care control regimen.

**Results:** Median baseline viral load was 4.7 log<sub>10</sub> copies/ml and CD4 count 100 cells/ $\mu$ l.

48 week results IIT (NC = F)	400 mg	800 mg	Control
Mean $\Delta$ VL (log <sub>10</sub> copies/ml)	-0.88**	-1.01*	-0.14
% >1 log <sub>10</sub> decrease	31%*	34%*	8%
% <50 copies/ml	23%	22%	0%
$\Delta$ CD4 cell count	+58	+61	+13

(P-value versus control at week 48 - \*P < 0.01 \*\*P = 0.02)

At week 48 in the combined TMC125 groups, 88% of those patients with a viral load <50 at 24 weeks remained <50 copies/ml; an additional six patients also achieved <50. Virological failure on TMC125 400 and 800 mg bid was 9% in both groups. In the control arm, 98% of patients discontinued study, 78% due to virological failure. The high rate of premature discontinuations on the control arm confounded the comparison of safety given the lower median duration of treatment in the control arm of 17.9 weeks, versus 47.7 weeks in both TMC125 groups. Grade 3/4 AEs (all causes) were reported in 43% of patients on TMC125; 17% discontinued due to AEs.

**Conclusion:** In this study, TMC125 showed high rates of sustained efficacy in heavily pre-treated patients with substantial NNRTI and PI resistance. These data are the first to show durable efficacy at 48 weeks with an NNRTI in subjects with NNRTI resistance.

P3

### Efficacy of TMC114/r in treatment-experienced HIV patients: factors influencing outcome in the pooled 24-Week analysis of POWER 1, 2 and 3

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**Aims:** Data from the randomised, PI-controlled POWER 1 and 2 studies (TMC114-C213 and C202) and the open-label roll-over study, POWER 3 (TMC114-C215), were pooled to examine factors contributing to the efficacy of TMC114 with low-dose ritonavir (TMC114/r) in treatment-experienced HIV patients.

**Methods:** Patients randomised to receive TMC114/r 600/100 mg bid ( $n = 458$ ) or control PI(s) (CPI,  $n = 124$ ) were included in this analysis. Regimens were optimised using  $\geq 2$  NNRTIs with or without enfuvirtide (ENF). Week 24 efficacy data were analysed by baseline (BL) viral load (VL), TMC114 EC<sub>50</sub> fold change (FC), concomitant and previous ENF use, number of IAS-USA primary PI mutations, and number of sensitive NNRTIs and CPI(s).

**Results:** Overall, BL mean VL was 4.6 log<sub>10</sub> copies/ml, median CD4 count was 128 cells/ $\mu$ l and 73% had  $\geq 3$  primary PI mutations. Overall BL median TMC114 FC was 3.5, 4.9 and 3.2 for POWER 1, 2 and 3, respectively. HIV RNA <50 copies/ml was reached by 42% of TMC114/r patients, 24% with a susceptible CPI, and 7% with a resistant CPI. Multivariate analyses showed that BL FC, number of sensitive NNRTIs and concomitant use of ENF correlated with response. Subgroup analysis showed BL FC was highly predictive of virological outcome: 50, 25 and 13% of TMC114/r patients with BL FC  $\leq 10$ ,  $10 < FC \leq 40$  and  $FC > 40$  respectively reached HIV RNA <50 copies/ml. All subgroup analyses showed a higher proportion of responders in the TMC114/r group compared to control, regardless of concomitant ENF use.

**Conclusion:** TMC114 FC was the strongest predictor of regimen efficacy. The magnitude of the incremental benefit for all other factors was determined by BL TMC114 susceptibility. TMC114/r 600/100 mg bid was uniformly superior to CPI, regardless of CPI predicted activity.

P4

**POWER 3 trial: 24-week efficacy and safety results of TMC114/r in treatment-experienced HIV patients**J-M Molina<sup>1</sup>, Cal Cohen<sup>2</sup>, Christine Katlama<sup>3</sup>, Beatriz Grinsztejn<sup>4</sup>, Artur Timmerman<sup>5</sup>, R Pedro<sup>6</sup>, Sandra de Meyer<sup>7</sup>,Marie-Pierre de Bethune<sup>7</sup>, Tony Vangeneugden<sup>7</sup> and Eric Lefebvre<sup>8</sup><sup>1</sup>Hopital Saint-Louis, Paris, France, <sup>2</sup>University of the Witwatersrand, Johannesburg, South Africa, <sup>3</sup>Hospital Pitie Salpetriere, Paris, France,<sup>4</sup>Inst de Pesquisa Clinica Chagas, Rio, Brazil, <sup>5</sup>PAM Heliopolis, Sao Paulo, Brazil, <sup>6</sup>HC Unicamp, Campinas, Brazil, <sup>7</sup>Tibotec BVBA, Mechelen, Belgium, <sup>8</sup>Tibotec Inc., Yardley, USA

**Objectives:** In the POWER 1 and 2 (TMC114–C213 and C202) studies, TMC114 with low-dose ritonavir (TMC114/r) provided a sustained efficacy compared to control. The efficacy and safety of the selected dose for treatment-experienced HIV patients, 600/100 mg bid, were further investigated in the non-randomised, open-label TMC114–C215 trial of POWER 3.

**Methods:** Study inclusion/exclusion criteria were the same as for POWER 1 and 2. Patients received TMC114/r 600/100 mg bid plus an optimised background regimen based on screening, resistance testing and treatment history. Analysis was intent-to-treat (TLOVR algorithm).

**Results:** In total, 303 patients were enrolled; 235 reached week 24 and are included in this analysis. Median baseline characteristics were similar to those of POWER 1 and 2: viral load was 4.6 log<sub>10</sub> copies/ml and CD4 count was 116 cells/μl. HIV RNA <50 copies/ml and a reduction in HIV RNA of ≥1 log<sub>10</sub> copies/ml were achieved by 40% and 66% of patients, respectively. Baseline TMC114 fold change was the strongest predictor of virological response. CD4 counts rose by a mean of 82 cells/μl. The most common AEs were diarrhoea (14%) and nausea (10%). Grade 3/4 triglyceride, cholesterol, ALT and AST elevations occurred in 5.5%, 4%, 2.4% and 1.8% of patients, respectively. Individual grade 3/4 AEs occurred in ≤4% of patients; 8 (2%) discontinued due to AEs. Serious AEs occurred in 13% of patients but no individual SAE occurred in (1% patients. The six deaths (2%) were not treatment-related.

**Conclusion:** POWER 3 efficacy and safety results confirm and extend those observed in POWER 1 and 2. TMC114/r 600/100 mg bid provided patients with a substantial reduction in viral load and an increase in CD4 counts, and was generally safe and well-tolerated.

P5

**The inhibitory quotient (IQ) of ritonavir-boosted protease inhibitors (PI/r): correlation with virological response.**Laura Waters<sup>1</sup>, Alan Winston<sup>1</sup>, Nimesh Patel<sup>1</sup>, David Back<sup>2</sup>, Saye Khoo<sup>2</sup>, Steve Bulbeck<sup>1</sup>, Anton Pozniak<sup>1</sup>, Mark Nelson<sup>1</sup>, Graeme Moyle<sup>1</sup>, Brian Gazzard<sup>1</sup> and Marta Boffito<sup>1</sup><sup>1</sup>St Stephens Centre, Chelsea and Westminster Hospital, London,<sup>2</sup>Department of Pharmacology, University of Liverpool, Liverpool, UK

**Aims:** IQ is a measure of plasma drug exposure corrected for resistance; we compared methods based on genotype (GIQ), virtual phenotype (VIQ) and population-adjusted or normalised IQ (NIQ) in terms of predicting virological response in experienced HIV-positive subjects.

**Methods:** In a prospective study of therapeutic drug monitoring (TDM), individuals commencing a PI/r-based antiretroviral (ARV) regimen underwent measurement of trough PI concentration (C<sub>trough</sub>). Week 4 C<sub>trough</sub> was adjusted for (a) total/significant genotypic PI mutations (sigGIQ/totGIQ), (b) virtual phenotypic fold-change (VIQ), and (c) VIQ corrected for 80% clinical cut-off and population C<sub>trough</sub> (NIQ). Associations between IQ and time-weighted change in HIV-RNA up to 48 weeks were assessed with linear regression modelling and z-transformation used to compare different PIs.

**Results:** 53 treatment-experienced patients commencing a new PI/r-based regimen between June 2004 and August 2005 were included. Baseline viral load (VL) was undetectable (<50 copies/ml) in 18 (34%) subjects and a mean of 3.68 log<sub>10</sub> copies/ml in the remainder. Median time-weighted change in log HIV-RNA was 1.82 log copies/ml. In a multivariate analysis only baseline HIV-RNA and NIQ were significantly associated with time-weighted change in HIV-RNA ( $P < 0.001$  and  $0.021$ , respectively); C<sub>trough</sub>, FC, sigGIQ, totGIQ and VIQ showed no significant association.

**Conclusion:** NIQ may be a useful tool in predicting response to boosted-PI based regimens in ARV-exposed subjects.

P6

**Virological outcome in naive and switch patients receiving TDF/DDI as their 2NRTI backbone**

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**Aims:** To look at outcomes following the use of didanosine (ddl) and tenofovir (TDF) as a 2NRTI backbone in patients naive to treatment or switching to this combination with a viral load (VL) <50 copies/ml without previous ARV failure.

**Methods:** Data were retrieved from pharmacy lists, databases, and case notes. Virological failure (VF) was defined as two consecutive VLs >400 copies/ml following <50 copies/ml or failure to achieve <50 copies/ml by 3 months (naive group only). Statistical analysis was by chi-squared and student *t*-tests.

**Results:** Thirty-nine patients were identified: 24 naive (21 NNRTI, 3 PI/r) and 15 switch (11 NNRTI, 4 PI/r). 14/24 (58%) naive patients failed treatment of whom eight were VF. Those with a baseline VL >10<sup>5</sup> were more likely to fail treatment (91% versus 31% <10<sup>5</sup>;  $P < 0.005$ ). 7/8 patients who had VF had genotypic resistance testing. All had significant RT mutations (7 NNRTI, 2 K65R). 67% (10) of switch patients maintained a VL <50 copies/ml (median follow-up 23 months) with only three demonstrating VF. Treatment failure occurred earlier in naive patients than those switching to TDF/DDI (mean 98 day versus 539 days;  $P < 0.005$ ). Of 10 naive and 10 switch patients achieving/maintaining a VL <50 copies/ml, 13 (65%) had their 2NRTI backbone changed because of concerns over TDF/DDI efficacy. All of these patients remain with a VL <50 copies/ml (median follow-up 6 months). None of the patients on PI/r-TDF/DDI who developed VF had PI mutations.

**Conclusion:** As in other studies, the 2NRTI backbone of TDF/DDI has been shown to produce unacceptably high rates of VF in naive patients, associated with high baseline VL and NNRTI and K65R resistance. However, patients switching with an undetectable VL and no likely previous ARV failure or drug resistance may remain successfully suppressed for a prolonged period on TDF/DDI.

P7

**Does gender or ethnicity influence treatment outcomes in antiretroviral-naive patients commencing NNRTI-based HAART?**

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**Aims:** To determine whether gender and ethnicity are associated with time to virological success or treatment failure in ART-naive patients commencing HAART.

**Methods:** ART-naive individuals commencing efavirenz (EFV) or nevirapine (NVP) with dual NA backbone were identified between 1/1/1998 and 1/7/2004 from a prospectively collected database. Virological success was defined as VL <500 copies/ml. Treatment failure was switch/discontinuation of NNRTI or documented virological failure ( $2 \times VL > 500$  copies/ml).

**Results:** Nine hundred and ninety-four patients were identified; 85.8% male and 69.1% Caucasians. 72.7% commenced EFV and 27.3% NVP-containing HAART. There was no difference between the two treatment groups for age and ethnicity, although significantly more females commenced NVP while the converse was true for males ( $P < 0.001$ ). In univariate analysis, neither gender nor ethnicity (black Africans versus Caucasians) were associated with time to virological success ( $P = 0.299$  and  $P = 0.322$  respectively) or time to treatment failure ( $P = 0.703$  and  $P = 0.499$  respectively).

**Conclusion:** We have shown that in a large NNRTI-experienced cohort there is no significant difference for gender or ethnicity with respect to time to virological success or treatment failure.

P8

### Cost-effectiveness of NNRTI versus PI-containing HAART regimens in UK NPMS-HHC Clinics, 1996–2002

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**Aims:** To estimate the cost-effectiveness of NNRTI versus PI-containing first-line HAART regimens.

**Methods:** Cox's proportional hazard regression models were used to estimate likelihood of treatment failure for different first-line HAART regimens. Analyses were adjusted for gender, age, baseline viral load, CD4 count and CDC diagnosis and stratified by year of starting HAART. Log rank survival analyses were extrapolated using least-squares maximum-likelihood method to estimate treatment-failure time. Annual cost of care estimated for different regimens and discounted at 3.5% (2002 prices). The cost-effectiveness analyses compared different PI-containing first-line HAART regimens with 2NRTIs + NNRTI.

**Results:** Median time to treatment failure for 2NRTIs + NNRTI was 4832 days (IQR = 2332–7332), 1571 days for 2NRTIs + PI (IQR = 738–2404), 2378 days for 2NNRTIs + 2PIs (IQR = 1128–3628) and 1631 days for 2NRTIs + PI<sub>boosted</sub> (IQR = 798–2464) ( $P < 0.001$ ). Annual hospital care cost was £12 199 for 2NRTIs + NNRTI, £14 060 for 2NRTIs + PI, £19 703 for 2NNRTIs + 2PIs and £14 049 for 2NRTIs + PI<sub>boosted</sub>. The cost-effectiveness of first-line 2NRTIs + NNRTI versus 2NRTIs + PI was £8079 per life year gained (LYG), £8236 per LYG for 2NRTIs + NNRTI compared with 2NRTIs + PI<sub>boosted</sub> and £1962 per LYG for 2NRTIs + NNRTI compared with 2NRTIs + 2PI.

**Conclusion:** People on first-line 2NRTIs + NNRTI had longest estimated time to treatment failure, lowest annual hospital costs and regimen was cost-effective compared with the PI-containing first-line regimens. Given the increasing number of people living with HIV in high, middle and low income countries, cost and cost-effectiveness of regimens are becoming increasingly important criteria for deciding which particular regimen to use for first-line HAART.

P9

### Kaletra monotherapy – a real-life experience

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**Aims:** Despite limited evidence, dual and single protease-inhibitor (PI) regimens are used increasingly in experienced subjects. We present our experience of boosted lopinavir monotherapy (mLPV/r) outside a clinical trial setting.

**Methods:** We identified all mLPV/r prescriptions up to September 2005 from a prospectively collected database. Baseline data including treatment history, resistance, CD4 count and viral load (VL) were collected. CD4 and VL changes over a 12-month period were analysed.

**Results:** 35 patients prescribed mLPV/r were identified; mean CD4 count and VL at switch were 248 cells/ $\mu$ l and 54 866 copies/ml, respectively and subjects had had a median of 5 previous drug regimens. Two switched for toxicity, five were lost to follow-up. 14/28 (50%) achieved VL <50 copies/ml and 73% a >1log<sub>10</sub> reduction. Mean CD4 rise was 115 and 73 cells/ $\mu$ l in the undetectable and viraemic groups respectively. Five patients with major PI mutations at baseline were identified and three experienced satisfactory responses (CD4 increase; two undetectable, 1 < 400 copies/ml). 10 had genotyping on mLPV/r; two exhibited new minor mutations. In total, 8/28 subjects switched therapy (three virological failure, two for blips, one immunological failure and two unclear reasons) and 20 remain on mLPV/r; 12/20, 60% are undetectable after a mean of 13.5 months (range 3–34).

**Conclusion:** In our series of drug-experienced individuals mLPV/r was associated with improved immunological parameters regardless of virological response. 50% achieved an undetectable (less than 50 copies/ml) VL and 73% a greater than 1log<sub>10</sub> reduction. As most subjects switched to mLPV/r for poor compliance these data support this strategy for poorly adherent drug-experienced patients.

P10

### Tipranavir/T20-containing salvage regimens highly effective and durable in heavily PI-treatment-experienced HIV-1-infected patients in clinical practice

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**Aims:** Highly antiretroviral-experienced individuals with failing HIV-1 therapy pose a challenge. Cross-class and triple-class resistance is resulting in reliance on new drugs. Tipranavir (TPV) has a resistance profile distinct from other PIs and although phase 3 trial data have shown boosted TPV to be superior to other PIs, there is little clinical practice data. This study evaluates the ongoing efficacy, durability, safety and tolerability of TPV-containing regimens in a clinical cohort.

**Methods:** A retrospective clinical case review was undertaken of triple-class-experienced HIV-1-infected patients who had failed previous PI regimens and were receiving new optimised boosted TPV-containing regimens with up to 27 months follow-up. ART resistance was determined by RT and PR sequence analysis using IAS-USA scoring and TPV resistance score (TPV-RS) at baseline and failure.

**Results:** 12 patients were commenced on TPV-containing therapy with median age 48 (IQR = 31–63) years, baseline CD4 count 46 (IQR = 12–276) cells/ $\mu$ l, VL 4.96 (IQR = 4.84–5.50) log<sub>10</sub> copies/ml, five previous PIs (range 3–7) and median exposure to TPV of 11 (range 3–27) months. 5/12 patients were <50 copies/ml after median 21 months (range 15–27), and 1/12 <700 copies/ml after 10 months. 6/12 patients failed after 9 (range 3–12) months and were more likely to have  $\geq 3$  TPV-RS mutations than non-failures ( $P = 0.06$ ). Presence of a major IAS-USA mutation at baseline was strongly associated with absence of a VL drop at 6 months ( $P = 0.02$ ).

**Conclusion:** TPV-containing regimens showed impressive efficacy and tolerability in this heavily experienced cohort, with 42% suppressed at 21 months. Baseline TPV-RS of three or greater appeared to be predictive of failure.

P11

### Nevirapine once a day may be safer than previously thought

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**Background:** Interest in once-daily HAART has increased with availability of newer once daily (OD) nucleoside/nucleotide backbones. Data from the 2NN study suggests that OD nevirapine (NVP) may be associated with increased hepatotoxicity and rash. As excess toxicity tends to occur in the first 6 weeks, it may be safe to switch to NVP OD after this time. We report our experience with NVP OD use.

**Methods:** All patients receiving NVP OD between 2001 and 2005 were identified from the clinic database. Demographic details, CD4 cell count, viral load (VL) (current and at OD switch), concurrent antiretrovirals and co-infection with hepatitis B/C were recorded. LFT measurements and occurrence of any skin rash after OD switch were noted; disposition was also recorded.

**Results:** Data was collected from 89 patients receiving NVP OD. 79 were male, 10 female; median age 43 (range 25–68); 92% Caucasian; 82% MSM. Median CD4 count at OD switch: 499 cells/ $\mu$ l (range 95–1168). 92% had VL <50 at time of OD switch. Three patients had Hepatitis B co-infection; two Hepatitis C (HCV). Median time to OD switch after starting NVP: 1248 days (range 31–3241). One patient had ACTG Grade 4 (G4) ALT (>10  $\times$  ULN) at 32 weeks on NVP OD (due to acute HCV). One had G3 Bilirubin at 76 weeks (receiving atazanavir). ALT G1:  $n = 16$ ; ALP G1:  $n = 7$ ; Bilirubin G1:  $n = 4$ , G2:  $n = 1$ . No patients reported rash on NVP OD. 94% patients remain on NVP OD [median follow-up 228 days (range 19–979)]; reasons for stopping NVP OD: virological failure 3; for/after pregnancy 2; own choice 1. No patient discontinued because of toxicity.

**Conclusion:** 2NN reported Grade 3 or 4 hepatotoxicity in 13.6% of patients starting NVP OD. NVP may be given safely OD if a lead period of bid dosing is used in predominantly Caucasian patients without HBV/CV co-infection.

P12

### Prospective trial to evaluate the role of therapeutic drug monitoring (TDM) in HIV-positive patients starting/changing antiretroviral (ARV) regimen

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**Background:** TDM is useful in specific clinical situations but its application in routine clinical practice is controversial. The study aim was to investigate the role of TDM in determining the need for ARV dose adjustments to ensure virological response or limit toxicity.

**Methods:** In this non-comparative, prospective trial, patients starting NNRTIs or PIs had TDM at weeks 0/4/24/48. Dose adjustments were planned according to suggested target concentrations (TC) at 12 or 24 h (C<sub>t</sub>) and clinical information (virological failure or drug-related adverse events).

**Results:** 109 patients consented; 48 naive, 61 switching regimen. Median (range) baseline HIV-RNA and CD4 were 2.76 (1.69–5.69) log<sub>10</sub> copies/ml and 279 (14–905) cells/μl. TDM results at week 0/4/24/48 were available for 49/77/50/23 patients. 40 patients received atazanavir/ritonavir (ATV/r), 23 efavirenz (EFV), 17 saquinavir/r (SQV/r), 14 lopinavir/r (LPV/r), 7 fosamprenavir/r (FPV/r), 1 nevirapine (NVP). Two patients on ATV/r, 5 on EFV, none on SQV/r, one on LPV/r, and none on FPV/r had a C<sub>t</sub><TC, none showed virological failure, no dose adjustment was performed. Three on EFV had C<sub>t</sub>>4000, but no major adverse event was reported and the patients continued EFV therapy. C<sub>t</sub> inter-individual variability (coefficient of variation, CV%) was 51% for ATV/r and EFV, 91% for SQV/r, 42% for LPV/r, and 47% for FPV/r. Of 199 tests, 23 results were not interpretable due to frequent errors occurring when requesting TDM.

**Conclusion:** Despite wide variability in C<sub>t</sub>, clinicians were reluctant to dose-modify in the minority of patients with abnormal results. TDM is a complex (though feasible) investigation to implement, and is frequently not performed correctly. The benefit of TDM in unselected patients is unclear, because patients with low C<sub>t</sub> still responded to therapy.

## Standard

P13

### Tenofovir and didanosine in combination with a boosted protease? 48-week clinical experience of boosted atazanavir with tenofovir and didanosine

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**Background:** Boosted atazanavir (ATV), tenofovir (TDF) and didanosine (ddl) is a once-daily antiretroviral combination used in our centre with little clinical data to support its use. The combination has complex drug interactions as well as concerns over the immunological consequences of combining TDF and ddl. We identified 71 patients who began on this combination at a large central London HIV centre and followed them prospectively. We looked at virological and immunological outcomes as well as laboratory markers and reported adverse events.

