2.8 IDENTIFICATION OF PERSON OR PERSONS WITH RESPONSIBILITY FOR THE PROGRAMME

Cancer screening is a multidisciplinary activity involving clerks, nurses, midwives, cytotechnicians, pathologists, gynaecologists, surgeons, GPs, epidemiologists, economists, etc. All these professionals need coordination. A committee should be created to monitor and update the local policy. The chairman of the committee should be elected or named by the health authority as programme manager. Specific responsibilities should be assigned to the chairman for organisation, mass media relationship, budget, quality assurance, evaluation, etc. The responsible persons should be officially appointed, and they should have authority for implementing the decisions of the committee. Consensus on a screening programme is not a sufficient condition for its success, but is highly desirable.

2.9 RESOURCE IMPLICATIONS AND ECONOMIC EVALUATION

Continuity of financial resources for the programme should be ensured at the start. A monitoring system should be designed to document the costs at appropriate times. The collection of these data should be performed either by continuous monitoring of the costs or by periodic surveys of the financial system. Parameters such as the cost per woman or per smear are necessary for improving the organisation and planning the strategy.

Screening competes for scarce resources with other health interventions. On a longer time scale, data should therefore be provided to the decision makers about costs and health effects of the programme, including the costs of diagnosis, treatment and organisation.

Economic evaluation can be performed as a cost-effectiveness analysis (cost per year of life saved) or as a cost-utility analysis (also taking quality of life into consideration). Simulation of different scenarios such as those illustrated in Table 2.3, with the utilisation of computerised mathematical models allows one to select the most cost-effective option for running the programme.

2.10 MECHANISMS FOR GATHERING DATA

Before cervical screening can be implemented mechanisms for gathering essential data for the day to day operation of the programme and for statistical purposes must be in place. A comprehensive registration system for women at risk is a prerequisite for an organised screening programme as is a system for registering the Papanicolaou smear reports. Ideally the systems should be computerised and linked.

A register of biopsies and the histology reports from women referred for treatment are also required and a regional cancer register should be in place. Minimum data requirements are itemised in Chapter 5.

2.11 ESTABLISHMENT OF A FAIL SAFE SYSTEM

The value of the cervical screening programme will be diminished if action is not taken whenever an abnormal smear report is issued. The responsibility for ensuring this action is taken lies with the person who took the smear. However, smears may be taken in many different situations and there is a need for a back up system (fail safe system) to ensure that there is appropriate follow up of every woman with an abnormal smear. Fail safe measures are recommended in Chapter 4.

3. Screening Methodologies

3.1 INTRODUCTION

FOR THE past 50 years, the Papanicolaou smear test has been used to screen for preinvasive and early invasive cancer in asymptomatic women. This test involves removing a sample of cells from the epithelium of the transformation zone of the cervix and examining the cells with a light microscope.

Abnormal cells present in the sample can be recognised by the experienced cytologist. In this chapter we describe (i) methods for collecting cervical smears (ii) methods of processing the smear and (iii) preparation of the smear report.

3.2 EQUIPMENT REQUIRED FOR TAKING A CERVICAL SMEAR

(i) There should be an examination couch for vaginal examination of patient in either the left lateral or dorsal position with good illumination from an adjustable halogen spot light.
(ii) Disposable vinyl or latex gloves should be available.
(iii) Various sizes of specula must be available. They may be of a disposable pre-sterilised plastic type or sterilised non-disposable stainless steel. These must be thoroughly cleaned before being re-sterilised by steam sterilisation in an autoclave for a minimum of 15 min at 121°C or in a hot air oven at 180°C for 120 min. Chemical disinfectants are not sufficient to prevent the spread of infection.
(iv) Other essential items are: frosted ended glass microscope slides 7.6 × 2.5 cm; a lead pencil; fixative (95% alcohol and carbowax or 5% acetic acid) in a dropper bottle slide jar or as commercially available cytospray; a slide box for transportation and a request form.

3.3 PROCEDURE FOR TAKING A CERVICAL SMEAR

(i) Explain to the patient the procedure, what to expect and give reassurance. Ask about her general health and whether she has any symptoms such as irregular bleeding or discharge.
(ii) Label the slide clearly in pencil on the frosted end with the patient's name, date of birth and identification number. Other methods of marking may be removed during processing of the slide.
(iii) Ensure that the woman is lying comfortably on the examination couch in either the dorsal or lateral position so as to visualise the cervix clearly and position the light.
(iv) Select the largest speculum that can be inserted comfortably and bring to body temperature. Insert the speculum along the axis of the introitus and when halfway up the vagina rotate 90° and open when fully inserted. Lubricants

are not usually necessary but if used must not contaminate the cervix as this impairs the smear quality. Bring the cervix into view by gentle movement of the speculum encouraging the patient to relax. If this proves difficult, digital examination or change in position may be beneficial. The appearance of the cervix should be noted and smear takers taught the various normal and abnormal appearances of the cervix and suspicious symptoms. If a non-medically qualified person is concerned about the clinical appearance of the cervix, a medical opinion should be obtained.

