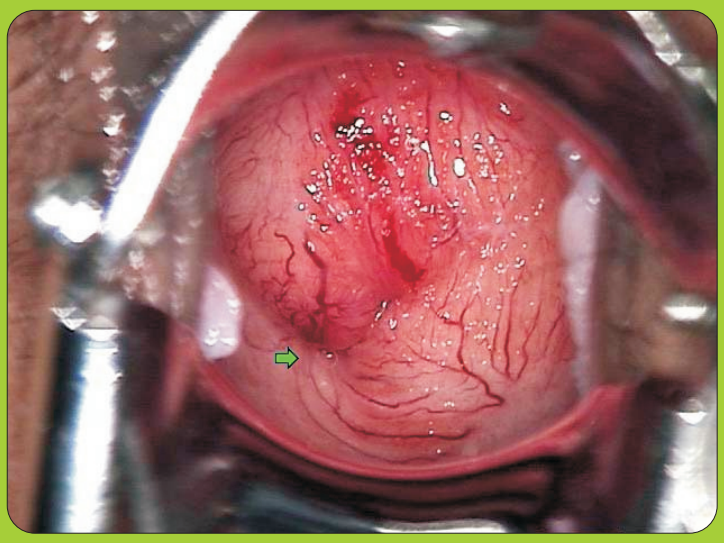
A Practical Manual on Colposcopy and Cryotherapy Procedures For Medical Professionals



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INDICATIONS FOR COLOPOSCOPY

Given the availability of a colposcope and trained colposcopists, there are a number of indications for this examination, of which positive cervical screening tests constitutes the most frequent indication for colposcopy (e.g., Positive cytology, positive on visual inspection with acetic acid etc.)

1. Suspicious looking cervix
2. Invasive carcinoma on cytology
3. CIN 2 or CIN 3 on cytology
4. Persisting (for more than 12-18 months) low-grade (CIN 1) abnormalities on cytology
5. CIN 1 on cytology
6. Persistently unsatisfactory quality on cytology
7. Infection with oncologenic Human Papilloma Viruses
8. Acetopositivity on visual inspection with acetic acid using magnification
9. Positive on visual inspection with Lugol's Iodene

INSTRUMENTATION

Hinselmann (1925) first described the basic colposcopic equipment and its use, establishing the foundation for the practice of colposcopy. A colposcope is a low-power, stereoscopic, binocular, field microscope with a powerful variable-intensity light source that illuminates the area being examined (Figure 1.2).

The head of the colposcope, also called the 'optics carrier', contains the objective lens (at the end of the head positioned nearest to the woman being examined), two ocular lenses or eyepieces (used by the colposcopist to view the cervix), a light source, green and/or blue filters to be interposed between the light source and the objective lens, a knob to introduce the filter, a knob to change the magnification of the objective lens, if the colposcope has multiple magnification facility and a fine focusing handle. The filter is used to remove red light, to facilitate the visualization of blood vessels by making them appear dark. Using a knob, the head of the colposcope can be tilted up and down to facilitate examination of the cervix. The distance between the two ocular lenses can be adjusted to suit the inter-pupillary distance of the provider, to achieve stereoscopic vision. Each ocular lens has diopter scales engraved on it to facilitate visual correction of individual colposcopists. The height of the head from the floor can be adjusted by using the height adjustment knob, so that colposcopy can be carried

out with the colposcopist comfortably seated, without strain to the back.

Modern colposcopes usually permit adjustable magnification, commonly 6x to 40x usually in steps such as, for example, 9x, 15x, 22x. Some sophisticated and expensive equipment may have electrical zoom capability to alter the magnification. Most simple colposcopes have a single fixed magnification level such as 6x, 9x, 10x, 12x or 15x. Most of the work with a colposcope can be accomplished within the magnification range of 6x to 15x. Lower magnification yields a wider view and greater depth of field for examination of the cervix. More magnification is not necessarily better, since there are certain tradeoffs as magnification increases: the field of view becomes smaller, the depth of focus diminishes, and the illumination requirement increases. However, higher magnifications may reveal finer features such as abnormal blood vessels.

The location of the light bulb in the colposcope should be easily accessible to facilitate changing them when necessary. Some colposcopes have bulbs mounted in the head of the instrument; in others, these are mounted elsewhere and the light is delivered via a fibre-optic cable to the head of the colposcope. The latter arrangement can use brighter bulbs, but less overall illumination may result if the cables are bent or twisted. A colposcope may be fitted with halogen, xenon, tungsten or incandescent bulbs. Halogen bulbs are usually preferred, as they produce strong white light. The intensity of the light source may be adjusted with a knob.

Focusing the colposcope is accomplished by adjusting the distance between the objective lens and the woman by positioning the instrument at the right working distance. Colposcopes usually have fine focus adjustments so that, if the distance between the base of the scope and the woman is kept fixed, the focus of the scope may be altered slightly using the fine focusing handle. The working distance (focal length) between the objective lens and the patient is quite important - if it is too long (greater than 300 mm) it is hard for the colposcopist's arms to reach the woman, and if it is too short (less than 200 mm), it may be difficult to use instruments like biopsy forceps while visualizing the target with the scope. A focal distance of 250 to 300 mm is usually adequate. Changing the power of the objective lenses alters the magnification and working distance.

Colposcopes are quite heavy and are either mounted on floor pedestals with wheels, suspended from a fixed ceiling mount, or fixed to the examination table or to a wall, sometimes with a floating arm to allow for easier adjustment of position. In developing countries, it is preferable to use colposcopes mounted vertically on a floor pedestal with wheels, as they are easier to handle and can be moved within or between clinics.

The instruments needed for colposcopy are few and should be placed on an instrument trolley or tray (Figure 1.1) beside the examination table. The instruments required are: bivalve specula (Figure 1.3), vaginal side-wall retractor (Figure 1.4), cotton swabs, sponge-holding

forceps, long (at least 20cm long) anatomical dissection forceps, endocervical speculum (Figure 1.5), biopsy forceps (Figure 1.6), endocervical curette (Figure 1.7), cervical polyp forceps and single-toothed tenaculum. In addition, the instrument tray may contain instruments necessary for treatment of CIN with cryotherapy or loop electrosurgical excision procedure (LEEP). The tray should also contain the consumables used for colposcopy and treatment.

In view of the different sizes of vagina, varying widths of bivalve specula should be available. One may use Cusco's, Grave's, Collin's or Pedersen's specula.

One should use the widest possible speculum that can comfortably be inserted into the vagina to have optimal visualization of the cervix. Vaginal side-wall retractors are useful to prevent the lateral walls of a lax vagina from obstructing the view of the cervix. However, they may cause discomfort to the patient. An alternative approach is to use a latex condom on the speculum, the tip of which is opened with scissors 1 cm from the "nipple". Sponge-holding forceps or long dissection forceps may be used to hold dry or moist cotton balls. The endocervical speculum or the long dissection forceps may be used to inspect the endocervical canal. The endocervical curette is used to obtain tissue specimens from the endocervix. Several types of sharp cervical biopsy punch forceps with long shafts (20-25 cm) such as Tischler-Morgan, Townsend or Kevrokian, are available. A single-toothed tenaculum or skin (iris) hook may be used to fix the cervix when obtaining a punch biopsy. Cervical polyps may be avulsed using the polyp forceps.

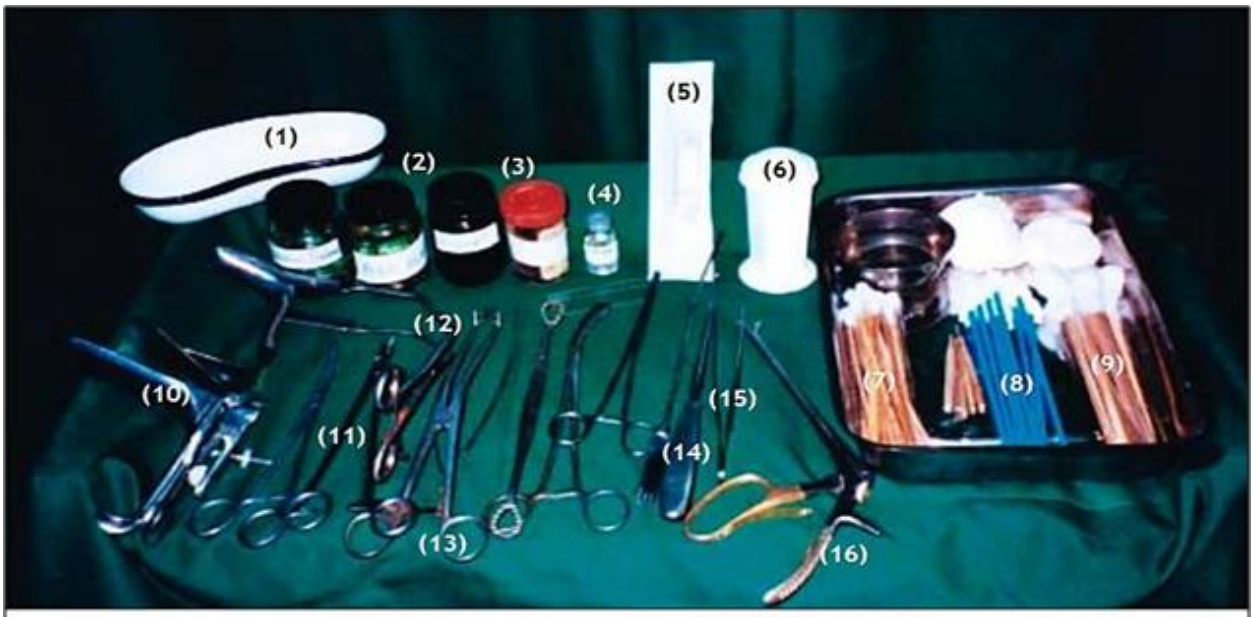


FIGURE 1.1: Colposcopy instrument tray

1: Kidney tray
2: Bottles with normal saline, 5% acetic acid and Lugol's iodine
3: Monsel's solution
4: Bottle containing formaline
5: Local anaesthetic syringe
6: Jar containing alcohol for cervical smear fixation
7: Cotton-tipped fine swab sticks
8: Cervical cytology brushes
9: Larger cotton-tipped swab sticks
10: Vaginal speculum
11: Sponge-holding forceps
12: Vaginal side-wall retractor
13: Endocervical speculum
14: Endocervical curette
15: Dissecting forceps
16: Punch biopsy forceps

