sexual partners over the 3 years prior to entry in the study. Compared with subjects reporting no or one sexual partner, the OR were 1.2 for those reporting two to five sexual partners and 1.4 for six or more; the trend in risk however was not statistically significant. No relationship emerged with age at first intercourse. Compared with men with no homosexual intercourse, the OR for HBsAg positivity was 1.6 (95% CI 0.8–4.2) for those reporting homosexual intercourses. An about twofold increased OR of HBsAg positivity was associated with TPHA positive assay (OR 2.6, 95% CI 1.1–6.3) and HIV status (OR 2.3, 95% CI 1.0–6.4), but no relationship emerged with the results of VDRL test.

This study included subjects from a population at high risk of HBV infection (subjects attending STD clinics) and cannot be considered representative of the general population. Nevertheless these results may in relative terms offer some quantitative estimates of the role of major determinants of HBsAg positivity in Italy. The results of this study are in general agreement with studies from other populations. The frequency of HBsAg positivity becomes more frequent with age (although it is not understood whether this is due to an age or cohort effect)^{2,3} and the male-female ratio of HBsAg prevalence was reportedly greater than unity in several countries.^{3,4} In this study intravenous drug use and number of heterosexual partners explained respectively 19% and 12% of HBsAg positive cases. In the USA, the proportion of HBV infected males in the late 1980s accounted for by parenteral drug use and heterosexual exposure were respectively 27% and 26%.⁵ Another finding is the positive relation between history of STD, TPHA positive test and HBsAg positivity. No relationship emerged, however, between VDRL test results and HBsAg positivity. According to the specificity of these tests for syphilis and their different reactivity in early and late stages of the infection, it is conceivable that an association of HBsAg with TPHA, but not with VDRL, could be observed if both hepatitis infection and syphilis had similar modality of transmission and the two infections occurred in the same period in the past. More in general, the association between TPHA and HBsAg positivity may be interpreted in terms of similar risk factors or of an easy way of infection for HBV in patients with vaginal infection.

Finally, HIV infection was strongly related with the risk of HBsAg positivity and this finding persisted after taking into account the effect of drug use and number of partners. This suggests that specific high-risk behaviours may be the underlying "mechanism" favouring both HIV and HBsAg positivity, for example, unprotected promiscuity in subjects with a high number of sexual partners or exchange of needles by intravenous drug users.

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- 1 Parazzini F, Naldi L, Sena P, *et al*. Risk factors for HIV infection in adults attending sexually transmitted disease clinics in Italy. *Int J Epidemiol* 1991;20:758–63.
- 2 Toukan AU, Sharaiha ZK, Abu-El-Rub OA, *et al*. The epidemiology of hepatitis B virus among family members in the Middle East. *Am J Epidemiol* 1990;132:220–32.
- 3 Centers for Disease Control. Racial differences in rates of hepatitis B virus infection. United States, 1976–1980. *MMWR* 1989;38:818–21.
- 4 Tsega E, Mengesa B, Hansson B-G, Lindberg J, Nordenfelt E. Hepatitis A, B and delta infection in Ethiopia: A serologic survey with demographic data. *Am J Epidemiol* 1986;123:344–81.
- 5 Alter MJ, Hadler SC, Margolis HS, *et al*. The changing epidemiology of hepatitis B in the United States. *JAMA* 1990;263:1218–22.

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Emerging incidence of vulval intra-epithelial neoplasia in young women with genital warts

Historically, vulval intra-epithelial neoplasia (VIN) has been considered to be an uncommon disease, seen usually in the post-menopausal woman. In a study at The Middlesex Hospital in London, the mean age for females with VIN was 63 years¹ although recent reports from Campion *et al*² suggest a modal age of 30 years and that the incidence in the young female is increasing.

In our clinic, in the short space of 11 months, we have diagnosed nine cases of VIN and we feel its incidence is probably even commoner in young females than it is generally believed to be, especially amongst those attending genitourinary clinics.

All new patients with genital warts were questioned to assess the presence or absence of pruritus, burning, dyspareunia or discolouration of skin. These are the commonest symptoms of VIN. All patients denied past histories of sexually transmitted diseases (STDs), including HSV. All suspicious lesions were biopsied. Of 11 cases biopsied, nine showed VIN on histology (table). The other two showed hyperkeratosis and wart virus changes but no VIN. Seven of the nine positives were graded as VIN III. All of them had colposcopies and four (44.5%) were found to have CIN.

The nine females with VIN had a mean age of 31.3 (range 19–57) and 6 (67%) had solitary vulval patches.

