PRACTICE OBSERVED

*Practice Research***Colposcopic assessment of the accuracy of cervical cytology screening**

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Abstract

Two hundred asymptomatic women in a general practice were screened both cytologically and colposcopically for evidence of cervical intraepithelial neoplasia. The prevalence detected by cytology alone was 5%, but the prevalence detected by cytology and colposcopy together was 11%. None of the larger lesions of cervical intraepithelial neoplasia (affecting more than two quadrants of the cervix) was associated with negative cytology. The false negative cytology rate for smaller lesions was 58%.

The clinical importance of the smaller lesions that were not accurately detected by cytology screening is unknown. As these lesions affected 6% of the screened population further studies of their clinical course are urgently required. Local destructive treatment in such cases may represent considerable overtreatment. If these lesions prove to be clinically important, however, the results of this study predict an increasing epidemic of preinvasive and invasive disease of the cervix.

Introduction

The incidence of preinvasive squamous carcinoma of the cervix has risen dramatically in recent years, and some authorities have referred to it as an epidemic.^{1,2} Without considerable improvements in screening programmes for cervical intraepithelial neoplasia it has been estimated that mortality from cervical carcinoma will rise by 70% by the 1990s.³ The British Medical Association has suggested that this is a conservative estimate.⁴ Because cervical cancer can be prevented by simple treatment of cervical intraepithelial neoplasia,⁵ often on an outpatient basis, it is vital that screening programmes identify all women at risk of cervical cancer while the disease is in its preinvasive stage.⁶ Recent articles suggest that the use of colposcopy in addition to cytology for screening might establish the true prevalence of cervical intraepithelial neoplasia and also the rate of false negative results for cytology alone.^{7,8}

This study reports the findings of the first five months' experience of a combined cytology and colposcopy screening service established in a general practice.

Patients and methods

A cervical screening service, combining cytology and colposcopy, was offered to all adult female patients of a general practice on the borders of London and Hertfordshire, irrespective of when they had had their last cervical smear. Details of the service, explaining the use of the colposcope, were described in a leaflet that was freely available at the practice reception and in all the doctors' consulting rooms. The practice was in a predominantly middle class area and had 2879 female patients over the age of 21.

Once a medical and cytological history had been taken, all patients were examined by one of the authors (JG). A cervical smear was taken by rotating a wooden Ayre spatula twice through 360° over the transformation zone. Then a standard colposcopic examination was performed with solutions of normal saline, 5% acetic acid, and Lugol's iodine. Biopsy specimens were

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taken from any abnormal areas of the epithelium⁹ (with the patient's consent) using Eppendorpher biopsy forceps. The specimens were fixed in formolsaline and sent for histological examination.

All the cytology specimens were independently screened and reported on by both EH and DW.¹⁰ The histological specimens were first reported on by the Royal Free Hospital histopathology service and then reviewed blind by JC.^{11,12}

Each consultation lasted roughly 15 minutes. Results of these examinations were communicated to both the patient and the general practitioner and suitable arrangements made for further follow up or treatment, as indicated.

Results

In the first five months after the introduction of the service 231 women were seen. Fourteen were referred by their general practitioner, either because of a recent abnormal smear result or because of abnormal vaginal bleeding. All other patients attended of their own accord or had been advised that they were due to have a cervical smear.

TABLE I—Details of patients with a diagnosis of cervical intraepithelial neoplasia

Case No	Results of histology (Cervical intraepithelial neoplasia grade)	Age	Time since last normal smear (years)	Results of cytology
1	3	44	4.6	Severe dyskaryosis
2	3	25	0.25	Severe dyskaryosis
3	3	29	1.0	Severe dyskaryosis
4	3	28	3.5	Mild dyskaryosis
5	Pregnant	22	2.0	Moderate dyskaryosis
6	2	50	1.0	? Reliable
7	2	35	1.0	Negative*
8	2	26	3.0	Negative
9	2	34	2.5	Negative
10	1	39	2.0	Moderate dyskaryosis
11	1	28	1.5	Mild dyskaryosis
12	1	53	1.0	Mild dyskaryosis
13	1	25	3.9	Mild dyskaryosis
14	1	40	10.9	Very mild dyskaryosis
15	1	28	1.1	Insufficient
16	1	29	2.8	Unsatisfactory
17	1	28	2.1	? Reliable
18	1	19	1.5	? Reliable
19	1	30	0.5	Negative*
20	1	31	6.5	Negative*
21	1	45	2.25	Negative*
22	1	43	1.5	Negative*

*Endocervical cells present.

who had been screened before was two years (range three months to 21 years). Ten women (5%) had never had a cervical smear.

