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European guidelines for clinical management of abnormal cervical cytology, Part 2

J. Jordan*, P. Martin-Hirsch†, M. Arbyn‡, U. Schenck§, J.-J. Baldauf¶, D. Da Silva**, A. Anttila††, P. Nieminen‡‡ and W. Prendiville§§

*Birmingham Women's Hospital, UK, †Department of Obstetrics and Gynaecology, Royal Preston Hospital, UK, ‡Unit of Cancer Epidemiology, Scientific Institute of Public Health, Brussels, Belgium, §Technical University, Munich, Germany, ¶Department of Obstetrics and Gynaecology, Hôpitaux Universitaires de Strasbourg, France, **Centro de Oncologica de Coimbra, Portugal, ††Mass Screening Registry, Finnish Cancer Registry, Helsinki, Finland, ‡‡Department of Obstetrics and Gynaecology, Helsinki University Central Hospital, Helsinki, Finland and §§Department of Obstetrics and Gynaecology, Coombe Women's Hospital, Dublin, Ireland

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J. Jordan, P. Martin-Hirsch, M. Arbyn, U. Schenck, J.-J. Baldauf, D. Da Silva, A. Anttila, P. Nieminen and W. Prendiville

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The current paper presents the second part of chapter 6 of the second edition of the *European Guidelines for Quality Assurance in Cervical Cancer Screening*. The first part of the same chapter was published in a previous issue (*Cytopathology* 2008;19:342–54). This part provides guidance on how to manage and treat women with histologically confirmed cervical intraepithelial neoplasia. The paper describes the characteristics, indications and possible complications of excisional and ablative treatment methods. The three options to monitor the outcome after treatment (repeat cytology, HPV testing and colposcopy) are discussed. Specific recommendations for particular clinical situations are provided: pregnancy, immuno-suppression, HIV infection, post-menopause, adolescence and cyto-colpo-histological disparity. The paper ends with recommendations for quality assurance in patient management and some general advice on how to communicate screening, diagnosis and treatment results to the woman concerned. Finally, a data collection form is attached.

Keywords: cervical cancer screening, colposcopy, clinical management, cervical intraepithelial neoplasia, European guidelines, treatment

Introduction

A histological diagnosis of cervical intraepithelial neoplasia (CIN) indicates the presence of a lesion which, if untreated, may progress to invasive cancer. The lowest grade is CINI (low-grade CIN) which may represent no more than changes due to human papillomavirus (HPV). On the other hand CIN2-3 (high-grade CIN) definitely has the potential to progress to invasive cancer and always requires treatment.

The key to management is colposcopy – no patient should be treated unless first seen and assessed by a colposcopist who is appropriately trained. The colposcopist must be thoroughly familiar with diagnostic colposcopy and ideally be trained in the various techniques of therapeutic colposcopy. Local excision of CIN is the preferred method of treatment thereby allowing a full and proper histological assessment of all the tissue removed. Ablation is an acceptable alternative but only if certain strict criteria are adhered to and only if the diagnostic colposcopy and initial biopsy/biopsies have been carried out by an expert colposcopist.

Correspondence:
Joe Jordan, Birmingham Women's Hospital, Birmingham, UK
Tel.: +44 121 4542345; Fax: +44 121 4545129;
E-mail: j.jordan@tiscali.co.uk

Treatment is not without morbidity and the various complications of treatment need to be considered before treatment is carried out. Any woman treated for CIN requires careful follow-up and this is the responsibility of the colposcopist. The colposcopist must be familiar with the problems associated with abnormality in pregnant women, adolescent women, postmenopausal women, post-hysterectomy women and immunocompromised women. The colposcopist must also know how to manage women in whom there is a discrepancy between cytology, colposcopy and histology. Patient information before during and after colposcopy is important and the responsibility of the colposcopist.