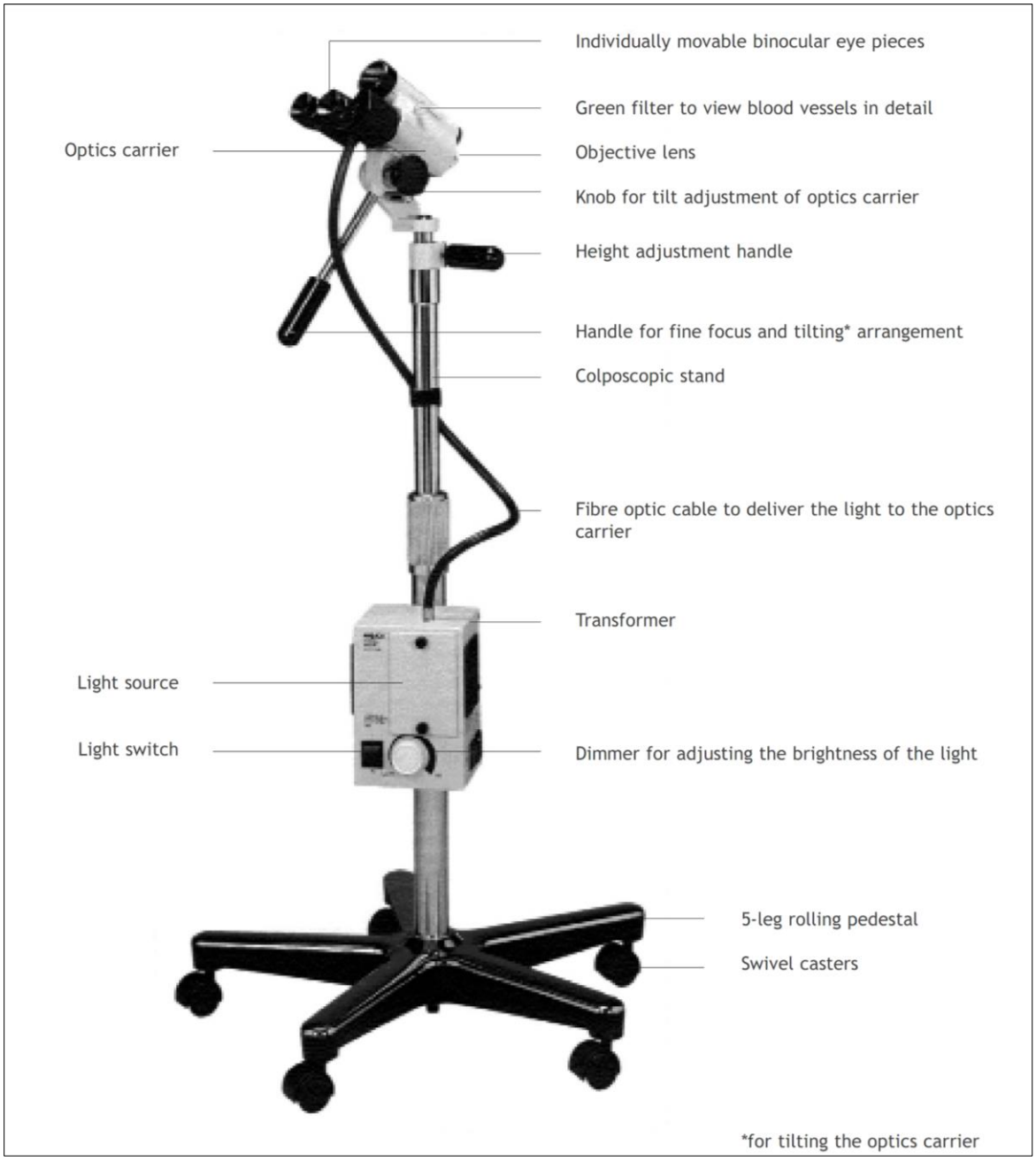


Figure: 1.2 Colposcope

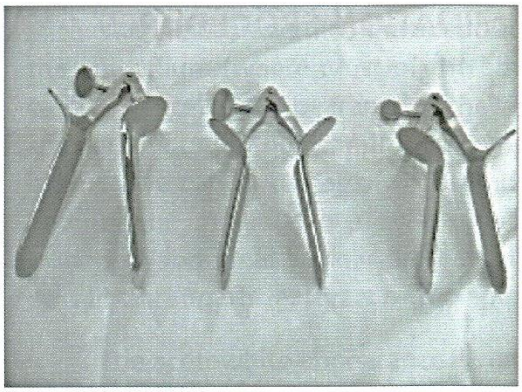


FIGURE 1.3: Collins bivalve specula of different sizes

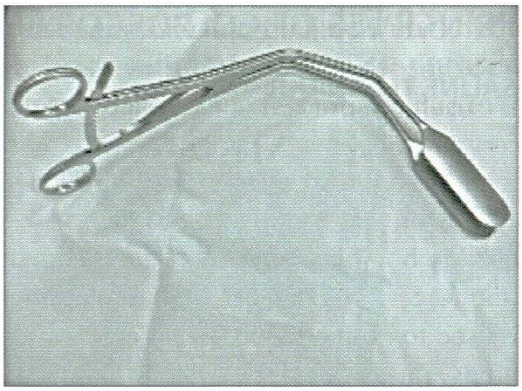


FIGURE 1.4: Vaginal side-wall retractor

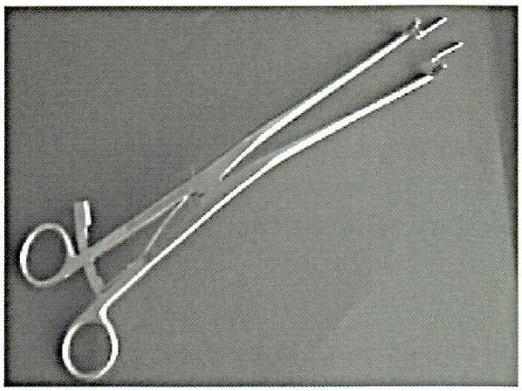


FIGURE 1.5: Endocervical speculum

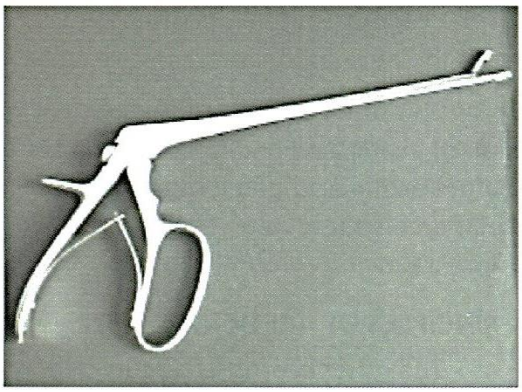


FIGURE 1.6: Cervical punch biopsy forceps with sharp cutting edges

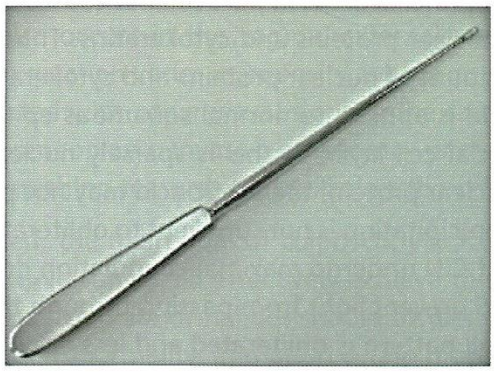


FIGURE 1.7: Endocervical curette

PRINCIPLES OF COLPOSCOPY EXAMINATION PROCEDURES

SALINE TECHNIQUE

The key ingredients of colposcopic practice are the examination of the features of the cervical epithelium after application of saline, 5% dilute acetic acid and Lugol's iodine solution in successive steps.

The study of the vascular pattern of the cervix may prove difficult after application of acetic acid and iodine solutions. Hence the application of physiological saline before acetic acid and iodine application is useful in studying the sub-epithelial vascular architecture in great detail. It is advisable to use a green filter to see the vessels more clearly.

PRINCIPLES OF ACETIC ACID TEST

The other key ingredient in colposcopic practice, 5% acetic acid, is usually applied with a cotton applicator (cotton balls held by sponge forceps, or large rectal or small swabs) or with a small sprayer. It helps in coagulating and clearing the mucus. Acetic acid is thought to cause swelling of the epithelial tissue, columnar and any abnormal squamous epithelial areas in particular. It causes a reversible coagulation or precipitation of the nuclear proteins and cytokeratins. Thus, the effect of acetic acid depends upon the amount of nuclear proteins and cytokeratins present in the epithelium. When acetic acid is applied to normal squamous epithelium, little coagulation occurs in the superficial cell layer, as this is sparsely nucleated. Though the deeper cells contain more nuclear protein, the acetic acid may not penetrate sufficiently and, hence, the resulting precipitation is not sufficient to obliterate the colour of the underlying stroma. Areas of CIN undergo maximal coagulation due to their higher content of nuclear protein and prevent light from passing through the epithelium. As a result, the subepithelial vessel pattern is obliterated and less easy to see and the epithelium appears white. This reaction is termed acetowhitening, and produces a noticeable effect compared with the normal pinkish colour of the surrounding normal squamous epithelium of the cervix, an effect that is commonly visible to the naked eye.

With low-grade CIN, the acetic acid must penetrate into the lower one-third of the epithelium (where most of the abnormal cells with high nuclear density are located). Hence, the appearance of the whiteness is delayed and less intense due to the smaller amount of nuclear protein compared to areas with high-grade CIN or preclinical invasive cancer. Areas of high-grade CIN and invasive cancer turn densely white and opaque immediately after application of acetic acid, due to their higher concentration of abnormal nuclear protein and the presence of large numbers of dysplastic cells in the superficial layers of the epithelium.

The acetowhite appearance is not unique to CIN and early cancer. It is also seen in other situations when increased nuclear protein is present: for example in immature squamous

metaplasia, congenital transformation zone, in healing and regenerating epithelium (associated with inflammation), leukoplakia (hyperkeratosis) and condyloma.

While the acetowhite epithelium associated with CIN and preclinical early invasive cancer is more dense, thick and opaque with well demarcated margins from the surrounding normal epithelium, the acetowhitening associated with immature squamous metaplasia and regenerating epithelium is less pale, thin, often translucent, and patchily distributed without well-defined margins. Acetowhitening due to inflammation and healing is usually distributed widely in the cervix, not restricted to the transformation zone. The acetowhite changes associated with immature metaplasia and inflammatory changes quickly disappear, usually within 30-60 seconds.

Acetowhitening associated with CIN and invasive cancer quickly appears and persists for more than one minute. The acetic acid effect reverses much more slowly in high-grade CIN lesions and in early pre-clinical invasive cancer than in low-grade lesions, immature metaplasia and sub-clinical HPV changes. It may last for 2-4 minutes in the case of high-grade lesions and invasive cancer.

Acetowhitening also occurs in the vagina, external anogenital skin, and anal mucosa. The acetowhite reaction varies in intensity, within and between patients. The reaction is often associated with other visual signs in the same area, and is not specific for intraepithelial preneoplasia. Invasive cancer may or may not be acetowhite; it usually has other distinguishing features that will alert the colposcopist.

As previously stated, the main goal of colposcopy is to detect the presence of high-grade CIN and invasive cancer. To effectively achieve this, the entire epithelium at risk should be well visualized, abnormalities should be identified accurately and assessed for their degree of abnormality, and appropriate biopsies must be taken. The colposcopic documentation and the biopsies taken by a colposcopist are important indicators for quality management in colposcopy clinics.

PRINCIPLES OF SCHILLER'S (LUGOL'S) IODINE TEST

The principle behind the iodine test is that original and newly formed mature squamous metaplastic epithelium is glycogenated, whereas CIN and invasive cancer contain little or no glycogen. Columnar epithelium does not contain glycogen. Immature squamous metaplastic epithelium usually lacks glycogen or, occasionally, may be partially glycogenated. Iodine is glycophilic and hence the application of iodine solution results in uptake of iodine in glycogen-containing epithelium. Therefore, the normal glycogen-containing squamous epithelium stains mahogany brown or black after application of iodine. Columnar epithelium does not take up iodine and remains unstained, but may look slightly discoloured due to a thin film of iodine solution; areas of immature squamous metaplastic epithelium may remain unstained with

iodine or may be only partially stained. If there is shedding (or erosion) of superficial and intermediate cell layers associated with inflammatory conditions of the squamous epithelium, these areas do not stain with iodine and remain distinctly colourless in a surrounding black or brown background. Areas of CIN and invasive cancer do not take up iodine (as they lack glycogen) and appear as thick mustard yellow or saffron- coloured areas. Areas with leukoplakia (hyperkeratosis) do not stain with iodine. Condyloma may not, or occasionally may only partially, stain with iodine.

Routine use of iodine application in colposcopic practice is recommended; as this may help in identifying lesions overlooked during examination with saline and acetic acid and will help in delineating the anatomical extent of abnormal areas much more clearly, thereby facilitating treatment.

DOCUMENTATION OF COLPOSCOPIC FINDINGS

The record of colposcopic findings for each visit should be documented carefully by the colposcopists themselves, immediately after the examination. This record, which can be stored on paper or electronically, forms the backbone of any medical record system that can be used for continuing patient care and performance.

PERFORM CERVICAL BIOPSIES, IF NECESSARY

Once an abnormal transformation zone is detected, the area is evaluated and compared with other areas of the cervix. If any other abnormal zones are present, the colposcopist should then decide from where a biopsy or biopsies should be taken. It is essential to obtain one or more directed punch biopsies from areas colposcopically identified as abnormal and/or doubtful. Biopsy should be obtained from the area of the lesion with worst features and closest to the squamocolumnar junction. Biopsy always should be done under colposcopic control by firmly applying the biopsy instrument (Figure 1.6), with the jaws wide open (Figure 1.8), to the cervical surface to be sampled. The cervix may move back somewhat with this manoeuvre, but that is normal.

To obtain a tissue sample, the biopsy forceps is guided under colposcopic visualization to the area from which the tissue specimen is to be obtained. The cervix may tend to slip away on pressure, but it is usually easy to grasp and remove tissue if the forceps used for biopsy has wide and sharp cutting edges, with one or two teeth to anchor the forceps while taking the biopsy (Figure 1.8). A tenaculum may be also used to fix the cervix before taking the biopsy. The jaws are then closed completely, and the specimen is removed and immediately placed in formalin. The biopsy performed should be deep enough to obtain adequate stroma, in order to exclude invasion. Cutting the specimen should be carried out by quick and firm closure of the jaws. Repeated cutting and rotation of the forceps should be avoided, as they can crush the tissue sample. The procedure is usually painless if carried out efficiently using a sharp and

toothed biopsy forceps. A skin hook is sometimes useful to anchor a potential biopsy site if it is difficult to grasp with the biopsy instrument.