There was a close correlation between the cytology reports of EH and DW, and the results of the initial screening by EH were used as the basis of this report. The "review" histology differed from the Royal Free Hospital's departmental report in 11 cases. The grade of cervical intraepithelial neoplasia was considered to be higher in five cases and lower in six cases, reflecting the acknowledged subjective element of reporting the lower grades of cervical intraepithelial neoplasia.¹³ These changes did not significantly alter the overall prevalence of cervical intraepithelial neoplasia (JC 11%, RFH 10.5%). The results of the "blind" review were used as the definitive histological findings for the diagnosis of cervical intraepithelial neoplasia in this report.

Twenty four (12%) of the smears taken at the colposcopic assessment were reported to be unsatisfactory or unreliable, and a repeat smear was requested in these cases. All the other smears (88%) were considered to be suitable for cervical cytology screening.

Cervical intraepithelial neoplasia was diagnosed in 22 (11%) patients (table I). The diagnosis was histological in 21 cases. One patient was pregnant at the time of the initial assessment, and no biopsy specimen was taken. The cytological and colposcopic impression in this case was of cervical intraepithelial neoplasia grade 2, and the patient was thus included as such. The mean age of those with disease was 29.5 (range 19-53), and the mean time since the last smear was two years (range three months-10.9 years). All lesions were colposcopically visible on the ectocervix.

Four patients had histological evidence of cervical intraepithelial neoplasia grade 3, and cervical cytology identified cervical intraepithelial neoplasia in all cases, although in one patient only mild disease was predicted. Five patients had cervical intraepithelial neoplasia grade 2, but cervical smears taken at the time of the colposcopic assessment failed to diagnose a cervical abnormality in three of these cases (a false negative rate of 60%). Thirteen women had colposcopic and histological evidence of cervical intraepithelial neoplasia grade 1, cervical cytology failing to diagnose any abnormality in four women (a false negative rate of 31%). In considering the false negative cytology we restricted ourselves solely to those smears considered to be suitable for accurate screening. These results assume that all unsatisfactory or unreliable smears would have shown disease when repeated.

Recently interest has been aroused by a possible association between human papillomavirus infection and cervical intraepithelial neoplasia.¹⁴ Seventeen (81%) of the 21 cervical biopsy specimens from patients with cervical intraepithelial neoplasia also showed histological evidence of human papillomavirus infection. In our study a further 10 patients (5%) had colposcopic and histological evidence (koilocytosis) suggestive of human papillomavirus infection alone. Eight of these patients yielded normal results on cytology. There seems to be no agreement on how patients diagnosed as having human papillomavirus infection alone should be managed.¹⁵

TABLE II—Results for 200 patients screened, by age group

Age (years)	<20 (n=4)	21-25 (n=18)	26-30 (n=22)	31-35 (n=34)	36-40 (n=44)	41-45 (n=23)	46-50 (n=24)	51-55 (n=10)	56-60 (n=12)	61-65 (n=4)	66-70 (n=3)	71-75 (n=1)	>76 (n=1)
No with cervical intraepithelial neoplasia	1	3	8	3	2	3	1	1	0	0	0	0	0
No with human papillomavirus infection	0	1	0	4	2	1	1	0	0	1	0	0	0
No with negative results	3	14	14	27	40	19	22	9	12	3	3	1	1

TABLE III—Results in 200 patients screened in relation to time since last normal smear result

	Time since last normal smear results (years)										
	<1 (n=49)	1.1-2 (n=53)	2.1-3 (n=37)	3.1-4 (n=10)	4.1-5 (n=9)	5.1-6 (n=5)	6.1-7 (n=7)	7.1-8 (n=8)	8.1-9 (n=3)	>9 (n=9)	Never (n=10)
No with cervical intraepithelial neoplasia	6	6	5	2	1	0	1	0	0	1	0
No with human papillomavirus infection	4	5	1	0	0	0	0	0	0	0	0
No with negative results	39	42	31	8	8	5	6	8	3	8	10

Thirty one patients were excluded from the study group; 13 had previously had an abnormal smear result, 11 had undergone surgery for benign cervical conditions (and so did not have a normal transformation zone), and seven patients reported abnormal vaginal bleeding and so could not be included in a normal screened population.

