Abnormal cervical smear test results: old dilemmas and new directions

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SUMMARY. Primary care professionals play a major role in the cervical screening programme in the United Kingdom, especially since the new contract for general practitioners. Many aspects of the programme are still the subject of broad debate and detailed research. New policies regarding the programme are generated at various levels; feedback is not always made directly available to primary care teams. This review article attempts to summarize the current available literature on cervical screening, focusing on the meaning of minor degrees of dysplasia, cervical cancer in younger women, the role of the wart virus, frequency of smear tests, diagnosis and treatment, counselling, and concludes with practical advice to help the practice team.

Keywords: cervical cytology abnormalities; cervical screening; subject reviews.

Introduction

GENERAL practitioners and their practice teams have played an important and increasing role in the cervical screening programme since its inception in the United Kingdom in the 1960s.[1] The cytology programme grew up sporadically in the UK and, unlike other countries with better organized programmes,[2] has failed to achieve a reduction in morbidity and mortality from the disease. This is despite huge expenditure on the programme, and the evidence from case control studies that even one negative cervical smear result affords a relative 'protection' for the disease.[3,4] Some still question the whole basis of the screening programme, which has never been fully evaluated by randomized controlled trials and never can be.[5] Recent evaluations of the performance of the programmes in the UK are depressingly poor.[6-9] The dilemmas are compounded by decades of problems with cancer registration, which have never been adequately addressed, causing women's pre-cancerous lesions to be misclassified as invasive cancers.[10]

However, on balance, most still agree that cervical screening can work if administered properly. The advent of computerized call and recall systems in each health authority, with a named individual with overall responsibility for the programme, is probably the most important advance in attempts to improve the efficacy of the screening programme.[11,12] But it will take many years before an effect is seen on morbidity and mortality rates from cervical cancer.

Carcinoma of the cervix is the second commonest cancer in women worldwide. Between 1950 and 1980 there has been considerable variation in the age specific mortality rates from the disease, with an incidence of invasive carcinoma of the cervix currently approximately 15 per 100 000 women per annum.[13] Primary care has diligently carried out this time consuming screening programme despite its high cost and poor return in terms of lives saved, and has done so with no formal mechanism for receiving central feedback.[5,6] The new contract[14] has encouraged an increase in screening activity and the proportion of cervical smears taken by general practitioners and practice nurses continues to increase.[15] Many authors have described the problems of implementing this aspect of the contract, which has been particularly difficult for inner city practices.[15-19]

There are many areas where new thinking has altered both the basic information and the management which should be offered to women at various stages through the screening and diagnostic process. These range from new hypotheses about the causality and risk of cervical intraepithelial neoplasia, through new treatments for preinvasive lesions, to changes in strategies for gaining optimum efficiency in the delivery of the screening programme. As pieces of the puzzle are published in a fragmented way throughout the literature, this flux understandably leads general practitioners to ask a variety of questions, which, it is hoped, will be dealt with in this paper. This may help general practitioners to make informed decisions as to what is the best care for their patients.

The meaning of minor degrees of dysplasia

Although the overall incidence of severe cervical intraepithelial neoplasia (CIN 3) has not altered over a number of decades, there has been a great increase in mild cervical intraepithelial neoplasia (CIN 1).[20] The reasons for this are not entirely clear, although increasing prevalence of wart virus may play a part.[21] This is a worrying phenomenon for patients, who often believe that any abnormality of the smear test means cancer.[22,23] Managers of screening programmes are also worried that full population coverage and the current abnormality rates will result in the swamping of colposcopy clinics.[24]

There is general agreement that the higher grades of cervical intraepithelial neoplasia (CIN 2 and CIN 3) should be treated, but the correct management of the woman with a mildly dyskaryotic smear or a woman with proven mild cervical intraepithelial neoplasia is uncertain. A review of 15 prospective studies of the progressive potential of minor dysplasia yielded variable and confusing results.[25] It is therefore important that any persistent degree of cytological abnormality, for example two abnormal smears over a six month period, even if mild, warrants colposcopic investigation, in view of the poor understanding of the natural history of cervical intraepithelial neoplasia.