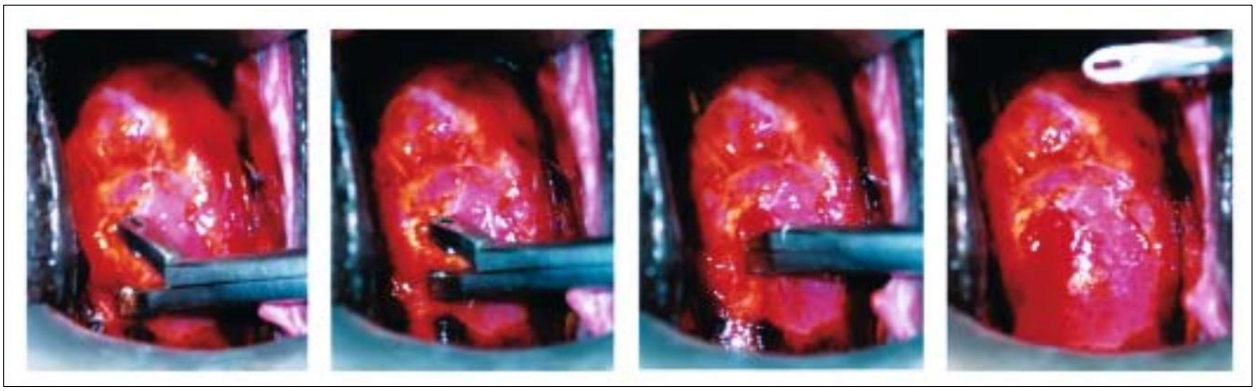


FIGURE 1.8: Biopsy technique: A toothed and sharp cutting biopsy forceps should be used for biopsy. Firmly apply the biopsy punch onto the cervix with the jaws wide open; fix the lower lip of the biopsy punch and close the jaws completely. Cutting the specimen should be carried out by quick and firm closure of the jaws. Repeated cutting and rotation of the forceps should be avoided, as this can crush the tissue sample. The removed specimen should be immediately placed in formalin. The biopsy site may be cauterized.

After the biopsy has been obtained, it is advisable to indicate the site of the target area which has been biopsied, on the diagram of cervix in the reporting form. It is important to place the freshly obtained biopsy specimen in a labeled bottle containing 1O% formalin. The biopsy site(s) may be cauterized immediately after the procedure to control any bleeding.

PERFORM ENDOCERVICAL CURETTAGE. IF NECESSARY

There are three commonly encountered circumstances, in which endocervical curettage (ECC) should be performed using an endocervical curette (Figure 1.7).

1. First, if the colposcopic examination of the ectocervix has not revealed any abnormality, yet the woman has been referred because of a cytological abnormality an ECC should be performed to properly evaluate the endocen/ical canal, which may contain a hidden invasive cancer or other lesion.
2. Second, if the referral cytology indicated that a glandular lesion may be present, an ECC should be performed (regardless of the findings of the colpocopic examination).
3. Third, an ECC should be performed if the colposcopic examination has been unsatisfactory (whether or not a cervical lesion has been detected).

However, it should be mentioned that the yield of an ECC is very low in inexperienced hand as it is frequently associated with inadequate tissue sampling. Thus, in such situations, a negative ECC should not be taken as unequivocal evidence of the absence of neoplasia in the endocervical canal. In the above three situations, and particularly in the case of an acetowhite

lesion extending into the canal, it may be prudent to excise the cervix with a cone (by LEEP or cold knife conization, as appropriate).

However, this approach places a large work load on histopathology services. ln the assessment of women in such situations, it is left to the discretion of the colposcopist to decide whether an ECC and/or cone biopsy should be performed.

Before ECC is performed, the posterior fornix must be dry to avoid the loss of curetted tissue in the acetic acid solution which accumulated during its application on the cervix. When performing ECC, the colposcopist holds the curette like a pen and scrapes the endocervical canal in firm, short, linear strokes until it has been completely sampled. During the procedure the curette should remain in the canal. When extracting the curette, care should be taken to twirl it in order to encourage the contents of the curette basket to remain trapped therein. The curettings should be put onto a piece of either gauze or brown paper, and then promptly placed into formalin. Any residual tissue can be removed from the canal with forceps.

Awareness of and ability to identify the colposcopic features of the normal cervix provide the basis for differentiating between normal and abnormal colposcopic findings.

Chap 2: Colposcopic Appearance of the Normal Cervix

AFTER APPLICATION OF NORMAL SALINE SOLUTION

SQUAMOUS EPITHELIUM

The original squamous epithelium is darker pink in colour compared with the light pink or whitish-pink colour of the metaplastic squamous epithelium. If one looks closely, it is apparent in some women that a few crypt openings, which look like tiny circular holes, are scattered over the surface of the squamous epithelium (Figure 2.1 & 2.2). In some women, alternatively, one may look for the nabothian follicles. Looking distally, away from the os towards the outer part of the ectocervix, one comes to a point where no more crypt openings and/or nabothian follicles are apparent. An imaginary line drawn connecting the most distal crypt openings and/or nabothian follicles that one can see in the cervical lips colposcopically define the original squamocolumnar junction (the junction between the original or native squamous epithelium and the metaplastic squamous epithelium). The original squamocolumnar junction forms the outer, distal, or caudal border of the transformation zone through its entire 360-degree circumference. Sometimes, it is the subtle colour variation between the native and metaplastic squamous epithelium that defines the original squamocolumnar junction.

The next task is to identify the proximal or inner border of the transformation zone, which is defined by the new squamocolumnar junction (the line of demarcation where the metaplastic squamous and columnar epithelia meet), throughout its entire 360-degree circumference. If the colposcopist is able to trace the entire new squamocolumnar junction successfully, the colposcopic examination is classified as adequate or satisfactory with respect to evaluation of the transformation zone (Figure 2.1 & 2.2).

The new squamocolumnar junction tends to recede towards, and eventually into, the canal as a woman ages (Figure 2.3). If the junction is proximal to the os, in the canal, it requires additional effort to visualize the entire junction. Opening the blades of the vaginal speculum and using a cotton-tipped applicator to pry the anterior lip upward or the posterior lip downward will often allow visualization of the squamocolumnar junction, if it is close enough to the os. The endocervical speculum (Figure 2.4) or the tips of a long dissection forceps also can be used, and will often allow a greater length of canal to be inspected. The skill for these manoeuvres comes with practice. The vast majority of CIN lesions occur in the transformation zone and the most severe changes tend to be closer to or abutting, rather than farther from, the new squamocolumnar junction.

COLUMNAR EPITHELIUM,

On first looking at the normal cervix in a young woman, one sees the cervical os. It usually appears to be encircled by the columnar epithelium, appearing dark red in colour with a grape-like or sea anemone tentacles-like or a villous appearance in contrast to the smooth, light pink squamous epithelium. Each columnar villous structure contains a fine capillary and the blood in the capillary and the vascularity of the underlying connective tissue give the columnar epithelium its strikingly reddish appearance. Small polyps may be detected during examination of the endocervical canal.

VASCULATURE

The next most important feature to observe is the vasculature. The examination of the blood vessels is facilitated by applying normal saline on the cervix and using the green (or blue) filter on the colposcope to enhance the contrast of the vessels. Use of a higher power of magnification (about 15x), if available in the colposcope, also is helpful. Depending on the thickness or opacity of the overlying squamous epithelium, smaller vessels may or may not be visible. The smaller vessels that may be visible are capillaries that are in the stroma below the epithelium.

Two types of capillaries are apparent in the native or original squamous epithelium: reticular (network) or hairpin-shaped capillaries (Figure2.5). The reticular pattern is especially visible because the epithelium is thinner in women taking oral contraceptives and in postmenopausal women. The hairpin capillaries actually ascend vertically, loop over, and then descend back into the stroma from where they came. Since these loops are seen 'end on', the colposcopic view usually is of dots with only a slight, if any, appearance of a loop at each. Inflammation of the cervix (e.g., trichomoniasis) often causes hairpin vessels to form stag horn-like shapes so that the vessels become more prominent and the loop appearance is more apparent (Figure 2.5). Often no vascular pattern is seen on the original squamous epithelium.

The ectocervical vessel appearances described above are more prominence towards the outer transformation zone, nearer to the original squamocolumnar junction. In the more recently formed immature metaplastic squamous epithelium nearer the new squamocolumnar junction, other vascular patterns become more prominent. These are large (compared to capillaries) branching surface vessels with three recognizable basic patterns (Figure2.5). The first pattern is much like a tree branching and the second is commonly seen overlying nabothian cysts (Figure 2.6). The regular structure and decrease in the calibre of the vessels towards the ends of the branches all suggest a benign (normal) nature. A third pattern sometimes occurs when healing has taken place after therapy for CIN (Figures 2.5 and 2.7): the vessels are long and run parallel to one another. The lack of other abnormal epithelial features that would suggest neoplasia is a

helpful clue that the vasculature is normal. If there is any doubt, it is always prudent to take a biopsy.

The vessels in the columnar epithelium actually are terminal capillary networks. One capillary network is confined to the stromal core of each grape-like villus, which projects up to the epithelial surface. With the colposcope, the rounded tips of the individual villi are the main features seen and the top of the vessel network in each villus appears as a dot. Large, deep branching vessels may be seen in some cases.

AFTER APPLICATION OF 5% ACETIC ACID SOLUTION

SQUAMOUS EPITHELIUM

After acetic acid has been allowed to take effect (1-2 minutes), certain changes in the features seen with saline are usually apparent in the normal cervix of a young woman. The colour of the squamous epithelium tends to be somewhat dull in contrast to the usual pink hue, and the translucence is diminished so that it looks somewhat pale (Figure 2.2). In postmenopausal women the colour usually is paler than in a premenopausal woman. The landmarks and full extent of the transformation zone should again be observed carefully. The squamocolumnar junction may be prominently visible as a sharp, step like white line due to the presence of actively dividing immature squamous metaplasia around the edge, medial (proximal) to the junction (Figure 2.8). The atrophic postmenopausal squamous epithelium looks more pale, brittle, without lustre, sometimes with sub-epithelial petechiae due to the trauma to sub-epithelial capillaries resulting from the insertion of the bivalved vaginal speculum (Figure 2.9). Often the new squamocolumnar junction may not be visible in postmenopausal women as it recedes into the endocervical canal.

COLUMNAR EPITHELIUM

The columnar epithelium should be inspected next. It is usually noticeably less dark red than it was with saline and the pale acetowhitening of the villi may resemble a grape-like appearance (Figure2.10). After the endocervical mucus among the villi has been coagulated by the acetic acid and wiped away, the topography may be seen more easily. If a polyp is covered by the columnar epithelium (which has not yet undergone metaplastic changes), the typical grape-like appearance may be visible. More often, especially when it protrudes, the epithelium covering the polyp undergoes metaplastic changes and presents features of various stages of metaplasia.

SQUAMOUS METAPLASIA

During the different stages of the development of metaplasia, a vast range of colposcopic appearances may be seen. This can present a challenge to an inexperienced colposcopist, who needs to differentiate between these normal findings and the abnormal features associated

with CIN. Immature metaplastic squamous epithelium that may turn mildly white after the application of acetic acid is a common source of confusion for the beginners. It is acceptable to take a biopsy when in doubt.

Colposcopically, three stages of development of squamous metaplasia may be recognized (Coppleson & Reid, 1986). In the earliest stage, the translucence of the columnar epithelial villi is lost and the villi become opaque at their tips; the villi widen and flatten and successive villi fuse in clusters and sheets with a pale pink colour (Figures 2.11, 2.12 and 2.13). Consequently the metaplastic epithelium looks like a patchily distributed pale cluster, or sheet-like areas, in the ectopic columnar epithelium.

As the metaplasia progresses, the grape-like configuration of the columnar epithelium disappears and the spaces between the villi are fused with glassy, pinkish-white, finger- or tongue-like membranes pointing towards the external os (Figures 2.14 and 2.15). There may be numerous crypt openings and islands of columnar epithelium scattered throughout the metaplastic epithelium. The rims of the crypt openings may not turn white with acetic acid early in the process of metaplasia, but may turn mildly white as the metaplastic process progresses. Gradually, the tongue-like metaplastic areas fuse together to form a continuously advancing glassy, shining, pinkish-white or mildly pale membrane-like area (Figure 2.16).

