AIDS briefs

1 in 40 patients presenting to UK emergency departments has HIV

An anonymous survey in Brighton of male patients aged 18 - 50 reporting to GPs and to hospital accident and emergency (A&E) departments with symptoms suggestive of HIV infection has found an overall HIV prevalence of 1% in those previously undiagnosed with HIV. However, it found a higher prevalence of 2.5% among the patients turning up at A&E, suggesting that, at least in a high-prevalence town like Brighton, there is scope for 'opt-out' HIV testing to be introduced in emergency settings.

The study, presented recently at the BHIVA Conference, Belfast, was carried out using residual blood samples left over from patients who had presented to local GP practices and emergency departments between January 2006 and June 2007 and was an anonymous unlinked survey.

In order for samples to be tested, patients had to have presented with flu-like symptoms, muscle and joint aches, fever, night sweats, rash or mouth ulcers or a combination of other symptoms suggestive of primary HIV infection.

Samples were tested for HIV antibodies and the HIV p24 protein (which appears earlier than HIV antibodies in infected people). Pooled samples were also tested for HIV RNA (i.e. given a viral load test) in order to identify people in primary infection before seroconversion.

A total of 686 samples were tested, and 7% of these tested HIV positive. Eliminating patients known to have HIV, this left 1% of patients (7 samples) who tested positive for HIV and were undiagnosed. One of these samples tested positive for primary HIV infection. It was recorded that 33 of the 686 patients had taken a same-day HIV test, but all were negative.

A total of 71% of samples were collected from GPs and 29% from A&E departments; the proportion of undiagnosed patients attending GPs was only 0.4% (1 in 250) but the proportion attending A&Es was 2.4% (1 in 40). Patients presenting with flu-like symptoms to a GP are unlikely to have investigations carried out.

The study therefore did not support the use of pooled RNA testing as a means of picking up on primary HIV infection in the community. However, the author did suggest that there is a case for routine HIV testing in A&E departments.

Nambiar K, *et al.* 2008. Fourteenth BHIVA Conference, Belfast. Abstract O5.

Concentrate on reducing partner numbers and on male circumcision

A commentary published recently in *Science* calls for HIV prevention efforts to be focused on reducing the number of sexual partners and on male circumcision. The authors argue that limited resources mean that concentrating on condom use and treating sexually transmitted infections are of limited value. They dismiss traditional explanations for the high prevalence of HIV in the 9 African countries where it is over 12%, such as poverty, gender inequality and war, pointing out that HIV prevalence is higher in the richer portions of African society and not always brought into the relationship by the man. They add that Rwanda, Congo and Angola, countries that have suffered war, genocide and rape, have a lower HIV prevalence than their stable and peaceful neighbours Swaziland and Botswana.

However, where multiple and concurrent sexual partners are uncommon, and where male circumcision is common, such as Niger (with an HIV prevalence of less than 1%), HIV prevalence is low. They point out that at the moment, the largest donor investments are being made for interventions for which the evidence for large-scale impact is increasingly weak. They state that promoting condom use may be successful only for high-risk populations such as gay men and sex workers, but that promoting condom use has not lead to reductions in prevalence in countries with large-scale epidemics. Voluntary counselling and testing has little use among people who test negative, they argue, and recent studies on the effect of treating sexually transmitted infections have been disappointing. Equally unlikely to be of value in the near future are vaccines and microbicides, leaving the most common – and most politically sensitive – issue of multiple concurrent partners, that appears to be the main reason for the high prevalence in the 9 African countries.

They are also optimistic about the effects of male circumcision, citing 45 observational and biological studies from the past 20 years that have shown that male circumcision reduces heterosexual transmission of HIV.

I wonder how they explain the high HIV prevalence among Xhosa men in South Africa – but otherwise their reasoning appears sound.

Potts M, *et al. Science* 2008; 320: 749-750.

Dual drug class resistance in two-thirds of those failing antiretroviral therapy in South Africa

Almost two-thirds of individuals failing first-line antiretroviral therapy in a KwaZulu-Natal cohort had resistance to drugs from two classes, and one-third had at least one mutation that could reduce response to the entire nucleoside analogue class, researchers from the South African Resistance Cohort Study Team report in a recent edition of *Clinical Infectious Diseases.*

The commonest mutations were associated with non-nucleoside reverse transcriptase inhibitor (NNRTI) and nucleoside reverse transcriptase inhibitor (NRTI) classes of drugs, with resistance to 3TC most frequent within this class.

The study findings highlight the controversy over how to monitor for the failure of antiretroviral treatment and when to switch patients experiencing treatment failure when viral load is not readily available and second-line treatment can cost 5 - 10 times as much as first-line treatment.

Current World Health Organization guidelines for antiretroviral treatment in resource-limited settings suggest that if viral load testing is not available, as is the case in most of sub-Saharan Africa, treatment should be switched to a second-line regimen if an individual develops new symptoms of serious immune suppression (WHO stage 3 or 4 symptoms), or if the CD4 cell count declines by 50% from its peak or 33% within the past 6 months (after a confirmatory test).