3.4 SAMPLING THE TRANSFORMATION ZONE

Sampling the transformation zone may be carried out using wooden or plastic spatula of various types or cotton swabs (wet and dry). Various forms of brushes or suction pipettes may be used as supplementary methods for sampling the endocervical canal or the vaginal pool, respectively. Pipettes are not much used at present and are not recommended.

The original Ayre spatula was designed with the purpose of sampling the ectocervix as well as the endocervical canal. The original design has been modified with a view to improving sampling. Comparative trials of these modified spatula (such as providing the spatula with an extended tip) have been carried out, some of these controlled. The decision as to which instrument to use to sample the cervix is a personal one. However, regardless of the spatula used, both the ectocervix and the endocervix in the region of the cervical os must be sampled.

To obtain an adequate sample the pointed end of the spatula should be inserted into the cervical os until the inner curved surface is applied to the cervical surface. The spatula is then rotated through 360°, keeping it firmly applied to the surface. This can be repeated should the spatula fail to contact an area during rotation.

If the patient has a small cervical os, if the transformation zone is invisible or treatment for a previous abnormality has been done, an endocervical brush sample should be taken in addition to the cervical scrape. The brush is inserted into the os so that the lower bristles are still visible and rotated once and removed.

To prepare the slide, the material obtained on the spatula or brush should be evenly spread over the whole of the non-frosted part of the slide on the same side as the name. The spatula should be placed flat on the slide and the material spread lengthwise. The spatula should be turned over and the motion repeated so that all the material is removed. Clinging mucus and material can be removed by scraping the spatula on the edge of the slide. Material from a brush sample can be transferred to a slide by a gentle rolling motion.

3.5 FIXING THE SMEAR

It is critical that smears are fixed immediately to prevent air drying which will distort cellular detail. The smear should be flooded with fixative from a dropper bottle or placed immediately in a container of fixative which covers the whole of the cellular area. The slide should be fixed for at least 10 min. It should be placed in a slide box for transportation. It should be noted that smears from post menopausal patients and blood stained smears dry very rapidly. Normally one smear should be sufficient but excess material should be spread onto a second slide.

The request form should by *fully* completed with the patient's name, date of birth and other identifying features clearly written. The number of smears, sampling technique, clinical observations such as irregular bleeding or suspicious looking cervix must be recorded. The smear taker should ensure that the patient has understood the procedure and is aware of when she will receive the report.

3.6 THE SATISFACTORY SMEAR

A satisfactory smear has been defined in various ways. A satisfactory smear should accurately reflect the underlying histology. It should contain cells from the whole of the transformation zone. The quality of material is more important than the quantity. The cells should be evenly spread and cell details clearly displayed.

Some cytologists consider the presence of immature metaplastic cells and endocervical cells or endocervical mucus as evidence of an adequate smear, and claim that slides without these elements should be an indication for a repeat smear. However, it is now acknowledged that the presence of these elements is only an indication that the cervix has been seen and sampled and not evidence that the transformation zone has been completely sampled. In women after the menopause, in pregnant women, women who have had cervical cautery or coagulation and in women using oral contraceptives, the number of endocervical cells may be very small or absent. It does, therefore, not seem justified to claim immediate repetition of a smear in which endocervical cells have not been found. However, it has been recommended that a comment to the effect that "endocervical cells not seen" may be included in the report. Within each local programme there must be an agreed policy for "repeat" smears.

There are several causes for unsatisfactory smears. These include inadequate cellular material, inadequate fixation or air drying. The presence of large numbers of leucocytes, erythrocytes or contaminants may make the smear inadequate if they obscure the epithelial cells. Smear takers who persistently produce unsatisfactory smears should be identified and offered training. To obtain optimal smear quality, smears should be taken midcycle.

It is important to recognise that a normal or unsatisfactory smear can occur in the presence of an invasive carcinoma of the cervix or endometrial carcinoma and a clinical suspicion of cancer should overrule a normal smear report.

All reports should be seen by a responsible person before filing.

3.7 REPORTING CERVICAL SMEARS

The report should be descriptive. It should contain a description of the content of the smear and predict the underlying histology. It should include a statement as to whether the smear is satisfactory or unsatisfactory. If the latter is the case, a reason should be given.

Different classification systems for evaluation of cervical smears are available. The European Commission Training Programme for Cervical Cancer Screening (ECTPCCS) has prepared a document on equivalent terminology for the reporting of cervical smears. A table containing translations between different classification systems is in Appendix B.

