Prevalence of antibodies to HPV16-E7-protein does not differ between AIDS-patients with and without Kaposi's sarcoma

Modern ideas about Kaposi's sarcoma (KS) centre around its relationship to the lymphoid system, immunological mechanisms, a genetic predisposition and the question of viral origin. The hypothesis that the cause of KS in patients with AIDS is an infectious agent that is different from HIV is supported by the report of KS in HIV-seronegative homosexual men. Emphasis had been placed on agents more readily sexually transmitted among homosexuals men in the USA and among heterosexual black men and women in Africa. The observation that KS is less frequently associated with parenterally than with sexually transmitted HIV suggests that the causative agent may not normally be present in the blood. In this context it is noteworthy that KS is rarely seen in women with AIDS in the USA. In contrast, the tumour is more common among female sexual partners of bisexual men (3%) than among those of exclusively heterosexual intravenous drug users (0-7%).

Although several lines of evidence had linked cytomegalovirus (CMV) to the classic and endemic African forms of KS and AIDS-KS, subsequent studies have not confirmed the presence of CMV sequences in the DNA of various KS tissues. Recent, papillomaviruses have been considered further candidates for the agent of AIDS-KS. This is based on the increasingly frequent detection of HPV16 and HPV18 in the anorectal mucosa of homosexual men in Europe and USA, and the possible association of these viruses with anal intraepithelial neoplasia and anal cancer.

Biggar and coworkers contrasted the previously presented findings suggesting the presence of human papillomavirus (HPV) type 16 DNA and papillomavirus related common antigen in both AIDS-related KS and endemic (HIV-negative) KS.

If HPV 16 was involved in the development of AIDS-KS, antibodies reactive with the early proteins of this HPV type should be significantly more prevalent in sera from HIV-positive patients suffering from AIDS-KS, than in sera from HIV-positive patients without evidence of a KS. We analysed a total of 48 sera from HIV-positive men by Western blot technique for the presence of antibodies against HPV 16-E7 protein, because particularly anti-E7 antibodies were shown to be more prevalent in patients with cervical cancer associated with HPV 16 than in controls. Sixteen sera were from HIV-positive patients with an AIDS-KS, 16 sera from HIV-positive homosexual men and 16 sera from HIV-positive male intravenous (iv) drug abusers.

For the expression of the E7 gene of HPV 16 a Sau 3 A fragment of HPV 16 DNA (+622-870), whose sticky ends were filled by Klenow polymerase, was inserted into the EcoRV site of pROS. The E7 protein was synthesised in bacteria as a fusion protein, separated from the α-galactosidase part by cleavage with the protease FXa and used for Western blot analysis as described before.

Eighteen out of 48 sera (37.5%) were positive for anti HPV 16–E7 antibodies (table). Five out of 16 (31.25%), 7/16 (43.75%) and 6/16 (37.5%) of the homosexual KS patients, the iv drug addicts and the male homosexual patients without KS, respectively, revealed these serum antibodies. The results indicate a seroprevalence of anti HPV 16–E7 antibodies in these 48 HIV-positive male patients which is by far higher than in the general population (4%) and even higher than in virologically uncharacterised cervical cancer cases (20-5%).

From our serological studies there is no evidence, however, that HPV type 16 is a possible KS agent, since no differences in the seroprevalence were seen between the three different patient groups. The immunocompromised state of HIV infected patients allowing a reactivation of persistent HPV infections may be responsible for increased values.

Our preliminary serological observations underline ongoing HPV DNA in situ hybridisation studies of AIDS-KS using probes for HPV 6, 11, 16, 18, 31, 33, 35 and an omniprobe which were so far negative for HPV DNA and which are in line with the negative in situ hybridisation results of Biggar and coauthors.

Thus it is very unlikely that these most common sexually transmissible HPV types play a causal role in the pathogenesis of KS. However, the possibility that so far unknown or less investigated virus types are involved in the aetiology of KS cannot be ruled out. Therefore the need is emphasised to investigate KS tissue for the presence of other HPV specific DNA sequences using more meticulous molecular biologic techniques such as the polymerase chain reaction.