Treatment procedures

The management of colposcopically confirmed disease can be ablative, excisional or in some circumstances observational. There is no obviously superior conservative surgical technique for treating and eradicating CIN.[1] This is true if success/failure rates are the index of superiority. Excisional techniques are preferred in the majority of circumstances because of their clear superiority over ablation in terms of histological evaluation of the transformation zone (TZ). Histological examination of the excised tissue allows the pathologist to recognize or rule out microinvasive cancer, glandular disease, margin involvement and depth of excision. It also allows the colposcopist to self-audit his/her diagnostic skills.

Excision of the lesion

The aim of an excisional treatment is to remove the lesion in its entirety. The entire excised specimen is then submitted for histological assessment. The sample can only be planned safely by colposcopic assessment of the lesion by an experienced colposcopist.

Excision of the TZ should not be performed for CIN1, unless the lesion has persisted over a period of more than a year. It should be performed without delay in the presence of high-grade intraepithelial neoplasia or suspicion of early stromal invasion or microinvasion.

Techniques used for the complete excision of the TZ are LLETZ, cold knife conisation, laser excision and needle excision of the transformation zone (NETZ). Large loop excision of transformation zone (LLETZ) consists of the excision of cervical tissue using a diathermy loop. Loop electrosurgical excision procedure (LEEP) is a North American term used to describe the same technique as LLETZ. The terms LLETZ and LEEP are used synonymously, but in this guideline only the European term LLETZ will be used. In cold knife conisation cervical tissue is removed using a knife and the excised product has the shape of a cone. Laser excisional conisation or laser excision means that cervical tissue is removed using a CO_2 laser in cutting mode. NETZ means that the TZ is excised with a straight diathermy wire. Straight wire excision of the transformation zone (SWETZ) and NETZ refer to the same technique.

When performing the excision the following recommendations should be followed:

1. The procedure should be carried out under colposcopic control.
2. The lesion together with the entire TZ should be removed.
3. It is helpful to mark the excised specimen with a thread at 12 o'clock, thereby facilitating the histopathologist to orient the specimen.
4. Surgeons should avoid damage of the ectocervical epithelium or of the endocervical canal.
5. A cervical dilator for orientation of the excision specimen is unhelpful.
6. The size and shape of the excised specimen will be determined by the colposcopic delineation of the lesion.
7. Excision should be mandatory if the lesion involves the endocervical canal.
8. If the lesion involves the endocervical canal, endocervical sampling should be considered after the excision.
9. Thorough histological assessment by a pathologist skilled in gynaecological pathology is essential.
10. The histopathologist should be informed of the cytology and colposcopic findings.
11. Cold knife conisation gives excision margins that are not affected by thermal artefact, whereas the margins of laser excisional cone or diathermy loop excision cone may be damaged. In skilled hands, the thermal artefact is generally minimal. In the meta-analysis of Martin-Hirsch et al[1] there was a clear advantage of cold knife cone biopsy over laser or LLETZ.
12. Excision of the TZ in multiple fragments can complicate histopathological assessment. Furthermore, if microinvasive disease is present, it may be impossible to allocate a substage or define completeness of excision in fragmented exci-

sional specimens. When using LLETZ, the external os and lower canal should be removed in a single sample. Disease lateral to the central area can be removed separately.

13. If cold knife conisation is performed great care must be taken to minimise side effects such as haemorrhage and cervical stenosis. Haemorrhage can be minimised by injecting the cervix preoperatively with adrenalin 1 in 200,000. If haemorrhage is controlled with diathermy and the use of Monsel's solution (see annex 1)[2] cervical stenosis is much less likely to occur than if cervical sutures are used to control bleeding at the time of conisation.

Local destructive therapy

The aim of local destructive therapy is to destroy CIN by the use of radical diathermy, laser vaporisation, cryotherapy or cold coagulation.

Radical diathermy (or electrocoagulation) uses a straight electrodiathermy needle and aims to destroy tissue to a depth of approximately 1 cm.

Diathermocoagulation is a technique which uses heat to destroy cervical epithelium only to a depth of 2–3 mm. The depth of destruction is too superficial for it to be recommended for the treatment of CIN.