**Results:** The mean age of the cohort was 39 years (range 27–63). 52 patients were male, 24 were black African, four black Caribbean, one Asian and 42 white. Ten patients were of low weight (<60 kg). The median time on antiretroviral therapy (ART) prior to this combination was 48 months (range 0–156), 33 (46%) were triple-class experienced. The median CD4 count at time of starting this combination was 260 (0–650 cells/μl). 18 patients had undetectable viral loads (<50 copies/ml) at the time of switching to this combination. At week 48, 20 patients had discontinued, eight due to jaundice. The median CD4 count rise OT was 115 (range 0–610), although 11 patients experienced CD4 decline (range 10–200 cells/μl). 41 patients had undetectable viral load (80% OT, 58% IIT analysis). 10 were viraemic.

**Conclusion:** The combination of DDI-TDF-ATV/r was reasonably well tolerated and resulted in good virological and immunological outcomes in the majority of this treatment-experienced cohort. These data support the use of this combination in clinical practice. Safety data will be presented in the poster.

**Results:** Six subjects with detectable viraemia after a median of 12 months (range 6–12) TFV/ddl/ATV/r (four inadequate suppression, two rebound from undetectability) met study criteria. Patients had received a median of 6 (2–12) previous regimens. All were 3TC-experienced (4/6 had M184V, two had received 3TC as part of a non-suppressive regimen) and were fully susceptible to ATV (IAS database); 3/6 had mutations conferring intermediate resistance to TFV, 2/6 to ddl. VL at intensification ranged from 89 to 1035 copies/ml and all reached undetectability (<50 copies) within 6 months. 5/6 remain undetectable (median follow-up 10.5 months; range 6–12).

**Conclusion:** We demonstrated the successful use of FTC to intensify HAART in subjects with viraemia and a history of 3TC resistance/failure. This may be due to residual activity of FTC despite M184V and/or increased susceptibility to TFV and/or reduced viral fitness with M184V. TFV/ddl/ATV/r may lack potency in drug-experienced patients.

P15

### Response to efavirenz (EFV)-containing regimens in previously antiretroviral-naïve patients: the role of gender

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**Objectives:** We investigated the role of gender in the response to efavirenz (EFV)-containing regimens.

**Methods:** All previously antiretroviral-naïve individuals starting EFV from 1996 onwards in a single large clinical centre were included. Virological failure (VF) was defined as the first of two consecutive viral loads >400 copies/ml.

**Results:** Of 81 women starting EFV, 61 (73%) were black African, 80 (95%) heterosexual and the median pre-ART CD4 count was 120 (IQR = 34, 215) cells/μl. 199/297 (66%) men starting EFV were white, 210 (70%) homosexual and the median pre-ART CD4 count was 181 (92, 261) cells/μl. 34% (95% CI: 24–45%) women had stopped EFV by 48 weeks compared to 26% men (21%, 31%; *P* = 0.1). CNS effects was the reason given for stopping in 44% of men and 26% of women discontinuing EFV; 10% of men and 7% of women discontinuing did so due to treatment failure. After 48 and 96 weeks 4.1% (1.6–6.6%) and 6.4% (3.1–9.7%) of men and 2.9% (0.0–7.0%) and 4.6% (0.0–9.6%) of women respectively had experienced VF (ignore treatment changes, censor when discontinue all ART; HR = 1.26; 95% CI: 0.42–3.74; *P* = 0.68). This became 27.5% (22.2–32.8%) and 43.1% (36.8–49.5%) for men and 34.7% (24.1–45.3%) and 49.0% (37.2–42.9%) for women when considering those discontinuing EFV as experiencing failure (HR = 0.77; 95% CI: 0.54–1.10; *P* = 0.15). The median (IQR) change in CD4 count after 48 weeks was +165 (+85, +238) cells/μl in men and +183 (+111, +265) cells/μl in women (*P* = 0.31).

**Conclusion:** We found no evidence for gender differences in virological and immunological response to efavirenz-based regimens. Larger studies are necessary to further explore these questions.

P14

### Success despite resistance: emtricitabine intensification of a tenofovir, didanosine and boosted-atazanavir regimen in individuals with low-level virological failure

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**Aims:** Tenofovir (TFV) and didanosine (ddl) backbones lack potency when combined with a non-nucleoside in naive subjects; evidence for boosted PI-based regimens is less clear. We describe treatment-experienced individuals on TFV/ddl/ritonavir-boosted-atazanavir (ATV/r) with low-level virological failure who added emtricitabine (FTC) despite previous lamivudine (3TC) failure.

**Methods:** Using a prospectively collected database we identified all individuals who had FTC added to ATV/r-based HAART during virological failure; all were receiving TFV/ddl. Treatment history and resistance were analysed; viral loads (VLs) following addition of FTC were collected to 12 months.

P16

### A retrospective analysis of the efficacy and tolerability of antiretroviral regimens containing dual-boosted protease inhibitors

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**Aims:** To describe the characteristics and evaluate the virological and immunological responses, toxicity and tolerability of regimens containing dual-boosted protease inhibitors (DBP).

**Methods:** All subjects ( $n = 178$ ) who had ever been prescribed a regimen containing two protease inhibitors and low-dose ritonavir at our hospital were assessed retrospectively (observational study). The time of virological failure (VF) was defined as the date of the first of two consecutive viral load (VL) measurements  $>400$  copies/ml (a) at any time for subjects initially  $<50$  copies/ml; (b), more than 6 months since starting DBP for subjects starting DBP with VL  $>50$  copies/ml (treatment changes and discontinuations ignored).

**Results:** Subjects were predominantly male (83%), Caucasian (73%) and MSM (69%). At baseline, median CD4 count was 402 cells/ $\mu$ l (IQR: 213–586), median CD4 nadir 90 (20–198) cells/ $\mu$ l and 63 (35%) had a VL  $< 50$  copies/ml. 12 (7%) were previously treatment-naïve and 115 had experienced VF on a previous regimen. Median time previously spent on ART was 5.5 years, and median number of ARVs previously received was 5 (3–6). 127 (71%) were prescribed lopinavir-saquinavir, and 160 (90%) were receiving other ARVs simultaneously. Median length of follow-up was 18 months (m) (10–24) during which 71 (40%) discontinued DBP [reasons for discontinuation: GI symptoms ( $n = 23$ ), VF ( $n = 18$ ), abnormal lipids ( $n = 6$ )]. No significant liver toxicity was observed. After 12, 18 and 24 months, 12% (95% CI: 7–18; Kaplan–Meier), 17% (11–23) and 28% (18–8) had experienced VF, respectively. At 6 and 18 months, median change in CD4 count from baseline was +63 (46, +186;  $n = 148$ ) and +91 (20, +202;  $n = 102$ ) cells/ $\mu$ l.

**Conclusion:** DBP regimens in this treatment-experienced cohort study resulted in viral load suppression and CD4 count increase in the majority of subjects.

P17

### 60-week clinical experience of boosted lopinavir (LPV) with tenofovir (TNF) and didanosine (DDI), in treatment-experienced patients

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**Background:** The current BHIVA guidelines do not recommend using TNF/DDI as an NRTI backbone in naïve patients because of concerns over toxicity, immunological and virological control. However, there is little data on its use in treatment-experienced patients.

**Methods:** We identified 46 patients who had commenced on this combination at a large HIV centre. We looked at virological and immunological outcomes and laboratory markers and reported adverse events.

**Results:** The mean age of the cohort was 40 years. The median time on treatment prior to this combination was 57 months (range 0–168). 18 were triple-class experienced. The median nadir CD4 count was 130 cells/ $\mu$ l (range 10–450) and at time of starting this combination was 250 (range 40–1003). No patients had an undetectable viral load (VL) at the time of switching to this combination. We report 60-week data for this cohort and 27 patients reached this endpoint. 11 patients discontinued this combination; one renal tubular acidosis, five GI intolerance, five others, no virological failures. The median CD4 count at week 60 was 490 cells/ $\mu$ l (range 150–1006), representing an increase of 240 cells/ $\mu$ l. 21 patients had an undetectable VL (77% OT, 46% ITT); 5 had low level viraemia ( $<400$  copies/ml) 2 had viraemia (451 and 5717 copies/ml).

**Conclusion:** Of the patients still taking lopinavir/r/TNF/DDI 76% still have an undetectable VL. It was well tolerated with only one reported serious adverse event. These data support the use of this combination in clinical practice.

P18

### Does cessation of didanosine (ddl) influence CD4 count rise in cholesterol in individuals receiving tenofovir (TDF)/ddl as the nucleoside backbone?

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**Aims:** To establish whether cessation of didanosine (ddl), as part of the nucleoside backbone in individuals who are also receiving tenofovir, is associated with an increase in CD4 count and changes in cholesterol.

**Methods:** A retrospective case-note review was performed on 21 individuals exposed to a backbone of TDF/ddl during the period 2002–2006. CD4 count and cholesterol levels were reviewed over a nine-month period prior to cessation of ddl and nine months post-switch. All patients included had an undetectable viral load at the time of switch.

**Results:** The 21 individuals ceased ddl (250 mg  $>60$  kg, 200 mg  $<60$  kg). Prior to switch, the mean rate of CD4 decline was 12 cells/ $\mu$ l per three-month period. After switch, the CD4 count gradually rose and at 9 months was 45 cells/ $\mu$ l above baseline. No patient stopping or switching from ddl virologically failed during this period. Mean cholesterol while on ddl remained stable but after cessation cholesterol fell by a median of 0.6 mmol/l over a three-month period; this was maintained to the nine-month status point.

**Conclusion:** In individuals who were receiving TDF/ddl, cessation of ddl or replacement with another antiretroviral agent was associated with improvements in CD4 count and cholesterol. It is suggested that all patients who are presently receiving TDF and ddl should be reviewed by their physicians with regard to alteration of antiretroviral backbone.

P19

### Emtricitabine may be associated with greater changes in cholesterol than lamivudine

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**Background:** HAART is associated with changes in lipid homeostasis including hypocholesteremia, hypertriglyceridaemia and lipodystrophic syndrome. We have assessed HAART-naïve individuals receiving an efavirenz (EFV)-based regimen with either tenofovir(TFV)/lamivudine(3TC) or TFV/emtricitabine(FTC) and changes in cholesterol 6 months after initiating therapy.

**Results:** Sixty-eight individuals commenced TFV/3TC/EFV, and 88 TFV/FTC/EFV. Baseline median was CD4 count 196 versus 175 cells/ $\mu$ l, viral load 83 507 versus 85 500 copies/ml and cholesterol 4.2 versus 4.2 mmol/l and were not significantly different. Only two individuals had cholesterol  $>6.5$  on TFV/3TC and six on TFV/FTC at baseline. At 6 months median CD4 counts were 318 and 337 cells/ml, median viral load of 50 copies/ $\mu$ l in both groups, and the median cholesterol 4.7 mmol/l in both groups. However, at 6 months, four individuals (5.8%) had cholesterol  $>6.5$  on TFV/3TC/EFV, and 21 individuals (23.8%) had cholesterol  $>6.5$  mmol/l on TFV/FTC/EFV,  $P = 0.002$ . This was despite three individuals receiving statins in the TFV/3TC/EFV group and 12 receiving statins in the TFV/FTC/EFV group.

**Conclusion:** Although median cholesterol was not different between the two groups at 6 months, a greater proportion of individuals on TFV/FTC had cholesterol  $>6.5$  mmol/l, the level at which treatment is mandatory at our unit. Further studies should be performed on changes in cholesterol dependent on 3TC or FTC therapy.

P20

### Once daily atazanavir/saquinavir/ritonavir (ATZ/SQV/r) double-boosted protease inhibitor therapy in treatment-experienced patients

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**Background:** The use of double-boosted protease inhibitors (PIs) in treatment-experienced patient groups has been described but discussion continues over which combination is best. Double-boosted ATZ/SQV/r offers the convenience of once-daily administration. However, there are no clear recommendations on optimal dosage when combined.

**Methods:** A retrospective case-note review was performed on patients receiving once daily ATZ/SQV/r at doses of 300 mg/1500 mg–2000 mg/100 mg respectively.

**Results:** Sixteen patients were identified: 9/16 male, 11/16 black African, median age 39.5 years, mean duration of HIV infection 9.7 years. 7/16 had AIDS, 10/16 had  $\geq 3$  combination switches. One patient had primary resistance. Median (range) baseline CD4 429 cells/ $\mu$ l (144–909). Seven patients had detectable VL prior to switch: 6/7 achieved VL $<$ 50 at 20 weeks, 1/7 lost to follow up. Nine patients maintained VL $<$ 50 both pre-and post-switch. Median (range)-projected ATZ trough concentration was 763 ng/ml (195–2403); median (range) trough concentrations for SQV 1500 mg ( $n = 8$ ) and 2000 mg ( $n = 8$ ) were 933 ng/ml (191–1710) and 298 ng/ml (100–2732), respectively. Three patients developed scleral icterus though none discontinued. No trends in lipid profile were seen at week 20. Two patients were on a lipid-lowering agent prior to switch and continued. No trends in ALT or glucose levels were observed.

**Conclusion:** Double boosting with ATZ and SQV was well tolerated in our cohort and once-daily dosing makes this combination attractive. ATZ and SQV plasma concentrations were variable but no patients had trough concentrations below target for either ATZ (100 ng/ml) or SQV (100 ng/ml).

P21

### A retrospective study examining the use of four or more antiretroviral agents in the treatment of HIV infection in Edinburgh

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**Objectives:** To identify reasons for the use of four or more antiretrovirals (FOMARVs), and to examine some of the positive and negative effects of antiretroviral polypharmacy.

**Methods:** HIV patients receiving FOMARVs for at least six months were included. Low dose ritonavir ( $\leq 400$ mg) was not counted. Data was collected from a database and case records in the following areas: patient demographics, reason(s) for use of FOMARVs, resistance testing, drug related adverse events, viral load and CD4 count. Physicians were interviewed to identify reasons for the use of FOMARVs.

**Results:** At the time of data collection 86 patients had been on FOMARVs within the last six months (26.0% of the treated cohort). Nine patients were treatment naive and 77 were experienced. 8/9 naive patients and 41/77 experienced patients had no clearly documented rationale for starting on FOMARVs. In the experienced group 61/77 had at least one previous virological failure on HAART. 48/77 of the experienced patients had been previously treated with mono or dual therapy. 49/86 patients (57% of all those on FOMARVs) had experienced a drug related adverse event in the last year. 48/86 patients had undetectable viral load after six months (HIV RNA  $<$  50 copies/ml). At the time of data collection 74/86 patients had an undetectable viral load.

**Discussion:** These results identify a sizeable group of patients on FOMARVs. These regimens are being selected despite an increased potential for drug interactions and adverse events. We attempted to identify reasons for the use of FOMARVs in naive and experienced patients. The factors influencing these treatment decisions will be discussed.

P22

### Induced sputum is a simple and non-invasive means of combining interferon- $\gamma$ assays with microbiology in diagnosing active tuberculosis (TB) in HIV-infected subjects

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**Introduction:** Detecting interferon- $\gamma$  (IFN- $\gamma$ ) secretion in blood is helpful in diagnosing latent TB. How useful such tests are in immunosuppressed subjects, especially with active TB, is unclear. We have previously demonstrated that clinically relevant responses in the lung are maintained even in advanced HIV using broncho-alveolar lavage fluid. We have sought to adapt an approach which allows immunological techniques to be combined with microbiology within a single induced sputum sample.

**Methods:** Nebulised 3% hypertonic saline was inhaled for 20 min. Sputum was mucolysed and then divided. Following overnight incubation with PPD, the frequency of Type 1 cytokine-synthetic CD4 lymphocytes was measured.

**Results:** Eight HIV-infected TB patients have undergone sputum induction at baseline. The characteristics of this group are: median blood CD4 cell count (range): 209 cells/ $\mu$ l (14–493); pulmonary TB = 6 of 8; AFB smear negative = 6 of 8. Six of eight had positive TB cultures from induced sputum. Using flow cytometry, seven of eight had CD4+IFN- $\gamma$ + frequencies in response to PPD  $>$ 0.5%. Eight of eight had CD4+IL-2+ frequencies  $>$ 0.5%. In comparison, of 16 HIV-uninfected TB patients (5 of 16 with non-pulmonary TB; 14 of 16 smear negative) who had sputum induced, 14 of 16 displayed CD4+IFN- $\gamma$ + frequencies to PPD  $>$ 0.5% and 15 of 16 CD4+IL-2+  $>$ 0.5%. In BCG-vaccinated healthy HIV negative controls, CD4+IFN- $\gamma$ +/IL-2+ frequencies were  $>$ 0.5% in 0 of 8 subjects.

**Conclusion:** We have shown that a simple lung-orientated approach to TB immuno-diagnosis in HIV-positive individuals allows rapid microbiological and immunological investigation to be performed on a single sputum sample.

P23

### Utility of an antigen-specific interferon- $\gamma$ assay for the detection of tuberculosis (TB) in patients with HIV-1 infection

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**Aims:** T-cell-based assays measuring interferon- $\gamma$  production by TB-specific cells are significantly more sensitive and specific than tuberculin skin tests (TST) in the diagnosis of both active and latent tuberculosis in HIV-negative patients. There are limited data on the usefulness of immune-based tests in the diagnosis of TB infection in HIV-1 infection. The aim of this study was to examine the relationship between antigen-specific TB responses and CD4 T cell counts in HIV-1 patients with either active or latent TB infection.

**Methods:** Interferon- $\gamma$  responses to the TB-specific proteins [early secreted antigenic target 6 (ESAT-6) and culture filtrate protein 10 (CFP-10)] have been performed using enzyme-linked immunospot (ELISPOT) technology in HIV-1 patients with clinically suspected TB disease or those at increased risk of TB infection.

**Results:** A positive ELISPOT result was found in 24/100 ELISPOTs performed to date (10 with active TB disease and 14 with latent infection). There was no significant difference in the magnitude of ESAT-6 and CFP10 responses between those with active TB disease or latent infection. There was a negative correlation between number of ESAT-6/CFP10 spots and absolute CD4 T-cell count.

**Conclusion:** ELISPOT technology to detect TB infection may be a more rapid, sensitive and specific test than TST in patients with HIV-1 infection.

P24

### Analysis of natural-killer-cell subsets in the gastrointestinal tract of HIV-1-infected individuals

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**Aims:** Recent findings document rapidly progressive loss of CD4 cells in the lymphoid tissue of the gastrointestinal tract caused by HIV-1 infection. This suggests that the gradual decline of CD4 cells observed in blood is not mirrored in the gut and that the detrimental effects of HIV may have their impact during acute infection. Natural killer (NK) cells are part of the innate immune system and react to viral infections by cytolysis of infected cells and production of cytokines. Little is known about the phenotype or distribution of NK cells in the gut and the effect of HIV in this compartment.

**Methods:** We have studied patients with HIV, HIV-negative patients with inflammatory bowel disease (IBD), and uninfected controls. Gut biopsies were obtained by endoscopy from consenting patients along with blood samples. Biopsies were cleaned and digested with enzymes to yield lymphocytes that were subsequently stained with monoclonal antibodies to NK receptors and activation markers, and analysed by four-colour flow cytometry. Mann-Whitney U test was used for statistical analysis.

**Results:** Significant differences were observed in the expression of CD16 between NK cells from blood and those from the gut. Furthermore, differences have been observed between patients with HIV, those with IBD and the uninfected controls.

**Conclusion:** The gut contains a phenotypically distinct subset of NK cells, which lack CD16 and are highly activated compared to blood NK cells. Biopsies from patients with damage to the gastric mucosa, through HIV or IBD, have increased numbers of CD16<sup>+</sup> NK cells present in the lamina propria compared to uninfected controls. This may be through infiltration into inflamed tissue or as a result of compromised capillary integrity.

P25

### Three case histories of abacavir hypersensitivity reaction

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**Introduction:** Up to 5% of individuals exposed to abacavir (ABC) may experience a hypersensitivity reaction (HSR). African ethnicity, male gender and the absence of the HLA-B5701 allelic variant have all been associated with a reduced risk of HSR. Cutaneous patch testing has been recently investigated as a tool to assist the determination of true ABC HSR. Testing for HLA B5701 has recently been made available at our centre case histories from three subjects are presented below.

**Methods and results:** Case 1: a 63-year-old Caucasian male presents with an itchy macular rash 17 weeks after starting ABC. Rash resolves after ABC is stopped. Skin patch test equivocal and ABC reintroduced with patient developing generalised macular rash. HLA-B5701 subsequently tested positive. Case 2: a 37-year-old Caucasian male, HLA-B5701 negative, develops symptoms of fever, rash, nausea, dyspnoea and myalgia exacerbated by ABC dosing 7 weeks after starting the drug. ABC stopped and symptoms resolve within 48 hours, skin patch test pending. Case 3: a 59-year-old Caucasian male, HLA-B5701 negative, develops symptoms of fever, nausea and myalgia 3 weeks after starting ABC. Patient stops ABC and symptoms resolve within 24 h, skin patch test pending.

**Conclusion:** These three case histories are presented to illustrate the complexity of ABC HSR as a clinical entity and the limitations of relying exclusively on genetic markers for diagnosis. They demonstrate the need for a large controlled trial to determine the appropriate application of HLA-B5701 and cutaneous patch testing in routine clinical practice.

P26

### Functional capacity of natural killer cells from treatment-naive HIV-1-infected individuals

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**Aims:** Natural killer (NK) cell killing is tightly regulated by inhibitory and activating NK cell receptors, which recognise MHC class I or pathogen-derived ligands on the surface of virally infected cells. However, chronic HIV-1 infection upsets the balance of activating and inhibitory receptors on NK cells, promoting the expression of inhibitory receptors whilst inhibiting the expression of activating receptors. Exceptionally, some types of activating NK receptor increase during HIV-1 infection. In particular, an activating receptor called NKG2C is present on a much higher proportion of cells in HIV-1-infected individuals compared with uninfected healthy controls whilst the opposite is seen for its inhibitory counterpart, termed NKG2A. We have tested the ability of these receptors to function properly on NK cells from HIV-1-infected individuals.

**Methods:** Firstly, the ability of NKG2C<sup>+</sup> cells to degranulate and kill MHC class-I negative K562 cells has been compared to K562 cells transfected with HLA-E, the natural ligand for this receptor. Secondly, the ability of NKG2C<sup>+</sup> NK cells to respond to HIV-1 permissive T-cell lines, either uninfected or infected with laboratory strains of virus, has been studied.

**Results:** NKG2C<sup>+</sup> NK cells from HIV-1-infected individuals efficiently degranulate and lyse target cells transfected with HLA-E whereas this is reduced in cells bearing the inhibitory receptor NKG2A. The response of NKG2C<sup>+</sup> cells to CD4<sup>+</sup> T-cell lines is enhanced in a significant proportion of individuals when these are infected with HIV-1.

**Conclusion:** NKG2C<sup>+</sup> NK cells are highly functional in chronically infected HIV-1-positive individuals but may have a pathogenic rather than a protective role in HIV-1 infection.