The longstanding model of cervical dysplasia as a continuum of increasing abnormality has been brought into question. Some have suggested new classifications which would dichotomize the condition, grouping mild cervical intraepithelial neoplasia with borderline changes.[26] Although severe cervical intraepithelial neoplasia is an obvious tissue diagnosis, histologists find it hard to agree about whether mild cervical intraepithelial neoplasia is present or not.[27] Epidemiological research and studies on oncogene expression support the impression that severe cervical intraepithelial neoplasia is a more definite and predictable lesion than the lower grades of dysplasia.[1,28]

If the disease is perceived as a dichotomy, this opens the door to changes in management for minor degrees of dysplasia. A working party from the national coordinating network of the National Health Service Cervical Screening Programme has recently published guidelines stating that it is not possible to

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say with certainty when mild cervical intraepithelial neoplasia should be treated, but if a surveillance policy is adopted, local circumstances such as the patient default rate, must be taken into consideration.[29]

Changing management offers increased potential for researching the mechanisms of regression for these lesions. The Imperial Cancer Research Fund has recently made a public appeal for women who have mild cervical intraepithelial neoplasia and are willing to be entered into different intervention groups. The Harris Birth Right Centre in Aberdeen is conducting a prospective study to observe a large cohort of women with minor cytological abnormalities which may shed further light on the safety of surveillance for such women (H Kitchener, personal communication).

Therefore, there is still debate about the dangers of observing, rather than treating, any dysplastic lesions. No step in the diagnosis of dysplasia is foolproof, and increased conservatism may allow clinically significant lesions to be missed. Failure to provide adequate follow up to women with mild abnormalities has been a problem in the past.[8,30] Women with persistent inflammatory smear results should be followed up with high vaginal swabs as the inflammation may be associated with infection. Women with three or more inadequate smears should be considered for investigation. It is important to remember that early invasive lesions which may produce a negative or inadequate smear result are best recognized by their clinical presentation.[31]

Given the level of the debate, general practitioners will follow different management strategies in different areas. Wherever a decrease in treatment patterns occur, attention should be paid to increased surveillance to prevent women with mild abnormalities being lost to follow up. Women over 65 years of age should be encouraged to have a smear if they are consulting the doctor and have not been screened previously.[29]

Is the disease different in younger women?

There has been an increase over the past three decades in the incidence of cervical cancer in younger women (those under 35 years of age).[32] This is thought to be largely due to changes in the risk status of this cohort of women.[33] Although the disease is more frequent, it does not appear to be more aggressive, with survival rates similar among older and younger women. Fortunately, young women tend to be well covered in screening terms. However, the overall increase in the prevalence of the disease in this age group should raise general practitioners' level of suspicion, especially if a young woman presents symptoms which could be due to an early invasive lesion.

It is rare for teenagers to develop invasive cervical cancer,[34] although it is worrying that one prospective study demonstrated that 3.3% of women referred for colposcopy were under 20 years of age.[35] Although there is no case for routine screening in this age range, it presents a dilemma for general practitioners who may feel a test is warranted especially if a young woman requests one.

The role of the wart virus

The focus of the search for a causal organism of cervical cancer changed from the herpes virus in the 1960s and 1970s[36] to the human papillomavirus in the 1980s and 1990s. The latter has been the subject of much epidemiological confusion.[37,38] Some studies have shown that a large percentage of women with normal cytology carry the human papillomavirus[39] but other research has demonstrated a lack of human papillomavirus in the most aggressive variants of cervical cancer.[40] However, there is general agreement that there is some relationship between certain strains of human papillomaviruses and cervical intraepithelial neoplasia.

Various tests have been developed in an attempt to identify the virus accurately.[41,42] One of these, the polymerase chain reaction, can be reduced to a very simple test and is currently in use in parts of the United States of America as a screening tool. British researchers have opted to avoid such unevaluated screening, and warned of the anxiety that could be caused by its use.[43] There is not enough known about the wart virus to make any firm conclusions. It is tempting to hypothesize that, in the presence of certain cofactors, some types of wart virus may become oncogenic.

There is wide variation in the management of women who have the cell change koilocytosis identified in their cervical smear but have no clinically apparent warts. Clinically apparent warts should be treated but women with koilocytosis but no evidence of dyskaryosis should be followed up as normal.

New ideas about diagnosis and treatment

Colposcopy is an old and delicate art, but it may disappear with the introduction of one stage treatments. The two stage procedure of colposcopically directed punch biopsies followed by laser ablation is still widely practised, but there is evidence that the small biopsies obtained are unreliable:[44] such biopsies may miss areas of microinvasion. Lasers are expensive pieces of equipment, and laser ablative techniques yield no further chance to make a histological diagnosis. This has resulted in an increasing trend towards large loop excision biopsy of the transformation zone using a diathermy loop.[45] This is a simple way of removing the whole transformation zone, effecting a simple treatment and allowing thorough histological examination. The long term consequences remain to be seen. There has been recent reassurance regarding fertility following laser treatment, but patients who had had treatment with a diathermy loop were not included in this report.[46]

Cervicography, a technique of cervical photography, has recently been assessed as a screening tool.[47] Unfortunately, there is a high rate of false positive lesions, limiting the value of this technique. Therefore, it seems unlikely that the technique will be widely introduced.