Finally, the immature metaplastic epithelium becomes a fully developed mature metaplastic squamous epithelium resembling the original native squamous epithelium, except for the presence of some crypt openings (Figure 6.1) and nabothian retention follicles in the metaplastic epithelium.

AFTER APPLICATION OF LUGOL'S IODINE SOLUTION

As described in the previous chapter, glycogenated cells take iodine, so that they have a uniform dark mahogany brown colour when stained with Lugol's iodine solution. Therefore, the normal vaginal and cervical squamous (both native and mature metaplastic) epithelium in women in the reproductive age group will take up the stain and become mahogany brown or black (Figure 2.17). This is helpful in distinguishing normal from abnormal areas in the transformation zone that have show faint acetowhitening. The columnar epithelium does not stain with iodine (Figure 2.17). The immature squamous metaplastic epithelium usually does not stain with iodine or may partially stain if it is partially glycogenated (Figure 2.18). The vascular features, so easily seen with saline, may be difficult to observe after application of Lugol's iodine solution. Cervical polyps do not stain with iodine, as they are usually covered with columnar or immature metaplastic epithelium (Figure 2.19). lf the maturation of the metaplastic epithelium varies, one may observe various fields of no uptake or partial to full iodine uptake on the polyp. In postmenopausal women, the ectocervix may not stain fully' with iodine, due to atrophy of the epithelium.

CONGENITAL TRANSFORMATION ZONE

The congenital transformation zone stains white after application of acetic acid. In this condition, the metaplastic epithelium formed during the latter portion of fetal life, lying distal to the transformation zone formed after birth, is located far out on the ectocervix, some distance from the cervical os and, in some cases, may even extend onto the vagina. It is important to recognize this as a normal condition for which no treatment is necessary.

With acetic acid, the congenital transformation zone will usually take on a mild acetowhite stain and the capillary vasculature may have a fine mosaic pattern vasculature.

The most important feature to observe is the vasculature. The examination of the blood vessels is facilitated by applying normal saline on the cervix and using the green (or blue) filter on the colposcope to enhance the contrast of the vessels. Use of a higher power of magnification (about 15x), if available in the colposcope, also is helpful. Depending on the thickness or opacity of the overlying squamous epithelium, smaller vessels may or may not be visible. The smaller vessels that may be visible are capillaries that are in the stroma below the epithelium,

Two types of capillaries are apparent in the native or original squamous epithelium: reticular (network) or hairpin-shaped capillaries (Figure 2.5). The reticular pattern is especially visible because the epithelium is thinner in women taking oral contraceptives and in postmenopausal women. The hairpin capillaries actually ascend vertically, loop over, and then descend back into the stroma from where they came.

Since these loops are seen 'end on', the colposcopic view confined to the stromal core of each grape-like villus (Figure 2.20), which projects up to the epithelial surface. With the colposcope, the rounded tips of the individual villi are the main features seen and the top of the vessel network in each villus appears as a dot. Large, deep branching vessels may be seen in some cases.

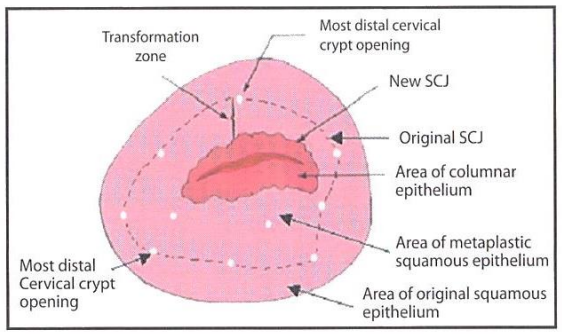


FIGURE 2.1 A method of identifying outer and inner borders of the transformation zone (SCJ: Squamo columnar junction)

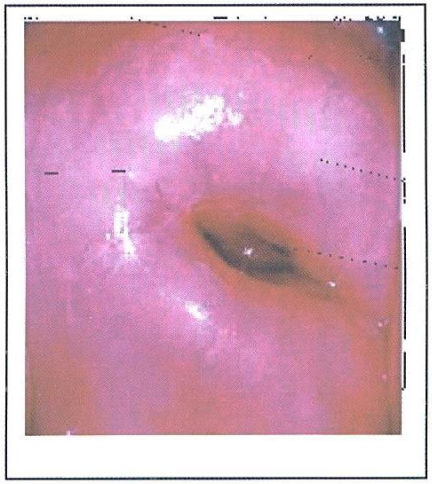


FIGURE 2.2 : The entire new squamocolumnar junction (SCJ) is visible, and hence the colposcopic examination is satisfactory; the transformation zone (TZ) is fully visualized. The metaplastic squamous epithelium is pinkish-white compared to the pink original squamous epithelium

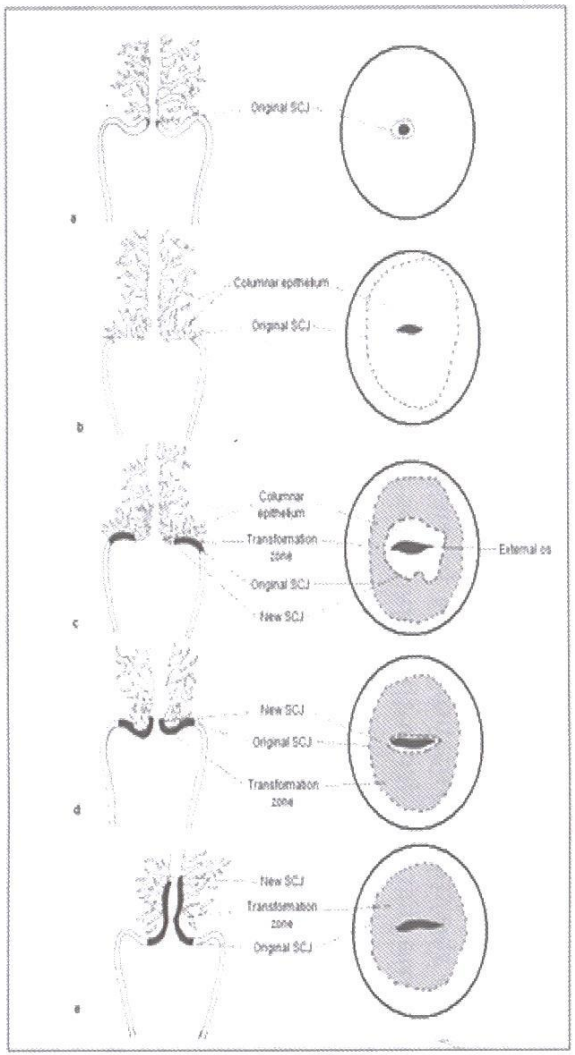


FIGURE 2.3 Location of the squamocolumnar junction (SCJ) and transformation zone; (a) before menarche; (b) after puberty and at early reproductive age; (c) in a woman in her 30s; (d) in a perimenopausal woman; (e) in a postmenopausal woman.

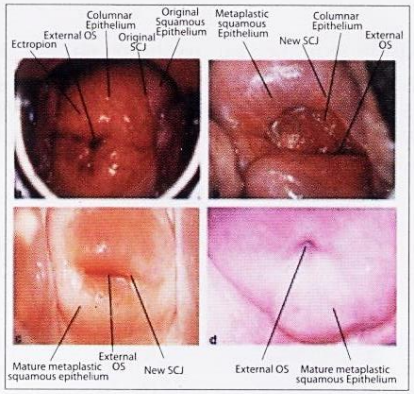


FIGURE 2.4 Location of squamocolumnar junction (SCJ)

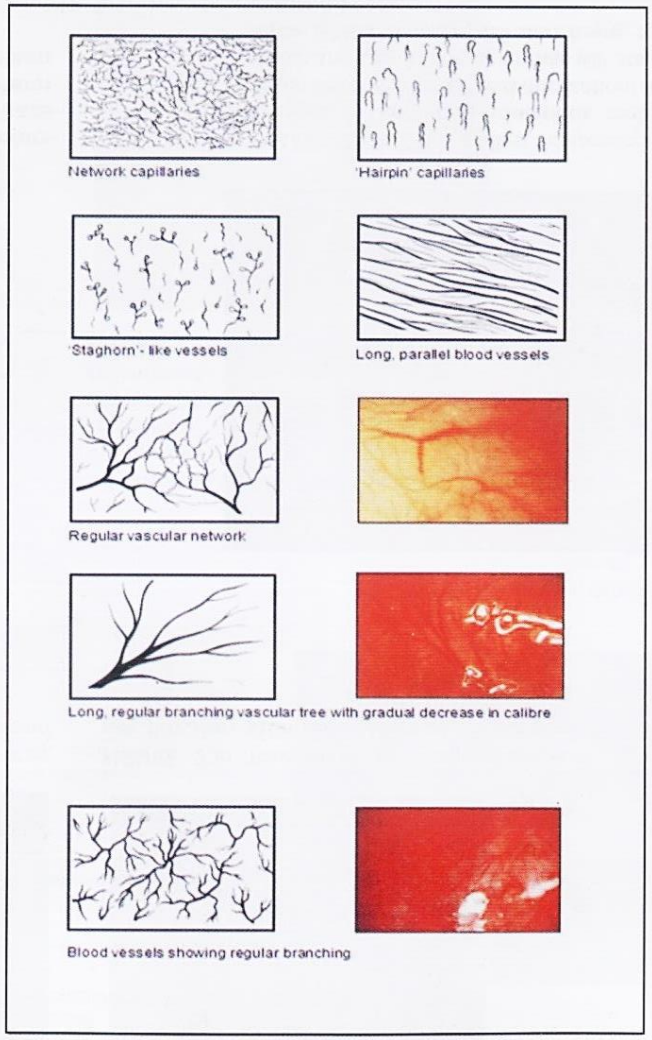


FIGURE 2.5 Normal vascular patterns

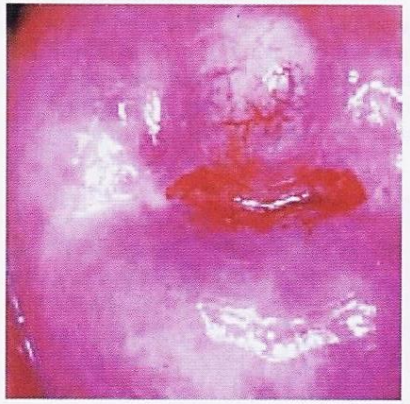


FIGURE 2.6: Nabothian cyst with regularly branching tree-like vessels (a)

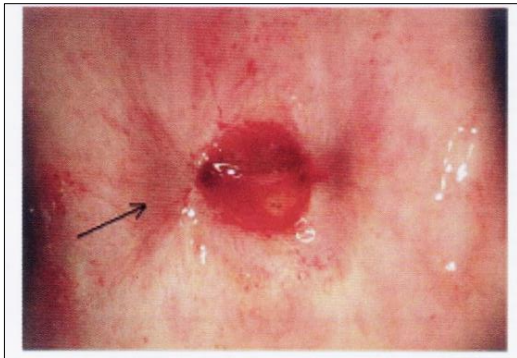


FIGURE2.7: Appearance of the cervix three months after LEEP; note the parallel blood vessels in the healed cervix (arrow).