P27

### The causes of immuno-suppression of HIV-infected patients in the era of highly active antiretroviral therapy

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**Aims:** To investigate the reasons for low CD4 cell counts of HIV-infected patients attending an HIV clinic in a teaching hospital.

**Methods:** Cross-sectional observational study on immunosuppressed patients attending a Department of HIV Medicine, between July and October 2005. Immunosuppression was considered as having CD4 cell counts of less than 250 cells/ $\mu$ l during the study period.

**Results:** A total of 42 (9%) of all HIV-infected patients had CD4 cell counts of less than 250 cells/ $\mu$ l within the study period. Fifteen (35%) patients were diagnosed for less than 48 weeks [median: 14 (IQR 8–31) weeks]. Thirty-three (78%) of all patients were on HAART for a median of 22 (IQR 10–56.5) weeks and 22 (67%) had undetectable VL. There was no significant difference between the duration of therapy of patients with undetectable viral load and that of those with detectable viral load ( $P < 0.10$ ). Seven (17%) patients had CD4 cell counts of less than 200 cells/ $\mu$ l after more than 48 weeks of undetectable VL with treatment [median: 98 (IQR 57–147) weeks].

**Conclusion:** Late diagnosis of HIV, poor adherence to medication, and failure to have CD4 cell recovery with treatment were the main causes of immunosuppression of studied patients. Strategies that reduce the number of patients with immunosuppression may further improve the survival of HIV-infected patients.

P28

### Long-term valproate therapy does not significantly alter the rebound kinetics of viral replication after cessation of antiretroviral therapy

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**Aims:** Activation of latent HIV infection with sodium valproate and intensification of pre-existing antiretroviral therapy (ART) was recently shown to enhance HIV-1 clearance from CD4+ memory T-cells. The aim of this study is to report the clinical outcome in a single patient on long-term sodium valproate therapy who interrupted his ART.

**Methods:** Baseline and serial bloods for viral load, lymphocyte subsets, valproate levels, episomal cDNA circles and CD8+CD38++ immune activation were taken.

**Results:** A 54-year-old man with a history of cerebral toxoplasmosis and recurrent grand mal seizures attended our clinic requesting help to interrupt his ART. Sodium valproate levels had been in the therapeutic range and he had well controlled disease with a viral load below the limit of detection for over 2 years. Baseline bloods revealed a normal CD4 cell count (776 cells/ $\mu$ l), normal CD8+CD38++ status, a viral load (VL) less than 50 copies/ml and no evidence of episomal cDNA circles. Within 3 weeks of stopping ART there was a rapid rebound of HIV-1 VL with concomitant marked rise in CD8+CD38++ immune activation and fall in CD4 T-cell count. Analysis of the kinetics of viral relapse showed a viral rebound rate constant 0.34/day<sup>1</sup>, which falls within the range previously reported: 0.12–0.91/day.

**Conclusion:** Further controlled studies are needed to establish the relative contribution of intensification of pre-existing ART and sodium valproate in the clearance of HIV-1 from CD4+ memory T cells.

## Large

P29

### Analysis of treatment costs for HIV RNA reductions, full virological suppression, and CD4 increases for treatment-experienced, HIV-infected patients

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**Aims:** To compare additional cost per incremental 25-cell rise in CD4 cell count, 0.5 log<sub>10</sub> reduction in HIV RNA, or per patient with HIV RNA <50 copies/ml, in treatment-experienced HIV patients.

**Methods:** For all approved antiretrovirals in treatment-experienced patients, plus TMC114/r with low-dose ritonavir (TMC114/r), 24-week efficacy (benefit over control in log<sub>10</sub> reduction of HIV RNA, increase in CD4 count, percent HIV RNA <50 ITT) was extracted from pivotal trials in published reports, and compared with the additional UK treatment cost versus the control arm of each trial (source: BHIVA guidelines). Treatment costs in the POWER 1 and 2 trials were calculated from the treatment use database, assuming the UK administrative fee for TMC114 as the annual cost.

**Results:** Data from 11 clinical trials in over 4000 treatment-experienced patients was used: Gilead 907 (TDF versus placebo), TORO1/2 [enfuvirtide (ENF)/OBR versus OBR], RESIST 1/2 (TPV/r versus CPI), BMS-045 (ATV/r versus LPV/r), CONTEXT (fAPV/r versus LPV/r), CAESAR (3TC versus placebo), CNA3002 (ABC versus placebo), POWER 1/2 (TMC114/r versus control PI). Additional cost per 0.5 log<sub>10</sub> reduction in HIV RNA was £709 for TMC114/r, £2685 for 3TC, £2796 for ABC, £3103 for TDF and £9726 for ENF. Cost per 25-cell rise in CD4 ranged from £617 for TMC114/r to £11 835 for ENF. In the POWER trials, treatment cost per patient with HIV RNA <50 copies/ml was £48 030 for TMC114/r versus £146 971 for control PI.

**Conclusion:** Multi-antiretroviral combinations are always required due to sub-optimal efficacy of individual drugs in treatment-experienced patients. Efficacy is associated with a range of costs across antiretroviral drug classes. Effects on clinical progression and toxicity could add to cost savings.

(70%) male, 41 (74%) of whom were gay. Black and ethnic minorities were over-represented ( $P \leq 0.01$ ) in the late group. 66 had full medical records available. Of these, 41 (62%) had presented to secondary care prior to their diagnosis; 11 (26%) presented with symptoms possibly or probably related to HIV but HIV testing was not offered. Primary care data will be presented. The mortality rate was 6% (5 deaths) in the 'late' cohort compared with 4% in the 'not late' group. Compared to the previous study period ( $n=70$ ), fewer individuals were diagnosed 'late' (14.5% versus 24%,  $P \leq 0.001$ ) and the death rate fell from 19% to 4%.

**Conclusion:** Despite targeted efforts, this study, compared with previous research, showed no significant change in the proportion of new diagnoses that are late ( $P$  less than or equal to 0.20). However, mortality appears to have improved in this patient group comparing our study period to that previously. The majority (62%) of individuals have previously presented to secondary care representing missed opportunities for diagnosis. This study has focused on testing in the context of symptoms but, given the number who presented to secondary care (including symptoms unrelated to HIV), an even stronger argument exists for routine testing.

P31

### HIV service re-design: an audit of the contribution that specialist nurses make to managing patients with non-complex health and social care needs

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**Background:** In-house research demonstrated a need to develop a new model of HIV outpatient care that would reflect the management of long-term conditions seen in other areas of primary care. As a result, in April 2005, two specialist nurses were appointed to manage patients with non-complex health and social care needs.

**Aims:** To outline a new advanced practice role for nurses and demonstrate their contribution in the HIV outpatient setting.

**Methods:** Prospective data were collected during the first 8 months of this new service development. Data were entered and analysed in an Excel database. **Results:** The specialist nurses perform six key roles: (a) manage an ongoing cohort of patients with non-complex care needs; (b) STI screening, cytology and contraception care; (c) follow-up treatment for facial lipoatrophy (poly-l-lactic acid injections); (d) HIV treatment support; (e) follow-up of individuals receiving post exposure prophylaxis (f) at-home results clinic. Following an induction and training period of 3 months, the specialist nurses started seeing a select group of 'well' patients who would normally see a doctor for their routine care. In the subsequent 6 months, over 700 episodes of patient care were managed by the specialist nurses. Nurse prescribing-training was completed and training for facial lipoatrophy treatment is underway. Further audit data will be presented.

**Conclusion:** New roles for nurses help redistribute workload so that patient-care needs are better matched with professional expertise. Such models of nurse-led care will undoubtedly help to manage the increasing HIV workload seen across the UK. Further evaluation is required to demonstrate safety, cost-effectiveness and acceptability.

P30

### Diagnosing HIV: better late than never...but better never late

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**Background:** Late diagnosis of HIV is associated with poorer outcome. Research has shown that many late presenters have received secondary care without HIV being diagnosed. Efforts have focused on normalising HIV testing in an attempt to reduce such late diagnosis and improve outcome.

**Methods:** Subjects were those with an AIDS-defining illness not previously known to be HIV-positive, between January 2000 and June 2005. Medical records in secondary and primary care (where consent was given) were studied; illnesses possibly related to HIV were noted. Results were compared to the previous research period (1997–2000).

**Results:** Of 536 new diagnoses, 78 individuals (14%) fulfilled the criteria for late diagnosis: 49 (63%) were white, 29 (37%) black or black African and 55

P32

### Designated lipid clinics are effective in improving HIV-related dyslipidaemia

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**Introduction:** Altered lipid metabolism occurs at all stages of HIV infection. The aim of this study was to assess the effect of an HIV-lipid clinic on hyperlipidaemia.

**Methods:** Lipid measurements were extracted prior to attendance at the lipid clinic, 6 and 12 months post-attendance. In the remainder of the HIV-infected population, the max lipid values were extracted for 6-month periods (January 2002–June 2003).

**Results:** 1456 patients were under active follow-up in 2002, of whom 111 attended the lipid clinic. Those attending the clinic were significantly older (44 years versus 38 years) and more likely to be male (95% versus 76%), non-black (94% versus 74%), homosexual (88% versus 60%) and to have received HAART (92% versus 72%) including a protease inhibitor (78% versus 54%) than those not attending. Significant differences in lipid values were observed between those who did and did not attend the lipid clinic. Significant improvements were observed for all lipid values among those attending the lipid clinic. In contrast, those not attending the clinic experienced no significant changes in LDL-c or TG level and a worsening in HDL-c. Among those attending the clinic, 51% were prescribed an omega-3 fish oil, 34% a fibrate, 40% a statin and 9% a cholesterol absorption inhibitor. 15 (14%), 35 (32%) and 49 (44%) individuals received three drugs, two drugs and one drug, respectively. There was a highly significant linear trend ( $P < 0.001$ ) associated with the number of lipid-lowering drugs prescribed and mean cholesterol level. 0 drugs: 6.68 mmol/l; 1 drug: 7.27 mmol/l; 2 drugs: 8.16 mmol/l; and 3 drugs: 9.33 mmol/l.

**Conclusion:** Attendance at this clinic was associated with significant improvements in lipid measurements over the subsequent year. The use of lipid specialists and designated lipid clinics should be promoted for HIV-infected patients with dyslipidaemia.

## Standard

P34

### The utility of a multidisciplinary lipodystrophy service in clinical practice

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**Aims:** Evaluate the effectiveness of a dedicated lipodystrophy service.

**Methods:** Prospectively collected demographic, HIV, antiretroviral (ARV), metabolic, fat loss (FL) and accumulation (FA) baseline data were analysed. FL and FA (patient questionnaire, physician examination, and biometric measurements), glucose homeostasis [random glucose, oral glucose tolerance test (GTT) and/or glycated HbA1c] and full lipid profile were measured. Outcomes examined were dietary and exercise advice, ARV switch, advice on metabolic moderating drugs, and referral for NewFill.

**Results:** Over an 18-month period, 52 patients (85% male, 94% white, median age 41.5 years, median time since diagnosis 8.5 years) were reviewed. Previous and current history of exposure to D4T were 90% and 8%, respectively, ZDV 83% and 20% and PIs 81% and 28%. FL was present in all and severe in >1 site in 63% (face 35%, buttocks 37%). FA was present in 52% and severe in 16% (abdominal 10%, neck 6%). Dyslipidaemia was evident in 54% and 23% were on lipid-lowering agents. 17% had abnormal glucose homeostasis (↑HbA1c and/or abnormal GTT). Dietary and exercise advice was given to all patients and metabolic-moderating drugs or ARV switch initiated/advised in 16%; 83% proceeded to facial NewFill treatment and 11% to research studies.

**Conclusion:** The majority of patients were referred because of facial lipoatrophy for consideration for NewFill. 30% were still on a thymidine drug and many had symptoms of metabolic syndrome. The lipodystrophy clinic allowed collection of BL assessments and ARV switch. It also enabled advice on cardiovascular risk-factor-reducing and metabolic management to be given, as well as facilitating recruitment to clinical studies.

P33

### Does a designated PEP clinic improve follow-up rates?

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**Background:** Attendances for HIV PEP (post-exposure prophylaxis), in particular PEPSE (PEP after sexual exposure) in GUM clinics are increasing as awareness of its availability rises. Historically, PEP completion and follow-up have been poor.

**Aims:** The aim of this study was to investigate if a designated PEP clinic improves access, completion and follow-up rates.

**Method:** An observational study of PEP/PEPSE comparing two periods of time. Prospective data collection was undertaken for the year 2004 and for the first 6 months of 2005 when the PEP service started. Data collection included: demographics, HIV risk, management, completion and follow-up rates. Comparisons were made using the chi-squared test.

**Results:** In 2004, 36 patients were prescribed PEP: 20 (55%) for SE and 16 for needle-stick/occupational exposure (NSI/O). From 1/1/05–30/6/05 there were 26 patients: 19 (73%) PEPSE and 7 NSI/O. All PEPSE recipients fell within BASSH guideline recommendations. There appeared to be a trend towards earlier access for PEPSE. Completion rates in 2005 compared to 2004 for all PEP were 74% versus 61% and for PEPSE 75% versus 53% although this failed to reach statistical significance. HIV testing at 3 months for all PEP was 84% in 2005 versus 59% in 2004 ( $P = 0.06$ ), and 81% in 2005 versus 47% in 2004 for PEPSE ( $P = 0.04$ ). There was one HIV-positive test result in 2004 after a physical assault with no recognised risk for PEP failure.

**Conclusion:** This study suggests that a designated PEP service can successfully support adherence to a course of PEP with high completion rates including 3-month follow-up. The number of patients receiving PEPSE has increased in 2005, but notably, all fall within recommended indications.

P35

### HIV partner notification has limitations but could reduce transmission by identifying primary infections

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**Aims:** Partner notification (PN) has a crucial role to play in reducing undiagnosed STIs. The aim of the study was to identify factors influencing the effectiveness of HIV PN.

**Methods:** A retrospective study was undertaken on a sample of newly diagnosed HIV patients from 2003 to 2005 (119/345). Factors studied included demographics, STI screening, partner status and relationships, prospective PN follow-up, contact testing and outcome. In 2005 we undertook purposive sampling for primary HIV infection (PHI).

**Results:** One hundred and nineteen patients were studied. 76% were men who have sex with men and 18% were African. 72 (61%) patients had an STI screen within 3 months of diagnosis and 26 (36%) had an STI. PN completion improved from 55% in 2003 to 94% in 2005. A total of 116 regular partners (RPs) were reported: 28 (24%) were known to be HIV-positive and 58/88 (66%) tested, of whom 17 (29%) were found to be positive. 202 casual partners (CPs) were reported (range 0–30), the majority of whom were uncontactable: five were known HIV-positive and 17/197 (9%) tested, of whom two (12%) were found to be positive. Contacts per case was 0.74 in RPs and 0.11 in CPs. Index cases with PHI were more likely to have partners with PHI (33%) compared to index cases with non-PHI (17%).

**Conclusion:** Despite high STI rates in new HIV diagnoses, many patients were not screened. PN identified more undiagnosed HIV in RPs than CPs. The contacts per case in CPs fall well below the standard for other STIs as the majority are uncontactable. Nevertheless, the association of PHI index cases with PHI contacts supports the utility of PN in identifying other individuals at the same stage of high infectivity, potentially reducing onward transmission.

P36

### How useful are adherence support follow-up clinics for recipients of post-exposure HIV prophylaxis following sexual exposure (PEPSE)?

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**Objectives:** To assess the effectiveness of an adherence-support follow-up clinic for PEPSE recipients.

**Methods:** Case-note review of PEPSE recipients who attended a new adherence-support follow-up clinic between February 2005 and October 2005. Management was audited against recent draft BASHH PEPSE guidelines and compared to an audit performed before the clinic was established (2000–2004).

**Results:** Thirty-four patients received PEPSE. These were predominantly white (79%), male (97%), homosexual (91%), of median age 32 years and given PEPSE predominantly after receptive anal sex (50%). 76% (26/34) patients completed therapy (previous audit 53%, BASHH target 75% met). 82% (28/34) attended at four weeks and 62% (21/34) received the 3-month follow-up HIV test (previous audit 64% and 45%). Of the patients who had reached the 6-month follow-up stage, 42% (8/19) received the six-month HIV test (previous audit 12%, BASHH target 75% not met). 74% (25/34) of PEPSE prescriptions were given in accordance with BASHH-recommended indications (previous audit 79%, BASHH target of 90% unmet). Where the time from exposure to receiving PEPSE was recorded, 94% (29/31) patients received it within 72 h (previous audit 97%, BASHH target of 90% met). Ninety-four percent (32/34) patients received a recommended PEPSE combination (previous audit 91%). To our knowledge no patients have seroconverted to HIV so far.

**Conclusion:** A clinic for PEPSE recipients that places emphasis on adherence support and recall of clinic absconders has ensured we have achieved the BASHH target for completing PEPSE and significantly improved the HIV testing rates at three and six months.

P37

### Nursing experience of recruitment into a randomised control trial at primary HIV infection (PHI)

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**Objectives:** There is a common perception that it is often not an optimal or appropriate time to recruit patients into a clinical trial when they present with PHI. We present data of how, over six years, nurse-led consultations with patients with PHI has positively effected recruitment into trials.

**Methods:** Reports of nursing experience in managing PHI over six years. Examining questions and issues presented to nursing staff by patients with PHI as well as discussing the factors associated with participants choosing to be included in a clinical trial.

**Results:** Discussion around the common issues raised by patients with PHI promotes informed decision-making by patients as to whether to or not to participate in clinical trials. Issues include viral transmission (the source as well as onwards transmission), disclosure (especially partner notification), prognosis and misconceptions about antiretroviral therapy. Recruited  $n = 151$  into clinical trials over six years of PHI studies. For example, over 18 months, out of 80 patients approached, 56 (70%) agreed to participate in the trials. The main reason for non-participation was declining to take antiretroviral agents.

**Conclusion:** PHI presents specific issues which, when handled in an objective, confident, and sensitive manner by expert nursing staff, do not exclude clinical trial participation.

P38

### Are we meeting the sexual health needs of HIV-infected gay men?

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**Aims:** To assess the sexual health risk profile of HIV-infected men having sex with men (MSM) and the sexual healthcare provided at our clinic.

**Methods:** A questionnaire was completed by the healthcare worker on all male patients attending HIV clinics for routine clinic appointments and for nurse-led STI screens.

**Results:** Of a total of 90 MSM, sexual activity and risk had previously been assessed in only 60%. 25% of men had not had a sexual health screen in the past year and 5% had never had a screen. 26 episodes of STIs were diagnosed amongst 14 patients in the past year. When asked about high-risk sexual activity, 57% of patients had two or more partners in the previous 3 months, 34% engaged in unprotected anal intercourse (UPAI) and 8% were fisting. 28% had UPAI and more than one partner in the last three months. 14% of patients had had UPAI with a contactable HIV-discordant partner. 40% of those with discordant partners were unaware of post-exposure prophylaxis. 84%, 82% and 71% of patients had syphilis, hepatitis C and hepatitis B serology screened, respectively, in the past year but most patients were unaware of outbreaks. 33% said they had erectile dysfunction.

**Conclusion:** HIV-infected MSM engage in high-risk sexual behaviour. Healthcare workers do not always ask about sexual activity and must be encouraged to do so consistently, and to enquire about sero-discordant partners more actively. There is limited awareness among HIV-infected men of sexual health issues.

P39

### Free antiretrovirals (ARVs) do not reach children who need them because treatment centres focus on adults and attitudes to testing are outdated: experience from eastern Uganda

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**Aims:** To determine factors leading to a very low uptake of free ARVs for children in eastern Uganda.

**Methods:** In September 2005 we visited regional referral hospitals in two districts, all organisations offering HIV treatment and testing in these and two other districts, and examples of health centres in remote rural areas of east and north-east Uganda. We assessed facilities for children and interviewed staff about policies and practices related to testing children for HIV and access to care, particularly for children orphaned by AIDS.

**Results:** In-patient facilities for children were extremely overcrowded, with as many as three patients per bed and others cared for outside the ward. Out-patient facilities had been designed for adults and only one organisation had an area dedicated to children, which was in a converted shipping container behind a large spacious building for adults opened in 2004. Child inpatients were tested for HIV only when they had advanced HIV-related disease. The two organisations providing the majority of free HIV care to adults had ratios of children to adults on free ARVs of 5:900 and 10:800. One organisation undertook the majority of HIV tests (27 000) in the region, including outreach clinics in the remote rural areas we visited. They operated a policy of testing children for HIV only if the child's mother requested it. Before ARVs were available, national guidelines had advised against HIV testing for children to avoid discrimination and rejection. This practice had continued and when guardians brought an AIDS orphan they were counselled and specifically advised against testing.

**Conclusion:** Lack of facilities for children and outdated attitudes to testing limit access to free ARVs for children and particularly for orphans in eastern Uganda.

P40

### What lies ahead? Paediatric HIV and future challenges for adult services

**Elizabeth Hamlyn, Melinda Tenant-Flowers, Sally Hawkins and Colin Ball**  
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**Aims:** To establish the management issues likely to face adult services in the near future, as children with HIV and multiple drug exposure survive through adolescence into adulthood.

**Methods:** Data were collected using a proforma by case-note review from all patients born prior to January 1997 attending the King's College Hospital Paediatric and Adolescent HIV clinic, to capture those aged 9 years and over.

**Results:** Of 54 patients attending the clinic, 30 (56%) were born prior to January 1997 and their median age was 12 years (range 9–22). Patients' demographics were: 25 (50%) female, 27 (90%) black African, 29 (97%) patients acquired HIV from vertical transmission. Twelve (40%) were born outside the UK. Six (20%) patients were antiretroviral (ARV)-naïve, 6 had received prior therapy but were now

off medication and 18 (60%) were receiving current therapy. Nineteen (63%) patients had received two or more ARV combinations and of these 7 (23%) had received 4–6 combinations. Only five patients had achieved complete virological suppression on their current regime. Of 11 patients who had resistance tests, 1 patient was resistant to 1 class of ARVs and 6 were resistant to 2 or more classes. Eight patients had switched ARV regimes due to drug toxicity. Twelve patients had CDC class C disease. Thirteen (43%) were aware of their diagnosis, the age of disclosure starting at 9 years. Eight patients had lost a parent or sibling to AIDS. All were attending school or college.

**Discussion:** This cohort of patients and those in other centres will present many difficult HIV management issues including: multi-drug experience, toxicity and resistance, suboptimal viral suppression, ill health, adherence issues complicated by adolescence and complex social and sexual health needs.

## Large

P41

### A prospective study of paradoxical reactions in individuals co-infected with HIV and tuberculosis

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**Background:** Paradoxical reactions (PRs) during anti-tuberculosis treatment have been widely reported since HAART became available. Disseminated tuberculosis (TB), early use of HAART, low baseline CD4 counts and rapid CD4 count rises have all been proposed as important factors. However, no systematic study has been undertaken.

