SCREENING FOR CERVICAL CANCER

Cervical cancer is the commonest malignancy among black South African women, highlighting the need for effective screening programmes.

M MOODLEY

MB ChB, FCOG, MMed (O&G)

Principal Specialist and Senior Lecturer

Department of Obstetrics and Gynaecology
Nelson R Mandela School of Medicine
University of KwaZulu-Natal
Durban

Dr Moodley trained at King Edward VIII Hospital, Durban, and obtained his Fellowship in 1996. His current field of interest is oncology and he is in charge of the Gynaecology-Oncology section at the Nelson R Mandela School of Medicine.

Cervical cancer remains a major health concern worldwide, especially in developing countries. It is the commonest malignancy among black women in South Africa. The quoted incidence of cervical cancer is approximately 30/100 000 women.[1] Mortality is higher in developing countries, mainly due to the lack of availability of screening and late-stage presentation. Cervical cancer has well-defined risk factors, namely precursor lesions which can be detected by screening. Treatment of these lesions leads to a reduction in incidence and mortality. In Finland, where a sophisticated screening programme exists, both the incidence of and mortality from cervical cancer have decreased by 80%,[2] and are now 3.8/100 000 and 1.6/100 000 women, respectively. However, in spite of knowledge of cervical screening and its availability, women from higher social and educational levels often do not take up screening.[3] The mere provision of a screening service is in itself not sufficient to ensure successful uptake, as screening is a complex process.

Important aspects of cervical cancer screening include the age at which screening is started, frequency of screening, ideal and cost-effective technique, provision of screening services to the most needy members of the population, and treatment of precursor lesions.

SCREENING RECOMMENDATIONS

Age at which screening should start

Various recommendations have been made as to the age at which cervical cancer screening should start, e.g. 18 years, or at the age of onset of sexual activity. Based on data from Cali, Colombia, the impact of starting cervical screening at different ages shows that starting screening at the age of 25 is as effective as screening from the age of 20 in reducing the cumulative incidence of invasive cervical cancer (Table I). It has been reported that in order to detect 1 case of cervical cancer in the age group 25 - 29 years, 13 965 women would have to be screened, whereas 3 786 women would have to be screened in the 35 - 39 age group. It would therefore appear more cost-effective to screen older women than younger women. However, among HIV-positive women, the age incidence of invasive cervical cancer shows that women are presenting with invasive cancers at younger ages. Cervical cancer screening should therefore begin at age 25. If the patient is HIV positive, screening should begin at a younger age, or at age of onset of sexual activity if the virus has not been sexually transmitted.

Table I. **Reduction in the cumulative incidence of invasive cervical cancer for different ages at initiation of screening**

Age screening initiated (yrs)	Frequency of screening (yrs)	Percentage reduction in cumulative incidence (%)	Tests (*N*)
20	5	84	9
25	5	84	8
35	5	77	6
20	2	52	10

FREQUENCY OF SCREENING

Women with a negative smear have low rates of developing invasive cancer for 5 years. The rates are even lower for women who have had two negative smears. It is therefore unnecessary to screen women annually, as is the case in some parts of the developed world and even in the private sector in developing countries. The effects of screening frequencies on the estimated risk of developing invasive cervical cancer are illustrated in Table II. These results, based on a report by the World Health Organisation (WHO),4 demonstrate that screening every year or every 2 years has an insignificant effect on the percentage reduction in cervical cancer. While screening every 3 years is probably more effective, screening every 5 years offers substantial benefits. These estimates assume total coverage of the population. However, this is often never achieved.

It would therefore be more cost-effective to screen a greater percentage of the population infrequently, especially high-risk populations, than to recruit a low proportion and screen them often. This is illustrated in Table III. Based on the above evidence, it would probably be ideal to screen women every 3 years from the age of 25. However, the cost implications of this approach are self-evident. If only one smear is available to women in their lifetime, it should be done at age 40 years as per WHO recommendation. Currently there is no screening policy in South Africa. The National Health recommendation is that women should be screened only 3 times in their lifetime, at 10-yearly intervals, with the first smear commencing after age 30. A recent South African study showed that the incidence of cervical cancer is still reduced for women who have ever had a smear.[5]

METHODS OF CERVICAL CANCER SCREENING

Various methods of screening have been described. The attributes of an ideal screening test are the following:

- reasonable sensitivity
- reasonable specificity
- wide availability
- low morbidity
- cost-effectiveness.

Whereas the ideal screening technique should have 100% sensitivity and specificity, this is rarely accomplished.

Papanicolaou smear

For many years the Papanicolaou (Pap) smear has been the conventional method of cervical cancer screening. However, in developing countries Pap smear screening is available mainly in the private sector or in the more urban areas of the population. Women who most require screening often live in rural areas where such screening is not practical, because the technical capabilities, systems for transportation, communication, follow-up and training are beyond the capacity of the health infrastructure. For many years the Ayre spatula was used exclusively to collect cell samples for Pap smear tests. However, it has been shown to be the least effective device and should be superseded by extended-tip devices for primary screening (e.g. Aylesbury).[6] Such devices should detect ectocervical as well as endocervical cells and include the combination of the spatula and an endocervical brush or the Cervexbrush or Baynebrush, which can collect both cell types. It is therefore recommended to use a Cervexbrush alone, or a combination of the Aylesbury spatula and an endocervical brush. The smears should be fixed with cytofix within 10 seconds and an effective system to check smear results and recall patients needs to be established. To date, Pap smear screening remains the most viable method of screening for the GP. Other methods of screening have been described, but these are not readily available in the GP setting.

