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Enhanced risk of HIV sexual transmission during structured treatment interruption

We report a case of HIV transmission through sexual intercourse while the sexual partner underwent antiretroviral structured treatment interruption. We would like to underline that giving proper information about a higher contamination risk during structured treatment interruption is a critical issue. Moreover, we consider that it is the responsibility of a medical investigator and physician to deliver a clear message in order to reinforce prophylaxis indications for sexual intercourse during this period.

A patient was infected with HIV for 9 years when he started HAART. At this time, his CD4 count was 280 × 10^3/ml and plasma viral load was 5.1 log_{10}/ml. A first structured treatment interruption (2 months’ duration) was proposed after 2 years, while plasma viral load was undetectable. He was asked to use preservatives strictly at this time. A peak of HIV RNA reappeared in blood within days of stopping HAART (mean increase 0.2 log/day). HAART treatment decreases HIV RNA concentration in blood and is generally associated with a decrease of seminal HIV RNA. Moreover, an increase of HIV RNA in plasma is known to enhance the risk of transmission. Finally, we may assume that a sudden increase in HIV RNA in blood during structured treatment interruption may induce a viral rebond in semen.

Some key messages have to be taken into account. Firstly, the impact of sexual transmission during clinical trials assessing the benefit/risk ratio of structured treatment interruption has to be evaluated prospectively as a side effect of the strategy. Secondly, patients have to be informed that they are particularly at risk of HIV transmission during this period and that sexual relations have to be heavily protected when antiretroviral treatment is stopped. It is the responsibility of investigators involved in such trials to inform patients. Thirdly, in order to avoid complaints against physicians, we believe that patients must be informed of this very high risk period.

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Chaperoning in genitourinary medicine clinics

In 1996 the General Medical Council recommended, where possible, offering chaperones to patients during intimate examinations. This advice was incorporated into a report by a Royal College of Obstetricians and Gynaecologists working party. Subsequently, Torrance et al performed a postal survey of practice in 175 genitourinary medicine (GUM) clinics in the United Kingdom. This study also concluded that chaperones should be offered to patients more widely during genital examinations in genitourinary medicine (GUM) clinics. In contrast, other studies about chaperoning identified two interesting observations (table 1). Firstly, there was a significant difference in provision of chaperones for female patients, depending on whether the person carrying out the examination was a female doctor (12/20) or a female nurse (1/20); Yates’s corrected χ² test = 11.40, 1 df, p<0.001. Secondly, there was a difference in provision of chaperones for female patients examined by female doctors (12/20) compared with male patients examined by male doctors (2/20); Yates’s corrected χ² test = 6.90, 1 df, p<0.003 (table 1). In addition, it was noted that in 18 clinics not offering routine availability of chaperones for male patients being examined by a male doctor.

We carried out a postal survey of the use of chaperones in 31 GUM clinics in the North Thames Region in order to assess current practice. Responses were received from 20 centres (64.5%). Only two (10%) clinics had a written clinic policy and only one (5%) had carried out a patient survey on views about the provision of chaperones. None of the clinics had carried out a staff (nurses and doctors) survey of their views about chaperoning.

We identified two interesting observations (table 1). Firstly, there was a significant difference in provision of chaperones for female patients, depending on whether the person carrying out the examination was a female doctor (12/20) or a female nurse (1/20); Yates’s corrected χ² test = 11.40, 1 df, p<0.001. Secondly, there was a difference in provision of chaperones for female patients examined by female doctors (12/20) compared with male patients examined by male doctors (2/20); Yates’s corrected χ² test = 6.90, 1 df, p<0.003 (table 1). In addition, it was noted that in 18 clinics not offering routine availability of chaperones for male patients being examined by a male doctor.

Table 1. Results of a postal survey of practice in 20 GUM clinics in the North Thames Region

<table>
<thead>
<tr>
<th>Chaperone offered</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female doctor</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Female nurse</td>
<td>1</td>
<td>19</td>
</tr>
<tr>
<td>Male doctor</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Male nurse*†</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Male patient:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female doctor‡</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>Female nurse§</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Male doctor</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Male nurse†‡</td>
<td>1</td>
<td>18</td>
</tr>
</tbody>
</table>

*Seven clinics do not allow this interaction; †one clinic does not have male nurses; §one clinic does not allow the interaction; ‡two clinics do not allow this interaction.

