Cytological screening for cervical cancer and human papillomavirus in general practice

E Hiscock, G Reece

Abstract

In a retrospective study of cervical screening in a general practice in Birmingham 156 out of 1913 smears taken over three years showed some abnormality. Smears from 65 women showed severe non-specific inflammation, and 91 women had various grades of cervical intraepithelial neoplasia, of whom 53 were aged under 30 and 13 over 40. Of 35 women with clinical evidence of human papillomavirus, 21 had normal results on cervical testing and 14 abnormal results.

The incidence of genital warts among sexually active young people is growing, but the association of human papillomavirus with abnormal cervical smears is not clear. The efficacy of screening in the United Kingdom must be improved by actively encouraging younger patients to attend for regular screening.

Introduction

Over the past few years controversial evidence has suggested that human papillomavirus is associated with the development of cervical cancer. Human papillomavirus 16 and 18 sequences have been found in a high proportion of cervical carcinomas.¹ Cases of genital warts seen at clinics for sexually transmitted diseases in the United Kingdom have increased from 20 334 in 1973 to 49 884 in 1984.² Exophytic condylomas have been reported in up to 6% of women with vulval warts,^{3,5} and genital warts are common in women who attend gynaecology clinics and clinics for sexually transmitted diseases. Numerous reports have attempted to link the incidence of human papillomavirus infection with abnormal results of cervical screening but we do not know of any reports of screening for cervical cancer and human papillomavirus in a general medical practice.⁶

Recent reports show that the overall death rate from cancer of the cervix has declined but the death rate in younger age groups has increased. Between 1968 and 1984 deaths from cervical cancer fell from 12.53 to 9.10 per 100 000, but in women aged under 30 they increased more than fourfold from 0.22 to 0.91 per 100 000. Further rises are predicted in this younger group, which will cause a decrease in the overall downward trend in mortality in the next 10 years unless effective intervention by cervical screening is undertaken.^{7,8}

Several reports from different countries have shown that screening of the population has been followed by a decrease in the incidence of invasive disease.^{9,10} In 1964 a large scale cervical cytological screening service was started in Britain; since then mortality from cervical cancer has declined at 1% a year.^{11,12}

We report the findings of cervical screening in our general practice and give details of four women under 30 with grade III cervical intraepithelial neoplasia, three of whom had human papillomavirus infection.

Patients and methods

Our general practice is an inner city suburb of north Birmingham and has a list size of 9900 patients, of whom 3301 are women aged 16-65. Organised screening for cervical cancer was started in 1984 for all National Health Service patients who were:

Women aged 16-65 who were sexually active; those attending for maternity care, gynaecological conditions, or family planning consultations; and patients who on their own initiative requested the service.

All women who had not had a smear in the past five years were identified from the age-sex register of the practice and invited to attend for screening.¹³ Patients who had had an abnormal smear before January 1985 were also invited for rescreening; these patients are not reported on here. When personally approached few women declined the opportunity to have a smear test.

When the smear was taken the external genitalia were examined for any lesions and especially for genital warts and the appearance of the cervix was noted. Patients with visible warts were treated in the surgery with podophyllin. Patients reported to have severe non-specific inflammation or cervical intraepithelial neoplasia grade I were called for repeat smear tests at appropriate intervals,¹⁴ and subsequent smears were referred to a gynaecologist. Patients reported to have moderate dysplasia compatible with cervical intraepithelial neoplasia grade II were given repeat smear tests after three months and then referred for colposcopy. All patients with severe dysplasia found to be compatible with cervical intraepithelial neoplasia grade III were immediately sent to the gynaecological department of Birmingham Women's Hospital for colposcopy and biopsy. Any warts found on colposcopy were treated in the department of gynaecology with a laser.

Results

Of 1913 initial smears taken over three years, 156 showed some cytological abnormality (table I). The 65 cases of severe non-specific inflammation entailed many repeat smears, which showed no change over three years, and no microbiological cause of the inflammation was discovered. The remaining 91 smears showed cervical intraepithelial neoplasia, which was classified as grade I in 42, grade II in 34, and grade III in 15. Five of the patients with cervical intraepithelial neoplasia grade III had not had a smear in 10 years, but in the 10 others smears had progressed from showing no abnormality or cervical intraepithelial neoplasia grade I to showing cervical intraepithelial neoplasia grade III in an average of 33 months, with a range from 4 months to 8 years.

Thirty five women had clinical evidence of human papillomavirus infection, of whom 21 had normal cervical smears. Of the remaining 14, two had had

Streetly Road Surgery,
Erdington, Birmingham
B23 7AH
E Hiscock, MB, principal
G Reece, SRN, practice nurse

Correspondence to:
Dr Hiscock.

recurrent infections with herpes simplex virus. Colposcopy confirmed human papillomavirus infection in 10 women who had cervical intraepithelial neoplasia, six who showed viral effects on the cervical smear, and four who showed no viral effects; nine of these were aged under 40 and were symptomless. Of the 91 patients with cervical intraepithelial neoplasia, 22 were shown either clinically or colposcopically to have human papillomavirus infection (table II). In a further 30 cases the smear showed "viral effects"; these were later attributed to koilocytotic atypia.

Altogether 53 women were aged under 30 when cervical intraepithelial neoplasia was diagnosed (30 with grade I disease, 18 with grade II, and six with grade III), 12 were 30-35, 13 were 35-40, and 13 were over 40; the average age of women with cervical intraepithelial neoplasia was 29.9 years.