The ECTP classification is set out in Table 3.1. The categories are hierarchically structured. This means that the most severe category should be used if it is possible to place a given smear in more than one category. Adherence to the terminology recommended by the ECTP working party will permit comparison of results of screening between one country and another and between individual screening centres within a country. It will permit effective monitoring of the programme.

Table 3.1. *Cervical smear and biopsy classification based on ECTP reporting terminology*

1. Invasive cancer includes
   - Invasive squamous carcinoma
   - Adenocarcinoma
   - Other malignant neoplasms
   - Possible invasive squamous carcinoma
2. Cervical intraepithelial neoplasia (CIN3) includes
   - Carcinoma *in situ*
   - Severe dysplasia
3. Adenocarcinoma *in situ* [glandular intraepithelial neoplasia (GIN3)]
4. CIN2/moderate dysplasia
5. CIN1/mild dysplasia includes
   - Koilocytic atypia
6. Other intraepithelial neoplastic lesions
   - Mixed glandular + squamous neoplastic lesions
   - Intraepithelial neoplasia of vagina and/or vulva
7. Squamous or glandular abnormality not amounting to neoplasia but requiring early repeat
8. Other abnormal changes to include
   - Abnormal findings of benign endometrial cells
   - Hormonal evaluation incompatible with age + history
9. Satisfactory — smear within normal limits/negative for neoplasia — to include smears where quality is considered to be suboptimal and smears where infection and/or inflammation have been identified
10. Unsatisfactory

3.8 PROCESSING CERVICAL SMEARS

3.8.1 *Staining*

The smear should be stained by the Papanicolaou method using reputable, high quality stains which are within the stated expiry dates. The haematoxylin should give excellent nuclear definition and the formulation of Harris haematoxylin is preferred. The cytoplasmic stains, OG 6 and EA 50, should produce the correct coloration, a steady colour balance, subtle contrasts and delicate coloration to allow cytologists to identify different types of squamous cells and define cytoplasmic margins. In order to maintain a consistent coloration of cervical smears, staining machines are recommended. The stains should be replaced at regular intervals or when there is any noticeable deterioration in the coloration.

3.8.2 *Coverslipping*

The majority of the cellular material on the slide should be covered by a glass coverslip. A 22 × 50 mm coverslip is recommended. The mountant should be dry before the slide is screened. If xylene is used as the clearing agent, the mounting procedure should be performed in a ducted fume cabinet to meet safety requirements.

3.8.3 *Labelling*

The slide should be labelled with the slide laboratory number and name of patient, bar code or other relevant information. The slide should then be matched with the request form.

3.9 MICROSCOPIC EXAMINATION OF CERVICAL SMEARS

The slide should be examined using a binocular microscope with 10 × and 40 × objectives, 10 × eyepieces and a mechanical stage. The slide should be placed on the mechanical stage and screened by starting in one corner of the coverslip and the stage should be moved either vertically or horizontally in straight lines. On reaching the edge of the coverslip the stage should be moved to overlap part of the previous field and the procedure reversed. Screening should continue until all the fields within the coverslipped area have been viewed.

Making available reports of previous smears and biopsies will facilitate the interpretation of the current smear.

3.10 STORAGE OF SLIDES

Both smears and reports should be kept for at least 5–10 years, in order to allow re-evaluation or comparison with new smears. In general, laboratories will deal with smears performed both for screening purposes and because of symptoms. Although the reason why a smear was performed should be clearly identifiable, it is advisable that a single registration system includes all smears performed for any reason. This will reduce errors and allow data for evaluation and eventually for an integrated screening programme.

3.11 THE REQUEST FORM

The form should be designed to allow easy computer entry and reporting of data. It should allow hard copy for laboratory record and copy for originator and general practitioner. A sample request form is appended (Table 3.2).

3.12 OTHER METHODOLOGIES

3.12.1 *Colposcopy*

This involves the illuminated observation of the cervix (and vagina) through a stereoscopic microscope. It is used as a screening method in some areas. Colposcopy plays an important role in the follow-up of abnormal cytology findings (see chapter 4). As a screening method, it suffers from the relative high cost and the insufficient number of skilled colposcopists. Low specificity due to overinterpretation of aceto-white areas on the transformation zone and limited sensitivity with regard to endocervical lesions are other reasons for not using colposcopy as a screening test. Early invasive cervical carcinoma may be misinterpreted as CIN because abnormal vessels are not always readily recognised at colposcopy.