Laser vaporisation employs a CO_2 laser at a high power setting: under colposcopic control the laser beam is aimed directly at the tissue to be removed: it works by vaporising the water in the cells at the speed of light.

Cryotherapy (or cryocautery) employs a probe which is applied directly to the tissue to be destroyed by freezing: the depth of destruction is 3–4 mm.

Cold coagulation uses a probe similar to a cryocautery probe, but destroys the tissue by heating it to 100 °C.

All of these techniques can be performed on an outpatient basis. The dilemma is that the tissue is destroyed rather than being sent for histological assessment: the fear is that occasionally cervical glandular intraepithelial neoplasia (CGIN), adenocarcinoma in situ (AIS) or early invasive carcinoma will remain undetected and, therefore, be treated inappropriately by destruction rather than by excision. This is one of the reasons why excisional techniques are preferred. However, provided that certain selection criteria are adhered to, the various techniques can be safe and very effective.

The selection criteria are as follows:

1. The entire transformation zone must be visible.
2. One or more biopsies should be taken from the area or areas that colposcopically show the most severe change.
3. The result of the biopsy or biopsies should be available prior to the destructive therapy.
4. Cryotherapy should not be offered to women with large lesions, occupying more than 75% of the ectocervix, extending to the vaginal wall or extending more then 2 mm beyond the cryoprobe.[3,4] This applies also to cold coagulation but not to radical diathermy.
5. There should be no evidence of invasive disease on cytology, colposcopy, or biopsy.
6. The Pap smear should not contain glandular atypical cells.
7. The destructive therapy should be carried out under colposcopic control by an experienced colposcopist.
8. There must be adequate follow-up.

When using an ablative therapy, destruction of the TZ should be to a minimum depth of 4 mm (it is probably safer to aim to destroy to a depth of 7 mm). Destruction should extend beyond the ectocervical and endocervical margins of the lesion.[5,6] The evidence from an extensive systematic review of the literature is that cold coagulation and laser ablation are effective in treating all grades of CIN when used by skilled operators.[1] Radical diathermy can be very effective. Chanen & Rome reported a cure rate of 98.3% with a single treatment.[7] Cryocautery should only be used for type 1 transformation zones and a double freeze-thaw-freeze technique should be used.[8] Ablative therapy should aim to destroy the entire TZ as more localised treatment produces higher recurrence rates.[9]

Management of histologically confirmed CIN

Management of CIN1

While some 60–70% of histologically suspected cases will revert to normal over time, some 15% will persist. Between 0% and 30% will ultimately reveal CIN2-3 and less than 1% will lead to invasive carcinoma.[10–12] However, colposcopists have to be aware that the diagnosis of CIN1 is not always reliable. This is illustrated by the wide range of intra-observer and inter-observer variability in the diagnosis of colposcopically directed biopsies initially classified as CIN1, as demonstrated in the

ASCUS/LSIL Triage Study.[13] In this study only 43% were confirmed as having CIN1 by expert panel review, 41% were downgraded to normal and 13% were upgraded to CIN2 and 3. Further evidence for the potential unreliability of colposcopic biopsies suggesting CIN1 is illustrated by studies that compared subsequent loop excisions of the TZ. These studies have demonstrated CIN2 and 3 in 23–55% of specimens.[14] The management of low-grade disease has to balance the high chance of spontaneous regression and negative histology with the possible risk of not treating underreported or missed high-grade disease. Observational and immediate treatments both have advantages and disadvantages. Two different situations can be distinguished: satisfactory and unsatisfactory colposcopy.

Satisfactory colposcopy. Two options can be recommended: follow-up or treatment. Follow-up consists of repeat cytology at 12 and 24 months or hrHPV DNA testing at 12 months, with referral for colposcopy when cytology reports atypical squamous cells of undetermined significance (ASC-US) or a more serious lesion or when the HPV test is positive. Observation tends to be the preferred management, particularly in young nulliparous women.[15] There is no reliable evidence on the optimal duration of follow-up or whether colposcopy increases the detection of high-grade disease during this period. Patients with CIN1 can also be offered treatment, which can be ablative or excisional. In case of recurrent CIN1 excisional methods should be preferred.