The mean age of the 200 women remaining in the study group was 39 (range 18-76), and the mean time since the last cervical smear among those

Table II shows the relation between age and the incidence of cervical intraepithelial neoplasia and human papillomavirus infection. Table III shows the relation between the time of the last smear and the incidence of cervical intraepithelial neoplasia and human papillomavirus infection.

The size of each lesion was assessed at the time of the colposcopic examination (table IV). Ten lesions (four cervical intraepithelial neoplasia grade 3, two cervical intraepithelial neoplasia grade 2, four cervical

intraepithelial neoplasia grade 1) affected more than two quadrants of the cervix, and there were no negative cytology reports in this group. There were 12 lesions (three cervical intraepithelial neoplasia grade 2, nine cervical intraepithelial neoplasia grade 1), however, affecting less than two quadrants of the cervix, and seven patients in this group yielded negative results on cytology (five with endocervical cells). Four smears were unsatisfactory or unreliable, and only one smear predicted mild disease. This is a false negative cytology rate for the smaller cervical intraepithelial neoplasia lesions of 58%.

TABLE IV—Results of cytology and diagnosis in relation to size of lesions detected

Size of lesions	Case No	Diagnosis (cervical intraepithelial neoplasia grade)	Cytology result
>2 Quadrants	1	3	Severe dyskaryosis
	2	3	Severe dyskaryosis
	3	3	Severe dyskaryosis
	4	3	Mild dyskaryosis
	5	2	Moderate dyskaryosis
	6	2	? Reliable
	10	1	Moderate dyskaryosis
	11	1	Mild dyskaryosis
	12	1	Mild dyskaryosis
	13	1	Mild dyskaryosis
	7	2	Negative*
	8	2	Negative
	19	1	Negative*
2 Quadrants	20	1	Negative*
	9	2	Negative
	14	1	Very mild dyskaryosis
	15	1	Insufficient
1 Quadrant	16	1	Unsatisfactory
	17	1	? Reliable
	18	1	? Reliable
	21	1	Negative*
	22	1	Negative*

*Endocervical cells present.

The addition of colposcopy to cervical screening did not always allow a definite diagnosis to be made. In a further 17 patients (9%) there was some evidence of disease, either cytological (7), colposcopic (11), histological (3), or a combination of these, but insufficient for the lesion to be classified as either cervical intraepithelial neoplasia or human papillomavirus infection. These patients were included as normals but are under review. Five of these women had an abnormal colposcopic appearance of rather dense acetowhite change within the transformation zone but with an irregular outline; the results of cytology were normal in these patients, but histologically they showed evidence of chronic inflammation.

The findings in 151 women (76%) were classified as normal by all three diagnostic methods.

Discussion

The prevalence of cervical intraepithelial neoplasia as diagnosed by a single cervical smear in this previously well screened population was 5%. This would rise to 7.5% if all unsatisfactory or unreliable smears in patients with cervical intraepithelial neoplasia showed disease when repeated. The addition of colposcopy as a screening procedure increases this prevalence to 11%. The overall false negative rate for cytology in all the patients with cervical intraepithelial neoplasia in this study was 32%. It must be acknowledged that in no patient with cervical intraepithelial neoplasia grade 3 (where the true premalignant potential of the disease has been established¹⁶) did cytology fail to detect dyskaryotic cells, although in one of the four patients with this grade of disease the report suggested only cervical intraepithelial neoplasia grade 1. In addition, none of the larger lesions, irrespective of grade, yielded negative results on cytology.