**Results:** 43 TB+HIV+ and 102 TB+HIV- patients have been enrolled. Pulmonary TB and TB at multiple sites were present in 58% and 40% in the TB+HIV+ versus 56% and 12% in the TB+HIV- group. At baseline, TB+HIV+ had significantly more systemic symptoms and raised inflammatory markers compared with TB+HIV- subjects. These variables did not predict PR, which occurred in 14/43 (33%) TB+HIV+ versus 16/102 (16%) TB+HIV-. 12/14 (86%) TB+HIV+ versus 4/16 (25%) TB+HIV- experienced systemic upset during PR. In those starting HAART: (1) within 2 months of anti-TB treatment; (2) after 2 months; or (3) pre-TB diagnosis (total 30 of 43), PR occurred in 40%, 33% and 45%, respectively. In those starting HAART after TB diagnosis, the baseline blood median (range) CD4 count in the HIV+ PR group was 30 cells/ $\mu$ l (11–114) compared to 82 cells/ $\mu$ l (3–844) in the no-PR group. No difference was seen in change in CD4 count between the two groups after 2 months of HAART. Site and extent of TB did not predict PR. Five of 14 (36%) TB+HIV+ PR were managed with observation; nine of 14 (64%) with corticosteroids. 0 of 14 stopped anti-TB treatment and one of 14 (7%) discontinued HAART during PR.

**Conclusion:** 1/3 of TB+HIV+ subjects develop PR, which often has marked systemic upset and requires treatment. Baseline blood CD4 count appears more predictive of this than CD4 change, systemic inflammation or disease extent.

P42

### The influence of HAART on HIV-associated primary cerebral lymphoma

**Danish Mazhar, Justin Stebbing, Chris Goode, Sundryha Mandalia, Mark Nelson, Brian Gazzard and Mark Bower**

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**Background:** The risk of primary central nervous system lymphoma (PCL) is increased in individuals infected with HIV-1. We investigated the effect of HAART on the presentation and outcome of HIV-associated PCL.

**Methods:** From a single-centre cohort of 9621 HIV-positive individuals, patients with PCL were identified. We compared pre-HAART and HAART era

clinico-pathological variables and investigated whether exposure to antiretrovirals with differing CNS penetrations protects from the development of this AIDS-defining illness.

**Results:** In 61 patients diagnosed with PCL and a median survival of 1.3 months, we observed a decreased incidence of PCL in the HAART era compared to the pre-HAART era ( $P = 0.0001$ ), and a significantly improved overall survival (log rank  $P = 0.032$ ). In the HAART era, there were fewer patients with prior AIDS-defining illnesses ( $P = 0.015$ ) and patients were significantly more likely to have the diagnosis confirmed histologically or by cerebrospinal fluid (CSF) PCR examination ( $P < 0.0001$ ). Exposure to specific antiretrovirals did not protect from the development of PCL, regardless of CSF penetration.

**Conclusion:** Although their prognosis remains dismal, the HAART era has decreased the incidence and prolonged the survival of individuals with HIV-1-associated PCL.

P43

### The management of meningeal lymphoma in patients with HIV in the era of HAART

**Danish Mazhar, Christina Thirlwell, Tom Newsom Davis, Anna Mary Young, Paul Holmes, Justin Stebbing, Mark Nelson, Brian Gazzard and Mark Bower**  
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**Background:** AIDS-related systemic non-Hodgkin's lymphoma (ARL) remains a significant cause of mortality in patients infected with HIV-1. Meningeal involvement in patients with ARL is common, conferring a dismal prognosis; therapy usually involves frequent lumbar punctures.

**Methods:** In a prospectively followed cohort of 137 individuals with ARL in the era of HAART, 22 had meningeal involvement at presentation. We compared the use of standard alternating intrathecal methotrexate and cytarabine ( $n=17$ ), with a sustained release formulation of intrathecal cytarabine (DepoCyt) ( $n=5$ ) that maintains concentrations in the cerebrospinal fluid (CSF).

**Results:** There were no differences in baseline characteristics between groups. For both intrathecal regimens, we observed no significant changes in overall survival ( $P=0.26$ ), the rate of fall of CSF protein ( $P=0.55$ ) and remission rates defined as absence of lymphomatous cells in the CSF and a CSF protein  $<0.4$  mg/l ( $P=0.46$ ).

**Conclusion:** DepoCyt is safe and effective in patients with ARL and meningeal disease, and reduces the number of intrathecal administrations required. In view of other data demonstrating an improved quality of life on this regimen, it should be considered as treatment for meningeal disease in these individuals.

P44

**Low sexual desire in HIV-infected men: a new treatment?****Daniel Richardson**, David Goldmeier, Graham Frize, Agnes Kocsis, Paul Lamba and George Scullard

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**Introduction:** Since the advent of successful HAART, men who have access to treatment for HIV experience good quality of life and expect to function normally in all aspects of life including sexual behaviour. However, it appears that men infected with HIV commonly complain of sexual problems. There is evidence that men on HAART develop low sexual desire that is associated with raised oestradiol levels. It has been postulated that abnormal fat metabolism (clinically presenting as lipodystrophy) seen in this group of men increases the aromatisation of testosterone to oestradiol. The current management of this problem is by giving testosterone. We hypothesised that letrozole, an aromatase inhibitor that inhibits the conversion of testosterone to oestradiol, would be beneficial in these men and we therefore set up a pilot study to compare the two treatments.

**Methods:** Local ethical approval was obtained. 13 men on HAART who had low sexual desire (clinically and confirmed by the Spector SDI inventory), as well as raised oestradiol levels ( $>120$  pmol/l), were randomly allocated to receive either parenteral testosterone esters (Sustanon 250 IM) ( $n = 6$ ) or letrozole 2.5 mg od ( $n = 7$ ) for 6 weeks. Sex steroid hormone assays, SHBG, virological, haematological and biochemical parameters were measured pre- and post-treatment. Each subject was given the Spector SDI, the Depression/Anxiety Stress Scale and the Rosenberg Self-Esteem Scale before and immediately after treatment.

**Results:** Inventory data suggested that both sexual desire and sexual activity levels increased in both treatment groups. Luteinising hormone increased in seven of seven men on letrozole, but only three of six men on Sustanon. Serum testosterone increased in seven of seven men on letrozole, but only one of six men on Sustanon ( $P < 0.05$ ). There were no adverse events or side effects from either medication.

**Conclusion:** Letrozole may be a useful adjunct in the management of men on HAART who have low sexual desire. Larger studies are needed.

P45

**Occult hepatitis B in HIV-infected persons: prevalence, predictive factors and kinetics in response to HAART****Ana Garcia<sup>1</sup>**, Gaia Nebbia<sup>1</sup>, Ursula Ayliffe<sup>2</sup>, Colette Smith<sup>1</sup>, Samir Dervisevic<sup>2</sup>, Margaret Johnson<sup>1</sup>, Richard Gilson<sup>2</sup>, Richard Tedder<sup>2</sup> and Anna Maria Geretti<sup>1</sup><sup>1</sup>Royal Free Hospital, <sup>2</sup>University College, London, UK

**Aims:** Determine the prevalence of HBV DNA in sera from sAg<sup>-</sup>/cAb<sup>+</sup> HIV-infected patients, its predictive factors and kinetics during HAART.

**Methods:** Patients entering two clinical cohorts (HA and HB) in Jan 2001–Apr 2005 were tested for sAg, cAb and sAb. Confirmed sAg<sup>-</sup>/cAb<sup>+</sup> patients underwent testing for HBV DNA by real-time PCR (lower 35 copies/ml). HBV DNA<sup>+</sup> patients were monitored prospectively.

**Results:** Among 1440 HA patients, 5.2% were sAg<sup>+</sup>; 39% were sAg<sup>-</sup>/cAb<sup>+</sup> and of these 196 were randomly selected for investigation. These included 75% male, 47% MSM, 50% white, 31% black and 13% HCV Ab<sup>+</sup> patients, with median CD4 273 (126–436) cells/ $\mu$ l, VL 4.6 (4.0–5.3) log<sub>10</sub> copies/ml, ALT 27 (19–46) IU/L. HBV DNA was found in 27/196 (14%) patients. At HB, 22/150 (14.6%) sAg<sup>-</sup>/cAb<sup>+</sup> patients had detectable HBV DNA. Median HBV DNA load was HA 342 (51–147 500) copies/ml and HB 60 (25–33 850) copies/ml. HBV DNA was not found in 50 sAg<sup>-</sup>/cAb<sup>-</sup> control patients. There was a trend for increased HBV DNA positivity among heterosexual and black patients. However, sAb status  $<10$  versus  $>100$  IU/L was the strongest independent predictor (RR: 12.13; 95% CI: 1.53–96.08;  $P = 0.02$ ). Follow-up of 18 HBV DNA<sup>+</sup> patients: (a) 3/18 drug-naïve patients were intermittently HBV DNA<sup>+</sup> over 4–12 months; (b) Five started 3TC and five 3TC/TDF-based HAART and were HBV DNA<sup>-</sup> at median 15 (12–31) months of therapy; (c) Five had been on 3TC or TDF/3TC-based HAART for median 3 (2–5) years at the time of initial HBV DNA detection, but were negative on 14 (12–24) months later.

**Conclusion:** We found high and comparable rates of occult HBV infection in two independent cohorts. HBV DNA detection was intermittent and not associated with HCV serostatus, CD4, VL or ALT levels. Lack of detectable sAb was a strong predictor of occult HBV DNA<sup>+</sup> status.

P46

**Acquisition of genotype 1a HCV infection after successful treatment for genotype 3 HCV infection in an HIVab+ male****Stephen Ash**, Karen Sheppard and Chrissie Green

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An HIVab+ gay male patient aged 40 on HAART (Combivir and nevirapine) with undetectable HIV viral loads and a CD4 count of 316 cells/ $\mu$ l (25%) was treated for HCV infection, genotype 3a, with 6 months of pegylated alpha interferon and ribavirin in 2002. HCV PCR values were undetectable on repeated occasions, 3 months, 6 months, 18 months and 3 years after the completion of treatment. However, 3.5 years after treatment, his PCR was rechecked and showed it had become positive again ( $1.53 \times 10^7$  IU/ml and then on rechecking,  $>6.9 \times 10^7$  IU/ml, Roche Cobas Taqman assay), but this time with genotype 1a infection and only 4 months after a negative HCV PCR result. Liver function tests showed progressive elevation of ALT and GGT, compatible with an acute, but otherwise subclinical HCV infection. The patient, who drinks little alcohol and does not inject drugs, revealed that he had had unprotected anal sex with two casual partners (status unknown) whilst on holiday abroad, 5 weeks before the positive HCV RNA PCR test. Clearly, this second infection with a different genotype would not have been detected except by continued screening for HCV antigen. Obviously, HCV antibody tests, being non-genotype-specific, remain positive for life after a first infection even though the HCV genotype 3 was eradicated in 2002. Patients need warning that, following treatment for HCV, they are not immune to infections with other genotypes.

P47

**Caspofungin in the treatment of severe *Pneumocystis jirovecii* pneumonia (PCP)****Laura Waters<sup>1</sup>**, Katie Darling<sup>1</sup>, J Min<sup>2</sup>, Mark Bower<sup>1</sup>, Brian Gazzard<sup>1</sup> and Mark Nelson<sup>1</sup><sup>1</sup>Chelsea and Westminster Hospital, <sup>2</sup>Imperial College School of Medicine, London, UK

**Aims:** PCP remains an important cause of morbidity and mortality in HIV-infected individuals. Caspofungin is the first of a new class of antifungals acting on the fungal cell-wall by inhibiting glucan synthesis; it has activity in animal models of PCP but human data on this agent are lacking. Here, we describe five cases of severe HIV-related PCP and the effect of Caspofungin treatment on disease course and survival.

**Methods:** Patients with PCP who had received Caspofungin during their admission were examined retrospectively and classified according to demographics, previous AIDS-defining illness (ADI), CD4 count, PaO<sub>2</sub> and respiratory symptoms at presentation. All patients studied had poor prognostic factors at presentation and as such risked a high mortality.

**Results:** Five patients were studied: three male and two female. Mean age was 42.8 years and none had a previous ADI. Mean CD4 count was 58 cells/ $\mu$ l\* (range 35–127) and mean PaO<sub>2</sub> was 7.3 kPa (range 5.13–8). All started high-dose Septrin as first-line treatment and were changed to second line following poor response. Caspofungin was commenced, either alone or in combination with other agents, when first-line or later options had failed, after an interval of 8–39 days: as second-line in three patients, third-line in one and fourth-line in one. Duration of Caspofungin treatment ranged from 13–41 days. All 5 patients survived after an in-patient stay of between 28 and 65 days. Time to discharge in patients receiving Caspofungin as second-line treatment was shorter than in those receiving it later.

**Conclusion:** Apofungin is effective in treatment of severe PCP following failure of first-line therapy. Prospective studies will identify prognostic indicators that may determine which patients will benefit from early Caspofungin use.

P48

**Incidence of tuberculosis and HIV among medical patients**

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This study examines the incidence of tuberculosis and HIV among patients attending various clinics in Abuja, Federal Capital Territory (FCT), Nigeria. A total of 1000 blood and sputum samples were collected and analysed for HIV and tuberculosis. This included 475 males and 525 females. Of these, 130 (13%) were infected while 870 (87%) were not infected with HIV, with the highest infection of 73 (7.3%) among the age group 20–29 years, while the least numbers of infection were in the 0–9 years and 60 years and above (0.1%) groups, respectively. Males were found to be more infected than females. A total of 69 (14.5%) males and 61 (11.6%) females were infected with HIV. The overall infection rate of 13% was found in both sexes. Among the 1000 patients screened for tuberculosis, 475 were males and 525 were females. Three hundred and thirty-eight of them were infected with tuberculosis. This gave a general tuberculosis infectivity of 33.8%. Among the 69 male patients infected with HIV, 82.6% of them also had the tuberculosis infection while 68.9% of the 61 HIV-infected females were also infected with tuberculosis. These represented 76.2% of patients screened being infected with both HIV and tuberculosis, i.e. 57 males and 42 females, which gives a total of 99 patients infected with both HIV and tuberculosis.

P49

**No association between HIV disease and its treatment and thyroid function**Sara Madge<sup>1</sup>, Colette Smith<sup>1</sup>, Fiona Lampe<sup>1</sup>, Mike Thomas<sup>2</sup>, Margaret Johnson<sup>3</sup>, Mike Youle<sup>3</sup> and Mark Vanderpump<sup>5</sup>*<sup>1</sup>Royal Free Centre for HIV Medicine and Department of Primary Care and Population Sciences, Royal Free and UC Medical School, <sup>2</sup>Department of Clinical Biochemistry, Royal Free Hospital, <sup>3</sup>Department of HIV Medicine, Royal Free Hospital, <sup>5</sup>Department of Endocrinology, Royal Free Hospital, London, UK*

**Objectives:** Retrospective analyses of thyroid function tests (TFT) in HIV-positive patients. To investigate the prevalence of overt and sub-clinical thyroid disease in HIV-positive patients. To determine risk factors associated with the development of thyroid dysfunction including HAART and individual antivirals. To observe the occurrence of thyroid dysfunction longitudinally over 3 years.

**Methods:** The period prevalence of and factors associated with clinical and sub-clinical thyroid dysfunction were investigated. Patients with normal TFT but previous thyroid disease were identified from pharmacy records and included in the overt category.

**Results:** 1565 (73% of the clinic population) had at least one TFT taken since 2001. 3584 samples were analysed. 1233 (79%) patients were male, 1043 (66%) were white, 365 (23%) were black African and in 969 (62%), the main risk for HIV was homosexual sex. Median age at baseline was 37 years. 900 (58%) were on HAART at the start of the study. 39 (2.5%) were found to have overt hypothyroidism; 8 (<1%) had overt hyperthyroidism. 61 (4%) had sub-clinical hypothyroidism; 5 (<1%) had sub-clinical hyperthyroidism and 263 (17%) had a non-thyroidal illness. 1118 (75.5%) had normal TFT. Multivariate analysis suggested no independent variables were significantly associated with overt hypothyroidism, including HAART and stavudine use specifically. Repeated measurements over 3 years were available for 825 patients and only eight new cases (1%) of overt thyroid disease occurred.

**Conclusion:** The prevalence of overt thyroid disease was low in this cohort, suggesting screening is not warranted.

P50

**Prolonged survival in patients with progressive multifocal leucoencephalopathy: a retrospective case series**

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**Aims:** To assess the survival of all patients presenting with progressive multifocal leucoencephalopathy (PML) over a 7-year period in a central London teaching hospital.

**Methods:** Retrospective case series. All patients with a definitive diagnosis of PML (compatible MRI imaging with positive CSF serology or brain biopsy for JC virus) were included.

**Results:** Four patients were identified, each with significant neurological deficits. All made excellent progress following treatment, initially with HAART including a protease inhibitor and subsequent use of cidofovir. All patients have survived with a median survival to date of 1148 days (range 496–2639 days).

**Discussion:** PML is associated with a high morbidity and mortality with median survivals of 131–646 days previously reported. We report the longest published survival to date of 1148 days (range 496–2639 days) in all four patients with confirmed PML presenting to our unit between 1998 and 2005.

# Standard

P51

**The presentation and survival of patients with non-cutaneous AIDS-associated Kaposi's sarcoma (AIDS-KS)**Carlo Palmieri, Justin Stebbing, Danish Mazhar, Christina Thirlwell, Tom Newsom Davis, Anna Mary Young, Mark Nelson, Brian Gazzard and Mark Bower  
*Chelsea and Westminster Hospital, London, UK*

**Background:** We describe for the first time a proportion of patients with AIDS-KS who presented with no evidence of cutaneous disease.

**Methods:** From our cohort of 5932 individuals infected with HIV-1 treated in the HAART era, 319 were identified with KS. Of these, 11 patients (5.4%) were

diagnosed with KS without the presence of any cutaneous disease. We compared their survival, clinical, immunological and virological characteristics to other individuals with KS.

**Results:** There were no statistically significant differences in survival, CD4 count or HIV viral load at KS presentation. We observed that tumour-associated oedema ( $P = 0.046$ ) and non-oral gastrointestinal KS ( $P = 0.042$ ) were significantly more common in patients with non-cutaneous KS. Only 1 case of non-cutaneous KS was observed prior to the era of HAART.

**Conclusion:** Non-cutaneous KS is a recognisable condition; patients should be treated with the standard of care as their prognosis is not inferior. This is likely to reflect a strong immune response in the era of HAART.

P52

**Hickman line infections during therapy for HIV-associated lymphoproliferative disorders**

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**Background:** As the incidence of OIs declines with HAART, lymphoproliferative diseases are of increasing importance. Hickman lines are routinely used for venous access and chemotherapy. Line infection is a major cause of morbidity particularly in the context of immunosuppression.

**Methods:** We undertook a retrospective review of the use and complications of Hickman lines in patients receiving chemotherapy and HAART for HIV-associated lymphoproliferative diseases.

**Results:** Over a 1-year period, 16 patients (15 NHL, 1 AML) received a total of 69 cycles of chemotherapy via Hickman lines. All patients received cotrimoxazole, itraconazole and azithromycin prophylaxis. 24 (35%) cycles were complicated by neutropaenic sepsis including 11 (46%) with microbiologically proven infection of the Hickman line. The pathogenic organisms isolated from Hickman line sepsis were: coagulase negative *Staphylococcus* (4), *Pseudomonas* (3), diphtheroids (1), *Escherichia coli* (1), *Achromatobacter* (1) and a mixed growth (1). The overall line infection rate was 1.37/100 line-days. This compares to previously reported rate of 0.97/100 line days for HIV-positive patients on maintenance treatment of cytomegalovirus retinitis.

**Conclusion:** A significant number of proven line infections was demonstrated. The main organisms associated with line infection were coagulase-negative *Staphylococcus* and *Pseudomonas*. The high infection rate is attributed to the high incidence of chemotherapy-related neutropaenia.

P53

**Audit of vitamin and mineral prescribing practices for HIV-positive patients**

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**Aims:** To review prescribing practices of vitamin/mineral supplements which account for a large proportion of non-HIV drug expenditure in the hospital setting.

**Methods:** A multidisciplinary (pharmacy/dietetic) literature review and audit of patient database and medical notes.

**Results:** Over 25% ( $n = 352$ ) of HIV-positive patients attending an inner London teaching hospital from January 2004–2005 were prescribed a daily vitamin and mineral supplement. Group characteristics were: 119 (34%) women; 233 (66%) men; white (40%); black African (43%); black Caribbean (12%); mean age of 41 years; mean weight of 68.8 kg (range 41–107 kg) in women; and 75.7 kg (range 59–119 kg) in men. Mean CD4 cell count was 356 cells/ $\mu$ l, 65% had a detectable viral load and 10% ( $n = 32$ ) had a diagnosis of AIDS at first prescription. The mean duration of vitamin prescription was 1159 days (range 1–2183 days). Duration of prescription was longest for white people and shortest for black Caribbean people ( $P \leq 0.0001$ ) and length of prescription increased with age ( $P = 0.013$ ). An audit of 62 medical notes showed a 'reason for prescription' documented in only 15% of notes, a prescription-review date in <2% and checking for other vitamins/products taken by patients in <2%. A referral was made to the dietician for a reason related to the prescription (e.g. malabsorption, loss of appetite/weight) in only 20% of cases.

**Conclusion:** Evidence is lacking to support the role of daily vitamin/mineral tablets as a general dietary supplement for HIV-positive patients. This audit shows a lack of clarity in rationale and expected outcomes, and inadequate documentation in medical notes. Clear guidelines are required to ensure prescribing is evidence-based, cost-effective and of genuine benefit to patients in future.

# Large

P54

**The safety of tenofovir DF (TDF) in the treatment of HIV infection: the first 4 years**Rachael Jones<sup>1</sup>, Mark Nelson<sup>1</sup>, David Cooper<sup>2</sup>, Robert Schooley<sup>3</sup>, Christine Katlama<sup>4</sup>, Julio Montaner<sup>5</sup>, Geraldine Reilly<sup>6</sup>, Sue Curtis<sup>6</sup>, Li Hsu<sup>6</sup>, Biao Lu<sup>6</sup>, Stephen Smith<sup>6</sup>, James Rooney<sup>6</sup> and Viread Global Expanded Access Program<sup>6</sup><sup>1</sup>Chelsea and Westminster Hospital, London, UK, <sup>2</sup>University of New South Wales, Sydney, Australia, University of California San Diego, USA, <sup>4</sup>Pitie-Salpetriere, Paris, France, <sup>5</sup>University of British Columbia, Vancouver, Canada, <sup>6</sup>Gilead Sciences, Foster City, USA

**Aims:** TDF is widely prescribed. This study evaluates the safety profile of TDF in the first 4 years of use.

**Methods:** Safety data were evaluated from international expanded-access programs (EAP) and post-marketing reports (PM). Serious adverse events (SAEs) were documented. Serum creatinine and phosphates were collected in over 1600 patients in the EAP.