Unsatisfactory colopscopy. If colposcopy is unsatisfactory then an excisional treatment, should be considered, because occult high-grade disease might be present.[16]

Unacceptable treatment approaches for CIN1

1. See and treat: this refers to seeing a patient for the first time in the colposcopy clinic and removing the transformation zone by loop excision because the cervical epithelium shows aceto-white changes. For low-grade cytological abnormality this will result in a very large number of women receiving unnecessary treatment.
2. Local destruction procedures are unacceptable for CIN1 in patients with an unsatisfactory colposcopic examination.[15]
3. Podophyllin or podophyllin-related products are unacceptable for use in the vagina or on the cervix.
4. Hysterectomy as the primary and principle treatment for biopsy-confirmed CIN1 is unacceptable unless there is another indication for hysterectomy such as a fibroid uterus.

Management of CIN2 and CIN3

The natural history of histologically confirmed high-grade CIN is documented only from a few small case-series, since these lesions are almost always treated. The review of Ostör[17] included six studies, showing the outcome of 423 women with biopsy-proven CIN2 or CIN3.[18–23] The pooled progression rate to carcinoma in situ or cancer was 20%, but varied widely (from 0% to 53%). The overall persistence rate was 50% (ranging from 15% to 96%) and the overall regression rate was 29% (ranging from 4% to 67%).

Women with high-grade CIN require treatment; observational follow-up is not an option. Local ablation or destruction, using laser ablation, cryotherapy, cold coagulation or radical diathermy is acceptable management strategies if colposcopy is satisfactory. In the case of recurrence or when colposcopy is unsatisfactory, excision using LLETZ or cold knife must be chosen.[24,25] Of these two approaches ablation or excision, excision is preferred. If destructive or ablative therapy is offered then the conditions outlined earlier must be adhered to.

Microinvasive cancer

If the degree of invasion is no more than early stromal invasion, then local excision is adequate treatment. If the lesion is microinvasive squamous carcinoma (FIGO Stage 1A1), it is still appropriate to use conservative excisional techniques alone, providing that the following conditions prevail:[24]

1. The excision margins are free of CIN and invasive disease.
2. The pathologist plus the multidisciplinary team have reviewed the histology and confirmed that the lesion is no more advanced than Stage 1A1.
3. If the invasive lesion has been excised but CIN extends to the excision margin (ectocervical and/or endocervical), then a repeat excision procedure should be carried out to confirm that the CIN has been excised completely and to confirm also that there are no further satellite foci of invasive disease. This should be carried out

even in those cases planned for simple hysterectomy, in order to exclude an occult invasive lesion requiring radical surgery.

Complications after treatment of CIN

Complications after conservative therapy have been reported, but these are uncommon. In the short term there may be bleeding, discharge and infection. Long-term complications include cervical stenosis, and cervical insufficiency causing mid-trimester abortions. The latter complications are generally associated with knife conisation.[26] Nevertheless, a recent systematic review indicated that all excisional procedures are associated with an increased frequency of low-birth weight and premature delivery when compared to women who never had cervical treatment.[27] Stenosis and unsatisfactory colposcoy and cytological follow-up are complications usually due to the use of haemostatic sutures.[1] Rarely the cervix will be stenosed completely in which case in premenopausal women haematometra will occur, and the efficacy of follow-up cytology may be compromised: in post-menopausal women, there is a further problem in that it will be impossible to rely on the presence of postmenopausal bleeding to suspect invasive endometrial carcinoma. Complete cervical stenosis is also a problem for women having hormone replacement therapy (HRT). They will need to use daily progestogen to suppress endometrial proli-feration due to oestrogen.