With the smaller lesions of cervical intraepithelial neoplasia, however (three cases of grade 2 and nine of grade 1), the false negative rate of cytology when used alone was striking. In this group, even when only satisfactory smears were included, the false negative rate for cytology was seven out of 12 cases, or 58%. There seem to be four possible explanations for the failure of cytology accurately to detect these small lesions. Firstly, sampling of the

transformation zone during the smear might have been inadequate. This seems unlikely, however, as all the smears were taken by a trained gynaecologist during a colposcopic examination. Secondly, there may have been a failure to identify abnormal cells on the smear during the cytology screening. This also seems unlikely as there was a close correlation between the independent reports of EH and DW, who are both experts in cytology screening. Thirdly, there might have been histological overreporting of cervical intraepithelial neoplasia grades 1 and 2 in the colposcopic biopsy specimens. Again, however, the correlation between the independent histology reports makes this unlikely. We suggest that the real explanation for the false negative cytology rate of 58% for the small lesions was the failure of these smaller lesions to exfoliate sufficient abnormal cells to enable accurate detection by cytology. Such lesions affected a significant number of our study group (6%), and their real biological potential is unknown.

Taking cervical intraepithelial neoplasia grade 1 lesions overall Campion *et al* showed that in a group of 100 women with lesions from which biopsy specimens were not taken, believed to be cervical intraepithelial neoplasia grade 1, only 7% of lesions regressed in over two years, but, more worryingly, 26 lesions progressed to cervical intraepithelial neoplasia grade 3, as shown by biopsy during that time.¹⁷ Similar findings have encouraged a change in gynaecological practice, so that now many units treat women with minor grades of cervical intraepithelial neoplasia, usually with local destructive techniques.¹⁸ As the number of women affected is so large, despite the fact that local treatments seem to have a low morbidity, it is important that further, larger studies of the clinical course of cervical intraepithelial neoplasia grade 1 should be carried out in case the current approach represents overtreatment. This is particularly important because when the patients with smaller, poorly exfoliating lesions identified in our study group were included the total prevalence for cervical intraepithelial neoplasia grades 1 and 2 was 9%—nearly one in 10 women.

Health districts in England and Wales are currently introducing cytology call and recall programmes. Many are starting screening at the age of 21 and thereafter every three years. This is an improvement on the previous policy of screening women over the age of 35, or those with three children, every five years. As fig 2 shows, however, in our study 13 (59%) of the 22 women with cervical intraepithelial neoplasia had had a normal cervical smear result within the past two years, and indeed two of these women had cervical intraepithelial neoplasia grade 3, as shown by biopsy. These numbers are small, but it could be argued that to avoid the potential consequences of false negative cytology, and to achieve the high rate of success reported in other countries with cytology screening programmes,^{19,20} a shorter interval between screenings may be required.

The alternative of using colposcopy as an additional screening technique may seem attractive because it identifies more women with cervical intraepithelial neoplasia, but such a policy would place considerable demands on resources and cause a clinical dilemma. When colposcopy is used for screening, as we have shown, a large group of women with smaller, more minor cervical lesions (cervical intraepithelial neoplasia grades 1 and 2 or human papillomavirus infection), who yield negative results on cytology, are identified. Such patients formed 8% of our study group. As the true clinical course of these lesions is unknown the problem of whether to treat these women or not arises.

We have confirmed that cervical cytology will detect women with larger and more severe cervical intraepithelial neoplasia lesions. If the smaller lesions that yield negative results on cytology are important, and progress, then they too should be detected when the lesions increase in size or severity. At present we are unable, cytologically, colposcopically, or histologically, to predict which lesions will progress to invasive disease. Until more information is available on the biological potential of the smaller lesions of cervical intraepithelial neoplasia that are not accurately detected by cytology their detection by colposcopy screening, cervicography, or other techniques currently being developed will place considerable strain on the already stretched colposcopy service and may result in considerable overtreatment. If these lesions prove to have an

invasive potential our results would predict a continuing epidemic of preinvasive and invasive disease of the cervix.