Routine tests for candida, *T vaginalis*, *G vaginalis*, gonorrhoea, *Chlamydia trachomatis* and syphilis serology were negative. Cervical

Table Profile of patients

No	Age	Signs & symptoms	Histology	STDs	CIN
1	39	Warts, Pruritus, Hyperpigmented pinkish patch	VIN II/III	none	neg
2	21	Warts, discomfort, pruritus	VIN II	none	I-1988(2 y prev)
3	33	Raised mauve patch	VIN III	none	I-1989(1 y prev)
4	57	Single wart/pruritus	VIN III	none	CIN I
5	38	Perianal wart, periclitiorial brown patch, pruritus	VIN III	none	neg
6	27	Irritation 4 y Exacerbation 1 y Pink brown lesion, pruritus	VIN III	none	neg
7	25	Pigmented warty area	VIN II/III	none	II/III
8	23	Warts	VIN I	none	neg
9	19	White patches 2 y	VIN II/III	History of gonorrhoea	II
10	26	Pruritus 6 months	VIN III	none	Wart Virus Change
11	17	Brownish lesions, pruritus	Acanthosis & keratosis	none	Focal inflammation
		Warts, discomfort, pigmented areas	Seborrheic keratosis	none	No CIN
		Blackish spots, irritation			CIN I

cytology was normal, except in cases 2 and 3, where dysplasia was reported.

Though VIN has been thought of as a rare phenomenon up to about 15 years ago, more recent reports indicate a higher prevalence and at a younger age—as does our small series of nine patients in 11 months. Most reports indicate a close association with HSV and other STD.³ We are unable to substantiate this, as none of our patients had associated STDs except warts. An association between CIN and VIN has been known and this was confirmed in four of our nine patients who had CIN too, even though Pap smears were negative. The clinical appearance of VIN is all important and cannot be overstated. Campion aptly reports that it is the most “productive diagnostic technique”.² Lesions are papular or macular, single or multiple, and over 60% are hyperkeratotic. In our series, contrary to published reports,⁴ 67% were solitary: pruritus in seven (78%) of the nine was the main presenting feature. None of our patients were immunocompromised⁵ though this is a known at-risk group.

Detection of VIN with Toludene blue is not reliable with false negative/positive results being common. Colposcopy is a better diagnostic tool.

In a series of 10 patients with co-existing proven CIN, biopsy of suspicious warts failed to substantiate the correlation that is said to exist between CIN and VIN.² We suspect that the same process that leads to CIN also leads to VIN but in the more resistant vulval skin, it takes longer to manifest. The hypothesis that VIN is more likely to follow CIN is now under investigation, following the chance finding of CIN in our VIN patients.

If this hypothesis were true, then any patient with VIN must also have/had CIN but this is not always the case. In our patient group, 50% were reported to have CIN compared with 20% reported to date.² We believe VIN is of multifactorial aetiology, some of which have yet to be identified. The possible presence of CIN should be investigated in the presence of VIN.

Though the malignant potential of VIN is uncertain, the intraepithelial changes may persist for long periods to accelerate rapidly at a later stage. The associated risk of neoplasia of other sites in the genital tract in general, and

cervix in particular, should trigger the clinician to be vigilant at all times.

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1 Graham A Barker. *Progress in Obstetrics and Gynaecology* 1990;25:389.
2 Campion MJ, Singer A. Vulval intraepithelial neoplasia: clinical review: *Genitourin Med* 1987;63:147–52.
3 Kaufman RH, Dreesman GD, Burek J. Herpes virus induced antigens in squamous cell carcinoma in situ of the vulva. *N Engl J Med* 1981;305:483.
4 Townsend DE, Levine RU, Richart RM, Crum CM, Petrilli ES. Management of vulvar intra epithelial neoplasia. *Obstet Gynaecol* 1982;60:49.
5 Woodruff JD, Hildebrandt EE. *Obstet Gynaecol* 1958; 12:414.

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Prodromal symptoms in genital herpes simplex infection

Many individuals with genital herpes simplex virus (HSV) infection report that they are able to predict at least a proportion of attacks through warning prodromal sensations. However the frequency and reliability of such sensations is not known.

The consistent use of condoms during intercourse will reduce the risk of transmission of HSV. However, the use of condoms is not always possible either because a couple desire a pregnancy or one or other partner is unwilling to use condoms. Under these circumstances warning sensations may be of value in reducing the risk of transmission if, in an individual, they reliably predict the onset of an attack and that individual makes appropriate changes in their sexual behaviour.

Ninety subjects suffering from recurrent genital herpes simplex virus infection (HSV), aged 19–60 years (mean, 34 years), 40 men and 50 women, were recruited from members of the Herpes Association (n = 60) and from a genitourinary medicine clinic (n = 30). The Herpes Association patients were sent a postal questionnaire (return rate = 60%). GUM clinic patients were approached while in the clinic (participation rate 100%). Subjects were asked about the frequency with which they experienced two different premonitory symp-