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References

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Cytokine profiles in HIV seropositive patients with tuberculous meningitis

The immunological response in pulmonary and pleural tuberculosis has been extensively studied. However, the response in tuberculosis meningitis has not been well documented. In pulmonary disease, exposure to tuberculous antigens results in a T cell and natural killer cellular response, elaborating various cytokines, mainly of Th helper type 1 (Th1) origin. Stimulated macrophages elaborate tumour necrosis factor (TNF) α, interleukin (IL) 12, and IL 1, promoting further recruitment and activation of macrophages and lymphocytes. TNF α correlates with disease severity and may contribute to tissue necrosis; however, TNFα has also contributed to survival in murine studies. Transforming growth factor β (TGF β) suppresses macrophage activation. IL 2 may be beneficial in promoting an immune response in HIV seropositive patients. Th1 and Th2 cytokine responses have been observed in cerebrospinal fluid (CSF) of HIV seropositive patients with tuberculous meningitis. Whether the response is similar in HIV seropositive patients with tuberculous meningitis is unknown.

We studied the cytokine response and its correlation with disease severity in HIV seropositive and HIV seronegative patients with tuberculous meningitis.

Tuberculous meningitis was diagnosed on clinical and CSF examination after exclusion of viral, acute bacterial, and other causes of aseptic meningitis. Disease severity was assessed according to the Medical Research Council stages 1 to 3. HIV ELISA was done on all patients. CSF samples were subjected to microscopy, culture, protein and glucose analysis, Venereal Disease Research Laboratory test, fluorescent treponemal antibody analysis, cryptococcal antigen analysis, viral studies, cystercocosis ELISA, CD4 counts, and determination of concentrations of adenosine deaminase (ADA), CSF IFN γ, and albumin.

For cytokine assays, CSF was centrifuged at 3000 g, and supernatant was aliquoted and stored at −70°C. TNF α, interferon (IFN) γ and IL 10 concentrations were measured by ELISA kits (Genzyme Diagnostics, Cambridge, Massachusetts, USA) with detection limits of 3 pg/ml, 3 pg/ml, and 5 pg/ml respectively.

Data were summarised as medians and ranges. Non-parametric Wilcoxon rank sum tests were used to compare HIV seropositive groups with HIV seronegative groups, tuberculous meningitis severity groups, and groups derived according to the blood brain barrier index for cytokine concentrations. Spearman’s rank correlation was used to derive correlations of cytokine concentration, ADA concentrations, and CD4 counts in CSF.

There were 27 patients: 18 (67%) women and 9 (33%) men. Seventeen were HIV seropositive and 10 HIV seronegative. The average interval between onset of symptoms and the first clinical assessment was 17 days (range 5–90 days) in 18 patients where this was recorded. The mean (SD) age was 26.8 (6.5) years. There was one patient aged 10 years and one aged 60, and the rest were between 25 and 40. The cytokine concentrations were not analysed according to age, as this would make it impossible to target a mean. However, the time and cost of resolving allegations against healthcare workers must be balanced against the costs of employing appropriate staff.

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References:
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Table 1 Differences between HIV seropositive and HIV seronegative groups and tuberculous meningitis severity

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>HIV positive</th>
<th>HIV negative</th>
<th>Stage 1</th>
<th>Stage 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median Range</td>
<td>Median Range</td>
<td>p Value</td>
<td>Median Range</td>
</tr>
<tr>
<td>IFN γ (pg/ml)</td>
<td>56.9 (16.0–2048)</td>
<td>890.6 (0–2048)</td>
<td>0.9</td>
<td>184.5 (0–1771.0)</td>
</tr>
<tr>
<td>TNF α (pg/ml)</td>
<td>1.6 (0–67.5)</td>
<td>9.8 (0–309.3)</td>
<td>0.11</td>
<td>0.65 (0–19.2)</td>
</tr>
<tr>
<td>IL 10 (pg/ml)</td>
<td>24.6 (0–127.9)</td>
<td>17.3 (0–296.3)</td>
<td>0.9</td>
<td>3.68 (0–53.0)</td>
</tr>
</tbody>
</table>

IFN, interferon; IL, interleukin; TNF, tumour necrosis factor.
significantly influence concentrations. Unfortunately, corresponding serum concentrations were not available. This would have been valuable. This is the first study correlating CSF cytokine responses to severity of tuberculous meningitis and comparing HIV positive with HIV negative groups. Further studies should be done to confirm these findings, perhaps to define their relevance to complications and to explore the possibility of IL-2 treatment in HIV positive patients.

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References


Hepatitis C testing in HIV infected patients

Numerous seroprevalence studies have shown a high rate of co-infection with hepatitis C among HIV-1 infected patients, ranging from 98% in haemophiliacs, 80% among injecting drug users, to 3–15% in homosexual/bisexual men. Although it is estimated that there are 200 000–400 000 people infected with hepatitis C (HCV) in the United Kingdom, the number of coinfected individuals is unknown. Data have shown that HCV increases the rate of HCV progression, and there is also some evidence suggesting that HCV worsens HIV progression, although this is more controversial.