Follow-up after treatment of CIN

In terms of success or failure, there is no obviously superior conservative surgical technique for the treatment of CIN.[1] All women treated for CIN, whether CIN1, 2 or 3, require regular follow-up. Excisional treatment procedures have the obvious advantage that they permit histological assessment of the biopsy. Histological examination of the entire TZ allows evaluation of the marginal status and exclusion of microinvasive or glandular disease. Women at increased risk of residual or recurrent disease should be considered for more intensive surveillance following treatment. Therefore, responsibility of the completeness of follow-up, using the intervals indicated below, needs to be clearly defined within the management process. Some factors may influence the frequency and duration of follow-up:

1. Patient's age: women aged 40 or over are at increased risk of persistent or recurrent disease.
2. Type of lesion: glandular disease requires careful post-operative assessment of the endocervical canal, usually with an endocervical brush sample.
3. Grade of lesion: high-grade lesions are more likely to persist or recur.
4. Histology of excised margins (suspicion of incomplete excision).

Women treated for **high-grade disease** (CIN2, CIN3, CGIN) require 6-, 12- and 24-month follow-up cytology and thereafter annual cytology for a further five years before returning to screening at routine interval. Colposcopy is performed in addition to cytology at the 6-month follow-up visit.[28] Most persistent/recurrent disease is detected within the first 24 months.[29,30] However, there is clear evidence that there is persistent long-term risk of invasive cancer for ten years after treatment.[31] Women treated for **low-grade disease** require 6-, 12-, 24-month follow-up cytology. If all results are negative, then women may be returned to screening at a routine interval. Women treated for AIS are at higher risk of developing recurrent disease than those with high-grade CIN.[32]

There is no clear evidence suggesting that the diagnostic performance of cytology in combination with colposcopy for the detection of persistent disease after treatment for CIN is superior to cytology alone. Some authors suggest that colposcopy does not increase the detection of disease.[33] Other authors[34–36] suggest that an initial follow-up colposcopy marginally enhances early detection of disease and reduces the false negative rate.

Significance of involved margins in the excised specimen

Several retrospective studies[29,33,37–44] of residual disease rates after LLETZ or knife cone biopsy have demonstrated that negative excision margins are associated with a lower risk of residual disease. Studies have demonstrated that disease at the endocervical resection margin is associated with increased risk of residual disease compared with involved ectocervical margins.[6,8,29,33,42,44–47] Women aged 40 or more[29,48] are particularly at risk of persistent or recurrent disease. All women over the age of 50 years who have CIN3 at the endocervical margin and in whom satisfactory cytology and colposcopy cannot be guaranteed should have a repeat excision to try to obtain clear margins. If the

pathologist has reported incomplete endocervical excision then an endocervical cytology sample is recommended.

The role of HPV testing in follow-up after treatment

The study of the sensitivity and specificity of HPV DNA testing to predict residual or recurrent neoplasia after treatment of CIN was the object of two recent systematic reviews[49,50] also discussed in Chapter 3 of the *European Guidelines for quality assurance in cervical cancer screening*.[51] The first systematic review concluded that there is evidence that HPV testing post treatment can more quickly and efficiently detect a treatment failure than follow-up cytology. Zielinski reached similar conclusions.[50] The data included in both studies were extended with newly published studies, and a formal meta-analysis was conducted.[52] From this meta-analysis it was concluded that HPV DNA detection predicted residual/recurrent CIN with significantly higher sensitivity (ratio: 1.27; 95% CI: 1.06–1.51) and not-significantly lower specificity (ratio: 0.94; 95% CI: 0.87–1.01) than follow-up cytology. HPV DNA testing was also more sensitive than histology of the section margins (ratio: 1.30; 95% CI: 1.05–1.62). HPV testing was even more specific but this difference in specificity was statistically insignificant.

Treatment of residual and recurrent lesions

The presence of residual disease warrants excision of the TZ although in skilled hands, destruction may be considered provided that the conditions relating to preoperative assessment are met. However, post-treatment recurrence frequently occurs in the endocervical canal where it is not colposcopically detectable and therefore not suitable for ablative therapy.[44,53]

Management of women in other clinical situations

There are several circumstances in which management and treatment may differ from the general recommendations given above. The following particular situations are distinguished:

1. Pregnant women
2. Adolescent women
3. Postmenopausal women
4. Hysterectomised women
5. Immunocompromised women
6. Discrepancy between cytology, colposcopy and histology.