TABLE 1—Results of initial cervical screening in women attending general practice, January 1985 to December 1987* (n=1913)

	No
Normal smear:	
Unrepeated	1731
Viral effects evident	5
Genital human papillomavirus present	21
Severe non-specific inflammation:	
Clinically normal	63
Genital human papillomavirus present	2
CIN grade I:	
Clinically normal	39
Genital human papillomavirus present	3
CIN grade II:	
Clinically normal	27
Genital human papillomavirus present	7
CIN grade III:	
Clinically normal	13
Genital human papillomavirus present	2

CIN=Cervical intraepithelial neoplasia.

*Results of repeat tests and of repeat smear tests for 52 women with cervical intraepithelial neoplasia discovered before January 1985 are not included.

TABLE II—Prevalence of human papillomavirus and cervical dysplasia in women attending general practice, January 1985 to December 1987

Results of cytological screening colposcopy	Grade of cervical intraepithelial neoplasia			Total (n=91)
	I (n=42)	II (n=34)	III (n=15)	
Cervical intraepithelial neoplasia only	21	10	8	39
"Viral effects" on smear testing	16	12*	2	30
Clinical evidence of human papillomavirus:				
Alone		4†	1	5
With viral effects in smear	3	3	1	7
Colposcopic evidence of human papillomavirus:				
Alone	2	1	1	4
With viral effects in smear	NA	4	2	6

NA=Not available.

*One patient had previously been infected with herpes simplex virus.

†One patient had previously been infected with herpes simplex virus and human papillomavirus.

Four patients under the age of 30 with cervical intraepithelial neoplasia grade III were of particular interest. The first had had a normal smear in 1977, when she was 21. A smear taken eight years later was graded as showing grade III disease; a biopsy showed invasive adenocarcinoma. She was treated by radical hysterectomy and vault radiotherapy early in 1986. The second patient was found at the age of 16 to have cervical intraepithelial neoplasia grade II, which had progressed to grade III by the next year. At the age of 14 she had suffered a protracted attack of cervical, vulvovaginal, perineal, and anal warts, which had been treated initially with podophyllin and later, after she was referred to a gynaecology clinic, with laser treatment. The third patient with cervical intraepithelial neoplasia grade III was 23 when her smear showed viral effects with cervical intraepithelial neoplasia grade II; seven months later this had progressed to grade III. Colposcopy showed grade II disease and human papillomavirus infection. She was given laser treatment. The fourth patient, a 29 year old

mother of two, had had a cervical smear five years previously. A routine smear taken when she attended for family planning advice showed cervical intraepithelial neoplasia grade II, and three months later grade III disease was evident. Colposcopy found high grade disease and early invasion. After laser excision histological examination confirmed grade III disease with glandular atypia and human papillomavirus infection.

Discussion

For many years the NHS has been complacent about cervical screening in general practice: the onus has been on women to present themselves at clinics and doctors' surgeries for this service, and health authorities have provided only limited facilities in cytology laboratories for smears to be checked. Most of the 91 patients (4.8%) found to have cervical intraepithelial neoplasia in this study would have been missed if they had not been actively encouraged to present for screening. In 87 of these women the neoplasia was found at an early stage, when treatment offers excellent results.

Condyloma acuminata of the cervix (exophytic condyloma) has been associated with characteristic findings of koilocytosis, dyskeratosis, and nuclear atypia on cytological examination.¹⁵ Human papillomavirus types 16 and 18 sequences have been found in a high proportion of cervical carcinomas and cases of cervical intraepithelial neoplasia; the human papillomavirus 16 sequence is reportedly more commonly found in invasive cervical cancers.¹ Meanwell *et al* suggested that the cause of cervical cancer is mediated by age.⁵ Our study found clinical evidence of human papillomavirus infection in 35 women, and on colposcopy in a further 10. Most of these women were under 40 years old and had no symptoms of cervical intraepithelial neoplasia.

Five smears were reported as normal but showing probable viral effects, and 30 smears were reported as showing cervical intraepithelial neoplasia and probable viral effects. The exact relevance of viral effects in cervical intraepithelial neoplasia is not clear; these lesions need to be carefully studied by Southern blot analysis and hybridisation for a full understanding of genital warts.

Mortality from cervical cancer has a strong social class gradient, the highest rate being found in social classes III, IV, and V.⁷ Patients in our practice are generally social classes III-V.

Pressure is growing for family practitioner committees to attempt a coordinated screening policy with cytology laboratories. The call and recall systems that are being introduced may produce more accurate figures for cervical disease.¹⁶ Nevertheless, the present complicated and bureaucratic system of remunerating general practitioners fails to encourage them to take cervical smears.

Though it is necessary to screen middle aged women, those cancers are currently not being identified until they are at an advanced stage, it is important not to become complacent about the younger age group. We strongly support the suggestion of Campion *et al* that all women whose cervical smear shows dyskaryotic cells should be referred for colposcopy, particularly as mortality in young women has increased appreciably.¹⁷ Our study shows that an age barrier cannot be placed on screening: 65 of the 101 women with cervical intraepithelial neoplasia (3.4% of initial smears) were less than 35 years old. Furthermore the incidence of genital warts is increasing in young people at an alarming rate. Though it is not possible to predict the potential importance and magnitude of this disease in the long term in this young group, the present

system does not allow for any monitoring. Screening should start much earlier if we are to prevent the untreatable cervical cancers in women over 40; extra pressure must be put on women at high risk so that they accept screening and attend when called. Many of these women are embarrassed about being examined; a large number adopt an ostrich approach and deny themselves routine tests through fear of an unfavourable diagnosis. Recall should be at least triennial if any difference in the mortality and morbidity from cancer of the cervix is to be achieved.

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