There is a growing recognition of the significant impact of co-infection on the management of HIV disease. Hepatitis morbidity and mortality among coinfected patients has increased fivefold in recent years. Furthermore the presence of HCV increases the frequency of hepatotoxicity with antiretroviral therapy, and may also impact on the choice of antiretroviral drug, with avoidance of drugs that are potentially hepatotoxic such as ritonavir and nevirapine. Most importantly there is now effective treatment available for the management of HCV infection.

Recent preliminary data suggest in HIV-HCV co-infected patients superior virological response in those receiving Peg-IFN-α2b with ribavirin compared to standard interferon with ribavirin. Finally, management of the HCV-HIV co-infected patients involves other interventions such as vaccination for other viral hepatitis A and B, and reducing alcohol intake.

These findings all highlight the importance of identifying those HIV infected patients who are co-infected with HCV. However, a recent survey at Kings’ College Hospital in March 2002 revealed that only 63% of a cohort of 850 current HIV infected attendees had been tested for HCV. The majority of those not yet tested for HCV were patients who had presented before the routine introduction of HCV testing in 1999. Similar findings have been reported from other European centres. In a French cohort of 4017 HIV infected patients only 2589 (64%) were tested for HCV. Although a substantial number of these patients have stored samples available on which retrospective HCV testing could be performed, the current guidance from Royal College of Physicians is that consent must be obtained before testing.

Current guidelines from the United States now recommends HCV testing for all HIV infected patients. Antibody based screening assays for HCV infection have evolved over the past decade and currently the most widely are third generation ELISA assays (Ortho). Confirmation of positive results by recombinant immunoblot assays (Chiron RIBA, others) is still recommended. As a proportion of positive tests may represent false positive results. Qualitative and quantitative PCR (polymerase chain reaction) tests that detect the presence of HCV RNA and have sensitivity in the range of 50–1000 equivalents per ml are now also available. We undertook a recent informal survey of 10 UK teaching hospitals, which showed differences in HCV testing policies. Seven clinical sites use serological testing for screening and confirm all initially positive results with a second serological assay, and then confirm positive results with a qualitative PCR test. Three sites use qualitative PCR testing for those with an initial positive serological test. For those with a negative PCR further confirmatory antibody assay are done at two sites and one site requests repeat PCR testing at 6 and 12 months.

What is the role of PCR testing in co-infection? At least 4–7% of HIV-HCV co-infected patients have no detectable antibodies in the presence of HCV viraemia as they fail to produce antibodies or have low titers (can’t be detected or give equivocal or indeterminate) or loss of detectable antibodies from serum despite persistent viraemia in immunosuppressed patients. Therefore, additional testing with PCR is often indicated. The guidelines recommend that all patients with positive HCV antibody tests and those patients thought to be at risk of HCV infection despite negative or indeterminate serological tests should undergo qualitative PCR testing of serum. A positive result confirms current viraemia whereas a negative test suggests non-viraemic infection. Patients with a positive ELISA but negative PCR should be tested with recombinant immunoblot assay to confirm antibody status.

In conclusion, we recommend that centres caring for HIV infected patients should develop clear policies and strategies for ensuring all their new and existing HIV infected patients have undergone testing for HCV.

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References


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First, do not harm: also an issue in NAA assay diagnostics for chlamydial infection

In his update on Chlamydia trachomatis diagnostics, Chernesy emphasises that nucleic acid amplification (NAA) assays can be useful for screening purposes, because of their increased sensitivity and the possibility of non-invasive sample collection. Since the introduction of these assays, many screening interventions have been undertaken and evaluated mostly in an optimal research context. However, a number of problems can be expected if these diagnostics are implemented in large scale routine diagnostic practice or in community screening programmes.

Firstly, multiple testing sites may be needed for accurate results, but cannot be realised for reasons of cost and inconvenience. Secondly, the positive predictive value of a test is low in low prevalence populations. To avoid false positive diagnoses in these situations repeat testing of the sample, preferably by a different technique, is highly recommended. However, in clinical practice a single
positive result is often considered to indicate that a patient is infected. Thirdly, reproducibility problems do occur and are varying in time, and confirmatory testing is required when test results are intermediate or near the cut-off value. A low positive test result that is not caused by the presence of amplification inhibitors points to a low number of target organisms in the sample. Repeat testing is then a matter of statistical chance of the second portion of the sample containing detectable numbers of target organisms. Such results should be transmitted to the clinician accompanied by interpretative comments.

Fourthly, diagnostic accuracy may be affected by contamination of the specimen during laboratory processing.

