CERVICAL SCREENING UPDATE

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INTRODUCTION

The screening programme is working. The incidence of cervical cancer has decreased by 42% since 1990, despite continuing and possibly increasing exposure to the two known risk factors of smoking and infection with certain serotypes of human papilloma virus (HPV). Invasive cervical cancer is now relatively uncommon in the UK, with an incidence of approximately 9.3 per 100,000 women and fewer than 1,300 deaths a year[1]. In many third world countries, however, it remains the commonest cancer in women.

The purpose of the national screening programme is to detect and treat pre-invasive disease at the stage of high-grade cervical intra-epithelial neoplasia (CIN2 and 3). In addition, screening may detect glandular pre-invasive disease, high-grade cervical glandular neoplasia (CIGN). This is more diffcult to diagnose in a smear than squamous abnormalities.

In this article I shall discuss the aspects of the screening programme about which I am most frequently asked.

THE NATIONAL GUIDELINES

'Are the national guidelines a form of rationing?'

The guidelines are an attempt to provide a comprehensive and effective screening programme which makes the best use of available resources. The laboratory has recently issued a protocol describing these guidelines but they are not new. The national cervical screening recall programme began in 1988; most of the present guidelines were issued in 1992 and reviewed in 1997[2,3]. They have been drawn up by the NHS Cervical Screening Programme (NHSCSP) using an evidence-based approach. The three issues which have caused most controversy are frequency, age group and so-called 'clinically indicated' smears.

FREQUENCY OF SCREENING

The DoH/NHSCSP guidelines advise a frequency of smears of at least once in five years for all 20-65-year-olds (in practice, recall at a maximum of 4.5 years). The screening interval is set by the local health authority and there are three main patterns throughout the country: three-yearly for all 20-65-year-olds, five-yearly for all 20-65-year-olds, and a biphasic pattern of three-yearly until the age of 35 and then five-yearly. The latter is the pattern chosen by Morecambe Bay Health Authority (MBHA) and has been the policy for several years. General practitioners should not be surprised, however, if their patients are recalled earlier. Some patients over 35 in South Cumbria may be recalled at three years as this was specifically stated on their last smear report, and this may also happen to patients moving from other areas.

Studies have shown that five-yearly smears prevent 84% of cancers, three-yearly smears prevent 90% and annual smears prevent 93%[4]. The benefit of screening more frequently than three-yearly is not cost-effective. The incidence of CIN peaks at 25-29 years of age, whilst that of invasive carcinomas is ten years later. The rationale of screening the younger age group more frequently is to detect and treat pre-invasive disease. The incidence of CIN3 in older women who have a history of regular negative smears is low and therefore screening can be less frequent. Women with a history of high-grade CIN should be screened three-yearly until age 65.

Although we have the biphasic policy in MBHA we have always accepted and screened all smears sent to us. Some laboratories are less compliant and return smears unscreened if they are outside their protocol. If we can keep smear-taking to the age group advised and abolish the so-called 'clinically indicated' smears we may have the capacity to provide a three-yearly service for all, but only when we have our full complement of trained staff.

AGE GROUP TO BE SCREENED

In 1992 screening of teenagers was no longer advised. This is because the incidence of minor reversible abnormalities is high in this group and invasive carcinoma rare. CIN3 does occur, but is said to progress more slowly than in older women. The average duration of high-grade CIN before it becomes invasive is given as 11 years, so it is very unlikely to become invasive before the age of 20[5].

CIN3 is rare in women over 50 who have been screened regularly and the feasibility of ceasing recall in selected women is being considered. Screening ceases at 60 in some parts of Scotland with no detriment to the effficacy of the service. As the incidence of invasive cancers in young women falls, those in the elderly constitute an increasing proportion of total cases, but there are no plans to increase the service to the over-70s. It may, however, be prudent to take a smear from an over-65-year-old woman who has not had regular smears prior to that age if she is thought to be at risk.

SMEARS OUTSIDE THE PROGRAMME

The cervical smear is a screening test, not a diagnostic test. Smears should not be taken as part of the investigation of a symptomatic woman unless due in the screening programme. If a smear is taken in the presence of symptomatic infection, it may be inadequate due to masking by inflammatory cells, or borderline as inflammatory changes are difficult to distinguish from dyskaryosis, and this will not help the patient.

Smears taken in the postnatal period can also be difficult to interpret and may be 'over'- or 'under-called'. This period should, therefore, be avoided and the smear delayed if possible. If a patient is due a smear, however, and is unlikely to attend at a later date, then a smear should be taken.

If the appearance of the cervix is suspicious of tumour the patient should be referred to a gynaecologist rather than a smear being taken. Conversely, symptoms cannot be ignored because a patient has had a recent negative smear. She may still have cancer.

SENSITIVITY OF THE CERVICAL SMEAR TEST

'What's the point? They get it wrong anyway'.