**Results:** Data from 10 343 individuals in EAP and PM reports, representing 455 392 patient-years of TDF exposure, were reviewed. In the EAP, 631 individuals (6%) reported SAEs. The most common were pneumonia (0.6%), renal (0.5%), pancreatitis (0.5%), fever (0.4%) and bacterial infection (0.3%). In the PM database, rates were highest for renal, pancreatitis, lactic acidosis and fever. Serious renal SAEs in the EAP/PM included renal failure (0.3% of patients; 0.24 cases/1000 patient-years, respectively), Fanconi/tubular disorder (0.07%; 0.22), and elevated serum creatinine (0.10%; 0.05). Risk factors for renal SAEs included concomitant nephrotoxic medications and low CD4 cell count. Grade 3/4 elevations in serum creatinine were reported in 0.3% of 1699 patients in the EAP. For PM, renal AEs with creatinine data, the median maximum serum creatinine was 2.3 mg/dl (IQR = 4.1), median time to resolution to  $\leq$ Grade 2 was 29 days (95% CI: 24–45). Mitochondrial toxicity, neuropathy and bone fractures were reported infrequently.

**Conclusion:** TDF is well tolerated. No new major toxicities have been identified in 4 years PM surveillance. The incidence of serious renal SAEs was 0.5% amongst 10,343 patients in the EAP; risk factors included concomitant nephrotoxic agents and low CD4 cell count. Bone fractures, neuropathy and mitochondrial toxicity were reported infrequently.

P55

**An overview of 10 years of reporting suspected adverse drug reactions to HIV therapy through spontaneous reporting**

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**Aims:** To analyse the trends in reporting of adverse drug reactions (ADR) to HIV therapy, which are used to detect signals of drug safety problems.

**Method:** All ADRs are entered onto the Adverse Drug Reactions On-Line Information Tracking database. This was interrogated and analysed using Business Objects (5.1.2, Microsoft, 1996).

**Results:** These figures can change due to identification of duplicate reports. N/ A—not applicable. YC—Yellow Card.

Year	Yellow card	Blue card <sup>1</sup>	Via MAH <sup>2</sup>	Pl <sup>3</sup>	Total HIV	Total No YC
1996	26	N/A	10	N/A	36	17107
1997	105	27	62	N/A	194	16627
1998	48	293	59	N/A	400	18053
1999	47	191	78	N/A	316	18483
2000	37	129	80	N/A	246	33151 <sup>§</sup>
2001	49	119	84	N/A	252	21460
2002	38	60	117	N/A	215	17619
2003	37	35	81	N/A	153	19245
2004	50	51	118	N/A	219	20016
2005	54	36	132	4	226	21125

<sup>1</sup>Blue card scheme was launched November 1997. <sup>2</sup>Marketing Authorisation Holder. <sup>3</sup>The patient reporting pilot scheme was launched in 2005. <sup>4</sup>Increase in numbers due to the Meningitis C vaccination programme.

**Discussion:** The Blue Card scheme produced an initial increase in reporting but this was not sustained. This may suggest that regular promotion of such schemes is necessary. Reports from patients may provide important additional information but are not a substitute for healthcare professional reporting.

P56

### Calculated creatinine clearance (CrCl) with two efavirenz (EFV)-based regimens in naive patients: tenofovir (TFV)/didanosine (ddl) versus ddl/lamivudine (3TC)

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**Aims:** Tenofovir has been implicated in case reports of renal dysfunction; we compare the changes in calculated CrCl observed in a randomised, prospective study of TFV/ddl/EFV compared with 3TC/ddl/EFV.

**Methods:** Antiretroviral-naïve subjects were randomised in an open-label study to receive TFV/ddl 250 mg/EFV (TFV arm) once daily (QD) with food or 3TC/ddl 400/EFV QD fasted (3TC arm). Routine biochemical data were collected at baseline and week 12. CrCl was calculated using the Cockcroft-Gault (CG) and Modified Diabetic Renal Diet (MDRD) methods. Mixed procedure was used to calculate time-weighted changes in CrCl and Mann-Whitney *U*-test to compare CrCl change between the two arms.

**Results:** 77 subjects were enrolled (36 to 3TC, 41 to TFV) prior to the early cessation of the study due to poor performance in the TFV arm. By CG baseline, CrCl was significantly greater in the TFV arm (107.1 versus 100.8 ml/min;  $P = 0.004$ ). No significant change in mean CrCl (CG) was observed at 12 weeks in either of the 2 treatment arms (TFV  $-4.1$  ml/min,  $P = 0.07$ ; 3TC  $+0.56$  ml/min;  $P = 0.806$ ). By MDRD calculation the difference in baseline CrCl was not significant (96.3 versus 92.2 ml/min in the TFV and 3TC arms;  $P = 0.109$ ). CrCl change from baseline was numerically smaller ( $P = ns$ ) using MDRD (TFV  $-1.45$  ml/min;  $P = 0.634$ ; 3TC  $-0.18$  ml/min ( $P = 0.938$ )). The mean change in CrCl between the two arms showed no significant difference by parametric testing.

**Conclusion:** In this randomised, open-label study the use of a TFV-containing regimen was not associated with significant reduction in calculated CrCl. Although baseline CrCl was significantly higher in the TFV-arm using the CG formula, this was not apparent using the MDRD calculation.

P57

### Tenofovir does not increase the incidence of chemotherapy-related nephrotoxicity

Rachael Jones, Mark Bower, Brian Gazzard and Mark Nelson

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**Background:** Both Tenofovir DF (TDF) and combination chemotherapy are associated with nephrotoxicity.

**Methods:** We have prospectively collected data on all patients treated with chemotherapy for haematological malignancies.

**Results:** One hundred and forty-two patients (16 female) were treated with anthracycline-based combination chemotherapy and concomitant HAART. HAART regimens were NNRTI based (80), PI-based (51), included both PI and NNRTI (5) or triple-nucleoside-based (6). Tenofovir was included in the regimen for 50 (35%). At the start of chemotherapy, 8 (6%) had CTC Grade 1–4 renal toxicity [elevated serum creatinine (Cr)  $>110$   $\mu\text{mol/l}$ ], including one patient on chronic haemodialysis. These included three patients on TDF and 5 not on TDF ( $P = 0.93$ ). The median peak serum Cr for these patients was 152  $\mu\text{mol/l}$  (range 137–234), and did not differ between TDF group and non-TDF group (Mann Whitney *U*  $P = 0.48$ ). During the course of chemotherapy, a further nine patients developed renal impairment; 2/50 on TDF and 7/92 not on TDF ( $P = 0.38$ ). The median peak serum Cr in this group was 274  $\mu\text{mol/l}$  (range 166–581); this was lower in the TDF group (median 176  $\mu\text{mol/l}$ , range 166–187) than in the non-TDF group (median 277  $\mu\text{mol/l}$ , range 207–581) (Mann Whitney *U*  $P = 0.04$ ).

**Conclusion:** Tenofovir did not increase the nephrotoxicity of anthracycline-based chemotherapy nor was it associated with a higher frequency of renal impairment at lymphoma diagnosis.

P58

### An audit addressing cardiovascular risk in a cohort of antiretroviral-treated HIV patients

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**Aims:** To assess the prevalence, investigation and management of cardiovascular problems in a cohort of antiretroviral-treated HIV patients.

**Methods:** HIV-infected patients, treated with antiretroviral medication within the 6 months preceding the audit, were included. British Hypertension Society, National Cholesterol Education Program and World Health Organization guidelines were used as audit standards. Using data from a departmental database, evaluations were made of 10-year risks of cardiovascular disease (CVD), and percentages with hypertension, hypercholesterolaemia and blood glucose abnormalities. Responses to abnormal test results were also assessed.

**Results:** 26.9% of subjects had a 10-year risk of CVD of  $\geq 10\%$ . 18.5% had at least Grade 1 hypertension. 6.2% had low-density lipoprotein (LDL) cholesterol levels requiring lipid-lowering medication immediately, of which 27.3% had not yet received such therapy. LDL remained high, despite drugs, in 30.4% of these patients. 4.8% had an LDL level where therapeutic lifestyle change (TLC) would be the initial management, but 94.1% of them had not received dietetic intervention. 25.6% of patients had at least two random glucose levels within the 'diabetes uncertain' range, 2% of which had further tests to investigate glucose control. No blood pressure (BP), LDL or random glucose measurements were made in 2.8%, 4.2% and 4.6%, respectively.

**Conclusion:** Prevalence of BP, cholesterol and glucose abnormalities were high, although some patients had no such measurements made. Failures to institute appropriate therapy for lipids, to control cholesterol with drugs or to investigate glucose abnormalities were often noted. Clearly, improvements in assessment/management of cardiovascular problems are necessary within our cohort.

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### Systolic blood pressure (SBP) and mean total cholesterol (TC) in HIV-infected patients

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**Aims:** To compare the mean systolic blood pressure and mean total cholesterol in an HIV cohort with a general population.

**Methods:** Prospective longitudinal cohort study estimating metabolic and cardiovascular risk (CVR) factors. Data from the first 200 subjects have been analysed in comparison with the Health Survey for England (HSE) 2003. SBP and TC were also examined in relation to HIV stage, antiretroviral therapy (ART) treatment and HIV surrogate markers. Analysis was done using SPSS 10. 75% were males, median age 39 years (range 22–66), Caucasians 52.5%, Africans 31%, Caribbeans 10%, 72% on HAART, 34% on PIs, median CD4 count 401 cells/ $\mu\text{l}$ , HIV-1 RNA  $<50$  copies/ml in 53%. 8% were on lipid-lowering drugs and 9% on antihypertensive treatment.

**Results:** Mean SBP was 119.9 mmHg in men and 117.6 mmHg in women compared to 131.4 and 125.9, respectively, in the HSE 2003. Mean TC was 4.7 mmol/l in men and 4.8 in women versus 5.5 and 5.6 in the HSE 2003 ( $P < 0.05$ ). Men in all age groups had significantly lower mean SBP and TC compared with similar population of the HSE ( $P < 0.01$ ), except those aged 55–64 years where TC was higher. In women, no differences were shown, except for those 35–44 where TC was lower. HAART-treated patients on PIs had significantly lower SBP than those not on PIs ( $P = 0.006$ ). Patients with viral load  $<50$  copies/ml had significantly higher TC than those with  $>50$  copies/ml ( $P = 0.025$ ).

**Conclusion:** Two of the main factors contributing to the CVR in the Framingham equation, BP and TC, were lower in our HIV cohort than the adult age-matched UK population. The reasons for this, e.g. increased patient awareness and better health care management of risk factors or other factors, need further investigation.

P60

**Renal toxicity in HIV/hepatitis C co-infected individuals exposed to tenofovir and/or ribavirin****Rachael Jones, Sundhya Mandalia, Mark Bower, Brian Gazzard and Mark Nelson**  
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**Introduction:** Hepatitis C co-infection is an increasing problem in HIV-1-infected individuals. When used in conjunction with interferon, ribavirin has been shown to be effective in the treatment of hepatitis C infection. Tenofovir remains a popular choice of nucleotide analogue, forming the backbone of many HAART regimens. Both agents have been linked to nephrotoxicity. This study investigates the prevalence of renal dysfunction in the HIV/hepatitis C co-infected population.

**Methods:** Individuals with HIV/hepatitis C co-infection were identified from a large clinical database. The treatment history of patients with at least two recorded creatinine values of  $\geq 120$  mmol/l was investigated.

**Results:** 350 co-infected individuals were identified. Of these, 156 had been exposed to tenofovir and/or ribavirin. In those exposed to tenofovir, the prevalence of abnormal creatinine was 32.1 per 1000 patients (95% CI: 10.4–73.2). In those exposed to ribavirin, prevalence was 19.2 per 1000 patients (95% CI: 4.0–55.1). In those exposed to both ribavirin and tenofovir, the prevalence was 12.8 per 1000 patients (95% CI: 1.5–45.6).

**Conclusion:** Renal toxicity was not increased in individuals exposed to both ribavirin and tenofovir. This study illustrates that these agents do not increase nephrotoxicity when used in conjunction in the control of HIV/hepatitis C co-infection.

P61

**10-year cardiovascular risk in an HIV cohort: associations and effects of HAART****Michael Aboud<sup>1</sup>, Elias Skopelitis<sup>2</sup>, Ali Elgalib<sup>1</sup>, George Panayiotakopoulos<sup>2</sup>, Kathryn Ludgate<sup>1</sup>, Alice Sharp<sup>2</sup>, Alastair Duncan<sup>1</sup>, Tony Wierzbicki<sup>1</sup>, Ranjababu Kulasegaram<sup>1</sup>, Fiona Lampe<sup>3</sup> and Barry Peters<sup>2</sup>**<sup>1</sup>Harrison Wing (HIV Department), Guy's and St Thomas' NHS Foundation Trust, <sup>2</sup>Academic Unit of HIV and STDs, St Thomas site of King's College, <sup>3</sup>Department of Population Sciences, Royal Free Site of UCL, London, UK

**Aims:** To evaluate cardiovascular risk (CVR) in an HIV cohort.

**Methods:** Prospective longitudinal cohort study estimating 10-year CVR commencing 2005. Data presented from the first 200 subjects (including demographics, disease stage, details of HAART, 10-year CVR-modified Framingham equation, and incidence of metabolic syndrome). Subgroups were compared with respect to high risk of CVR using the chi square test.

**Results:** Complete data on CVR were available for 183/200 patients. 75% (137/183) were male, median age was 39 years, 52.5% (95/183) were Caucasian (62.1% of non-Caucasian were African) and 72.1% (132/183) were on HAART. Median (IQR) 10-year CVR risk was 1% (1,4). Overall, 10.4% and 3.3% subjects had mean 10-year CVR  $>10\%$  and  $>20\%$ , respectively. The proportion of subjects with CVR  $>10\%$  was higher in men than women (13.9% versus 0%,  $P = 0.004$ ), and higher in Caucasians than non-Caucasians (16.8% versus 3.4%,  $P = 0.003$ ), but there were no significant differences according to current HAART use (12.1% versus 5.9%, for HAART and no HAART,  $P = 0.22$ ) or CD4 count (14.3% versus 9.5%, for  $CD4 < 200$  and  $\geq 200$ ,  $P = 0.57$ ).

**Conclusion:** Although overall, there was a similar incidence of high CVR  $>20\%$  compared with an historical age-matched HIV-negative population, several factors were associated with increased CVR. These included male gender and Caucasian ethnicity. Lack of association with HAART reflects the modest effect of lipid changes on calculated CVR. Also, the effects of HAART on CVR may not be captured by the Framingham equation. Further elucidation of the associations of increased CVR in HIV might inform management strategies and reduce long-term morbidity.

## Standard

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**Fish oils (omega-3 fatty acid supplementation) and cardiovascular risk in HIV-positive individuals with hypertriglyceridaemia****Danni Chilton<sup>1</sup>, S Mann<sup>2</sup>, Simon Edwards<sup>1</sup> and Paul Benn<sup>1</sup>**<sup>1</sup>Department GUM, Mortimer Market Centre, Camden PCT,<sup>2</sup>Centre for Sexual Health and HIV, University College London, London, UK

**Objectives:** To determine the efficacy and tolerability of fish oils and their impact upon the cardiovascular (CV) risk of HIV-positive individuals with elevated triglycerides (TG).

**Methods:** Retrospective case-notes review of clinic attendees receiving fish oils between January 2003 and November 2004. Demographics, disease stage, anti-retroviral (ARV) history and duration of fish oil therapy were recorded. Changes in lipid parameters and Framingham score were calculated 6 months after commencing fish oil therapy. Data were analysed using Wilcoxon matched pairs test.

**Results:** 23 individuals were identified, 14/23 (61%) CDC C, 5/23 (22%) B and 4/23 (17%) A. The median duration of ARV was 10 years (5–18); 16/23 including a protease inhibitor (PI), 14/16 including ritonavir. Median CD4 was 390 cells/ $\mu$ l (50–600), viral load was  $<50$  copies/ml in 16/23 and  $<1000$  in 20/23. CV risk factors include: (i) median age 45 (36–62); (ii) 10/23 smokers; (iii) 4/23 diabetic; and (iv) 8/23 hypertensive. 19/23 and 17/23 had received dietary advice and attended the lipid clinic, respectively. Following introduction of fish oils, the median TG declined from 7.0 mmol/l at baseline to 4.6 at 6 months ( $P = 0.0037$ ) and the median Framingham score from 13% (2–45%) to 8% (3–25%) ( $P = 0.0013$ ). 6/23 took Omacor (O), 17/23 Maxepa (M) for a median duration of 28 months (4–86). 5/23 received other lipid-lowering agents. Three switched M to O to reduce pill burden and 5/23 stopped due to side effects (1 = myalgia, also taking statin, 2 = rash, 2 = not recorded).

**Conclusion:** Fish oils are safe, effective and well-tolerated. We demonstrate significant reduction in lipids and CV risk in this cohort. Additional support is required to encourage smoking cessation.

P63

**Five years' experience of administering poly(lactic acid) (Newfill) implants to treat facial lipoatrophy in individuals with HIV infection****Stephen Ash, Paul Gomez and Marielle Perraut***Ealing Hospital, Middlesex, UK*

As part of a network, we have treated over 100 HIV-seropositive patients with poly(lactic acid) (PLA) injectable implants for the treatment of facial lipoatrophy over the last five years from our hospital cohort and those referred from neighbouring hospitals. Both the cheek and temple areas of the face were treated with PLA. The average number of sessions required per patient was six. The fifth and final sessions were often devoted to minor adjustments for aesthetic reasons to resolve minor imperfections and involved small volumes of PLA suspension. Injections into areas of the facial skin that had received many previous injections were often difficult due to the hard consistency of the collagen that had formed in these areas. Once large volumes of collagen had been formed, the aesthetic result was impaired due to the hardness and inflexibility of the mass. Large masses of induced collagen may become unnaturally visible during certain facial expressions. Because of this feature, there is probably a limit to the prolonged use of PLA for replacement of large volumes of lipoatrophic defects. Other types of implant, which are softer, such as Bioalcamid, may be more suitable in these cases. Patients often required retreatment after an average of 20 months, mostly due to continued lipoatrophy, but also due to slight shrinkage of the collagen formed from initial treatments. Temple areas seemed to be effectively treated with two or three sessions of PLA injections. Previous topical steroid use on the skin, which thins the skin, seems to make the hard collagen produced by PLA injections more visible and less natural in contour. Lumps in the dermis could be produced if the PLA fluid injected was allowed to pass back along the needle track, and the injecting technique was refined to prevent this. Overall, there were no failures of response to PLA injections, although there was a wide individual variation in response. There were no episodes of sepsis.

**Conclusion:** PLA is a safe and effective treatment with long-lasting effects for the treatment of HIV-associated facial lipoatrophy. It does, however, have some disadvantages; these may make some alternatives a better therapeutic option.

P64

### The use of lipid-lowering drugs in a cohort of HIV-infected patients: an intriguing association with surrogate markers

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**Aims:** To investigate the characteristics of lipid-lowering drug use in a prospective cross-sectional HIV cohort study.

**Methods:** Demographics, HIV surrogate/treatment data, systolic blood pressure, anthropometrics, serum lipid and glucose profile were obtained for 200 patients (74% males, median age 39 years, Caucasians 52.5%, Africans 31%, Caribbeans 10%, symptomatic/AIDS 49%, on HAART 72%, on PIs 34%, median CD4 401 cells/ $\mu$ l, HIV-1 RNA <50 copies/ml) 53%. Comparisons between groups were done using chi-square and Mann-Whitney U-tests.

**Results:** Eight per cent were on a lipid-lowering drug (LLD) compared with 2.3% in the general UK adult population. 86% were on statins, 7% on fibrates and 7% on other agents. 8% of females and 8.1% of males in our cohort were on LLDs compared to 2.6% and 1.9%, respectively, in the age-matched UK population. 6.3% of LLD-treated patients achieved total cholesterol (TC) <5 mmol/l compared to 4.2% in the UK. 37.5% of those not on LLDs had a TC  $\geq$  5 and 5.4% of them  $\geq$  6.5 mmol/l. All patients on LLDs were on HAART, 31% on a PI. Patients on HAART were more likely to be on LLD than others (11.1 versus 0%,  $P = 0.012$ ). Similar odds were found for those with VL<50 and >50 copies/ml (11.2 versus 1.4%  $P = 0.012$ ). LLD patients had higher CD4 counts than those on HAART but not on LLD (median 496 versus 371,  $P = 0.03$ ). LLD use did not differ significantly according to gender, ethnicity and HIV stage.

**Conclusion:** Use of LLDs in our HIV cohort, especially among those on HAART, was more frequent than in the age-matched UK population, which may in part indicate increased awareness and prompt intervention. It remains to be determined whether the favourable surrogate markers profiles are spurious or independently related to LLD use.

P65

### HIV-associated body shape changes in women from African backgrounds: a preliminary study

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**Background:** In the UK, HIV is increasingly affecting people from African backgrounds with almost twice as many women as men diagnosed. HIV and its treatment are associated with changes in body shape but little is known about the social and personal sequelae. The ways that the body with HIV is experienced, represented and understood are culturally defined and gender-specific. Such existing data are predominantly from studies of Caucasian men. We explore the implications of body shape changes for African women living with HIV in the UK.

**Methods:** A focused group interview was conducted in a community environment with 12 Zimbabwean women living with HIV in London. The group discussion was tape recorded, transcribed and subjected to thematic analysis.

**Results:** Alteration in self-identity was associated with somatic changes. The significance of the shape of buttocks and thighs was highlighted. Loss of weight from these areas was especially problematic. A sense of being less attractive or desirable led to withdrawal from social networks and support. Concerns were voiced about an HIV diagnosis being inadvertently divulged by bodily changes. The tension between having well-controlled HIV infection whilst also dealing with the difficulties that a change in self-identity produced was notable. The importance given to the problem by clinicians was not always felt to be adequate. Adhering to medication associated with changes in shape was seen as contradictory but essential.

**Conclusion:** HIV-associated body shape changes result in an altered self-identity, with particular challenges for women from African backgrounds, potentially reducing social networks and support. This needs to be understood and acknowledged by clinicians when considering therapy.

P66

### How well do we target hyperlipidaemia? A study to investigate total cholesterol results and statin use in a clinical cohort

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**Introduction:** Lipid abnormalities are increasingly common in HIV-infected individuals. Recent studies have highlighted the need to address these issues. National Cholesterol Education Programme guidelines identify a cholesterol value of  $\leq$ 5.1 mmol/l as 'desirable', 5.2-6.1 mmol/l 'borderline high' and  $\geq$ 6.2 mmol/l 'high'. This study investigates cholesterol values and statin intervention within our cohort.