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ONE HUNDRED YEARS AGO

A NOVEL but by no means an insignificant application was made recently to a magistrate at Thames Police Court, on behalf of an organised trade society of East End tailors by its secretary, himself a tailor, that proceedings should be taken in respect to the insanitary condition of 2,000 dwellings used as sweaters' dens. The complainant stated that he had a right to make the application, because he had reason to believe that the local authorities would not take any action in the matter, although they were fully cognisant of the evil. It would be, in our opinion, rather delicate for a magistrate to accede to such a course without some deliberation, because there was no evidence to show either the existence of 2,000 dwellings used as sweating dens, or that the administration of sanitary law with which local authorities are charged has been neglected to the extent stated. We have had ample proof, however, of the weakness of existing Acts on labour to grapple with this evil in places where adult labour only can be found, and we have also had an exposition of the inattention of local authorities to enforce cleanliness in those places wherein their several jurisdictions lie. But, whatever view be taken of the application, it seems clear that the sweated men and women in the East End are availing themselves of the various revelations lately made by official reports and declarations made in the House of Lords to rid themselves of the bondage under which they groan in having to work in such filthy places. It is singular that the persons complaining are not of the immigrant class, but London born, and it is they who cry out loudest against immigration, although their parents were introduced here under circumstances now so loudly complained of by their children. Mr. Slade stated that if any evidence could be adduced to prove that local authorities would not act after application to them, he would then grant process; but the Act of 38 and 39 Vict. cap. 55, known as the Public Health Act of 1875, says that the local authority has power to cause inspections to be made of any house as to the existence of any nuisance, and such inspection to be between 9 A.M. and 6 P.M.; and if any person make a written complaint that a nuisance exists, the local authority may authorise their officer to inspect, after twenty-four hours' notice, or without notice in case of emergency. A house is defined to include factories and other buildings in which persons are employed in any manufacture, trade, or business. There is nothing to show that other steps can be taken by a complainant, unless power such as is asked for here can be granted under 11 and 12 Vict. cap. 43, upon oath of complainant that by his personal application in writing, he failed to move the local authority. It is nothing short of a public disgrace that these 2,000 dwelling-houses should be converted into filthy dens or workshops, where not only are persons assembled for daily work, but where the rooms are occupied by the families of immigrants or of workers for the sweaters. There have been reports enough for years past to show that this great evil is not abated, and it is high time that the Acts, now seemingly inoperative, should be made living factors by defining the duties of all local authorities, and making it incumbent upon the inspectors under the Local Government Board, especially the medical staff, to see that local officers do their work as men ought who are entrusted

with important duties. The filthy condition of these workshop dens and dwelling-houses, which were built for bedrooms in small houses, where the atmosphere is pestiferous and over-crowding excessive, ought not to be allowed; such places are not to be found amongst our country people, but entirely amongst the foreign population, who import *inter alia* their dirty habits to the East End, at present stocked with at least 30,000 men, women, and children of foreign Jews. If the applicant can make good his case, and can show, as a deponent to facts, that the local authorities have failed in their duty, it will be good *prima facie* evidence that higher powers should be evoked to aid sufferers who seem resolved upon asserting their right as ratepayers to ask that the servants of the vestries be called upon to do their duty even though vested interests should, in some cases, intervene.

(*British Medical Journal* 1888;ii:603)

It is proverbial that to keep an Englishman in good temper he must be well fed, and the teachers in some primary schools appear to find it hard to work in the afternoon when unable to get any mid-day meal. The new schools must be built where they are wanted, and where space can be obtained at reasonable cost. This has led to schools existing in poor and densely populated neighbourhoods, without necessarily having any adjacent coffee-house or restaurant giving facility to the teachers for obtaining a good mid-day meal. Whenever there are cooking centres in connection with Board schools, no difficulties are experienced by the teachers and pupil teachers in buying well-cooked food for their dinners at reasonable cost, but there is no systematic arrangement by which provision of this kind is made. In very poor neighbourhoods there is but little choice for the teachers; they must either live near the schools, so as to get something to eat at their lodgings in the middle of the day, or dine off sandwiches, buns, etc., as some young teachers do. Teachers preferring to live at a distance would not get home till six in the evening, or later. There is a "teacher's common room" at each school, but it is not possible for teachers to cook food there, and in summer there is no fire. In every school a woman is placed as caretaker; it might reasonably be arranged as a part of her duty that she should cook a plain mid-day meal for the teachers, say a joint and vegetables with pudding, the teachers themselves paying the cost. To become a teacher in a Board school is to undertake important and onerous duties, and it is very important that the health and strength of teachers and pupil teachers should not suffer from want of properly prepared food. When food is wanted in schools, the means of providing it are at hand, and we trust that School Boards will see that the necessary arrangements are made in cases where local circumstances show that they are needed, especially as no question of expense would be involved thereby.

(*British Medical Journal* 1888;ii:311)