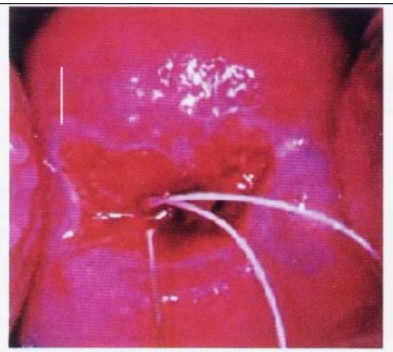


FIGURE 2.8: Prominent new squamo columnar junction after application of 5% acetic acid

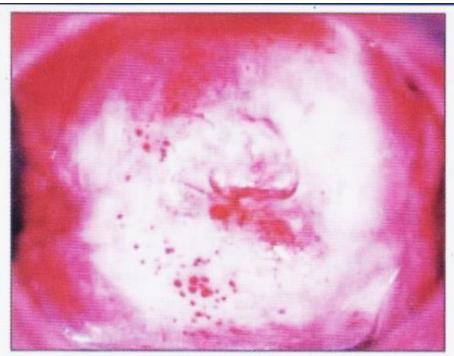


FIGURE 2.9: Postmenopausal cervix: The epithelium is pale, brittle and lacks lustre, showing sub-epithelial petechiae (a). Squamocolumnar junction is not visible

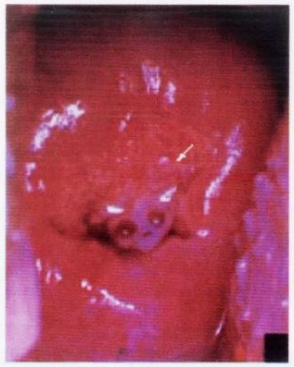


FIGURE 2.10: The colour changes in the columnar epithelium after the application of 5% acetic acid. The columnar villi turn white, obliterating the red colour of the columnar epithelium

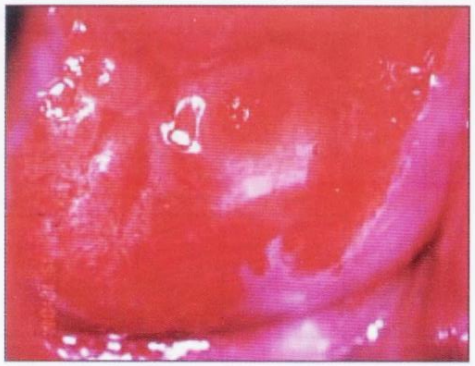


FIGURE 2.11: The earliest colposcopic changes in immature squamous metaplasia (after 5% acetic acid application) in which the tips of the columnar villi stain white (a) and adjacent villi start fusing together (b)

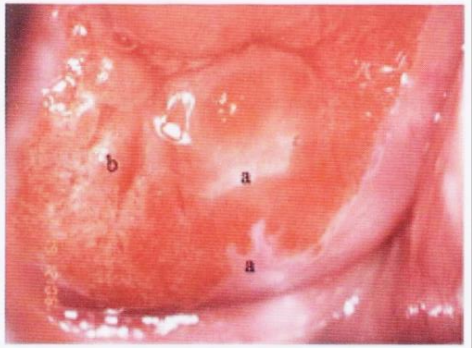


FIGURE 2.12 Immature squamous metaplasia: The columnar villi have fused together to form thin membrane (a). The adjacent villi are fusing together (b) (after 5% acetic acid application)

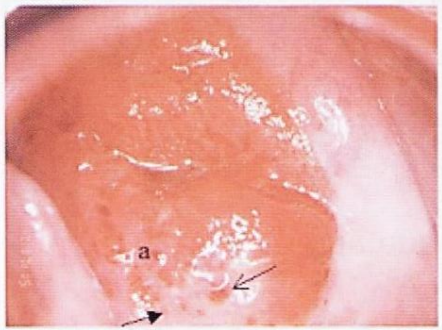


FIGURE 2.13 The glassy, pinkish white immature squamous metaplastic epithelium (a) with islands of columnar epithelium (narrow arrow) and crypt opening (bold arrow) (after 5% acetic acid application)

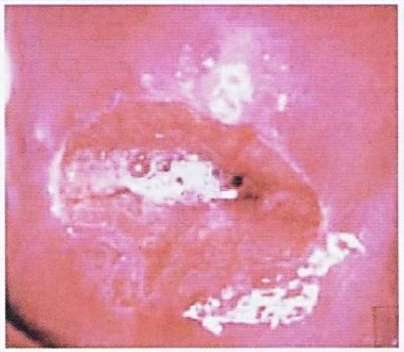


FIGURE 2.14: The prominent white line corresponds to the new squamocolumnar junction and tongues of immature squamous metaplasia (a) with crypt opening at 4-8 o'clock positions (b) (after application of 5% acetic acid)

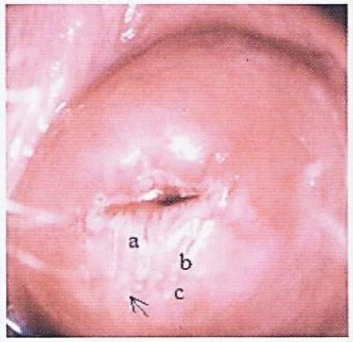


FIGURE 2.15 Appearance after 5% acetic acid application: protruding tongues (a) of immature squamous metaplasia towards the external os in the lower lip and the crypt openings (b) after application of 5% acetic acid. Some crypt openings are already covered by metaplastic epithelium (c) which may become nabothian cysts soon. Note the distal crypt opening indicated by the arrow and the pinkish white hue of the metaplastic epithelium compared to the pink colour of the original squamous epithelium

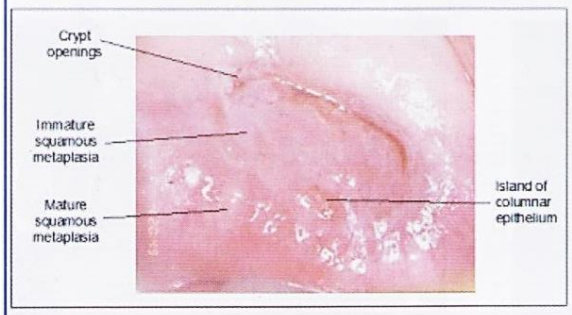


FIGURE 2.16 Pale, translucent acetowhitening due to immature squamous metaplasia with several crypt openings after application of 5% acetic acid

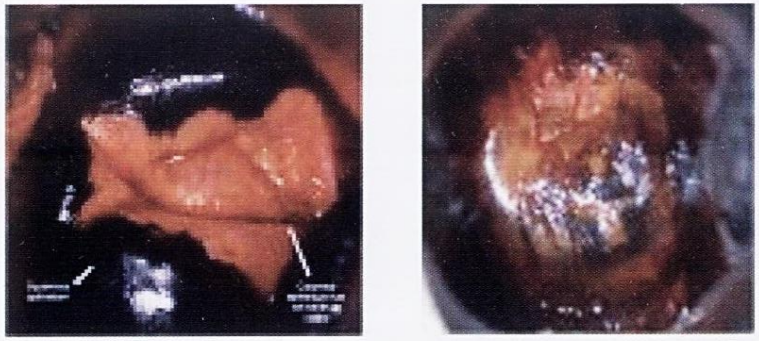
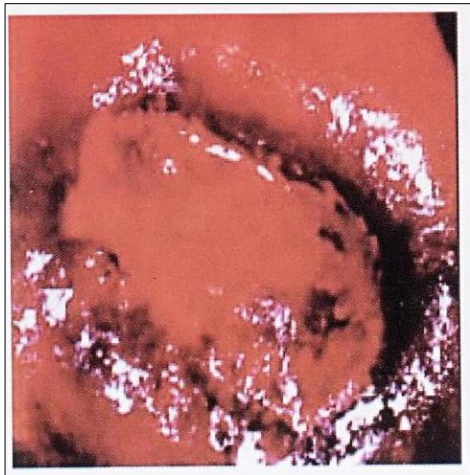


FIGURE 2.17: Colour changes after application of Lugol's iodine



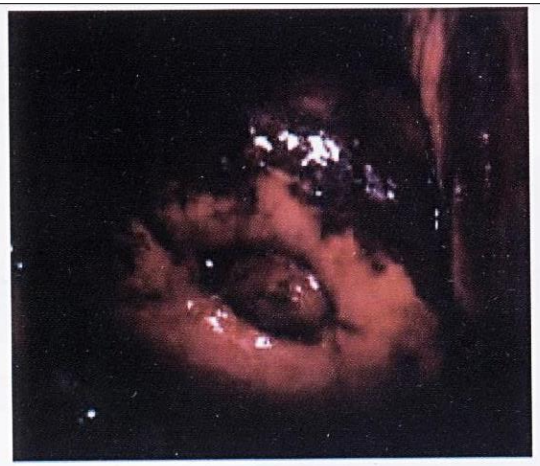


FIGURE 2.18: An Area Of No Or Partial Iodine Uptake In The Immature Squamous epithelium (a)

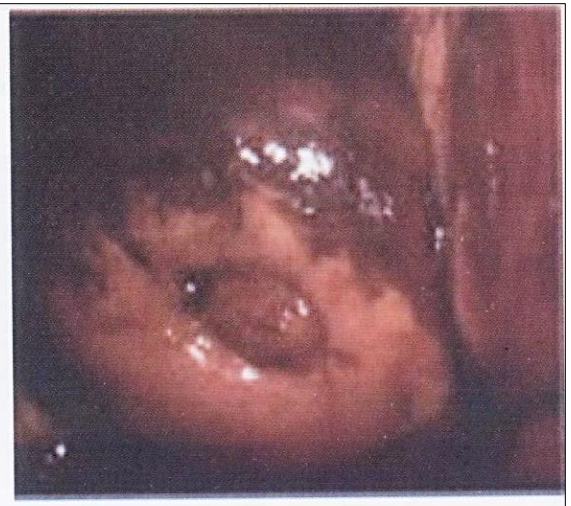


FIGURE 2.19 After application of Lugol's iodine solution the endocervical polyp and the immature squamous metaplasia surrounding the os partially take up iodine

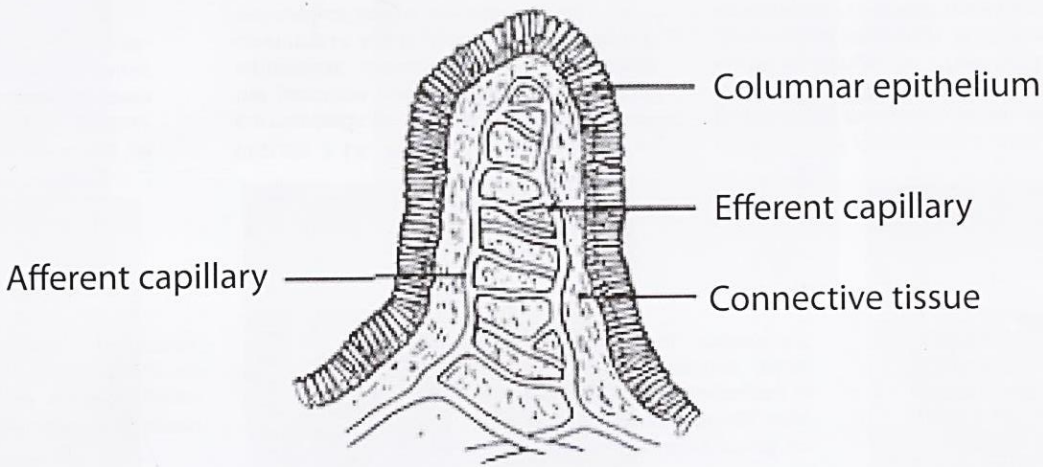


FIGURE 2.20: Capillary network in columnar villi

Chap 3: Colposcopic Assessment of Cervical Intraepithelial Neoplasia

The colposcopic features that differentiate an abnormal transformation zone from the normal include the following: colour tone of acetowhite areas; surface pattern of acetowhite areas; borderline between acetowhite areas and the rest of the epithelium; vascular features and colour changes after application of iodine.

AFTER APPLICATION OF NORMAL SALINE SOLUTION

Following application of saline, abnormal epithelium may appear much darker than the normal epithelium.

VASCULATURE

Using the green (or blue) filter and higher-power magnification when necessary, the best opportunity to evaluate any abnormal vasculature patterns is before the application of acetic acid, the effect of which may obscure some or all of the changes, especially in an acetowhite area. The abnormalities of interest are punctation, mosaics and atypical vessels.

CAPILLARIES

The afferent and efferent capillaries within the villi (Figure 2.20) of columnar epithelium become compressed during the normal metaplastic process and are not incorporated within the newly formed squamous epithelium. Instead, they form a fine network below the basement membrane. When CIN develops as a result of HPV infection and atypical metaplasia, the afferent and efferent capillary system may be trapped (incorporated) into the diseased dysplastic epithelium through several elongated stromal papillae (Figures 2.3 and 2.4), and a thin layer of epithelium may remain on top of these vessels. This forms the basis of the punctate and mosaic blood vessel patterns (Figures 3.1, 3.2 and 3.3). The terminating vessels in the stromal papillae underlying the thin epithelium appear as black points in a stippling pattern in an end-on view under the colposcope, making what are called punctate areas (Figures 3.1, 3.2 and 3.3). The inter-connecting blood vessels in the stromal papillae surrounding the rete pegs of the epithelium, running parallel to the surface, are observed colposcopically as cobbled areas of mosaic pattern (Figures 3.1 and 3.2). In mosaic areas, the epithelium appears as individual small, large, round, polygonal, regular or irregular blocks. Punctation and mosaic areas may be classified as either fine or coarse. Coarse changes tend to be associated with more severe degrees of abnormality. When both punctation and mosaic patterns are found to coexist, the same evaluation criteria for colposcopic prediction of disease are used as when they exist separately.

