Minor degrees of cervical intraepithelial neoplasia

Time to establish a multicentre prospective study to resolve the question

No longer is there argument that cervical screening can reduce deaths from cervical cancer. There is also agreement that the incidence of cervical intraepithelial neoplasia has risen appreciably in recent years[1,2] and that without intervention deaths from cervical cancer in the 1990s will rise by 70% or more.[3,4] The debate is now centring on what proportion of cases of cervical intraepithelial neoplasia will progress and over what period of time.

Introduction of the call and recall screening programme for cervical cancer in Britain in 1987 reflected a determined effort to detect the hidden pool of cervical intraepithelial neoplasia (and occult invasive carcinoma) but is beginning to highlight problems relating to the efficacy of cervical cytology and how to manage the woman with an abnormal smear result. Cervical cytology seems to be the only practical way of detecting cervical intraepithelial neoplasia, but even the best laboratories have admitted to a false negative rate of 10-15%—and recent work suggests that this may be a gross underestimate. Giles *et al* screened women with both cytology and colposcopy and found that the prevalence of cervical intraepithelial neoplasia was 5% when detected by cytology alone but increased to 11% when cytology and colposcopy were used together, and the overall false negative rate for cytology in patients with all grades of cervical intraepithelial neoplasia was 32%.[5] Reassuringly cytology detected all patients with cervical intraepithelial neoplasia grade III (carcinoma in situ). On the other hand, the false negative rate for small grade I and grade II lesions was 58%, a finding that was especially alarming since 6% of the population has these lesions. But is it as alarming as it seems? Four fifths of their patients with cervical intraepithelial neoplasia showed evidence of infection with human papillomavirus and since the highest false negative rate was in patients with grade I and grade II cervical intraepithelial neoplasia the debate must be reopened on whether these grades truly reflect a preinvasive disease or whether some are no more than changes caused by infection with human papillomavirus without the potential to progress.

Of a group of 45 patients referred to a colposcopy clinic with cytological abnormality and found to have no more than infection with human papillomavirus, 26 underwent spontaneous regression over a median period of 28 months.[6] Campion *et al* studied 100 women with cytological and colposcopical evidence of cervical intraepithelial neoplasia grade I and reported that regression over two years occurred in only seven, whereas the lesion progressed to cervical intraepithelial neoplasia grade III in 26.[7] Conversely, Woodman *et al* reported to the Australian Society of Colposcopy and Cervical Pathology in 1987 that in 80 women with histologically proved cervical intraepithelial neoplasia grade I or II with associated infection with human papillomavirus the lesions regressed in 32, there was no change in 27, and there was progression to cervical intraepithelial neoplasia grade III over a median period of 11 months in 20 (unpublished data). This raises the question of the importance of cervical intraepithelial neoplasia with or without associated infection with human papillomavirus and is of more than academic interest because the aim of any screening programme is to detect and treat cervical intraepithelial neoplasia at its earliest stage. As a result more and more women, especially younger women, are now being referred to colposcopy clinics for assessment of even the most minor cytological abnormality. This is not only putting an intolerable burden on existing colposcopy units but is also resulting in the treatment of some patients who probably do not need it. Such referrals put increasing stress on the patient even to the extent of causing psychosexual problems.[8]

Prospective study

In an attempt to sort out this dilemma Robertson *et al* have prospectively studied the clinical course of patients with a mild dyskaryotic smear who had not been treated (p 18). The patients were followed up by cytology alone, a test being taken every six months. Referral to a colposcopy clinic was made if the mild dyskaryosis persisted for 18-24 months, if the smear showed more dyskaryosis, or if the patient had abnormal bleeding or a cervix that looked abnormal on clinical examination. Their results confirm that a single smear result can underestimate the severity of epithelial abnormality, but in just under half the patients the cytological changes reverted to normal without treatment. In only one instance did cytological surveillance fail: the patient was later found to have invasive carcinoma. The authors emphasise that this was a patient who was observed throughout a pregnancy and who had also undergone colposcopy.

Finally, there is debate about the age at which screening should start. A report from the Lothian area colposcopy clinic states that 33% of patients referred with abnormal smears were under 20; the authors suggest that screening should start before this age (p 29). Others might argue that these young women are at no appreciable risk of developing cervical cancer even if their first smear was delayed until 20.

Everyone working in cervical cytology aims to detect and treat cervical intraepithelial neoplasia, but until the true importance of cervical intraepithelial neoplasia grades I and II and infection with human papillomavirus is known there will be different opinions on whether to treat these minimal lesions. Until this question is resolved many women, especially young women, will suffer the anxiety of referral to colposcopy clinics and may even be subjected to treatment which will eventually be shown to have been unnecessary. Individual units have done their best to resolve these problems, but surely the time has now come when we should establish a multicentre prospective study finally to settle the problem.

J A JORDAN

Consultant Gynaecologist,
Birmingham and Midland Hospital for Women,
Birmingham B11 4HL

1 Roberts A. Cervical cytology in England and Wales, 1965-1980. *Health Trends* 1982;**14**:41-3.
2 Wolfendale MR, King S, Usherwood MMCD. Abnormal smears: are we in for an epidemic? *Br Med J* 1983;**287**:526-8.
3 Beral V. Prediction of cervical cancer incidence and mortality in England and Wales. *Lancet* 1986;i:495.
4 British Medical Association. *Cervical cancer and screening in Great Britain*. London: British Medical Association, 1986.
5 Giles JA, Crow J, Walker P, Hudson E, Williams D. Colposcopic assessment of the accuracy of cervical cytology screening. *Br Med J* 1988;**296**:1099-102.
6 Woodman CBJ, Byrne P, Fung S, Wade-Evans T, Jordan JA. Human papillomavirus infection of the cervix—a self limiting disease? *Colposcopy and Gynaecological Laser Surgery* 1986;2:9-13.
7 Campion MJ, McCance DJ, Cuzick J, Singer A. Progressive potential of mild cervical atypia: prospective cytological, colposcopic, and virological study. *Lancet* 1986;ii:237-40.
8 Campion MJ, Brown JR, McCance DJ, *et al*. Psychosexual trauma of an abnormal cervical smear. *Br J Obstet Gynaecol* 1988;**95**:175-81.