### Table HPV 16-E7 Antibodies in HIV-seropositive men

<table>
<thead>
<tr>
<th>N</th>
<th>+</th>
<th>+ +</th>
<th>+</th>
<th>+</th>
<th>negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS-KS patients</td>
<td>16</td>
<td>5/16</td>
<td>31.25%</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>IV drug abusers</td>
<td>16</td>
<td>7/16</td>
<td>43.75%</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Homosexual men without KS</td>
<td>16</td>
<td>6/16</td>
<td>37.5%</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td>18/48</td>
<td>37.5%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Letters to the Editor


Accepted for publication 27 September 1993.

Screening for genital Chlamydia trachomatis infection in female patients

Chlamydia trachomatis is a major sexually transmitted pathogen with consequent serious morbidity such as pelvic inflammatory disease, tubal occlusion, and infertility in women. The prevalence varies in different parts of the world.1 2

The usual site chosen to screen for this pathogen is the cervix.3 4 In our clinic, the urethra and the cervix are also tested. We report the findings from our Department of Genitourinary Medicine in Sunderland, Tyne and Wear, United Kingdom.

Between the period of 1 January 1991 and 31 December 1991, 1461 women were screened (for sexually transmitted diseases). The ELISA method (Chlamydiazyme) was used in screening for Chlamydia trachomatis, while Gram stain and culture were used for the detection of gonorrhoea.

The results in the table show that 116 patients were positive for Chlamydia trachomatis, 22 were positive for N gonorrhoea while five patients had both conditions. Among the 11 patients with only urethral Chlamydia trachomatis eight (72%) were asymptomatic.

Infection of the female urethra by Chlamydia trachomatis has been previously reported.5 6 The female urethra is about 4 cm long and various ducts open into its lumen. Of particular importance are the ducts of Skene glands and ducts which are lined by columnar epithelium.

The positive yield of Chlamydia trachomatis from the urethra alone in our clinic was 9-5%. The implications of this result are threefold. First, colonisation of the female urethra by Chlamydia trachomatis may contribute to some patients being diagnosed with female urethral syndrome. In this condition, the patient has increased frequency of micturition, dysuria, but no significant bacteriuria. It is advisable to exclude Chlamydia trachomatis from the urethra of such patients. Secondly, the urethra may serve as a reservoir of infection despite a negative result from the cervix. The infection may subsequently be transmitted to the male partner. Thirdly, failure to screen the urethra may be responsible for some patients whose symptoms persist, despite negative results.

We recommend that the urethra be screened for Chlamydia trachomatis.

A A OPANEYE
K M SARAVANA MUTTU
S RASHID
Department of Genitourinary Medicine, Sunderland District General Hospital, Kayl Road, Sunderland, SR4 7TR, UK

Address correspondence to: Dr A A Opameye

5 Dunlop EMC, Hare MJ, Darougar S, Treharne JD, Dewry RC. Isolation of chlamydia from the urethra of a woman. BMJ 1972;1:386.

Accepted for publication 12 October 1993

HIV seroprevalence among eunuchs

Eunuchs (hijras) and their existence is well described in ancient Indian texts.1 In India, hijras are seen as a “third gender” role which is neither male nor female but contains elements of both. He is an intersexed impotent man

Number of patients with positive findings from different sites

<table>
<thead>
<tr>
<th>Location</th>
<th>Chlamydia n = 116</th>
<th>Gonorrhoea n = 22</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Urethra only</td>
<td>11 (9-5)</td>
<td>1 (4-5)</td>
<td></td>
</tr>
<tr>
<td>2 Cervix only</td>
<td>70 (60-3)</td>
<td>6 (27-3)</td>
<td>p &lt; 0-05</td>
</tr>
<tr>
<td>3 Urethra and cervix</td>
<td>11 (9-5)</td>
<td>5 (22-5)</td>
<td></td>
</tr>
<tr>
<td>4 Cervical involvement (2 + 3)</td>
<td>10 (9-5)</td>
<td>18 (81-8)</td>
<td></td>
</tr>
<tr>
<td>5 Urethral involvement (1 + 3)</td>
<td>46 (39-7)</td>
<td>14 (63-6)</td>
<td></td>
</tr>
<tr>
<td>6 Rectal involvement</td>
<td>5 (4-3)</td>
<td>7 (31-8)</td>
<td></td>
</tr>
<tr>
<td>7 Pharyngeal involvement</td>
<td>3 (13-6)</td>
<td>3 (13-6)</td>
<td></td>
</tr>
</tbody>
</table>

Among the 11 patients with urethral chlamydia alone, 8 (72%) were asymptomatic.