Letters to the Editor

Microsporidia: a new sexually transmissible cause of urethritis

Microsporidia are worldwide ubiquitous intracellular protozoan parasites, which have recently emerged as a significant cause of morbidity in immunocompromised patients, particularly in those with AIDS.¹ Multiorgan microsporidiosis is well described in these individuals, which underscores the severity of immunodeficiency in patients with microsporidial infection.^{2,3} In 15-30% of patients with advanced AIDS, *Encephalitozoon bienersi* is the causative agent of major chronic diarrhoea.¹ Many such patients have shown dramatic responses when treated with albendazole.⁴

The first case of urethritis associated with microsporidiosis has recently been reported in a 36 year old AIDS patient with urethritis, sinusitis and diarrhoea.⁵ *Encephalitozoon*-like spores were isolated in a smear of expressed urethral pus. Microsporidial spores were also isolated from faeces, nasal discharge, sputum and centrifuged urinary deposit. We now report a similar case of microsporidiosis in a 35 year old homosexual patient with AIDS, who presented with sinusitis, urethritis and diarrhoea.

Our patient had multiple episodes of gross urethritis with a profuse brown urethral discharge, which was only partially responsive to antibiotics. His urethritis persisted despite courses of doxycycline, erythromycin, azithromycin, rifampicin and ciprofloxacin. Clindamycin, chloramphenicol and metronidazole produced some improvement, but had to be stopped owing to the development of drug related rashes.

Our patient initially presented with urethritis at the same time as his partner had diarrhoea due to intestinal microsporidiosis. We believe he was persistently infected, or reinfected, by his partner during regular unprotected sexual intercourse. Four months later our patient developed diarrhoea and microsporidium was detected in his stool. He received a four week course of albendazole 400 mg bd. It was this course of therapy that finally cleared his symptoms of urethritis. It is likely that the urethritis responded to the albendazole, which is known to treat successfully microsporidial infections.^{4,5,6} However, it was at this time that his partner died, so it is possible that his lack of relapse was partially due to the fact that he was no longer being sexually exposed to microsporidia. Our patient died from multiple opportunistic infections three months later, but the urethritis never recurred.

We suggest that microsporidia represents an unlooked for cause of sexually transmissible urethritis. Microsporidia should be looked for actively in all non-responsive cases of urethritis in the immunocompromised. A study to this effect is currently underway.

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Vertical transmission of human papillomavirus in cytologically normal women

The sexual transmission of genital type human papillomavirus (HPVs) has been recognised since 1971, but clinical, epidemiological and laboratory evidence suggests that other ways of transmission can be important especially in children.^{1,2} In our department we conducted a polymerase chain reaction (PCR) based study with the following aims: (1) to evaluate the prevalence of HPV DNA in vaginal swabs of pregnant women clinically and cytologically free from HPV; (2) the prevalence of HPV DNA in nasopharyngeal aspirate of newborns and the frequency of perinatal transmission of HPV; (3) to evaluate the reliability of a single-point PCR test to predict the risk of perinatal transmission in clinical practice. For this purpose vaginal swabs were obtained from 124 pregnant women during the last three months of pregnancy and nasopharyngeal aspirates were collected, immediately after vaginal delivery, from 109 neonates born in the same hospital. All samples were coded and processed without knowing the presence and/or identity of mother/baby pairs. For HPV amplification and identification the protocol described by Bauer *et al* was used.³ Briefly, HPV DNA was amplified with consensus primers MY09-MY11 and the presence of amplified DNA was checked by Southern blot hybridisation with a generic and type specific probes for HPV 6, 11, 16, 18, 31 and 33.³ Hybridisation analysis of the PCR products with the generic probe was positive in 15/124 (12%) vaginal swabs and 10/109 (9%) nasopharyngeal aspirates. HPV typing of vaginal swab amplicates disclosed HPV6/11 in two cases, HPV16/18 in one, HPV31/33 in two and was negative in the remaining ten cases (unidentified HPV) (table). HPV typing of nasopharyngeal aspirates amplicates disclosed HPV6/11 in two cases, HPV16/18 in one case and HPV31/33 in one case. The other 6 samples positive with the generic probe were negative with the type specific probes (unidentified HPV) (table). On opening the code, we found 47 mother-baby pairs. Among this subgroup, HPV DNA was