**Methods:** The total cholesterol values and statin prescription in individuals attending clinic during the time period 01/07/05-15/07/05 were reviewed. Where available, cholesterol values subsequent to statin introduction were also documented.

**Results:** Five hundred and fifty-two individuals had visited the clinic during this time period. 14 individuals had no data recorded. Cholesterol values and statin prescription are illustrated below.

Cholesterol value (mmol/l)	$\leq$ 5.1	5.2-6.1	$\geq$ 6.2
N	300 (56%)	153 (28%)	85 (16%)
On statin therapy	18 (6%)	11 (7%)	18 (21%)
Subsequent statin prescription	4 (1%)	4 (3%)	14 (17%)
Number of individuals with latest cholesterol $\leq$ 5.2 mmol/l (where results available)	N/A	5 (3%)	6 (7%)

**Conclusion:** The majority of individuals had lipid measurements performed, with almost half having elevated cholesterol, illustrating the benefit of routine screening. Overall, more than a third of individuals with high cholesterol have received statin therapy, compared with one-tenth of those with borderline high values. This study reinforces the need for increased vigilance and intervention in individuals with elevated cholesterol values.

# Large

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## Combined detection of antigen and antibody should be the standard of care for screening of HIV infection in populations with a high rate of sero-conversion

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**Objectives:** Traditionally, first-line laboratory diagnosis of HIV has relied on the detection of HIV antibodies. However, there is a significant risk that patients who are seroconverting may not be identified if standard HIV antibody-only tests are used. Consequently, these patients may be wrongly classified as HIV uninfected. The inclusion of antigen detection in the screening assay should improve their detection. We identified how many such patients would have been missed if antigen detection had not been included.

**Methods:** Two commercial combined antigen/antibody EIA assays for HIV have been introduced to the diagnostic virology laboratory since May 2004. Up until this time, the laboratory used an antibody-only EIA method as a screening test. We aimed to identify all patients who had a negative antibody-only HIV result since the combined assay was introduced. Data were collected retrospectively for 18 months. Plasma HIV viral load was also measured at the time of diagnosis. To confirm the presence of p24 antigen and absence of antibody, samples were sent to a National Reference Laboratory where a variety of assays including HIV p24 antigen and Western Blot were performed. Serial samples were collected during the first 14 days and then every 7 days until the patient developed detectable antibody in the antibody-only assay.

**Results:** Over an 18-month period, 10 patients were identified as having a negative HIV-antibody-only test with positive combined antigen/antibody tests. All patients had a positive EIA 1 test, and 9 out of 10 had a positive EIA 2 test. All patients were confirmed to have detectable p24 antigen. Three patients were lost to follow up. All 7 remaining patients were shown to have seroconversion to HIV-1 antibody. The median time to develop an antibody response was 12 days with a range of 9–129 days.

**Conclusion:** The results indicate that 10 patients would have been wrongly classified as HIV-uninfected at this stage if our laboratory performed the conventional HIV-antibody-only assay alone. Although they all subsequently became HIV-antibody-positive, there is no certainty that they would all have re-attended for testing. Furthermore, one patient would have remained antibody-negative even after the suggested 3-month window period. We suggest that the combined HIV antigen/antibody assay should be adopted as the standard of care for HIV screening, especially in populations where there is known to be a high rate of sero-conversion.

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## Four cases of paediatric HIV infection due to seroconversion in pregnancy: should partners be tested and/or repeat third trimester HIV screening be recommended?

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**Background:** Recent estimates (2004) indicated that universal screening at antenatal booking now identifies 92% of HIV-infected mothers. However, seroconversion in pregnancy predisposes to foetal infection *in utero*, peripartum and during breastfeeding. Historically, infants infected during maternal seroconversion had greater mortality and morbidity, necessitating intensive, prolonged and costly treatment.

**Methods:** Descriptive case series of seven consecutive infants diagnosed at <1 year of age with HIV at our paediatric unit between 1 April 2004 and 31 December 2005.

**Results:** Four of seven infants were born to women who had tested HIV-negative at 12–16 weeks of pregnancy. Two were born to women who had declined testing. The seventh infant was born to a previously diagnosed mother who had declined antiretroviral therapy. Six of the seven infants presented between age 3–9 months with AIDS diagnoses (PCP, CMV and multi-organ failure). Of the four whose mothers seroconverted in pregnancy, three infants died, one sustained marked neurological sequelae and one made an intact recovery. Of the other three infants, one has ongoing problematic CMV viraemia, one made an intact recovery, and one was never symptomatic.

**Discussion:** We increasingly observe seroconversion in pregnancy leading to infant AIDS. This might reflect the rising incidence of new HIV in the UK and/or increased recognition of seroconversions, now that screening at booking successfully identifies most established infections. Thus, a negative antenatal test does not preclude an AIDS diagnosis in a sick infant. Also, safe sex advice and HIV screening of sexual partners should become part of normal ante- and post-natal care and repeat third trimester HIV testing, already routine in some countries, may be cost-effective in the UK.

P69

## Stavudine (d4T) and didanosine (ddI) use, low-level transaminitis (LLT), and hepatic steatosis in a cohort of HIV mono-infected subjects

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**Background:** Reports of slowly progressive hepatic steatosis, fibrosis and portal hypertension have been linked with the long-term use of d4T and ddI without lactic acidosis and acute liver failure. This is thought to be related to mitochondrial toxicity and associated with low-level transaminitis.

**Methods:** A retrospective cohort analysis of 1669 HIV-infected patients followed at our centre from January 1996 to determine the occurrence of AST/ALT > 40 U/l persisting for at least 3 months (LLT). Patients with documented HCV or HBV, those with a first AST/ALT measurement >40 U/l or with <2 AST/ALT determinations were excluded. Factors associated with LLT were investigated. A sensitivity analysis was performed excluding subjects with an AST/ALT >200 U/l during their LLT. Among patients with LLT, the occurrence of hyperlipidaemia (serum triglycerides >1.8 mmol/l or total cholesterol >6.2 mmol/l) was assessed, as was the correlation between LLT and hepatic steatosis (assessed by ultrasound). Poisson regression models were used to investigate factors associated with LLT, including: demographics; immuno-virological status; treatment with protease inhibitors (PI); d4T; AZT; ddI; or d4T/ddI; cumulative duration of ART and of PI, d4T, AZT, ddI or d4T/ddI.

**Results:** 75.9% (1266) were male and 60.7% (1013) homosexual. At study entry, 67.9% (1127) were naive for ART; 192 (11.5%) had ever received d4T, 147 (8.8%) ddI and 72 d4T/ddI (4.3%). During a total of 5524.8 person years (py), 388 LLT were observed, corresponding to a rate of 7.02/100 py (95% CI: 6.32–7.72). Females [relative rate (RR) 0.58, 95% CI: 0.44–0.76, *P*<0.001] and patients not on d4T (RR 0.68, 95% CI: 0.53–0.87, *P* = 0.001) and not on ART (RR 0.97, 95% CI: 0.89–1, *P* = 0.04) had a lower risk of LLT. Of 248 subjects with LLT, 130 (52.4%) had high triglycerides and 52 (21.0%) had high total cholesterol. Hepatic steatosis was found in 24 subjects (23.5%) with LLT and in five (3.9%) without (*P* = 0.0005) on ultrasound scan.

**Conclusion:** Identifying those patients at risk of liver damage may allow reversal of steato-hepatitis and reduce the risk of end-stage liver disease and ultimately transplantation.

P70

### Identifying early HIV infection: comparison of a guanidine-based HIV IgG avidity assay with the detuned EIA assay (STARHS)

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**Objectives:** To compare the performance of a guanidine-based HIV IgG avidity assay with that of the detuned EIA assay (STARHS) in differentiating between recent and established HIV infection.

**Methods:** Avidity assay: paired sera in triplicate or duplicate were tested by VITROS (Orthodiagnosics) at a 1:10 dilution in either PBS (reference) or 1 M guanidine (test). Results were reported as avidity index, with values  $\leq 0.80$  indicating seroconversion within the previous 4–6 months. Detuned assay: samples were tested according to the established STARHS algorithm, and results reported as incidence index, with values  $< 1.0$  indicating infection acquired in the previous 4–6 months. Discrepant samples were tested by the BED calypte (r) HIV-1 incidence EIA and the AxSYM IgG Avidity assay.

**Results:** Four hundred and thirty-two samples from newly diagnosed patients were tested by the avidity assay and the detuned assay. Of these, 425/432 (98%) gave concordant results. These comprised 134 (31%) recent infections, including 75% males, 81% white and 7% black Africans with median CD4 594 (59–1865) cells/ $\mu$ l; and 291 (67%) established infections, including 73% males, 51% white and 30% black Africans, with median CD4 359 (50–1287). There were 7/432 (2%) discordant samples with avidity indices of 0.61–0.76 (recent infection) and incidence indices of 1.0–7.3 (established infection). Five of these remained discrepant on repeat testing, including 4/5 from black Africans with non-B subtype, two of whom with CD4  $\leq 50$  cells/ $\mu$ l. Results of the BED and the AxSYM assay combined resolved 3/5 discrepancies.

**Conclusion:** The guanidine-based HIV IgG avidity assay shows very good agreement with the detuned EIA assay (Kappa value: 0.97). As is also recommended for the detuned assay, results of the avidity assay should be interpreted in the context of the CD4 counts, disease stage and infecting HIV-1 subtype.

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### The contribution of primary HIV infection to transmission clustering within a London HIV centre

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**Aims:** To investigate the role of individuals with primary HIV on transmission events.

**Methods:** Prospective observational study of newly diagnosed HIV infection 1999–2005. Blinded HIV *pol* genotypes were analysed from baseline sequences in two separate cohorts: primary HIV (PHI) (infection acquired within previous 6 months) and newly diagnosed chronic infection (acquisition greater than 6 months prior to diagnosis). Clusters were defined when there was 100% homology in bootstrap and a genetic distance of less than 0.015 nucleotide substitutions per site. Potential transmitting pairs were consented for further sequence analysis.

**Results:** A total of 130 sequences were analysed in each group. Of 260 sequences, 25 clusters were identified which included 2–4 individuals. 4/25 clusters occurred within the chronically HIV-infected population whilst 21 included at least one individual diagnosed with PHI. 4/21 involved only PHI individuals. 24 individuals with PHI appeared within clusters, genotypically 6 of which were supported by clinical history. More clustering was identified amongst individuals diagnosed with PHI than those with chronic infection.

**Conclusion:** Phylogenetic analysis indicating case-clustering suggests a role of PHI in the onward transmission of HIV. However, genotypic analysis in the absence of sexual network studies is unable to confirm the direction of transmission. Identification of PHI and subsequent safe sex counselling must play a critical role in HIV prevention.

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### Do primary HIV-1 infections amongst MSM contribute disproportionately to onward transmissions in the UK: a phylogenetic approach

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**Aims:** We aim to link phylogenetic and demographic analyses from surveillance programmes to measure the extent that MSM who have been recently infected with HIV may be contributing to onward transmission, relative to MSM with non-recent infections.

**Background:** The MSM epidemic is continuing, despite a 79% HIV testing uptake at GUM clinics, and 67% of diagnosed HIV-infected MSM being treated with antiretroviral therapy in 2004. MSM undergoing primary infection may be contributing disproportionately to onward transmissions due to high viral load and/or remaining undiagnosed at this time.

**Methods:** HIV *pol* sequences from the UK HIV resistance database and surveillance data from the UK HIV/AIDS patient database will be used to create a surveillance-sequence database representative of newly diagnosed HIV infections among MSM. The Serological Test Algorithm for Recent HIV Seroconversion will be applied to a subset of samples to allocate MSM into those recently infected with HIV and those not recently infected. We will determine the distribution of node types formed between the following category of sequence-pairs: recent with recent (R-R); recent with non-recent (R-NR); non-recent with non-recent (NR-NR). We will compare these distributions against a model that predicts the frequency of node types that would be expected if Rs and NRs had an equal risk of transmitting an infection onwards, thereby 'measuring' the relative importance of recent infections in contributing to onward transmission.

**Discussion:** If recently HIV-infected MSM are substantially contributing to onward transmission, HIV-testing promotion may have limited impact because such individuals will not yet have had the opportunity to have their infections diagnosed.

P73

### Prevalence of primary genotypic resistance in a single UK centre: a comparison of patients with primary HIV infection and newly diagnosed treatment-naïve individuals

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**Aims:** Transmitted drug resistance in a cohort of well-defined individuals with primary HIV infection (PHI) between 2000 and 2004 has been stable at 6%, although a recent study in the UK reports the prevalence of primary drug resistance to be as high as 19%. To further assess this disparity, we compared rates of resistance in patients with PHI with newly diagnosed treatment-naïve individuals.

**Methods:** Routine genotyping of two cohorts: (i) PHI, infection acquired within 6 months of diagnosis; and (ii) newly diagnosed, treatment-naïve patients. Mutations conferring resistance were identified using IAS guidelines.

**Results:** (i) PHI:  $n = 140$ ; 9/140 (6%) exhibited mutations conferring resistance to HIV-1. Of these, seven had resistance to one drug class only (6 of which occurred in reverse transcriptase and one in protease). The remaining two individuals had triple-class resistance. All cases of drug-resistant PHI were sexually acquired in the UK and occurred in white gay men infected with clade B viruses. (ii) Newly diagnosed, treatment-naïve:  $n = 134$ ; In total, 10/134 (7%) had mutations conferring resistance to HIV-1. 8/10 had resistance to one drug class only (either NRTI or NNRTI); two patients had resistance to two classes and no patient showed triple class resistance. 9/10 cases of drug-resistant infection in newly diagnosed, treatment-naïve patients were in MSM, and all but one of these were white; the remaining case was in a white, heterosexual female. (8/10) 80% were clade B.

**Conclusion:** Using a strict definition of PHI and newly diagnosed, treatment-naïve patients identified prospectively, a similar and lower rate of drug resistance is seen in both our populations than has been recently reported in the UK.

P74

### Impact of HIV-1 subtype on genotypic resistance to protease inhibitors in the UK

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**Objectives:** To identify whether specific drug-resistant mutations in the protease (PR) gene of patients infected with non-B subtype are the same as those with subtype B infection; and the presence of novel mutations in non-B subtype viruses.

**Methods:** Data consisted of PR sequences from all resistance tests in the UK HIV Drug Resistance Database, which has collated nucleotide or amino acid resistance test results since 1996 from clinical centres in the UK. Subtypes were assigned to sequences using the STAR algorithm. PR sequences for individuals who had been on a single first PI for at least 28 days were compared with those from PI-naïve patients with the same subtype using chi square test to detect significant differences in the prevalence of amino acids (AAs) at specific positions. Any significant differences ( $P < 0.05$ ) were considered potentially clinically relevant and compared with known IAS mutations.

**Results:** 15 624 genotypes were successfully subtyped. 11 692 were subtype B. The most frequent non-B subtypes were C ( $n = 2043$ ), A ( $n = 815$ ), D ( $n = 428$ ) and AG ( $n = 322$ ). After linkage with antiretroviral therapy (ART) data, 2505 sequences were classified as from PI-naïve and 1155 from PI-exposed patients for  $\geq 28$  days. We confirmed non-B subtype differences at known IAS positions 10, 20, 30, 33, 36, 46, 63, 71, 82, 90; identified  $>2$  non-B subtype differences at novel positions 12, 13, 14, 15, 16, 33, 35, 37, 41, 57, 61, 69, 74, 89, 93. There were significant subtype/PI interactions at positions 12, 63, 82, and 89.

**Conclusion:** In this large database of patients with diverse HIV-subtypes, novel non-B subtype-specific PR mutations were rare. However, the limited sample size after exclusion of individuals exposed to more than one PI, or with an uncommon subtype, highlights the need for collaboration with other large databases to validate these findings.

P75

### Virological failure and subsequent resistance profiles in individuals exposed to atazanavir

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**Aims:** Studies have failed to illustrate acquisition of PI resistance in HIV-1-infected individuals experiencing virological failure following exposure to the ritonavir-boosted PIs saquinavir, lopinavir and fosamprenavir. The aim of this study was to examine the resistance profiles of individuals failing regimens containing boosted atazanavir. Resistance was based on recently published atazanavir scores.

**Methods:** Individuals failing atazanavir-based therapy were identified from a large database. Previous PI experience and/or PI failure was noted. Resistance mutations present before and after atazanavir exposure were documented. TDMs were reviewed to monitor adherence.

**Results:** Twenty-four individuals who had previously failed PI therapy prior to atazanavir exposure and 14 PI-naïve/PI non-failure individuals were found to

have a viral load  $>50$  copies/ml whilst prescribed atazanavir. Overall, nine individuals had undergone TDM, of whom only two had undetectable atazanavir levels. Resistance tests performed at the time of virological failure in the previous PI-failure group revealed one individual had accumulated the mutations 24I, 63P, 71 V/T/S and 82T. A second individual accumulated a 63P. In the PI naïve/non-failure group, two individuals had developed 63P mutations and one developed the 20M.

**Conclusion:** In the previous PI-failure group, one individual developed new significant mutations, a second accumulated a secondary mutation. In the PI-naïve/PI non-failure group, three individuals accumulated secondary mutations. Ritonavir/atazanavir is not associated with the development of genotypic resistance in individuals failing this combination without previous PI failure. It is rarely associated with the acquisition of genotypic resistance in individuals with previous PI exposure.

P76

### Primary resistance in antiretroviral-naïve HIV patients

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**Objectives:** To review primary resistance to HIV drugs in antiretroviral (ARV)-naïve patients attending our HIV service.

**Methods:** All baseline resistance tests on patients over 16 years of age were reviewed. The tests were performed between June 2004 and December 2005. Ethnicity, ARV history and mutation patterns were documented.

**Results:** Thirty-seven HIV-positive patients (24 females and 13 males) underwent resistance testing prior to receiving ARV treatment. Median age was 32 years (range 19–75). The majority of patients harboured non-B subtypes and were from sub-Saharan Africa. All of these patients were heterosexual. Eight (33.3%) female patients were pregnant and diagnosed HIV-positive in this pregnancy.

Table 1. Viral subtype and patient ethnicity

	ANGOLA	BURUNDI	CONGO	ETHIOPIA	GHANA	GUAYANA	JAMAICA	KENYA	MALAWI	NIGERIA	PAKISTAN	SIERRA LEONE	UGANDA	UK	ZIMBABWE	TOTAL
A or CRF01_AE			1	1				1					1			4
A1			1					2					1			4
AG					2					1			1			4
B					1	2			1		1	1		2		7
C													1			1
COMPLEX RECOMBINANT	1												1			2
D		1												1		2
K				1												1
NOT AVAILABLE																1
TOTAL	1	1	2	1	2	1	2	4	1	1	1	2	2	1	6	27

One sample showed potential low-level resistance. The most commonly observed reverse transcriptase mutation seen in eight patients (21.6%) was the 211K. All patients had more than one polymorphic change in the protease gene.

**Conclusion:** In a small sample of chronically infected, ARV-naïve patients, we have not found a significant level of primary resistance. This is a homogenous group, mostly of patients who acquired infection through the heterosexual route in Africa. This may reflect the lower level of exposure to ARV drugs in the country where infection was acquired. Further observation is required to confirm this data, which is in contrast to some of the recently published data.

## Standard

P77

### Baseline genotypic resistance in pregnancy

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**Aims:** The 2005 BHIVA pregnancy guidelines recommend baseline resistance testing in pregnancy. More acquired resistance and recycling of antiretrovirals (ART) in subsequent pregnancies explain this strategy. This study examined baseline resistance results in pregnancy.

**Methods:** In three hospitals, consecutive pregnancies were reviewed and recruited where baseline, pre-treatment genotypic resistance testing was performed. Demographic and clinical parameters were collected. Genotypic testing methods and interpretation algorithms varied with hospital and time.

**Results:** 75 pregnancies in 70 women were identified with baseline resistance testing. 55 (78%) came from sub-Saharan Africa. Median age was 29 years (17–40); median pre-treatment CD4 count was  $348 \times 10^6/l$  (81–846) and viral load was 5883 copies/ml (49–325703). In 16 (21%) pregnancies, the woman was ART-experienced: 4 had previously taken zidovudine; 13 had taken HAART (one woman had zidovudine and HAART exposure). In the ART-naïve samples, one had K103N; one had V179E; one had 41L and one had a V substitution at 33. In the ART-experienced group, one had K103N, M184V and L90M; one had M184V; one had mutations at positions 30, 33 and 88 (history of stavudine, lamivudine, nelfinavir). 51 (68%) samples had PI polymorphisms (28 with two or more); one (1.3%) had NRTI polymorphisms and four (5.3%) had NNRTI polymorphisms.

**Conclusion:** To date, the prevalence of significant mutations in ART-naïve cases is low. Whether polymorphisms will increase the likelihood of resistance development impacting on future ART options is uncertain.

P78

### Assessing the possibility of an HIV outbreak happening in a major UK city using mathematical modelling

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**Objectives:** This major UK city has two concurrent, ongoing outbreaks of syphilis and hepatitis B. The highest risk group in these outbreaks is MSM, which is also a high-risk group for HIV transmission. Unlike many other British cities, the healthcare provision for sexually transmitted infections (STI) and HIV in this city is undertaken at two separate sites. This study focuses on determining the factors under which we would expect to see in an outbreak of HIV within the city by looking at MSM.

**Methods:** We construct a mathematical model to describe the disease transmission between individuals by assuming that an individual who has

already contracted one infection is more susceptible to infection by a second. Within the model structure, we consider the problem of healthcare provision by separating infected individuals into two categories: those who have been treated and those who have not. We can estimate some of the model parameters from published data.

**Results:** By estimating infection rates and times taken to get an STI screening appointment, the model suggests the possibility of an HIV outbreak happening in the next few years with the current sexual healthcare offered in this city.

**Conclusion:** Mathematical modelling is a useful tool which could allow us to determine conditions under which we would predict an HIV outbreak. This could provide further information in deciding where sexual healthcare infrastructure and resources could be diverted for MSM living with HIV/AIDS.

## Large

P79

### Completion rates and tolerability of post-exposure prophylaxis following sexual exposure to HIV: a prospective observational study

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**Aims:** To describe the completion rates and tolerability of post-exposure prophylaxis (PEP) following non-occupational exposure to HIV infection.

**Methods:** Individuals attending 10 GUM/HIV clinics between 11/2002 and 06/2005, receiving PEP following high-risk non-occupational exposures to HIV, were prospectively recruited. Details regarding PEP regimen, adherence, completion rates, side effects, absenteeism from work and psychological disturbance were recorded.