Vessels exhibiting punctation and mosaics are usually more strikingly obvious than the normal stromal vessels because these vessels penetrate into the epithelium and are thus closer to the surface. When acetic acid is applied, these abnormal vascular patterns seen to be confined to the acetowhite areas.

Fine punctation refers to looped capillaries - viewed end-on - that appear to be of fine calibre and located close to one another, producing a delicate stippling effect (Figures 3.1 and 3.2). Fine mosaics are a network of fine-calibre blood vessels that appear in close proximity to one another, as a mosaic pattern, when viewed with the colposcope (Figure 3.1). These two vascular appearances may occur together and may be found in low-grade (CIN 1) lesions. The patterns do not necessarily appear throughout the whole lesion.

Coarse punctation (Figure 8.3) and coarse mosaics (Figures 3.1 and 3.2) are formed by vessels having larger calibre and larger intercapillary distances, in contrast to the corresponding fine changes. Coarse punctation and mosaicism tend to occur in more severe neoplastic lesions such as CIN 2, CIN 3 lesions and early preclinical invasive cancer. Sometimes, the two patterns are superimposed in an area so that the capillary loops occur in the center of each mosaic 'ti|e'. This appearance is called umbilication (Figure 3.1).

LEUKOPLAKIA (HYPERKERATOSIS)

Leukoplakia or hyperkeratosis (Figure 3.4) is a white, well-demarcated area of the cervix that may be apparent to the unaided eye, before the application of acetic acid. The white colour is due to the presence of keratin and is an important observation. Usually leukoplakia is idiopathic, but it may also be caused by chronic foreign body irritation, HPV infection or squamous neoplasia. No matter where the area or leukoplakia is located on the cervix, it should be biopsied to rule out high-grade CIN or malignancy. It is not usually possible to colposcopically evaluate the vasculature beneath such an area.

CONDYLOMATA

An exophytic lesion on the cervix usually represents and exhibits the characteristic features of a condyloma (Figures 3.5- 3.8). Condylomata are multiple, exophytic lesions, that are infrequently found on the cervix, but more commonly in the vagina or on the vulva. Depending on their size, they may be obvious to the naked eye. The present as soft pink or white vascular growths with multiple, fine, finger-like projections on the surface, before the application of acetic acid. Under the colposcope condylomata have a typical appearance, with a vascular papilliferous or frond-like surface, each element of which contains a central capillary. Occasionally, the surface of a condyloma may have a whorled, heaped-up appearance with a brain-like texture, known as an encephaloid pattern (Figure 3.8). Often, the surface of the lesion may be densely hyperplastic. These lesions may be located within, but are more often found outside the transformation zone. After application of acetic acid, there is blanching of the surface with acetowhite change

persisting for some time. A condyloma at the squamocolumnar junction can sometimes be confused with a prominent area of columnar epithelial villi. Both tend to be acetowhite, but condyloma is whiter. lt is always prudent to obtain a biopsy to confirm the diagnosis of any exophytic lesion and to rule out malignancy. Condylomatous lesions may not take up iodine stain or may stain only partially brown.

AFTER THE APPLICATION OF 5% ACETIC ACID SOLUTION

The observation of a well demarcated, dense, opaque, acetowhite area closer to or abutting the squamocolumnar junction in the transformation zone after application of 3% acetic acid is critical. In fact, it is the most important of all colposcopic signs, and is the hallmark of colposcopic diagnosis of cervical neoplasia. The degree to which the epithelium takes up the acetic acid stain is correlated with the colour tone or intensity, the surface shine, and the duration of the effect, and, in turn, with the degree of neoplastic change in the lesion. Higher-grade lesions are more likely to turn dense white rapidly. Abnormal vascular features such as punctation, mosaicism and atypical vessels are significant only if these are seen in acetowhite areas.

The acetic acid dehydrates cells and reversibly coagulates the nuclear proteins. Thus, areas of increased nuclear activity and DNA content exhibit the most dramatic colour change. The most pronounced effects are observed in high-grade lesions and invasive cancer. A direct correlation exists between the intensity of the dull, white colour and the severity of the lesion. Less differentiated areas are associated with an intensely opaque, dull-white appearance of lesions in the transformation zone.

Flat condyloma and low-grade CIN may uncommonly present as thin, satellite acetowhite lesions detached (far away) from the squamocolumnar junction with geographical patterns (resembling geographical regions) and with irregular, angular or digitating or feathery margins (Figures 3.9 - 3.13). Many low-grade CIN lesions reveal less dense, less extensive and less complex acetowhite areas close to or abutting the squamocolumnar junction with well demarcated, but irregular, feathery or digitating margins (Figures 7.10-7.16) compared with high-grade CIN lesions (Figures 3.17-3.27). High-grade lesions show well demarcated, regular margins, which may sometimes have raised and rolled out edges (Figures 3.25 and 3.26). High-grade lesions like CIN 2 or CIN 3 have a thick or dense, dull, chalk-white or greyish-white appearance (Figures 3.17-3.27). They may be more extensive and complex lesions extending into the endocervical canal (Figures 3.22-3.27) compared with low-grade lesions. High-grade lesions often tend to involve both the lips (Burghardt et al., 1992 (Table 7.1). Severe or early malignant lesions may obliterate the external os (Figure 3.22 and 3.25).

As lesions become more severe, their surfaces tend to be less smooth and less reflective of light, as in normal squamous epithelium. The surfaces can become irregular, elevated and nodular relative to the surrounding epithelium (Figures 3.2 and 3.23-3.27).

The line of demarcation between normal and abnormal areas in the transformation zone is sharp and well delineated. High-grade lesions tend to have regular sharper borders (Figures 3.17, 3.18, 3.19, 3.21, 3.23, 3.25, 3.26) than low-grade lesions (3.13, 3.14, 3.15, 3.16).

Visualization of one or more borders within an acetowhite lesion ('lesion within lesion') (Figure 3.21) or a lesion with differing colour intensity (Figure 3.16) is a important observation indicating neoplastic lesions, particularly high-grade lesion. The crypt openings that are involved in high-grade precursor lesions may have thick dense and wide acetowhite rims called cuffed crypt openings (Figure 3.26). These are whiter and wider than the mild, line-like acetowhite rings that are sometimes seen around normal crypt openings.

The cardinal features that should differentiate between the CIN lesions and immature metaplasia are the less dense and translucent nature of the acetowhitening associated with metaplasia, and the lack of a distinct margin between the acetowhite areas of immature metaplasia and the normal epithelium. The line of demarcation between normal epithelium and acetowhite areas of metaplasia in the transformation zone is diffuse and invariably blends with the rest of the epithelium (Figures 2.1 and 2.16). The finger-like or tongue-like projections of the metaplastic epithelium often point towards the external os centripetally (Figures 2.14 and 2.15). The acetowhite lesions associated with CIN are invariably located in the transformation zone close to or abutting, and appearing to arise from, the squamocolumnar junction (Figure 3.11, 3.21). They spread centrifugally, pointing away from the external os. The line of demarcation between normal squamous epithelium, inflammatory lesions, are regenerating epithelium is also diffuse (Figures 5.2-5.5).

To summarize, acetowhite staining is not specific for CIN and may also occur, to some extent, in areas of immature squamous metaplasia, the congenital transformation zone, inflammation and healing and regenerative epithelium. However, acetowhite changes associated with CIN are found localized in the transformation zone abutting the squamocolumnar junction and well demarcated from the surrounding epithelium. Low-grade lesions tend to be thin, less dense, less extensive, with irregular, feathery, geographic or angular margins and with fine punctation and/or mosaic; sometimes, low-grade lesions may be detached from the squamocolumnar junction; and atypical vessels are seldom observed in low-grade lesions. On the other hand, high-grade lesions are associated with dense, opaque, grey white, acetowhite areas with coarse punctation and/or mosaic and with regular and well demarcated borders; these lesions often involve both lips and may occasionally harbour atypical vessels; CIN 3 lesions tend to be complex, involving the os.

AFTER APPLICATION OF LUGOUS IODINE SOLUTION

Lugol's iodine solution is abundantly applied with a cotton swab to the whole of the cervix and visible parts of the vagina. The periphery of the cervix, fornices and vaginal walls must be observed until the epithelium is strongly stained dark brown or almost black by iodine. Normal vaginal and cervical squamous epithelium and mature metaplastic epithelium contain glycogen-rich cells, and thus take up the iodine stain and turn black or brown. Dysplastic epithelium contains little or no glycogen, and thus does not stain with iodine and remains mustard or saffron yellow (Figures 3.28-3.32). This colour difference is helpful in distinguishing normal from abnormal areas in the transformation zone that have shown faint acetowhitening. Columnar epithelium does not stain with iodine and immature metaplasia only partially stains, if at all. Atrophic epithelium also stains partially with iodine and this makes interpretation difficult in post menopausal women. Condylomatous lesions also do not, or only partially, stain with iodine (Figure 3.33).

Atypical epithelium of CIN may be less firmly attached to the underlying stroma, from which it may easily detach or peel off, after repeated application with different solutions, resulting in a true erosion (epithelial defect) exposing the stroma. Such true erosions may easily be observed after iodine application, as the stroma does not stain with iodine.

DETERMINING THE NATURE OF THE LESION

The colposcopic detection of CIN essentially involves recognizing the following characteristics: the colour tone, margin and surface contour of the acetowhite epithetlium in the transformation zone, as well as the arrangement of the terminal vascular bed and iodine staining. Variations in quality and quantity of the above atypical appearances help in differentiating CIN from physiological, benign, infective, inflammatory and reactive changes in the cervix. Grading schemes, based on these variations may guide the colposcopic diagnosis.

The colposcopist is also encouraged to make a colposcopic prediction (or 'diagnosis') at the end of the colposcopic session in terms of normal (or negative), low-grade CIN, high-grade CIN, invasive cancer, other (e.g., inflammation etc.) and un-satisfactory colposcopy. Use of a scoring or grading system may guide colposcopic interpretation and diagnosis in a less subjective manner and helps developing a systematic approach to colposcopy. The modified Reid colposcopic score based on the colposcopic index proposed by Reid & Scalzi (1985) is quite useful for this purpose.

PRECLINICAL INVASIVE CARCINOMA OF THE CERVIX

The primary responsibility of a colposcopist is to ensure that if preclinical invasive carcinoma of the cervix is present in a woman, it will be diagnosed.

The colposcopist should be well aware that invasive cancers are more common in older women and in those referred with high-grade cytological abnormalities. Large high-grade lesions, involving more than three quadrants of the cervix, should be thoroughly investigated for the possibility of early invasive cancer, especially if associated with atypical vessels. Other warning signs include the presence of a wide abnormal transformation zone (greater than 40 mm2), complex acetowhite lesion involving both lips of the cervix, lesions obliterating the os, lesions with irregular and exophytic surface contour, strikingly thick chalky white lesions with raised and rolled out margins, strikingly excessive atypical vessels, bleeding on touch or the presence of symptoms such as vaginal bleeding.

The colposcopic findings of preclinical invasive cervical cancer vary depending upon specific growth characteristics of the individual lesions, particularly early invasive lesions. The early preclinical invasive lesions turn densely greyish-white or yellowish-white very rapidly after the application of acetic acid (Figure 3.34). The acetowhiteness persists for several minutes.

One of the earliest colposcopic signs of possible invasion is blood vessels breaking out from the mosaic formations and producing irregular longitudinal vessels (Figure 3.35). As the neoplastic process closely approaches the stage of invasive cancer, the blood vessels can take on increasingly irregular, bizarre patterns. Appearance of atypical vessels usually indicates the first signs of invasion (Figures 3.34- 3.38). The key characteristics of these atypical surface vessels are that there is no gradual decrease in calibre (tapering) in the terminal branches and that the regular branching seen in normal surface vessels, is absent. The atypical blood vessels, thought to be result of horizontal pressure of the expanding neoplastic epithelium on the vascular spaces, show completely irregular and haphazard distribution, great variation in calibre with abrupt, angular changes in direction with bizarre branching and patterns. These vessel shapes have been described by labels such as wide hairpin, waste thread, bizarre waste thread, cork screw, tendril, root-like or tree-like vessels (Figure 3.38).

They are irregular in size, shape, course and arrangement, and the intercapillary distance is substantially greater and more variable than that seen in normal epithelium.

If the cancer is predominantly exophytic, the lesion may appear as a raised growth with contact bleeding or capillary oozing. Early invasive carcinomas that are mainly exophytic tend to be soft and densely greyish-white in colour, with raised and rolled out margins (Figures 3.37 and 3.31).