This quote from a patient comes from a failsafe reply when the Kent and Canterbury enquiry was prominent in the national press.

It is acknowledged that cervical screening can never prevent all invasive cervical cancers. There are three main reasons for this:

1 certain cancers are difficult to detect because they develop high in the cervical canal or because they have a short surface pre-invasive phase or none at all.

2 a conventional smear, however well-taken and prepared, only contains a sample of the cells removed by the spatula or brush and this may not be representative. Smears taken at colposcopy from women with biopsy-proven CIN are sometimes truly negative, particularly if the lesion is small. This is why we need a series of negative smears before returning a patient to normal recall.

3 It is diffficult to distinguish between dyskaryosis and inflammatory change. This is the main reason for the borderline category, but although tempting it is impractical to call all inflammatory smears borderline.

Cervical screening involves difficult subjective judgement. Major errors are rare, and most laboratory false negatives are the result of misinterpretation of subtle changes whose significance only becomes apparent in retrospect. If a patient is regularly screened these problems of sampling and interpretation are reduced and the sensitivity increases, as described above. I have been unable to find a figure in the literature but a negative smear result means that the chances of a patient having pre-invasive or invasive disease is less than 1%. A negative smear result means low risk, not no risk, of cervical cancer.

QUALITY ASSURANCE

All laboratories take part in a mandatory training and quality assurance programme. This includes a minimum initial 18-24 month training period for screeners, ending in an examination. In addition, staff attend regular updates and there is a quarterly rolling audit of screener and pathologist performance and an external regional programme with test sets of smears. Laboratories have an accreditation inspection. All smears are fully screened by a trained screener. If negative or inadequate they are passed to a second trained screener for rapid re-screen. If positive, or possibly abnormal, they are passed to a consultant pathologist for reporting. The establishment of this training and quality assurance programme has lead to an improvement in the quality of screening. Most cases which reach the national press are historical and do not reflect present standards.

PATIENT INFORMATION AND CONSENT FORMS

It is tempting to print 'The laboratory accepts no responsibility in the event of the patient developing cervical cancer' on the back of our request forms, but this would not be ethical. The laboratory has an obligation to patients to maintain an acceptable standard of practice. If this standard means that diffficult smears are occasionally misinterpreted, is this negligent?

In the USA some screening laboratories are incorporating information on the risks of false negatives and false positive rates in a signed consent form[6]. There are no plans here to introduce a consent form, but we should not ignore the limitation of the test when encouraging patients to have a smear. The new NHS national cancer plan emphasises that patients should be given clear and honest information about screening programmes so that they can make an informed decision to take part. National information leaflets are to be introduced as the quality of information varies between health authorities.

SCIENTIFIC ADVANCES

There are two promising techniques which are now being piloted.

1 Liquid-based cytology. The smear is taken in the usual way but the spatula or brush is rinsed in a liquid transport medium resulting in a cell suspension. Special and expensive equipment is needed in the laboratory to produce a smear with a thin monolayer of cells. This preparation should be a more representative sample and quicker and easier to screen than a conventional smear, resulting in fewer inadequates and fewer false negatives. Pilot studies are being set up and if NICE approves this technique the government has promised to fund it.

2 HPV triage. Genital HPV infection has a prevalence of 15-30% in young women; most infections are transient and clear within 8-24 months[7]. All cases of high-grade CIN and invasive squamous carcinomas are thought to be associated with infection with high risk serotypes of HPV. The infection may have been acquired many years previously and persists as the viral DNA becomes integrated into the cellular DNA. Testing women with borderline changes and mild dyskaryosis for these serotypes should identify those most likely to have high-grade CIN, whilst those who are negative can be followed up more conservatively. Samples from the liquid-based preparation can be used for this, so these two techniques can be piloted together.

AUTOMATION OF SCREENING

Two automation systems have been trialled in the UK: PAPNET and Autopap. Both use a combination of image analysis and neural network techniques to identify abnormal cells in conventional smears. Although both were promising, neither was satisfactory in its present stage of development, largely because of the complexity of the conventional smear. The new liquid-based thin preparations should be more suitable for automated analysis than the conventional smear. A suitable automated screening system would competently report the most obviously normal smears but leave human screeners to check and grade those smears the computer recognises as potentially abnormal.

HPV VACCINATION

Work on this is still very much in the early stages. An effective vaccine is probably the only way of reducing the incidence of cervical cancer in developing countries. As well as preventing initial infection, animal studies have shown that vaccination can induce regression in papilloma virus-associated tumours, so this may also be used in treatment.

The cervical screening service throughout the country is having difficulty in maintaining a service because of shortages of skilled staff. If liquid-based collection and automation are adequately funded these problems will be resolved and the way in which we provide the service will change radically in the next ten years.

REFERENCES

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