Fifthly, it is not clear whether detection of a very small amount of chlamydial DNA always reflects relevant infection. The assays might identify residual DNA from a viable organism, or DNA of levels of pathogenicity which are too low to be infectious. assays might identify residual DNA from a viable organism, or DNA of levels of pathogenicity which are too low to be infectious.

Geographical focusing: an intervention to address increased risk for sexually transmitted diseases during repatriation and resettlement in post-war Mozambique

Countries in the early post-war phase face population movements contributing to increased vulnerability for sexually transmitted diseases (STD) and HIV. Mozambique chose geographically focused interventions to control STD spread in the first post-war years.

Mozambique was one of the poorest countries in the world in 1993 with per capita GNP of US$63 and life expectancy of 48 years.

Fifteen districts in five provinces were selected on the basis of existing population health facilities and projected influx of people. STD/HIV control. PHC services were strengthened over coming the shortages of staff, drugs, and materials. Clinical, laboratory, and health education skills of over 100 PHC workers were upgraded. The use of syndromic activities, was subsequently expanded to other districts. The use of syndromic management protocols contributed positively to STD management throughout the country.

Focusing interventions in areas with especially vulnerable populations, combined with an integrated approach to STD/HIV control, may have contributed to the decline in the spread of STD and HIV in early post-war Mozambique.

Acknowledgements

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References


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www.sextransinf.com

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A novel research approach in sex on premises venues (SOPV): objective measure of sexual behaviour and low level intrusion to patrons

Sex on premises venues (SOPV) are commercial venues where men who have sex with men (MSM) meet other MSM for casual, usually anonymous, sex. These venues are challenging environments for traditional methods of behavioural research—for example, interview surveys. An alternative research method adapted from a study with sex workers in Nicaragua may be used in SOPVs. This study counted the number of used condoms per client as a measure of “safe” sexual behaviour. A pilot study in two parts was conducted at a Melbourne SOPV to determine the feasibility of this approach. The merit of this method was dependent on the consistency of the ratio of used condoms per SOPV patron, and consequently the method's sensitivity to detect behaviour change.

Part 1 of this pilot aimed to establish a system of SOPV waste collection and condom counting. SOPV staff collected waste condom numbers and research staff counted the number of condoms in the waste that were free from condom packaging. Part 2 pilot the SOPV staff handing out anonymous, self-complete questionnaires to patrons during the time periods when waste was being collected. The questionnaire only asked about anal sex and condom use during the participant’s visit at the SOPV.

Part 1 operated on 16 Saturdays and Sundays during the day. An overall ratio of 0.8 condoms per patron was calculated (95% CI: 0.7 to 1.1), and the ratio for each day ranged from 0.3 to 1.6. It was suspected that inconsistent collection of waste on Saturdays and Sundays contributed to the variability of the calculated condom to patron ratio each day. To have the same SOPV staff collecting waste each time and to avoid weekend functions at the SOPV, collection continued on the following nine Wednesday and Thursday evenings. For these evenings an overall ratio of 0.56 condoms per patron was calculated (95% CI: 0.4 to 0.7), and the ratio for each day ranged from 0.2 to 1.0.

Part 2 of this pilot operated on Wednesday and Thursday evenings of the following 8 weeks. Approximately 180 patrons were given a questionnaire by SOPV staff, of which 76 (~40%) completed and returned the questionnaire (mean 43.8 (SD 13.3 years). Forty four (44%) completed and returned the questionnaire by SOPV staff, of which 76 (~40%) completed and returned the questionnaire by SOPV staff.

NOTICES

International Herpes Alliance and International Herpes Management Forum

The International Herpes Alliance has introduced a website (www.herpesalliance.org) from which can be downloaded patient information leaflets. Its sister organisation the International Herpes Management Forum (website: www.IHMF.org) has launched new guidelines on the management of herpesvirus infections in pregnancy at the 9th International Congress on Infectious Disease (ICID) in Buenos Aires.

XIX International Congress of the Society of The Fetus as a Patient

1–4 May 2003, Gran Hotel Sitges, Barcelona-Sitges, Spain

Further details: (fax: +34 934 11 10 38; email: info@icid-2003.com; web site: www.icid-2003.com).

Australasian Sexual Health Conference: Tango down South—2003!

4–7 June 2003, Christchurch Convention Centre, New Zealand


Editors’ Notice

Inadvertent failure to disclose an interest

Podophyllin office therapy against condyoma should be abandoned. Von Krogh et al (Sex Transm Infect 2001;77:409–12). The author Dr G Von Krogh inadvertently failed to disclose that he had received consultancy fees or reimbursement of expenses to attend educational meetings relating to anogenital papilloma virus infection from the following companies: 3M, Perstorp, Stiefel, Oclassen, and MSD. In addition clinical trials on anogenital HPV infection had been funded within his department by both 3M and MSD.