Management of women with cytological abnormality in pregnancy

Smears in pregnancy. Taking a smear should be postponed for pregnant women with negative screening histories unless the last smear was more than five years ago. If a woman has been called for routine screening and she is pregnant, the smear should usually be deferred. If a previous smear was abnormal and in the interim the woman becomes pregnant then the follow-up should not be delayed.

Colposcopy in pregnancy. A woman who meets the criteria for colposcopy still needs colposcopy if she is pregnant. The primary aim of colposcopy for pregnant women is to exclude invasive disease and to defer biopsy and treatment until the woman has delivered. Women who have low-grade cytology and in whom the colposcopy excludes high-grade disease, simply have a repeat colposcopy/cytology test 3–4 months after delivery. Women with high-grade disease and in whom colposcopy has excluded suspicion of invasive disease, should be reviewed at intervals of 3 months with a view to a final assessment 3–4 months following delivery. At that time a decision should be made on whether treatment is required.

The safety of delaying treatment of pregnant women has been shown in a number of cohort and retrospective uncontrolled studies.[54] The incidence of invasive cervical cancer in pregnancy is low and pregnancy itself does not have an adverse effect on the prognosis.[54] The risk of progression of CIN3 is low in pregnancy and the spontaneous regression rate is high. One study reported a spontaneous regression rate of 69% after pregnancy for histologically proven CIN3[55] If colposcopy has been performed during pregnancy, post-partum assessment of women with an abnormal smear or biopsy-proven CIN is essential. Excision biopsy in pregnancy cannot be considered therapeutic and these women should be seen for colposcopy post-partum. Colposcopic evaluation of the pregnant woman requires a high degree of skill. If invasive disease is suspected clinically or colposcopically, a biopsy adequate to make the diagnosis is essential. Cone, wedge and diathermy loop biopsies are all associated with a risk of haemorrhage[56] and such biopsies should be taken only where appropriate facilities to deal with haemorrhage are available. Punch biopsy suggesting only CIN cannot reliably exclude invasion.

Adolescent women. Invasive cervical carcinoma is virtually non-existent in adolescent women.[57] The prevalence of transient HPV infection after coitarche is high.[58] Cervical screening in this age group may detect prevalent low-grade disease which might have resolved spontaneously if screening were started at a later age.[58] This could result in un-necessary attendances at colposcopy, with the resultant possible negative consequences of increased anxiety and possible over-treatment. In addition screening has not been shown to be effective at reducing the incidence of invasive cancer in women under twenty.[15,59-61]

Post menopausal women. The incidence of abnormal cytology is extremely low in women of this age group who have previously had negative cytology. An episode of postmenopausal bleeding warrants a complete gynaecological assessment, with a cytology test, but is not an indication for colposcopy.

Hysterectomised women. Women who have had a hysterectomy with CIN present are potentially at risk of developing vaginal intraepithelial neoplasia (VAIN) and cancer. The incidence of VAIN following hysterectomy diagnosed with CIN is in the order of 1% in a series of 341 women[62] with no subsequent cases of invasive disease. In a similar series of 177 women[63] 4% developed VAIN, with 0.6% developing subsequent invasive disease. A meta-analysis of long-term results suggests that while recurrent intraepithelial disease is less common after hysterectomy for CIN than after local treatment of the cervix (522 vs. 1587 per 100,000 woman-years), the risk of invasive recurrence is similar in both groups (57 vs. 67 per 100,000 woman-years).[64] There is no clear evidence that colposcopy increases the detection of disease on follow-up. A possible guideline for post-hysterectomy follow-up is as follows:

1. For women who have been on routine screening for at least ten years but who have no CIN in the specimen, no vault cytology is required.
2. For women who have been on routine screening for less than ten years, and who have no CIN in the cervix, a smear six and 18 months from the vault and no further cytology follow-up if both are negative.
3. For women who have had a hysterectomy for CIN for some particular reason, and in whom the CIN has been excised completely, there should be a smear six and 18 months after the hysterectomy. If follow-up cytology at 18 months is negative, no further cytology is necessary.
4. For women with incomplete or uncertain excision of CIN, follow-up should be conducted as if the cervix were still *in situ* (i.e. as for low and high-risk CIN).