Table 3.2. *Information to be included on smear request form*

1. The patient's name and address with post code.
2. The patient's date of birth.
3. Any relevant identification number.
4. The sender's name and address.
5. The name and address of the patient's general practitioner if not the sender.
6. Date of smear.
7. Source of smear.
8. Date of last smear test and report if known.
9. First day of last menstrual period, duration of cycle.
10. Reason for smear, i.e. screening or diagnosis.
11. Specimen type, i.e. cervical shape, endocervical brush, vaginal pool.
12. Condition of patient (pregnant, post natal, post menopausal).
13. Relevant clinical data (current method of contraception, hormone therapy, specify symptoms such as discharge, into menstrual or post menopausal bleeding).
14. Cytology report.
15. Suggested management.
16. Laboratory code and number.
17. Signature of reporter and date.

3.12.2 *Cervicography*

This method involves interpretation of a photographic record of the exposed acetowhite-treated area of the cervix with a specially developed camera. It is still under development.

3.12.3 *Analysis of cervical scrapes and biopsy specimens for human papillomavirus (HPV) infection using molecular biological techniques*

Screening for HPV has been advocated recently in view of the association between HPV and cervical cancer. Since a definite causal relationship between HPV and cervical cancer has not been demonstrated and since no satisfactory treatment of HPV is available it is inappropriate at this time to recommend this approach.

4. Management of the Patient with an Abnormal Cervical Smear

4.1 INTRODUCTION

WHEN AN abnormal smear report has been issued, the patient must be recalled for further examination and referral for treatment if necessary. Experience shows that this is not always the case, and a fail-safe mechanism for ensuring follow up must be part of the screening organisation (see 2.11).

The subsequent management of a patient with an abnormal smear depends on the degree of abnormality, the age of the patient and local gynaecological practices. Follow-up and management of the patient with an abnormal smear form the basis for this chapter.

4.2 FOLLOW-UP OF AN ABNORMAL SMEAR REPORT: FAIL SAFE MEASURES

The primary responsibility for follow-up of a woman with an abnormal cervical smear rests with the smear taker. However, support from other services involved in the cervical screening programme is essential to maximise follow-up efforts. The following fail safe measures should be in place:

(i) An abnormal smear report should be clearly marked with the phrase "further action required".
(ii) A copy of the smear report must be sent to the smear taker and the patient's general practitioner if he or she is not the smear taker. The woman should receive a letter informing her of the smear result or advising her to contact her doctor within a specified time.
(iii) A check list of all smears taken must be kept by the smear taker who must ensure all reports are received within 3 weeks of smears being sent to the laboratory for processing.
(iv) The cytology laboratory is appropriately placed to check whether action has been taken on any abnormal smear reports that have been issued. The cytology laboratories should send out a reminder to the smear taker and/or general practitioner if no action has been taken within 3 months of issuing an abnormal smear report.
(v) Despite all attempts to ensure action is taken, some women will escape follow-up either because they refuse further investigation or because they cannot be traced.

The names of such women should be given to the programme manager (see 2.8) who should keep a record of the attempts that have been made to contact the women concerned.

4.3 MANAGEMENT OF MILD DYSPLASIA (CIN1)

There is no agreement on the management of women with mild dysplasia (CIN1) or koilocytic atypia. Each case needs to be decided on an individual basis. Due to the high spontaneous regression rate and long average duration of these lesions before progression to invasive cancer, a repeat smear in 6 months is usually recommended in the first instance. Since there is evidence that in a small proportion of cases a more severe lesion may be present than is apparent from the cytological finding, colposcopy is recommended if the repeat smear contains abnormal cells. Alternatively, 2–3 consecutive negative smears should be obtained within 12–18 months before the woman may be returned to routine screening. Referral for colposcopy is recommended for women aged 35 and over (and women with symptoms) who have a mild dysplasia (CIN1). A biopsy is advised in the event of an abnormal transformation zone being seen.

4.4 MANAGEMENT OF MODERATE AND SEVERE DYSPLASIA AND CARCINOMA *IN SITU* (CIN2, CIN3)

There is no international agreement on treatment, but the following recommendations are given. Immediate referral for colposcopy is advised if the smear shows CIN2 or more. If an abnormal area of the transformation zone is seen, a biopsy is essential in these cases. If the biopsy shows CIN2 or more, treatment must be instituted. Treatment regimes are of two types; (1) local destructive therapy or (2) conisation. Local treatment may be by cryotherapy, heat coagulation, laser coagulation or loop exisicion. Conisation may be by cold knife conisation, electric loop or laser.

4.5 CONDITIONS FOR LOCAL DESTRUCTIVE THERAPY OF CERVICAL INTRAEPITHELIAL NEOPLASIA

Before local destructive treatment can be instituted the following conditions must be fulfilled:

(i) The transformation zone must be visualised in its entirety.
(ii) The abnormal area must be clearly defined. If the lesion extends into the endocervical canal local treatment is not sufficient.
(iii) A biopsy specimen must be taken before any local treatment is instituted.