**Results:** Three hundred and thirty-three individuals were recruited with 309/333 (93%) following sexual exposure. 315/333 (95%) commenced a standard PEP regimen and 18/333 (5%) commenced alternative regimens. The median time to initiation of PEP was 24 h (range 20 min–72 h). 225/333 (68%) attended for follow up at 4–6 weeks with 203/225 (90%) completing the 28-day regimen. 22/225 (10%) stopped PEP early, 11/22 (50%) due to side effects. Of those completing therapy, 128/203 (63%) reported full adherence and 41/203 (20%) missed at least one dose, with a mean of 3 (range 1–18). 132/225 (59%) reported any side effect with a mean duration of 18 days (range 0–33). 24/225 (11%) experienced a Grade 3 or 4 adverse event (ACTG toxicity criteria). Among employed individuals, 50/189 (27%) required at least one day off work (range 1–30), 34/50 (68%) attributed this to drug side effects. 137/201 (68%) reported some degree of psychological disturbance following the exposure. Two individuals tested HIV positive 3–6 months following PEP; both reported further high-risk exposures.

**Conclusion:** Individuals receiving PEP frequently report side effects and require time off work. Strategies to improve follow-up, adherence and completion rates are required.

**Results:** 333 individuals were recruited: 264/333 (79%) MSM, 38/333 (11%) heterosexual males and 31 (10%) women; 80% of white ethnicity. 93% received PEP following high-risk sexual exposures and 146/309 (47%) were with known HIV-positive partners. 36/333 (11%) had previously received PEP. The median number of sexual partners reported in the 3 months prior to presentation was 3 (1–100); MSM reported more partners than heterosexual men or women, declining to one (0–30) partner in the three months following PEP. Direct comparison of number of partners at baseline and at three months in 93 individuals showed 56/93 (60%) reporting a decrease and 10/93 (11%) reporting an increase in the number of sexual partners. At baseline, 244/333 (73%) denied an additional exposure to HIV in the 3 months prior to receiving PEP, increasing to 204/225 (91%) and 145/172 (84%) at 4–6 weeks and 3 months following PEP, respectively. 200/225 (89%) were offered testing for sexually transmitted infections (STIs) in the first 2 weeks, 69/200 (35%) accepted, 16/69 (23%) had a bacterial STI.

**Conclusion:** High rates of STIs among those testing support routine screening in all. Compared to baseline, most individuals report fewer sexual partners in the 3 months following PEP.

P81

### Condom-use decision-making by HIV-positive black Caribbeans before and after diagnosis

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**Aims:** To understand decision-making around condom use of HIV-positive black Caribbeans before and after diagnosis.

**Methods:** In-depth, semi-structured interviews with 25 of 200 HIV-positive participants in the LIVITY study on the Impact of HIV Among Black Caribbeans in South London, based on a quota-based sample according to gender, age, sexuality and country of birth.

**Results:** Ten patients were homosexual/bisexual men, five heterosexual men, and 10 heterosexual women. 64% were born in the Caribbean. Patients report inconsistent or no condom use before diagnosis for reasons of pleasure, trust and intimacy, ignorance of risk, partner's wishes, loss of self-control, and the identification of safe partners through physical/behavioural cues. While desire to please the partner and fear of perceived promiscuity are mentioned particularly in women's accounts, loss of self-control (through passion/drugs/alcohol) is a feature of men's accounts. Post-diagnosis, lack of condom use is linked to lack of self-control (self-reported by men), pleasure, fear of reaction to disclosure and/or request for condom use, the perceived responsibility of the sexual partner to request condom use/ask about HIV status, the partner's wishes and the partner's HIV status. The withdrawal method may be used to compensate for non-condom use.

**Discussion:** Pre-diagnosis, emotional and sensual considerations, ignorance of HIV, and assumptions based on physicality and behaviour contribute to unsafe sex more than conscious risk-taking. Post-diagnosis, patients take risks for similar reasons: however, avoidance of stigma is a further factor. Unsafe sex is justified by attempts made to minimise risk and by relying on the partner to ensure safe sex.

P80

### No evidence of increasing risk behaviour following post-exposure prophylaxis for sexual exposure to HIV

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**Aims:** To describe the impact of non-occupational post-exposure prophylaxis upon sexual behaviour.

**Methods:** Individuals attending 10 GUM/HIV clinics between 11/2002–06/2005, receiving PEP following high-risk non-occupational exposures to HIV, were prospectively recruited. Demographic, behavioural and clinical data were collected at baseline, 4–6 weeks, 3 and 6 months.

P82

### HIV testing for African people and MSM: comparing needs, access and effectiveness in clinic and community settings in a UK city

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**Introduction:** Sub-Saharan Africans and MSM are currently at highest risk for HIV infection. This study compared HIV testing uptake in a UK sexual health clinic (SHC) and a community setting at the Terrence Higgins Trust (THT) in these groups.

**Methods:** A weekly rapid HIV testing (Abbott Determine HIV-1/2®) clinic at THT was offered as a walk-in, out-of-hours satellite HIV-testing service for 6 months. A self-completed questionnaire was used to establish demographic profiles, sexual histories, HIV-testing behaviours and reasons for using either of the services.

**Results:** There were 139 attendances at the THT and 133 HIV tests were undertaken. 117 (88%) attendees completed the questionnaire. Four (3.0%) tested positive for HIV of which three were serologically confirmed at the SHC. Of the 100 that attended the SHC, 82% completed the form and there were no HIV-positive results. The age of attendees did not vary across sites (mean of 31.4 years). Attendees at the SHC compared to THT were significantly more likely to be: female (47.6% versus 22.4%); heterosexual (79.3% versus 54.8%); live in city (70.1% versus 47.8%); white British (82.9% versus 72.6%); and UK born (89.8% versus 76.5%). 45.3% of all attendees had no previous HIV test and were significantly younger, female and heterosexual. 49.6% at THT attended because of same-day testing. 32.7% cited the convenience of a walk-in, out-of-hours service.

**Conclusion:** Walk-in, out-of-hours satellite HIV-testing services are feasible and acceptable in community settings and serve a more ethnically diverse and higher-risk population than in a standard SHC setting. Increasing patient choice helps reduce the burden of undiagnosed HIV infection.

P83

### The role of HIV testing in risk perceptions and safer sex strategies: qualitative results from an investigation into risk factors for seroconversion among gay men who HIV test

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**Objectives:** Recently acquired HIV infections among gay men continue to be diagnosed in the UK whilst behavioural studies indicate increases in risk behaviour. The INSIGHT study combines qualitative and quantitative methods to understand risk factors for recently acquired infections in gay men who are tested for HIV.

**Methods:** In-depth follow-up interviews exploring the context of seroconversion were conducted among 48 respondents to the case-control survey of men who had recently tested positive (cases) or negative (controls), having tested negative during the previous 2 years. Purposive selection ensured diversity in demographic, socio-economic and behavioural characteristics. Analysis, informed by grounded theory, was conducted with the aid of Framework.

**Results:** Regular testing and negative test results played an important role in affirming safer sex practices and risk perceptions. The period leading up to the test and receipt of the test results was used to review past sexual behaviour and possible exposures to HIV. During this time, men engaging in unprotected anal sex with partners of an unknown or serodiscordant status formed expectations of whether their test result would be negative or positive. Subsequent negative results were interpreted as evidence of immunity from HIV infection or imbued risk practices with a sense of diminished likelihood of HIV transmission.

**Conclusion:** HIV testing remains the cornerstone of HIV prevention, but without informed review of past sexual behaviour and understanding of the implications of a negative HIV test result, such test results are used to endorse continued risk behaviour and facilitate continued exposure to HIV transmission routes.

P84

### Decisions to disclose among HIV-positive black Caribbeans

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**Aims:** To understand decision-making around disclosure of HIV status among HIV-positive black Caribbeans (BC).

**Methods:** In-depth, semi-structured interviews with 25 out of 200 HIV-positive participants in the LIVITY study on the impact of HIV among black Caribbeans in south London, based on a quota-based sample according to gender, age, sexuality and country of birth.

**Results:** Ten patients were homosexual or bisexual men, five heterosexual men and 10 heterosexual women. 64% were born in the Caribbean. The decision to disclose to a family member or friend was guided by two related considerations: the avoidance of stigma and the quality of the relationship between the patient and the potential disclosee. Trust was the most important factor in determining whether the patient would disclose: trust that the person would not divulge the patient's status to others, which would expose the patient to stigma and discrimination; that the person would offer support; and that the person would not treat the patient differently as a result of disclosure, either through ostracism or pity. Patients may use active and passive assessment strategies (discussion of HIV and observation) with potential disclosees to decide on disclosure. However, fear of adding to family members' worries can override trust in determining disclosure. Patients will not disclose to sexual partners if they suspect rejection, violence or dissemination to others will result.

**Discussion:** Stigma and trust are powerful factors in decision-making to disclose. Patients evaluate their relationships with family and friends to mitigate potential stigmatisation as a result of disclosure.

P85

### Barriers to HIV testing in UK African communities

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**Background:** The UK African population is disproportionately affected by HIV infection and presentation is often late in the disease when treatment may be less effective. Much remains unknown about the cultural practices, beliefs and attitudes of Africans with or at risk of HIV against a background of economic deprivation, uncertain immigration status and 'dispersal' to settings where community-based support networks and prevention activity may not be extensive.

**Aims:** This study aims to explore potential barriers to HIV testing in UK African communities in a setting outside London.

**Methods:** This qualitative study uses in-depth interviews with a purposive sample of African participants of known and unknown HIV status, and key informants from a range of professional backgrounds. Interviews with experts explored their views, experiences and attitudes relating to HIV testing in Africans. Interviews with African participants explored health beliefs, perceptions of risk, cultural and behavioural norms, knowledge and experience of HIV, access to health-related services, and issues relating to immigration and racism. Data were analysed using the constant comparative method derived from grounded theory approaches.

**Results:** Key themes emerging from the data include fear, denial, stigma and risk. Cultural norms, health beliefs and spiritual beliefs are all important considerations. Knowledge of HIV is strongly influenced by negative experiences of HIV in Africa where medical care is often limited.

**Discussion:** This study helps us better understand the complex influences and beliefs, which may act as barriers to HIV testing amongst Africans in the UK. Raising awareness and understanding, and improving cultural competency amongst professionals may ameliorate some of these barriers.

P86

### Sexual orientation and activity according to country of birth among black Caribbean and black British HIV-positive individuals in south London: the LIVITY study

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**Background:** There remains considerable stigma and discrimination surrounding homosexuality in the Caribbean. Our objective was to investigate the relationship between country of birth and subsequent sexual orientation and activity.

**Methods:** The LIVITY study is an in-depth epidemiological and behavioural study on the impact of HIV in the black Caribbean community (BCC) in south London. Eligible patients were HIV-positive black Caribbeans (BC) registered at ten clinics in south London. Participants completed an 11-part self-administered sexual health questionnaire.

**Results:** As of 01/2006, 206 patients were enrolled. Median age was 38 years (IQR = 31–43), 31.5% were female and 61.6% of men were homosexual/bisexual (HoM/BM). Seventy-six (36.9%) were born in the UK, and 130 (63.1%) in the Caribbean (68.5% Jamaica, 14 from the Windward Islands, 9 from Trinidad and Tobago, 8 Guyana, and 10 other islands). A similar proportion of those born in the UK or Caribbean reported that they were HM (42.1% versus 40%), but a higher proportion born in the Caribbean identified themselves as BM (1.3% versus 12.3%,  $P < 0.01$ ). The median number of lifetime sexual partners was similar [20 (IQR = 7–100) versus 17.5 (IQR = 8–100)]. Importantly, none of those who identified themselves as heterosexual (either UK or Caribbean born) reported any male sexual partners. A higher proportion of those born in the Caribbean versus the UK likely acquired HIV from a person of BC ethnicity (43% versus 29%), but less likely from white (11.5% versus 23.7%) or black Africans (8.5% versus 14.5%).

**Conclusion:** Despite persisting stigma, a high proportion of BC men identified themselves as HoM/BM. There was no evidence of covert homosexual activity among BC heterosexuals, or for difference according to country of birth.

P87

### Public attitudes about HIV and AIDS in Great Britain: the results of a representative survey

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**Objectives:** To establish the attitudes and understanding of HIV and AIDS among the general public, as well as attitudes towards condom use.

**Methods:** A nationally representative quota sample of 2048 adults interviewed in Great Britain.

**Results:** Less than half of those with a new sexual partner in the last two years said they would always use a condom with a new sexual partner. In addition,

levels of knowledge about transmission routes have declined since a similar survey in 2000. Around one in five respondents said that they did not know enough about HIV risks. Those in less affluent groups were less knowledgeable about HIV. Overall, greater levels of knowledge were associated with holding fewer discriminatory attitudes against people living with HIV.

**Conclusion:** While levels of knowledge about HIV transmission are relatively high, a decline in knowledge since 2000 presents a worrying trend. There is also a need to respond to the inequalities in levels of knowledge among different social groups identified. The relationship observed between increased levels of knowledge about transmission and anti-discriminatory attitudes gives encouragement to educative initiatives aimed at challenging stigma and discrimination.

P88

### How does dispersal by the National Asylum Support Service (NASS) affect the health of asylum seekers living with HIV? A study of clinicians' views and experiences

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**Objectives:** Concerns have been expressed about the impact on the health of asylum seekers living with HIV of being moved to a different area of residence (dispersal). A national HIV charity researched the experiences of clinicians to provide recommendations to NASS on improving continuity of HIV care and treatment.

**Methods:** A questionnaire survey of clinicians sought quantitative and qualitative information on their experiences of the dispersal process.

**Results:** Issues identified were: insufficient notice of dispersal so that HIV treatment was interrupted and health harmed; asylum seekers with HIV being dispersed when too ill or vulnerable to travel; and ineffective links being made with healthcare providers to ensure continuity of care in the dispersal destination.

**Conclusion:** Following lobbying, NASS had accepted a number of recommendations for change in the dispersal of HIV-positive asylum seekers, including: the potential for dispersal to be delayed; the need for satisfactory arrangements for continuity of care according to the treating clinician; and an obligation for accommodation providers to arrange registration with a GP. The report made additional recommendations for better promotion of voluntary HIV-testing in initial accommodation centres; clearer instruction on the need for HIV-positive asylum seekers to alert clinicians when a dispersal notice has been given; mechanisms for improved transfer of patient information between healthcare providers in areas from and to which patients are dispersed; and better social and psychosocial support for HIV-positive asylum seekers. The charity will continue to examine the issue of dispersal of asylum seekers living with HIV.

## Standard

P89

### The importance of religion for people living with HIV

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**Objectives:** To examine the importance of religious beliefs for people living with diagnosed HIV.

**Methods:** HIV patients receiving treatment and care in outpatient clinics in northeast London were asked to complete a confidential, self-administered questionnaire in 2004–2005. Respondents were asked about their religion (if they had one), frequency of attending services and the importance of their religious beliefs.

**Results:** 1687 HIV patients returned a completed questionnaire (response rate 73% of eligible patients), including 480 black African heterosexual women, 224

black African men and 758 gay/bisexual men. Overall, 80% of respondents said they had a religion; gay men 59%, black African men and women 97% ( $P < 0.001$ ). The majority described themselves as Christian. Half the black African men and women attended a service once a week or more, compared with 10% of gay men ( $P < 0.001$ ). Three-quarters of the black African men and women (76%) and a quarter of the gay men said their religious beliefs were very important to them ( $P < 0.001$ ). For a quarter of black African men and women and 10% of gay men, religious beliefs influenced their use of HIV medication ( $P < 0.001$ ). In all groups, however, the overwhelming majority (>75%) did not think that prayer alone could effectively cure HIV.

**Conclusion:** Religion is central to the lives of most black African men and women with diagnosed HIV; religion also has an important place in the lives of some gay men with HIV. The role of faith leaders in supporting members of their congregation living with HIV needs to be explored further as does the influence of religion on use of HIV medication.

P90

### Understanding variation in prescribing of injectable therapy: the role of physician attitudes and beliefs

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**Background:** Despite its proven efficacy, enfuvirtide (ENF) is prescribed less than expected. This study assessed the impact of doctors' beliefs about ENF on prescribing decisions.

**Methods:** Four hundred and ninety-nine HIV doctors (EU/US) completed interviews assessing their history of prescribing ENF and beliefs about self-injectables. Doctors were divided into three prescriber (Rx) groups: non-Rxs (0 patients on ENF), lower Rxs (1–4) and higher Rxs (≥5). Doctors reviewed two case histories of patients generally indicated for ENF; an ex-IDU (case 1) and a non-adherent patient (case 2), and were asked to select either an ENF- or oral-based regimen for each. Doctors also recorded details of their next two experienced patients (≥8 ARVs).

**Results:** 24% non-Rxs; 41% lower Rxs; 35% higher Rxs of ENF. UK-based doctors were more likely to be non-Rxs ( $P < 0.001$ ). Non-Rxs had less confidence in the efficacy of an ENF-based regimen and its use in practice compared to an oral-based regimen, and were more likely to believe ENF is harder to justify (time/resources), is associated with non-adherence/treatment refusal and would jeopardise patients' trust ( $P < 0.05$ ). 66% chose ENF for case 1 and 45% for case 2. Doctors who chose ENF for case 1 had more confidence in its efficacy/usage and were less likely to believe a range of negative attributes [i.e. an association with non-adherence, risk associated with self-injecting and difficulty justifying ENF ( $P < 0.01$ )]. Doctors who chose ENF for case 2 had more confidence in its efficacy/usage and were less likely to believe ENF is associated with non-adherence or unsuitable for chaotic/previously non-adherent patients ( $P < 0.05$ ). Of 996 patient records evaluated, 77% were not receiving ENF. UK doctors submitted fewer records of patients receiving ENF ( $P < 0.05$ ).

**Conclusion:** Doctors varied in their beliefs about injectable ARVs, and their beliefs influenced prescribing.

P91

### The diagnosis of HIV in African men living in London: a qualitative study

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**Background:** In the UK, people from African backgrounds present with HIV infection later than their British-born counterparts and African men present with more advanced infection than African women. Little is known about the experience of HIV for African men to help develop appropriate health and social care in the UK.

**Methods:** A qualitative study based on narrative accounts from in-depth semi-structured interviews was carried out with HIV-infected African men attending 4 London HIV-treatment centres between October 2003 and September 2004. Interviews were tape recorded, transcribed and subjected to thematic analysis.

**Results:** Thirty-seven men from 13 different countries participated. Two were MSM, and 35 men who had sex with women. None was diagnosed as a result of routine testing. A majority were diagnosed as a result of symptoms or associated medical problems, some because of a partners' ill health, and over half had required an in-patient admission. Most were shocked by the diagnosis and assumed that they were facing imminent death. A majority required antiretroviral therapy at the time of diagnosis. An HIV diagnosis exacerbated current substantial co-existing life pressures, (e.g. immigration, finance) and added relationship difficulties with partners. Together, these factors served to undermine their identity as men.

**Conclusion:** The impact of a diagnosis of HIV on men's sense of self worth, strength and identity was profound and influenced their use of available services. These challenges must be recognised in designing diagnostic and treatment services for African men living with HIV.

P92

### Eating disorders and body image in HIV clinic attenders

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**Aims:** This study aimed to examine the prevalence of eating and body image problems amongst HIV-positive men and women attending a large HIV clinic. It was hypothesised that such individuals may be at risk of body image/eating problems for a number of reasons, including the stress of living with HIV, impact of HIV and HAART on the body and body image (including lipodystrophy), and the emphasis on physical appearance amongst gay men who make up a large proportion of clinic attenders.

**Methods:** Clinic attenders completed a short questionnaire pack including a demographic questionnaire, a body image measure and a standardised eating disorders screening tool.

**Results:** Preliminary results ( $n = 43$ ) are as follows: 7 participants were female, 1 transgender (M-F) and 35 male. Seven were overweight, 5 underweight and 31 normal weight. 70% were on HAART. 15% had been diagnosed with lipodystrophy, whilst a further 17% said they were worried about lipodystrophy, but had not been diagnosed. Overall, 15% (29% of women and 12% of men) scored above the cut-off on the eating disorder screen, suggesting they may have an eating disorder. (Prevalence of eating disorders in the general population is 0.2–3%). 67% of the sample described themselves as gay, 15% as heterosexual and 8% as bisexual. Gay or bisexual participants tended to be slightly lighter and have higher scores on the eating disorder screen, but neither of these differences was significant.

**Conclusion:** Early results suggest that eating problems may be over-represented amongst HIV-positive men and women. This may have implications for the management of HIV and for medication compliance. It may be useful to screen HIV clinic attenders for eating problems.

P93

### Discrimination experienced by people living with HIV

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**Objectives:** To examine the extent to which people with diagnosed HIV experience discrimination as a result of their infection.

**Methods:** HIV patients receiving treatment and care in outpatient clinics in northeast London were asked to complete a confidential, self-administered questionnaire in 2004–2005 concerning social, economic and behavioural characteristics. Respondents were asked 'Have you ever been treated unfairly or differently because of your HIV status (in other words discriminated against)?' Those who answered 'Yes' were then asked 'by whom'.

**Results:** 1687 HIV patients returned a completed questionnaire (response rate 73% of eligible patients), including 480 black African heterosexual women, 224 black African heterosexual men and 758 gay/bisexual men. Overall, 475 respondents (30%) said they had been discriminated against because of their HIV status; black African women 27%, black African men 21%, gay men 34% ( $P = 0.001$ ). Of the 475 respondents who reported being discriminated against, 121 (26%) said they had been treated unfairly or differently by their dentist, 85 (18%) by their GP and 48 (10%) by other hospital staff. Overall, 238 patients (51% of those experiencing discrimination) said they had been treated unfairly or differently by a healthcare worker (usually outside the GUM/HIV clinic) because of their HIV status.

**Conclusion:** Nearly one-third of patients diagnosed with HIV said they had been discriminated against because of their infection; half of those experiencing discrimination said this involved a healthcare worker. Tackling HIV discrimination in the healthcare setting should be given priority.

P94

### People with diagnosed HIV: risk of cross-infection within a relationship

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**Objectives:** To examine the sexual behaviour of people with diagnosed HIV and the risk of HIV cross-infection with their primary partner.

**Methods:** The east London project is a confidential questionnaire survey of patients diagnosed with HIV receiving treatment and care in outpatient clinics in northeast London in 2004–2005. Respondents were asked whether they were currently in a relationship, about the HIV status of their current partner and about their sexual behaviour with that partner.

**Results:** 1687 patients with HIV completed a self-administered questionnaire (response rate 73% of eligible patients) including 480 black African heterosexual women, 224 black African heterosexual men and 758 gay/

bisexual men. Between half and three-quarters of respondents said they were in a current relationship (black African men 72%, black African women 62%, gay men 53%). Of those in a relationship, up to a half said their partner was also HIV-positive (black African men 53%, women 37%, gay men 37%). Patients with an HIV-positive partner were more likely to report unprotected sex (vaginal or anal) with that partner than patients with a partner who was HIV-negative or of unknown HIV status (black African men, 26% versus 6%; black African women, 32% versus 15%; gay men 56% versus 13%; all  $P < 0.001$ ).