HPV identification in vaginal swabs and nasopharyngeal aspirates

	HPV positive	HPV 6/11	HPV 16/18	HPV 31/33	Unidentified
Vaginal swabs	15/124 (12.1%)	2	1	2	10 (66.6%)
Nasopharyngeal aspirates	10/109 (9.1%)	2	1	1	6 (60%)

demonstrated in 6/47 (12.7%) vaginal swabs and in 4/47 (8.5%) nasopharyngeal aspirates. In two cases both the mother and the neonate were HPV positive. One pair was concordant for HPV6/11 infection and the other was putatively concordant for unidentified HPV. In two cases the neonate was HPV positive (one HPV6/11 and one unidentified HPV) and the mother HPV negative and in four cases the mother was HPV positive (one HPV16/18 and three unidentified HPV) and the neonate negative. Our result is consistent with published data and again confirms that a substantial fraction of cytologically normal women is infected with HPV. The results of HPV typing in our female population may appear surprising. Our probes did not identify the HPV type in more than 60% of samples positive to the generic probe. This data seems to be in contrast with most published data according to which HPV 16 is the most frequent HPV type in cervical samples from apparently healthy women.⁴ However, our results also seem to be confirmed by data obtained at the Department of Pathology of Siena University where HPV amplification and typing is routinely carried out on cervical biopsies referred for histological evaluation. According to them more than 50% of HPV samples positive after amplification with MY09/MY11 primers were negative to type-specific PCR (R Santopietro, personal communication). It is therefore possible that HPV 16 is the most common HPV type among the most common genital HPV types but it is also likely that most amplified HPV will fall into the "unidentified" category, as already proposed by Schiffmann and Gravitt, when general-primers PCR protocols are used.⁵ In conclusion our results confirm previous observations on the frequency of HPV infection in apparently healthy women and show that these viruses can be transmitted vertically during delivery.⁶ Since this event may be the cause of laryngeal papillomatosis it is a matter of debate whether or not to perform a cesarean section in infected women. To date there are insufficient data to advocate the need of cesarean section in infected women⁷ and this position should be held until further studies will clarify the determinants of laryngeal papillomatosis. Our data also show that single-point sampling, which would have been useful for screening in clinical practice, is not a reliable method to assess the risk of vertical transmission of HPV for which multiple sampling in mothers and children is required.

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Cytomegalovirus retinitis in a healthy antiretroviral naive HIV positive male with a CD4 count of 277/mm³

Cytomegalovirus (CMV) retinitis is a common sight threatening complication of late HIV disease, occurring rarely with CD4⁺ lymphocyte counts above 100/mm³ and most frequently when the CD4⁺ lymphocyte count falls below 50/mm³.¹ Four cases of CMV retinitis occurring in HIV patients with CD4 counts greater than 200/mm³ have been described. In three of these cases, the CD4 counts were 255/mm³ and 235/mm³ and 355/mm³ at the time of CMV diagnosis.^{2,3} However, these patients were receiving zidovudine antiretroviral therapy which may complicate interpretation of CD4 counts. As demonstrated by Concorde,⁴ zidovudine may sustain CD4 counts without translating into clinical benefit. Although the reason for this is unclear, one suggestion was that zidovudine may alter the proportion of poorly functioning CD4 cells in the peripheral blood. In the fourth case, the patient had a CD4 count of 366/mm³ and although he had not previously had antiretroviral therapy, his CD4 count and immune function may have been altered by a previous splenectomy.⁴

We report a case of CMV retinitis occurring in a 42 year old HIV seropositive homosexual man, who was antiretroviral naive, in good health with no prior AIDS defining diagnosis and no other immunocompromising condition. He presented with a history of "floaters" preceding the development of a shadow in the vision of his right eye. He had a relatively stable