Fluid-based technology

Fluid-based technology uses cervical cytology specimens. The aim is to minimise the incidence of false-negative cytological findings by optimising collection, and by producing a monolayer of cells for analysis. Examples of such fluid-based technology are ThinPrep and CytoRich. Although these two systems vary somewhat, the basic concepts are similar. In a comparison between the traditional Pap smear,

Table II. **Reduction in the cumulative incidence of invasive cervical cancer with different frequencies of screening**

Frequency of screening (yrs)	Reduction in cumulative incidence	Tests (*N*)
1	93	30
2	93	15
3	91	10
5	84	6
10	64	3

Table III. **Reduction in the cumulative incidence of invasive cervical cancer with different proportions of the population screened and different frequencies of screening**

Frequency of screening (yrs)	Proportion screened (%)	Reduction in cumulative incidence (%)	Tests (*N*)
1	20	19	6
2	30	28	4.5
3	40	37	4
5	50	42	3
10	80	51	2.4

The quoted incidence of cervical cancer is approximately 30/100 000 women. Mortality is higher in developing countries, mainly due to the lack of availability of screening and late-stage presentation.

ThinPrep and colposcopy-directed biopsies, it has been shown that ThinPrep shows the same results in almost 90% of cases.[7] ThinPrep, however, costs twice as much as a Pap smear when all variables are considered.

Cervicography

Cervicography is the process whereby a photographic image of the ectocervix is taken and examined on colposcopic principles. It is performed using a cerviscope or specially designed 35 mm hand-held camera. The cervix is painted with 5% acetic acid and a panoramic photograph is taken of it. The procedure is simple and short but requires the expertise of a colposcopist for analysis. A negative cervigram implies that it is extremely unlikely that cervical disease is present and, if present, it may be exclusively within the endocervical canal. It is therefore more sensitive in younger women and in women not using progesterone-only contraception, in whom the transformation zone is ectocervical and visible on cervicography. Used together with a Pap smear, it can identify nearly 2.5 times the number of women with dysplasia compared with the use of a Pap smear alone. Owing to the false-positive results, its use in general screening is limited.

Speculoscopy

Speculoscopy is a visual endoscopic examination which uses specialised 'blue-white' chemiluminescent light, along with acetic acid and low-power magnification for screening. An activated blue-white light is attached to the inner aspect of the upper speculum blade. The cervix is painted with 3 - 5% acetic acid, followed by examination of the cervix with magnification.

Visual inspection of the cervix

Speculum-assisted visual examination of the cervix identifies women with signs of high-risk characteristics. These include cervical erosions, small visible growths or a suspicious-looking cervix. This method can preselect women with suspicious cervices, who can then undergo further evaluation. In this context, unaided visual inspection can detect 40 - 50% of early cervical cancers.

Visual inspection with acetic acid (VIA)

The cervix is washed with 3 - 5% acetic acid and then inspected with the naked eye for any disease. It is advantageous in low-resource settings where immediate feedback of test results are available to the patient, who can then be treated for any abnormalities. This method may give false-positive results which may lead to unnecessary referrals and possibly treatment.

Human papillomavirus (HPV) DNA testing

High-risk types HPV (16,18) are implicated in the pathogenesis of cervical cancer. Infection by types 16 and 18 has a higher rate of progression than low-risk types (6,11). Significant cervical lesions are unlikely to be present within 3 - 5 years after the onset of sexual activity. Most HPV infections in women aged less than 22 years tend to be transient, with 70% regression rates within 3 years and over 90% regression rates for low-risk types.[8] HPV DNA testing may be particularly useful in older women in whom regression rates are lower and infection is less likely to be transient. Several tests are currently described for detecting HPV DNA, including the Digene kit. HPV DNA testing with cytology for primary cervical cancer screening has not yet been approved by the FDA. The Hybrid Capture (HC2) has been approved by the FDA and detects 14 types of HPV DNA. Although it is considered easier to implement than cytological screening, especially for low-resource settings,[9] it is not cost effective for the GP setting.

SCREENING IN DEVELOPING COUNTRIES

While the Pap smear currently remains the most widely practised technique, further research and development are needed to determine the most cost-effective way of screening women in the developing world. Cytological examination, cervicography, VIA and speculoscopy appear not to be suited for screening in such settings because of low sensitivity of the cytological examination and low specificity of the other tests. A combination of the tests will increase the sensitivity, but the specificity remains low. For now, the Pap smear remains the only viable test for screening in the office setting. The ideal screening test for developing areas may be one which is simple, cost-effective, and widely applicable in a mobile unit for the rural areas, with on-site colposcopic examination and treatment in an endeavour to reduce the incidence of and mortality from cervical cancer. For a screening programme to be successful, the health care provider needs to give appropriate information to the patient and the patient needs to go for screening.

References available on request.

IN A NUTSHELL

Cervical cancer remains a major health problem worldwide, particularly in the developing world

The age at which screening should be started is controversial. However, evidence from several different analyses suggests that it should start before the age of 25 years.

Women with HIV infection should be screened at a younger age since data on the age incidence of invasive cervical cancer show that it occurs at a younger age in these women.

Screening should take place every 3 - 5 years.

For the GP the Pap smear still remains the most practical method of cervical cancer screening.