How often should cervical smears be repeated?

Despite persuasive evidence for a three year schedule, and some authors suggesting that a two year interval would be safer,[4,48] the government continues to recommend a five year interval between normal cervical smear tests. The cost benefit analysis of reducing the interval is difficult to estimate. Unlike other countries, accurate estimates of the true cost of the cervical screening programme in the UK are lacking.[49]

The recommended five year interval between cervical smears is based on indirect evidence from computer models for the disease which presupposes that all cervical intraepithelial neoplasia lesions take many years to become invasive.[50] However, reviews of the cytological history of women with known invasive cervical cancer arrive at the conclusion that many women had a series of normal smears preceding diagnosis.[51-53] It is difficult to know whether these women had rapidly developing lesions, or repeated false negative cytology.

Despite the government recommendation, many health authorities have taken local decisions to carry out cervical screening at three yearly intervals. Many general practitioners, perhaps because of their own perceptions of risk, or because they are under pressure from their patients, repeat the smear test even sooner. In our group practice, where 1483 women are eligible for screening, over 40% had two tests with normal results in

less than a three year interval. These figures are similar for South Glamorgan Health Authority as a whole.

For abnormal smear results, smears indicating mild dyskariosis should be repeated every three to six months. If the dyskariosis persists, patients should be referred for colposcopy. Women should also be referred for colposcopy if they have smears indicating moderate to severe dyskariosis. If treated successfully, there should be annual follow up for five years, and after this a return to three yearly screening.

Previous experience would suggest that the women who have their smears most frequently are also those at lowest risk from the disease.[18,22] Perhaps a more risk-sensitive policy would help to target the service more equitably and effectively, while reducing demand from women who are known to be at low risk.

Implications for counselling women

All of this information has important implications for the counselling role undertaken by general practitioners and practice nurses. Leaflets should be seen as supplementary to sympathetic counselling, and should be simple and reassuring. Women with abnormal smear tests are a particularly vulnerable group, and anxiety is common.[23,54] Treatment methods will cause far less anxiety if women fully understand what treatments are used and exactly what that treatment involves.

Practical advice

The review of the literature reveals some important changes in the cervical screening programme. In order to keep abreast of these changes as the programme is implemented, the following practical advice may be of use to primary care teams:

- Ensure good education for all practice staff who contribute to the programme, from reception staff to doctors, regarding general guidelines and local practices.
- Supplement the local failsafe system for women with minor abnormalities who are under observation by keeping a careful practice register of such women. The register can be manual or computerized, but ideally should have one clinician who takes overall responsibility.
- Avoid raising unnecessary anxiety in patients regarding overt human papillomavirus infection, and koilocytosis in smear reports.
- Investigate treatment methods and changing trends, encourage local clinics to produce videos of newly introduced treatments to educate primary care staff.
- Monitor and avoid excessive repeat tests in low risk women.
- Ask programme managers to send yearly statistics regarding the programme in your area to each practice.
- Ask the local laboratory to feedback detailed information regarding inadequate cervical smear rates by initiator, to enhance practice audit.

Conclusion

General practitioners and their practice nurses are central figures in the cervical screening programme in the UK. General practice is the ideal setting for the programme, which can be offered as part of each woman's general medical care, with the family doctor as the advocate of the patient throughout. Primary care teams should not be discouraged by the failure of the UK programme to date, it will take many years for their current efforts to alter these statistics.

New research is being accumulated rapidly in this field and, with the advent of new techniques in molecular biology, is likely to continue to accelerate. New treatment options and new management procedures for minor abnormalities must be appropriately reflected in the counselling of women who have an abnormal cervical smear test result.

Guidance has been produced which addresses the wide local variation in delivery of the programme.[29] A number of bodies are currently producing guidelines intended to strengthen the central coordination so badly needed in the UK and to accommodate the changing ideas about the natural history of the disease.[55] Further measures are underway to ensure quality control in the laboratories.[56]

General practitioners are in an excellent position to implement the cervical screening programme to maximum advantage and with minimum psychological distress to their patients.

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