Immunosuppressed patients. Patients with immunodeficiency due to immunesuppressing medication, transplantation and all other forms of immunosuppression will have an increased frequency of CIN. The risk of progression to invasive disease is higher and the success rate of treatment is lower. Continued patient surveillance is needed. The prevalence of abnormal cervical cytology in the renal transplant population of around 15% represents a five-fold increase from the normal population.[65] There is also an increased incidence of CIN in women with systemic lupus erythematosus treated with long-term chemotherapy.[66] There is debate as to whether immunosuppressed patients should be screened more frequently, and in some centres annual cytology combined with colposcopy is recommended.

HIV-positive women. Whereas the estimated prevalence of cervical disease in HIV seronegative women is approximately 3%,[67] a number of reports including cross sectional, case-control and cohort studies have indicated a greatly increased prevalence of squamous intraepithelial lesions, ranging between 20 and 40%[68] in HIV-infected women. Annual cytology should be performed with an initial colposcopy if resources permit. High-grade histologically-proven disease should be treated as the guidelines recommend for non-HIV patients.

Procedure in case of cyto-colposcopical discrepancies. Occasionally, following a high-grade abnormal Pap smear, the colposcopy is normal. Such women are at risk of having or developing subsequent CIN2 or worse. In this situation, before assuming that either the Pap test is falsely positive or before systematically recommending a diagnostic cone biopsy or loop excision of the TZ, smears should be repeated, and the original cytology should be reviewed.

Should cytological abnormalities persist, a second colposcopy is required. The colposcopic examination must be performed under optimal conditions, if necessary after treatment of any inflammatory or infective condition of the lower genital tract or after oestrogenic preparation in postmenopausal women.

Special attention must be given to identifying the squamo-columnar junction (SCJ). If the SCJ is visible and no colposcopic abnormality is apparent, the investigation should be completed by a detailed examination of the vagina. If again there is no obvious lesion, the endocervical canal should be assessed as thoroughly as possible. If no abnormality can be seen, then the TZ should be excised in its entirety; this should be combined with an endocervical curettage. If the SCJ is not visible, and no abnormality can be identified on the cervix or the vagina, then the TZ should be excised in its visible entirety and the lower third of the endocervical canal should also be removed. This should be followed by an endocervical curettage.

The management depends also on the severity of the cytological abnormality. With minor cytological abnormalities the risk of failing to detect a severe histological lesion is low provided colposcopic assessment, together with, if indicated, colposcopically directed biopsies and perhaps endo-cervical curettage, are all negative. However, when cytology is suggestive of high-grade disease the major problem is to eliminate high-grade CIN or an early invasive disease. Ideally, all cases with discrepant high-grade cytology, colposcopy or histology findings should be discussed in a multi-disciplinary forum to optimise management.

Quality assurance of patient management

To achieve optimum results from cervical screening, quality assurance at all levels is important. Each national cervical screening programme should produce guidelines that are relevant to its own country or region. The aim of quality assurance is to optimize compliance and effectiveness of patient management according to defined standards, to inform women, and to provide feedback to healthcare professsionals and decision makers. Multidisciplinary meetings involving the cytologist, the histopathologist and the clinician should be encouraged in both public and private hospitals. These meetings are useful for discussing general cytology, histopathology and colposcopy practice but are also useful for discussing unusual cases and where there is a discrepancy between results. Auditing of practice should be encouraged.

Measures to improve follow-up

There should be national or EU-agreed guidelines regarding management and follow-up. Fail-safe measures should be installed to maximise compliance of screen-positive women with follow-up recommendations.[69] Formally agreed-upon instructions should be developed to monitor the outcome of screen-detected lesions (see below and Chapter 7.[51] The purpose is to measure the accuracy of cytology and colposcopy, using histology as reference, and to evaluate follow-up compliance and treatment effectiveness.