Surface bleeding or oozing is not uncommon, especially if there is a marked proliferation of atypical surface vessels (Figures 3.34, 3.37 and 3.40). The bleeding may obliterate the acetowhiteness of the epithelium (Figures 3.34, 3.37 and 3.40). The atypical surface vessel types are varied and characteristically have widened inter-capillary distances. These may take the form of hairpins, corkscrews, waste thread, commas, tadpole and other bizarre, irregular branching patterns and irregular calibre (Figures 3.34, 3.38, 3.40). The abnormal branching vessels show a pattern of large vessels suddenly becoming smaller and then abruptly opening up again into a larger vessel. All of these abnormalities can best be detected with the green (or blue) filter and the use of a higher power of magnification; Proper evaluation of these abnormal vessel patterns, particularly with the green filter, constitutes a very important step in the colposcopic diagnosis of early invasive cervical cancers.

Early preclinical invasive cancer may also appear as dense, thick, chalky-white areas with surface irregularity and nodularity and with raised and rolled out margins (Figure 8.6). Such lesions may not present atypical blood vessel patterns and may not bleed on touch. Irregular surface contour with a mountains- and valleys- appearance is also characteristic of early invasive cancers (Figures 8.2-8.4, 8.6 and 8.7). Colposcopically suspect early, preclinical invasive cancers are often very extensive, complex lesions involving all the quadrants of the cervix. Such lesions frequently involve the endocervical canal and may obliterate the external os. Infiltrating lesions appear as hard nodular white areas and may present necrotic areas in the center. Invasive cancers of the cervix rarely produce glycogen and therefore, the lesions turn mustard yellow or saffron yellow after application of Lugol's iodine (Figures 3.34, 3.36, 3.37, 3.40).

lf a biopsy is taken of a lesion that is suspicious for invasive carcinoma and the report is negative for invasion, the responsibility rests with the colposcopist to ensure that a possibly more generous biopsy and an endocervical curettage (ECC) be taken at a subsequent examination. It is mandatory to take another biopsy if the pathologist reports that there is inadequate stromal tissue present on which to base a pathological decision as to whether invasion is present.

GLANDULAR LESIONS:

There are no obvious colposcopic features that allow definite diagnosis of adenocarcinoma in situ (AIS) and adenocarcinoma, as no firm criteria have been established and widely accepted for recognizing glandular lesions. Most cervical AIS or early adenocarcinoma is discovered incidentally after biopsy for squamous intraepithelial neoplasia. It is worth noting that often AIS co-exists with CIN. The colposcopic diagnosis of AIS and adenocarcinoma require a high degree of training and skill.

It has been suggested that most glandular lesions originate within the transformation zone and colposcopic recognition of the stark acetowhiteness of either the individual or fused villi in

discrete patches (in contrast to the surrounding pinkish white columnar villi) may lead to a colposcopic suspicion of glandular lesions. While CIN lesions are almost always connected with the squamocolumnar junction, glandular lesions may present densely white island lesions in the columnar epithelium (Figure 3.41). In approximately half of women with AIS, the lesion is entirely within the canal (Figure 3.41) and may easily be missed if the endocervical canal is not properly visualized and investigated.

A lesion in the columnar epithelium containing branch-like or root-like vessels (Figure 3.38) may also suggest glandular disease. Strikingly acetowhite columnar villi in stark contrast to the surrounding villi may suggest glandular lesions (Figure 3.42)

Elevated lesions with an irregular acetowhite surface, papillary patterns and atypical blood vessels overlying the columnar epithelium may be associated with glandular lesions (Figure 3.43). A variegated patchy red and white lesion with small papillary excrescences and epithelial buddings and large crypt openings in the columnar epithelium may also be associated with glandular lesions.

Invasive adenocarcinoma may present as greyish-white dense acetowhite lesions with papillary excrescences and waste threadlike or character writing-like atypical blood vessels (Figure 3.34). The soft surface may come off easily when touched with a cotton applicator. Adenocarcinoma may also present as strikingly atypical villous structures with atypical vessels replacing normal aectocervical columnar epithelium (Figure 3.45). Closely placed, multiple cuffed crypt openings in a dense acetowhite lesion with irregular surface may also indicate a glandular lesion (Figure 3.46).

The test outcome after application of Lugol's iodine solution depends upon the desquamation and the loss of cell layers containing glycogen. If desquamation is limited to the summit of the stromal papillae where the squamous epithelium is thinnest, a series of thin yellow spots are seen on a mahogany-brown background, giving a stippled appearance (Figure 4.6). When the inflammation persists and the infection becomes chronic, the small desquamated areas become confluent to form large desquamated areas leading to the so-called leopard- skin appearance (Figure 4.7). These features are often found with Trichomonas infection, but also may be seen with fungal and bacterial infections. If there is marked desquamation, the cervix appears yellowish-red in colour, with involvement of vagina (Figure 4.8).

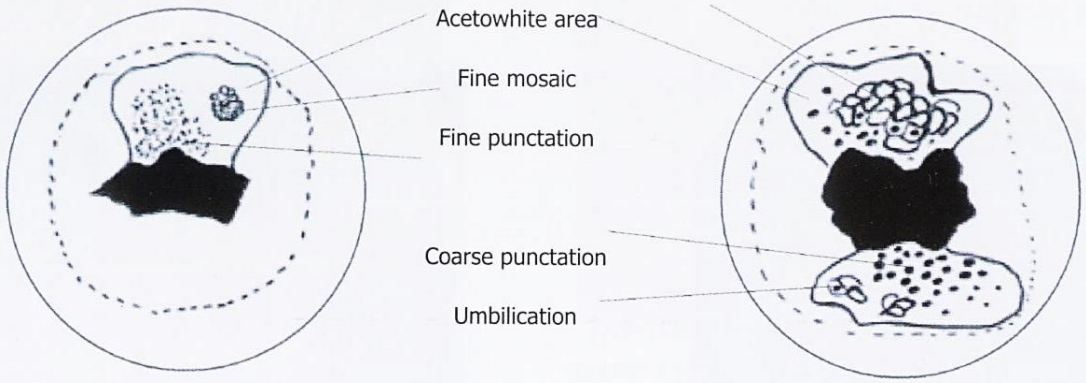


FIGURE 3.1: A schematic representation of punctation and mosaics

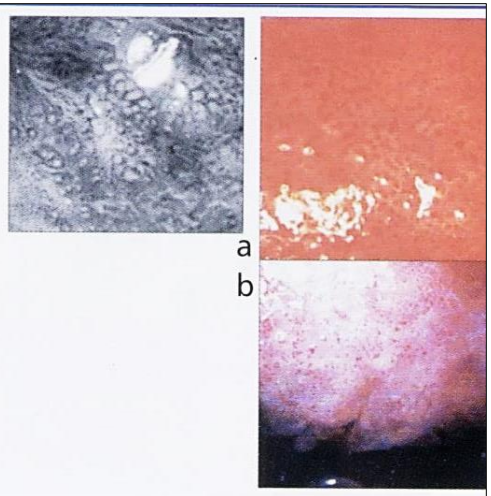


FIGURE 3.2: Fine punctation (a) and coarse mosaic (b) seen after application of normal saline

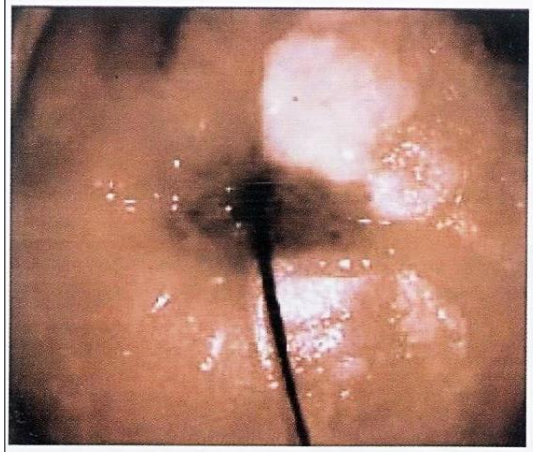


FIGURE 3.3: Coarse punctation before and after application of Acetic Acid acetic acid

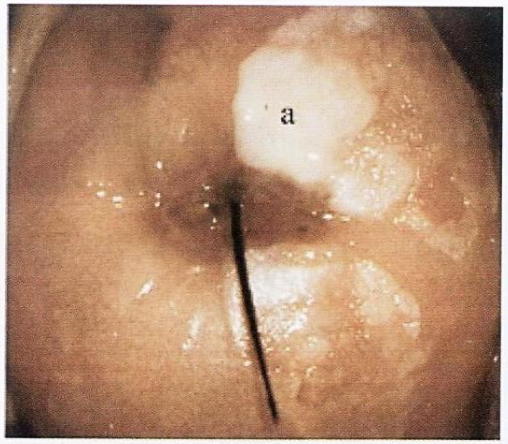


FIGURE 3.4: Hyperkeratosis (leukoplakia) (a)

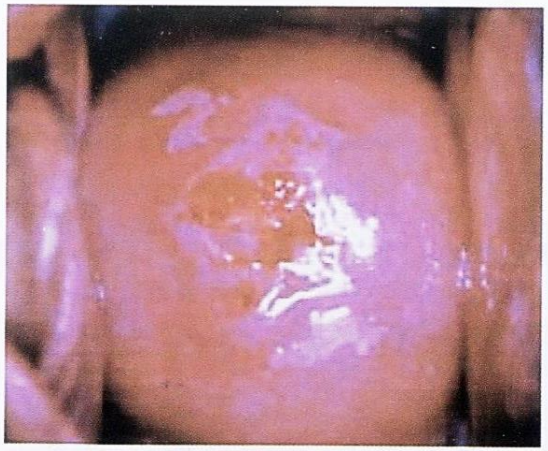
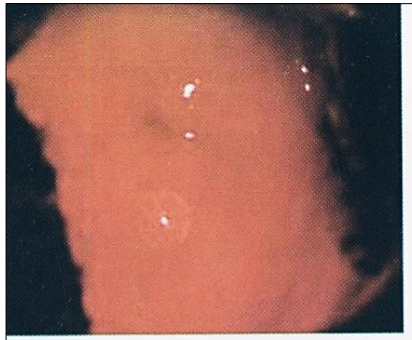


FIGURE 3.5: The geographic satellite lesions far away from the squamocolumnar junction suggestive of condyloma



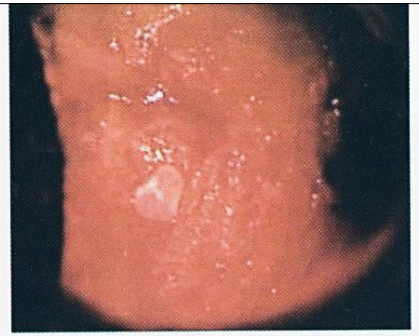
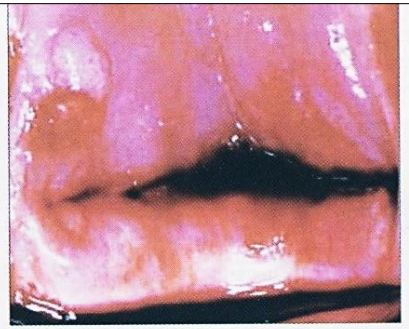


FIGURE 3.6: Exophytic condyloma in the posterior lip of the cervix before and after 3% acetic acid application



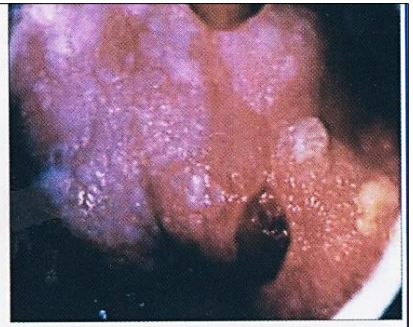


FIGURE 3.7: Exophytic condyloma in the cervix after application of acetic acid

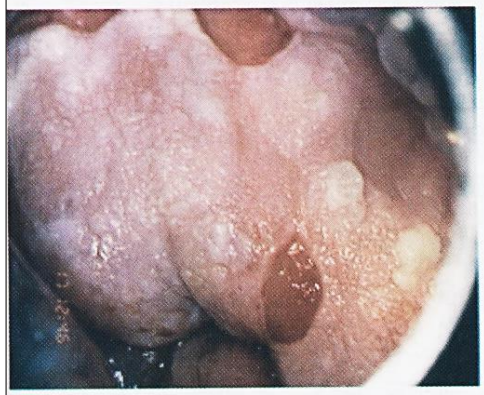
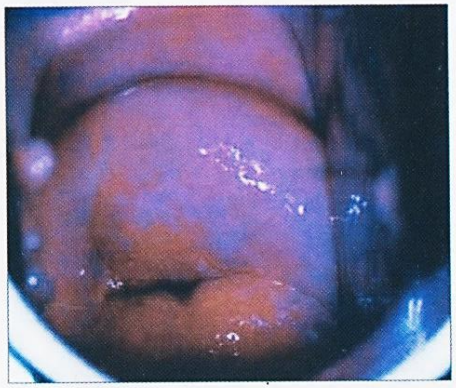


FIGURE 3.8: Condyloma with anencephaloid (cerebriform) pattern



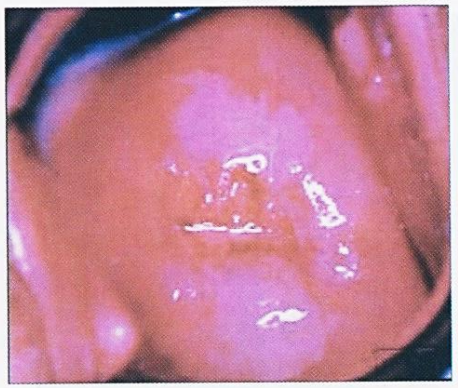


FIGURE 3.9: Thin acetowhite lesion with geographic margins in the upper tips. Historology indicated CIN 1.