**Conclusion:** Among people diagnosed with HIV who were in a relationship (married, co-habiting or living apart), 40–50% had an HIV-positive partner. Patients with HIV were more likely to report unprotected sex with an HIV-positive partner than with a partner of unknown or negative HIV status. While 'positive-positive' unprotected sex does not present a risk of HIV transmission to an uninfected person, there is a risk of cross-infection with resistant virus with a primary partner.

## Large

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### Rectal tuberculosis and lymphogranuloma venereum co-infection: a case report

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**Introduction:** The causes of gastrointestinal symptoms in HIV are many and varied, and multiple aetiologies for a single presenting complaint are common. The current lymphogranuloma venereum (LGV) outbreak among HIV-positive gay men has added to the diagnostic challenge.

**Case:** We report a rare and interesting cause of colitis in a 42-year-old Caucasian HIV-positive gay man, naive to HIV therapy, with a CD4 cell count of 350 cells/ $\mu$ l. He presented with a one-year history of intermittent diarrhoea, associated with blood, mucus and pain on defecation with exacerbation 7 weeks after a Belgian sexual contact. Colonoscopy showed mild inflammation, with CMV inclusions on histology, so he was started on HAART. After referral for sexual health screening, he tested positive by rectal swab for chlamydia, subsequently proven to be LGV. Treatment with doxycycline gave only partial symptomatic relief. Repeat rectal examination revealed a mass, a biopsy of which grew *Mycobacterium tuberculosis*. The patient had complete symptomatic resolution after quadruple anti-mycobacterial therapy.

**Discussion:** Tuberculosis is often HIV-related and is an AIDS-defining illness. In the UK, the incidence of tuberculosis in HIV is increasing. This case highlights an atypical presentation of tuberculosis within the current outbreak of LGV.

A 26-year-old homosexual male presented with difficulty walking, associated with ascending paraesthesia. Neurological examination revealed proximal muscle weakness of arms and legs with areflexia. Cerebrospinal fluid analysis showed elevated protein with paucity of cells and nerve conduction studies confirmed demyelination. The progression of the disease was complicated by mild respiratory and autonomic involvement. He was treated with a 5-day course of immunoglobulins, resulting in a slow but ongoing recovery. Pre-treatment CD4 count and viral load (VL) were 131 cells/ $\mu$ l and 53,000 copies/ml, respectively, but this had improved to CD4 156 and VL 57 at the time of presentation. In this case, as the disease occurred during a period of sharp decrease in viral load and because of the temporal association to ARV therapy initiation, we hypothesise that GBS was associated with immune reconstitution following antiretroviral therapy.

P97

### Avascular necrosis (AVN) of knee and ankle: improvement with calcitonin

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A 55-year-old HIV-positive man, diagnosed in 1991, and treated with a variety of antiretroviral agents since 1995, presented in September 2003 with rapidly increasing pain in the right knee. Later, pain developed in the left ankle. He had no systemic symptoms or signs of inflammation. In April 2003, stavudine was changed to tenofovir due to lipodystrophy, hyperlipidaemia, NIDDM and past MI. Alkaline phosphatase was mildly elevated; phosphate level was low but stable. Serum calcium and vitamin D were normal. Blood cultures and inflammatory markers were negative. X-ray of the right knee and left ankle revealed mild osteopenia. MRI showed subchondral marrow oedema in the right medial femoral condyle with linear subchondral low signal-intensity compatible with AVN. He was treated with rest and increasing analgesics, but the pain was poorly controlled. Tenofovir was replaced with abacavir without change of symptoms. Repeat MRI of the right knee showed new areas in the lateral condyle with oedema and AVN. MRI of the left foot showed oedema and AVN of the intermediate cuneiform. Calcitonin nasal spray (200 units daily) was commenced in January 2005 with significant improvement of symptoms and return to normal mobility in 6 months. HIV-infected patients are at higher risk for the development of AVN. In our patient, the causes included hyperlipidaemia, diabetes, antiretrovirals and HIV infection. Medical treatment has shown little benefit. Calcitonin may warrant further experiment for this condition.

P96

### Guillain Barré syndrome following immune reconstitution associated with antiretroviral therapy for HIV infection

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Guillain Barré Syndrome (GBS), although rare, may be a presenting feature of primary HIV infection. However, we report a unique case of GBS occurring one month after the initiation of antiretroviral (ARV) therapy (Truvada and efavirenz).

P98

**Plasma hyperviscosity syndrome secondary to HIV infection: a case report**Claire Ryan<sup>1</sup>, Olufunso Olarinde<sup>1</sup>, George Kinghorn<sup>1</sup> and Beverley Paul<sup>2</sup><sup>1</sup>Royal Hallamshire Hospital, Sheffield, <sup>2</sup>Bassetlaw District General Hospital, Nottinghamshire, UK

**Introduction:** We report the case of a young woman with plasma hyperviscosity syndrome secondary to a polyclonal hyper-gammaglobulinaemia in HIV. There is one previously reported case with a successful outcome following institution of HAART therapy. Our case is unique as we have demonstrated that a successful long-term outcome is possible with regular plasma exchange therapy.

**Case:** A 24-year-old woman was admitted to hospital in October 2004 with mucosal bleeding from the nasopharynx, vagina and urinary tract. Clinical

examination of the fundi revealed venous tortuosity and beading. Initial investigations revealed anaemia of Hb 7.8, a very high serum protein of 140 g/l, globulins of 116 g/l and a plasma viscosity (PV) of 6.19. A peripheral blood film showed marked rouleaux formation, pointing to a diagnosis of myeloma. However, protein electrophoresis revealed a polyclonal hyper-gammaglobinopathy, which led to testing for HIV antibodies. The HIV test was positive. CD4 count was 326 cells/ $\mu$ l, and HIV viral load >100 000 copies/ml. Initial treatment was with plasma exchange, which normalised the PV leading to gradual resolution of symptoms. HAART was added, but was never effectively taken. The patient has since been successfully managed for over a year with regular plasma exchanges to control her globulins and plasma viscosity.

**Conclusion:** Previous case reports have shown that plasma exchange is useful in the short-term symptomatic control of this syndrome and, in one case, HAART was shown to reverse the hyper-gammaglobulinaemia and raised PV. What we can extrapolate from this case is that plasma exchange alone appears to be an effective management for the longer term when HAART is unavailable.

## Standard

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**CMV cholangiopathy in HIV-infected man following HAART: immune recovery inflammatory syndrome**

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**Introduction:** The use of HAART has led to a decrease in the frequency of opportunistic infections. However, a subgroup of HAART-treated patients exhibited a paradoxical clinical deterioration. This is referred to as immune recovery inflammatory syndrome (IRIS). We describe a case of CMV cholangiopathy (CMV-CA) following HAART; while IRIS involving CMV retinitis, pneumonitis and ventriculitis has been reported, to our knowledge IRIS with CMV-CA has not previously been described.

**Case:** A 34-year-old man was diagnosed with HIV. The CD4 count was 9 cells/ $\mu$ l and HIV RNA was 350 000 copies/ml. HAART was initiated. Twelve days later, he presented with fever and vomiting. LFT showed markedly elevated gamma-glutamyl transferase and alkaline phosphatase with moderately elevated alanine transaminase and bilirubin. His HIV RNA was 257 and CD4 count was 69, 4 weeks following HAART. He had high CMV viral load and presumptive diagnosis of CMV-CA was made. He was treated with cidofovir and LFT improved.

**Discussion:** This case illustrates CMV-CA occurring in a patient who was commenced on HAART. Despite rapid decline of HIV RNA and improvement in CD4 count following HAART, our patient clinically deteriorated. In the view of this paradoxical clinical worsening, it was proposed this case is most likely a manifestation of IRIS. In conclusion, CMV cholangiopathy can present as IRIS in HIV-infected patients and should be considered in the differential diagnosis of abnormal LFTs.

P100

**A case report of seronegative pulmonary leishmaniasis in an HIV-hepatitis C co-infected patient**Andrew A Benzie<sup>1</sup>, Robert D Goldin<sup>2</sup> and John Walsh<sup>1</sup><sup>1</sup>St Mary's Hospital, <sup>2</sup>Imperial College, London, UK

We describe an antiretroviral-naïve 38-year-old Portuguese man with HIV/HCV co-infection [CD4 cell count 210 cells/ $\mu$ l (6%), viral load 34 053 copies/ml]. He presented in April 2005 with 6-month history of intermittent episodes of high fever, dry cough and shortness of breath on exertion. Over time, each episode had increased in severity. Previous episodes had settled either spontaneously or after treatment for a presumed community-acquired pneumonia. On admission, he was pyrexial with hepatosplenomegaly. He was thrombocytopenic ( $58 \times 10^9$ /ml) and had a mild neutrophilia. CRP was 127 mg/l and albumin was low at 25 g/l. CXR and bronchoscopy were normal. Stains and cultures for *Pneumocystis*, *Cryptococcus* and *Mycobacterium tuberculosis* were negative. Initially, he was again treated presumptively for community-acquired

pneumonia and PCP. Fever resolved and he was commenced on HAART. However, his condition again deteriorated with worsening thrombocytopenia, hypoalbuminaemia and oedema and respiratory distress. Plasma tested positive for both EBV and HHV8 DNA by PCR. Castleman's disease was suspected but, despite negative investigations including serology, bone marrow aspiration with culture for *Leishmania*, post-mortem revealed extensive pulmonary leishmaniasis. *Leishmania* and HIV co-infection, although rare in the UK, is becoming increasingly frequent elsewhere. Diagnosis of visceral leishmaniasis in HIV infection is difficult as only 40–50% of cases have positive *Leishmania* serology. Clinicians should have a high index of clinical suspicion for visceral leishmaniasis in patients who present with fever and hepatosplenomegaly, despite negative serology and bone marrow aspiration/culture.

P101

**An unusual cause of abnormal chest radiograph in an HIV-infected patient**Sumit Bhaduri<sup>1</sup>, Phillip Nottingham<sup>2</sup> and Kathir Yoganathan<sup>3</sup><sup>1</sup>Department of GU Medicine, Redditch, <sup>2</sup>Worcestershire NHS Acute Trust, Worcestershire, <sup>3</sup>Department of GU Medicine, Swansea, UK

**Introduction:** Disseminated histoplasmosis (DH) with extrapulmonary spread is common in HIV patients from endemic areas. To our knowledge, single organ involvement in patients from non-endemic areas has not previously been reported. We describe a homosexual Caucasian man with pulmonary histoplasmosis without any other organ involvement. His CD4 count was less than 100 cells/ $\mu$ l and he lived in a non-endemic area.

**Case:** A 37-year-old Caucasian homosexual man was diagnosed with HIV in 1990. Combination antiretroviral therapy (ART) was started in 1995. He stopped taking ART in 2000 and went to Australia in 2002 where his chest radiograph (CXR) was abnormal. He returned to the UK in 2003 when his CD4 count was 80. ART was re-started and his CXR showed an infiltrative lesion involving left hilum. CT thorax revealed a mass with satellite lesions for which he underwent a wedge excision. A histological diagnosis was made of histoplasmosis (crescent-like fungal spores with staining for *Cryptococcus* and *Pneumocystis* being negative). A bone marrow aspirate and trephine was normal. He did not have any other organ involvement and was successfully treated with itraconazole 200 mg bid for 12 weeks. To date (January 2006), he remains well without any recurrences or dissemination.

**Discussion:** DH is an acute infection with fever, dry cough and breathlessness, and is progressive and potentially fatal in immunocompromised patients. Military tuberculosis and *Pneumocystis carinii* pneumonia are important differential diagnoses. DH is often described in endemic areas, but our patient did not visit endemic areas and only had pulmonary involvement. Clinicians should be aware of this unusual cause of pulmonary infiltrates due to histoplasmosis in immunocompromised HIV-positive patients, even those living in non-endemic areas.

P102

### Seeing double: bilateral retinitis with different pathogens in a patient with advanced HIV infection

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A 41-year-old woman presented with visual disturbance in the left eye [visual acuity (VA) 6/24] 3 months after an untreated episode of left-sided maxillary shingles. There was acute retinal necrosis and peripheral retinal detachment in the left eye and a small area of retinitis in the right. Intravenous ganciclovir (5 mg/kg bid) was given for 7 days pending polymerase chain reaction (PCR) results. The left vitreous biopsy was positive for varicella zoster virus (VZV), but negative for cytomegalovirus (CMV) and herpes simplex virus (HSV). HIV serology was positive and CD4 count 16 cells/ $\mu$ l. The patient was treated with left intravitreal foscarnet injection, barrier laser and intravenous aciclovir (10 mg/kg tid) for seven further days. With valaciclovir, 1 g tid maintenance therapy VA improved to 6/12. Three weeks later she presented with bilateral visual deterioration [VA 6/12 right and counting fingers (CF) left]. Extensive right-sided retinitis was seen. PCR from right vitreous was positive for CMV, but negative for VZV and HSV. Intravitreal foscarnet injection and barrier laser therapy were performed. A combination of intravenous ganciclovir and foscarnet (60 mg/kg tid) was given for 21 days. HAART was commenced with emtricitabine, tenofovir and lopinavir/r. At three months viral load was <50 copies/ml and CD4 72. VA improved to 6/6 right but remains CF left. She remains on valganciclovir 900 mg bid with no relapse. She has returned to work. In severe immunosuppression, multiple opportunistic infections can occur even in the same organ system. This possibility should be suspected in apparent treatment failure. Combination antiviral therapy with foscarnet and ganciclovir may be effective in complicated bilateral retinitis with VZV and CMV to preserve vision.

P103

### HIV and systemic lupus erythematosus (SLE)

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Coexisting systemic lupus erythematosus (SLE) and HIV is a rare occurrence with fewer than 30 published cases. Overlapping immunological and clinical manifestations pose diagnostic and management challenges. The growing HIV epidemic in the developing world within a SLE-susceptible sub-population may increase these numbers. We describe a 41-year-old female African patient diagnosed with asymptomatic HIV and pancytopenia. At baseline, she had a CD4 count of 399 cells/ $\mu$ l and undetectable HIV viraemia (<50 copies/ml). HIV-1 infection was confirmed with proviral DNA testing and absence of HIV-2 antibodies. Two months later, she presented with a painful symmetrical polyarthropathy, discoid facial rash, positive anti-nuclear antibody and double-stranded DNA fulfilling the American Rheumatism Association criteria for diagnosis of SLE. She was commenced on hydroxychloroquine with reducing doses of prednisolone. During this six-month period, despite persistently undetectable HIV viraemia, her CD4 count declined to 150 cells/ $\mu$ l (11%). Recurrence of her polyarthropathy prompted the addition of mycophenolic mofetil (MMF), which was associated with a CD4 rebound to 725 cells/ $\mu$ l (24%). Her HIV viral load remains undetectable. In our patient, treatment of SLE was associated with CD4 cell depression despite the absence of HIV replication. Interestingly, the use of MMF was associated with immune restoration. This case provides further insight into the dynamics of coexisting SLE and HIV and the potential therapeutic role of MMF. We explore these issues further.

P104

### Lopinavir-associated hepatotoxicity in a pregnant woman: a case report

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**Aims:** To describe a case of severe hepatotoxicity in a pregnant patient started on lopinavir-based antiretroviral therapy (ART) to prevent mother-to-child-transmission (MTCT) of HIV. To contribute to knowledge base of safe prescribing of lopinavir in pregnancy.

**Methods:** (1) Case report and (2) literature review.

**Results:** (1) Case: A 32-year-old HIV-positive woman with a CD4 count of  $470 \times 10^6/\mu$ l (31.9%) and a viral load of 3300 copies/ml started ART consisting of boosted lopinavir (3 capsules bid) and Combivir (1 tablet bid) to prevent MTCT and allow vaginal delivery. Baseline liver function tests (LFTs) were normal. At 10 days, she experienced nausea, vomiting and anorexia. Toxicity bloods 4 days after onset of symptoms revealed AST 1560 IU/l, ALP 122 IU/l and bilirubin 47  $\mu$ mol. Coagulation screen, lactate level and liver ultrasound scan were normal. Viral hepatitis serology was negative. Combination therapy was immediately changed to ZDV monotherapy. By 8 days, liver function tests had returned to normal. She delivered a healthy baby by elective caesarean section.

(2) Literature review: Although hepatotoxicity with ART is well documented, little is published specifically on lopinavir-associated hepatotoxicity in pregnancy.

**Discussion:** The observed potentially life-threatening hepatotoxicity in this case is likely to be lopinavir-associated. Although this is a single case, it highlights the need to explore less-hepatotoxic regimens in pregnant women with low-level viraemia who wish to opt for vaginal delivery. There is an urgent need for better surveillance of adverse maternal events in addition to foetal and obstetric outcomes.

P105

### Neurocysticercosis with communicating hydrocephalus in an HIV-positive subject

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**Case:** A 26-year-old female patient from the Democratic Republic of Congo presented with a year-long history of seizures, following head trauma. An HIV test was positive, with an initial CD4 count of 378 cells/ $\mu$ l. Her CT head scan at this time showed characteristic changes of neurocysticercosis, which were confirmed on CSF and serum immunoblot tests. Treatment of cysticercosis was delayed due to pregnancy, reactivation of toxoplasmosis and non-progression of lesions; however, she presented two years later with worsening headaches, visual hallucinations and psychosis. CD4 count at the time was 600 cells/ $\mu$ l. An MRI scan showed communicating hydrocephalus. Treatment was commenced with praziquantel 50 mg/kg in three divided doses, together with dexamethasone. Her headaches improved and a repeat MRI scan showed reduction in size of all lesions. No deterioration in her mental state occurred and her HIV did not progress either. She remains on anticonvulsants and antipsychotic medication. Antiretroviral medication was only used whilst pregnant.

**Discussion:** Aggressive neurocysticercosis, with basilar meningitis, has previously been reported in immunosuppressed patients and in HIV. We describe a case where effective treatment given to a HIV-positive patient has been successful, in a patient not currently taking antiretroviral medication.

# Large

P106

## Lymphogranuloma venereum (LGV) presenting as haemorrhagic proctitis: first cases from Wales

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**Introduction:** The emerging UK epidemic of anorectal LGV presenting as haemorrhagic proctitis is often initially misdiagnosed and inappropriately treated. We report five cases of LGV in MSM who attended the department of genitourinary medicine. These are the first confirmed cases from Wales.

**Cases:** Five patients, aged 27–54 years, presented between Novembers 2004–2005. Symptoms included profuse rectal bleeding, mucous, severe anorectal pain, tenesmus, constipation, diarrhoea, weight loss and general malaise. Three of the five had previously been admitted to hospital for rectal bleeding, a fourth was on a waiting list. Three patients were taking mesalazine. Four of the five had severe haemorrhagic proctitis but none had inguinal lymphadenopathy. Positive serology for Psittacosis/LGV and *Chlamydia trachomatis* IFA was found in four of the five men. The remaining patient, seen within five days of symptoms, had negative serology but a positive rectal swab. Rectal swabs for LGV were positive for serotype L2 in 3/5 men and not taken/contaminated in two. Three of the five men were HIV-positive and one was hepatitis B e-antigen-positive, none had hepatitis C.

**Discussion:** Rectal bleeding is a common complaint and, particularly in relatively rural areas such as ours, patients may attend their general practitioner, gastroenterologist or colorectal surgeon who may be unaware of the patient's sexual orientation or of the possibility of LGV or HIV leading to inappropriate and delayed treatment.

P107

## Syphilis re-infection in HIV-positive men: a new challenge

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**Aims:** To study patients presenting with syphilis re-infection in two genitourinary medicine clinics.

**Methods:** A retrospective case note review between 1/1/2005 and 31/12/2005.

**Results:** In the study period, 34 patients presented with a syphilis re-infection. In total, these 34 patients had presented with 80 episodes of syphilis since the start of the syphilis epidemic in 1997. All were male, 33 were homosexual and 27 HIV-positive. 12 out of 34 patients presented with their third episode of syphilis infection; of these, 11 were HIV-positive. Other STIs diagnosed in 20/80 presentations with syphilis included five new HIV diagnoses. In the 3 months preceding presentation, 55% of HIV-positive patients and 60% of the HIV-negative reported high-risk sexual behaviour. Out of the 39 episodes with HIV who attended for follow-up at 6 months, 35 (90%) had a serological cure. In the eight without HIV who attended for follow up, serological cure was achieved in 7/8 (88%). Intramuscular penicillin was prescribed in 63 episodes (48 HIV-positive and 15 HIV-negative). The remainder received various treatment regimens. In those with HIV, 18/48 (38%) episodes were treated with 1 injection of benzathine penicillin; in the 9 who attended for follow up, 8 of these had a serological cure. The remaining 30/48 (62%) had longer courses of penicillin injections; 23 of the 24 who attended for follow up had serological cure.

**Conclusion:** HIV-positive status is a strong predictor of syphilis re-infection in homosexual men. High-risk sexual behaviour levels and overall cure rate were similar in both HIV-positive and -negative groups. Serological cure rates following single dose benzathine penicillin were comparable to those following prolonged penicillin courses, regardless of HIV status. Safer sex messages should target HIV-positive homosexuals.

# Standard

P108

## Lymphogranuloma venereum (LGV) is strongly associated with HIV infection in men who have sex with men (MSM)

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**Aims:** We carried out a study of all cases of LGV presenting to a UK clinic between December 2004 and October 2005 in order to examine the prevalence of HIV and other sexually transmitted infections (STIs) in men with LGV.

**Methods:** Data were gathered prospectively on patients diagnosed with LGV and checked by retrospective review of clinic notes. We assessed the results of screening for concomitant STIs. In patients with HIV infection, we recorded the results of surrogate markers and baseline tests for genotypic resistance.

**Results:** There were 34 cases of confirmed LGV, 32 (94%) of which were rectal and 2 (6%) urethral; all were in MSM. Two cases of asymptomatic rectal LGV

were found by routine screening (prevalence 0.4% in asymptomatic MSM). Twenty-six (76%) patients were HIV-1-positive, and five (15%) were co-infected with hepatitis C (one of these acquired hepatitis C infection at the same time as LGV). Amongst the 76% who were HIV-1 positive, 12 (50%) patients for whom a viral load result was available had a detectable plasma viral load. Four (15%) had evidence of baseline genotypic drug resistance. Two (6%) patients had concomitant rectal gonorrhoea, four (12%) had urethral chlamydia (non-LGV serovars). There were no cases of acute syphilis diagnosed in this group, but 21% had been treated in the past for early syphilis. Overall, 13 (38%) patients had at least one concomitant STI.

**Conclusion:** The majority of cases of LGV were seen in MSM with HIV infection. Half of all HIV-infected patients had a detectable viral load. Co-infection with other STIs was common. There is an obvious risk that patients acquiring infection with LGV may transmit or become infected with HIV and other STIs; active case-finding and treatment might limit the spread of HIV and other STIs.

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