Fail-safe measures to assure compliance with follow advice

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

1. An abnormal smear report should be clearly marked with the phrase ''further action required''. 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.
2. A check-list of all smears must be kept by the smear taker who must ensure that all results are collated and acted upon.
3. The cytology laboratory should 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 six months of issuing an abnormal smear report. Failsafe procedures could be a task of the screening programme manager, who has access to screening registries.
4. 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 who should keep a record of the attempts that have been made to contact the women concerned.

Correlation of cytology findings with the final histological diagnosis

Efforts should be made to correlate the reported cytological abnormality with the histological out-

come. Since the laboratory is the only common factor in the diagnosis and follow-up of women with abnormal cytology, it should be the responsibility of the cytology laboratory to collate this information. It could also be the responsibility of the programme manager, working in conjunction with the laboratories.

Where the original cellular changes have been minor, information of cytological regression will suffice. However, in those cases which require histological assessment and treatment, the original cytology should be correlated with the final histology.[70] This needs to be organised in a way such that the wish for quality improvement does not increase the risk of harm by over-diagnosis and over-treatment of the women. This correlation between cytology and histology is an important component of maintaining and improving the quality of the cytology screening programme.[71]

Patient information

Each woman must be informed (verbally or written) about the screening test result. Anxiety can be produced by the mere process of cervical screening[72] when an abnormality is found which requires referral for colposcopy or treatment.[73,74] To allay anxiety, the following points should be considered:

1. Each woman should receive verbal and/or written information before and after a cervical smear is taken. She should be reassured that she will be informed of the result either verbally (if necessary by telephone) or in a written form.
2. Each woman should receive verbal and written information before colposcopy.
3. Counselling should be available as an integral part of colposcopy.
4. Women should receive an appropriately worded invitation for colposcopy with a contact name, telephone number and clinic times.
5. Information following the colposcopy visit should be given to the patient verbally by the person performing the colposcopy. She should be told that the results of any investigations will be communicated to her within a few weeks.
6. If the visit to the colposcopy clinic has involved treatment then the results of histology of the excisional biopsy or punch biopsy should be communicated to the patient within a few weeks.
7. Information should be made available to ethnic minority and refugee groups.

Data collection on treatment and follow up of screen-detected lesions

A recommended minimum set of indicators should be permanently monitored. The minimum set of indicators can be monitored by hand-collecting items described in Tables 1 and 2, but the use of an audit system is highly recommended for practical reasons and because it facilitates homogeneous data recording. The potential benefits of audit are unlikely to be accomplished unless physicians (gynaecologists) take responsibility for it and see it as an opportunity for permanent education and professional improvement rather than an attempt to control their activity. Follow-up of outcomes such as cancers, residual pre-cancerous lesions after treatment of pre-cancerous lesions, deaths and survival rates after cancer treatments must also be included in the auditing process. Systematic outcome data can be acquired by linking the treatment information, e.g. operation and diagnosis codes, with cancer registry or death records.

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Table 1. Data to be collected on the treatment of lesions, and to be obtained from the cancer registry in case of occurrence of cancer.

Personal identification
- personal identifier
- date of birth

Diagnosis
- date of diagnosis
- diagnosis and diagnosis code
- stage
- grade

Treatment
- date of treatment
- treating physician
- hospital code
- operation code
  - radiotherapy
  - chemotherapy
  - radical hysterectomy
  - total hysterectomy
  - amputation of cervix
  - conisation/excision of the TZ
    - LLETZ
    - NETZ
    - laser
    - cold knife
  - local destructive therapy
    - laser vaporisation
    - cryotherapy
    - radical diathermy
    - cold coagulation

Compliance with
- treatment follow-up

Table 2. Carcinoma cases occurring during follow-up after treatment (from cancer registry and mortality records).

- personal identifier
- date of diagnosis of cancer
- diagnosis code
  - stage
  - grade
- vital status of the patient
- cause of death

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