But some, particularly in the USA, are critical of the WHO approach. In an accompanying editorial they suggest that if a choice must be made between

monitoring viral load and CD4 count during antiretroviral therapy, then monitor viral load. However, patients in this study were identified as having failing treatment through viral load testing, suggesting that rates of thymidine analogue resistance could have been much higher if viral load monitoring had not been available.

After the failure of first-line treatment in resource-limited settings international and national guidelines recommend switching to a protease inhibitor-based regimen in order to have the benefit of a new class of drug.

In KwaZulu-Natal, antiretroviral use increased more than 6-fold during the period 2002 - 2006. The study sites were two referral centres for antiretroviral therapy in KwaZulu-Natal. Study participants were HIV-1-infected patients aged 18 years or older who experienced virological treatment failure after 24 weeks of their first antiretrovirals, which consisted of either first- or second-line regimens or some combinations of drugs.

Virological failure was defined as an HIV-1 RNA level of more than 1 000 copies/ml. Genotypical resistance testing was performed on plasma virus samples from all patients who experienced virological failure. Drug resistance mutations and deletions in the reverse transcriptase and protease genes were identified by DNA sequencing.

A number of other laboratory parameters were measured at enrolment. These included CD4 counts, complete blood counts, HIV-1 RNA levels, haemoglobin, and liver and kidney function tests. Clinical and demographic data were also obtained.

In all, a total of 124 antiretroviral-treated adults who experienced virological failure were enrolled between January 2005 and August 2006. The predominant viral subtype was HIV-1C. Virus samples from 83.5% of participants carried one or more significant drug resistance mutations. Dual-class drug-resistant virus was present in 64.3% of participants while triple-class drug-resistant virus was present in 2.6%.

The commonest mutation was M184V/I, which was observed in 64.3% of patients; K103N was present in 51.3%, and V106M was present in 19.1% of the patients. In 39.1% of patients the M184V/I and K103N mutations were both present. Thymidine analogue and protease resistance mutations were found in 32.2% and 4.4% of patients, respectively.

Marconi VC, *et al. Clinical Infectious Diseases* 2008; 46: 1589-1597.

Oral HIV tests highly effective

Two oral HIV tests have been shown to be highly accurate in a study conducted in Namibia and reported in the *Journal of Acquired Immune Deficiency Syndromes*. The studies were conducted among patients infected with HIV subtype C and the OraQuick test was shown to be 100% accurate, with the OraSure test being 98.9% accurate. The investigators believe that oral HIV testing could be used to help to diagnose HIV in resource-limited settings, and assist in the gathering of surveillance information.

Two oral HIV tests have been approved in the USA (OraQuick and OraSure) and have been shown to be able to diagnose HIV infection accurately. But studies into the accuracy of these tests were conducted in countries where the majority of patients are infected with HIV subtype B. There is very little information about the accuracy of these tests in settings where the majority of HIV infections involve non-B subtypes.

In this study, investigators designed a cross-sectional (or 'snap-shot') study to assess the accuracy of these two oral HIV tests. The study population involved 273 pregnant women of unknown HIV status in Namibia. Subtype C is the predominate HIV subtype in this region.

Two oral fluid samples were collected using both the OraQuick and OraSure tests. Blood samples were also taken from the women and tested for antibodies to HIV to assess the accuracy of the oral tests.

Blood tests showed that 70 of the women (26%) were infected with HIV. OraQuick results were available for all 273 women and were 100% accurate. Six of the OraSure results were excluded because they were not labelled properly, and three results (1.1%) did not agree with the results from the paired blood test. This included two false-negatives and one false-positive.

Hamers RL, *et al. J Acquir Immune Defic Syndr* 2008; 48: 116-118.

Arm of international once-daily HIV treatment trial stopped

The independent drug safety and monitoring board of the ACTG 1571 study into three alternative once-daily antiretroviral combinations has prematurely stopped one of the study arms.

Interim results from the study, which involves patients taking anti-HIV treatment for the first time, showed that a once-daily antiretroviral combination of atazanavir, FTC and enteric-coated ddI (ddI-EC) was associated with poorer control of HIV. Patients taking this regimen will be switched to one of the other drug combinations being investigated in the study.

Enrolment to the study started in July 2007 and its primary focus is patients in low- and middle-income countries. Patients were randomised to either receive AZT, 3TC and efavirenz, regarded as the standard of care, or two alternative once-daily antiretroviral combinations. The alternative combinations were FTC, tenofovir and efavirenz, or atazanavir, FTC and ddI-EC. The study is titled 'Evaluation of once-daily PI and NNRTI regimens as initial HIV therapy in individuals from resource-limited settings'.

Conclusive evidence was presented to the study's independent over-sight board that patients who were treated with atazanavir, FTC and ddI-EC were less likely to achieve an undetectable viral load. They therefore took the decision to terminate this arm of the study. The US National Institute of Allergy and Infectious Diseases, which is overseeing the study, accepted this recommendation and had stopped this arm of the study.

www.aidsmap.com, 30 May 2008.

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