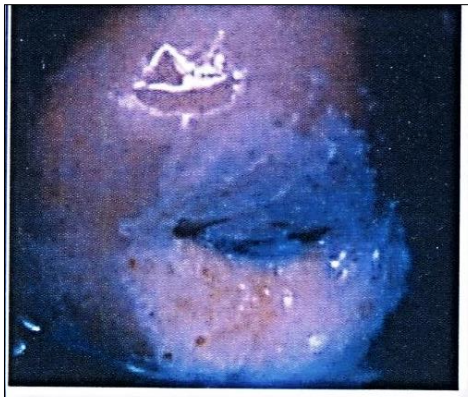


FIGURE 3.10: Mildly dense, thin, elongated acetowhite lesion with regular margins abutting the squamocolumnar junction. Note the fine mosaic at the distal end of the lesion. Histology indicated CIN 1

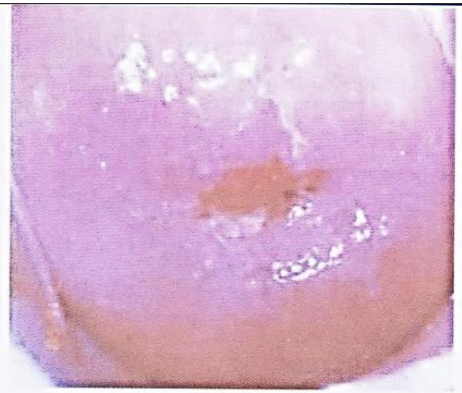


FIGURE 3.11: Mildly dense, acetowhite lesions arising from the squamocolumnar-Junction in 12 and 6'0'clock postion with irregular geographical margins, which on histology proved to be CIN 1 lesion.

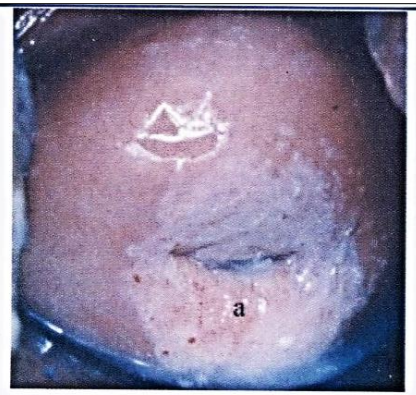


FIGURE 3.12: Circumorificial acetowhite CIN 1 lesion with regular margin and fine mosaece (a)

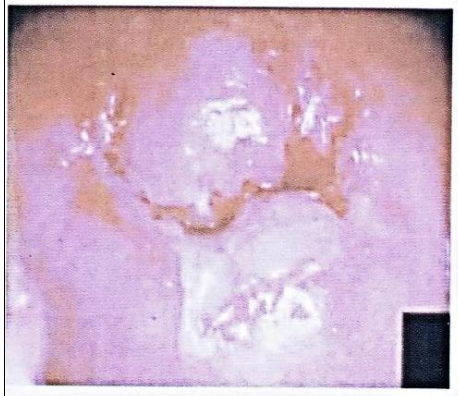


FIGURE 3.13: Moderately dense acetowhite lesions with irregular margins, in the anterior and posterior tips (CIN 1)

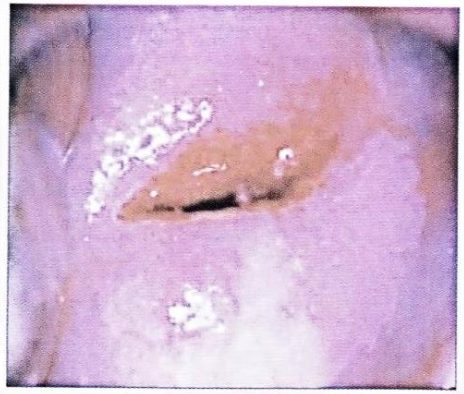


FIGURE 3.14: Note the circumorificial mild to dense acetowhite 1 lesion with fine mosaic, Histology indicated CIN 1. Note the internal borders within the lesion.

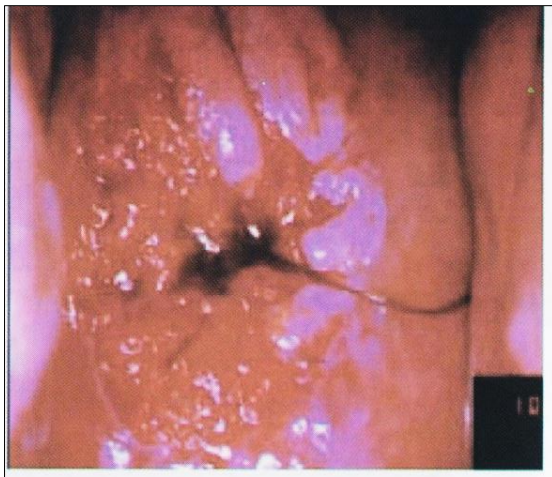


FIGURE 3.15: Moderately dense acetowhite lesions with well defined margins in the anterior lip and in 3'o'clock position (CIN 2 lesion).

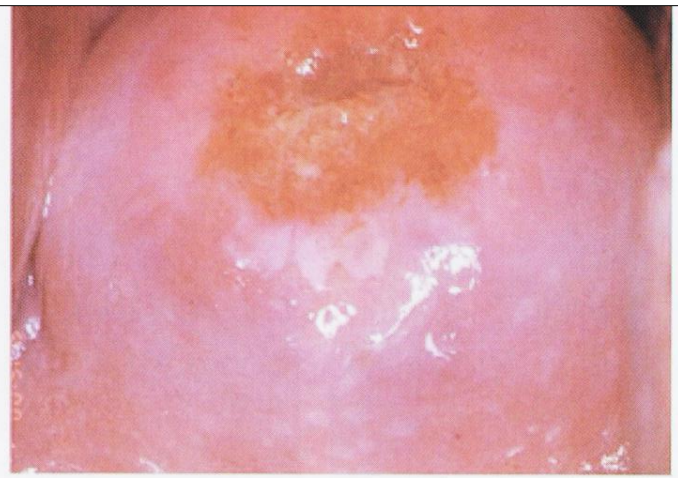
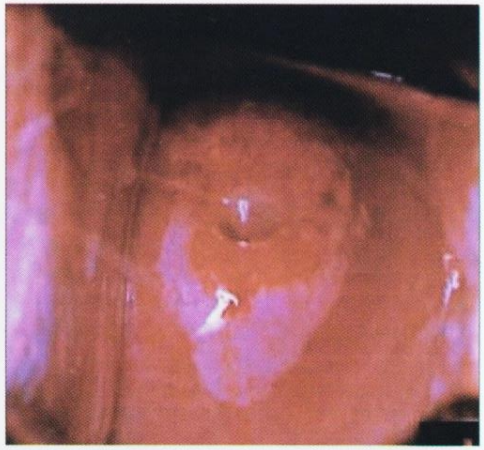


FIGURE 3.16: Dense well degined acetowhite area with regular margins and coarse mosaic (CIN 2 lesion)



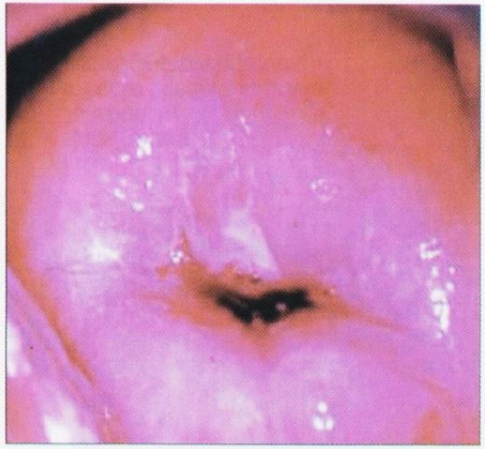


FIGURE 3.17: A dense acetowhite lesions with varging colour intensity and coarse mosaics in a CIN 2 lesion.

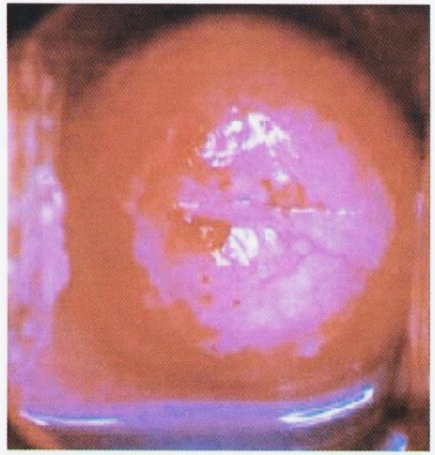


FIGURE 3.18: Acetowhite lesions with coarse punctation and mosaics in a CIN 2 lesion.

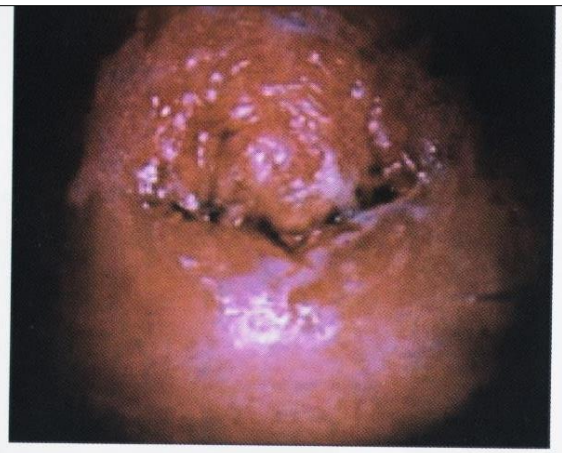


FIGURE 3.19: An acetowhite lesion arising at 12 o'clock position, abutting the squamocolumnar junction. Note the two colour intensities in the same lesion (a and b) with an internal border within the same lesion (c). This is an example of a lesion within a lesion

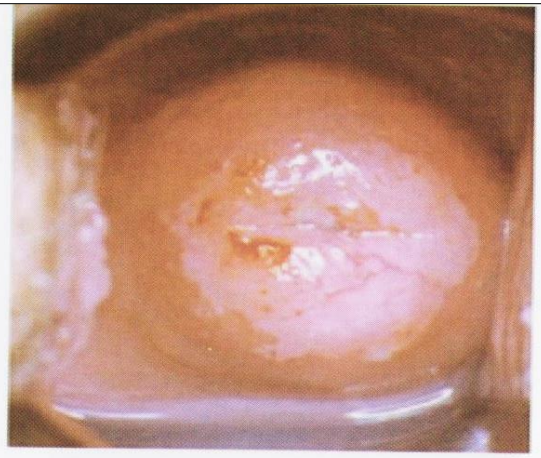
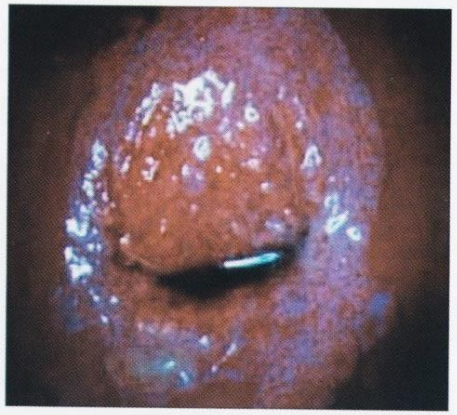


FIGURE 3.20:A circumorificial dense opaque acetowhite area with coarse mosaics (CIN 3 lesion)



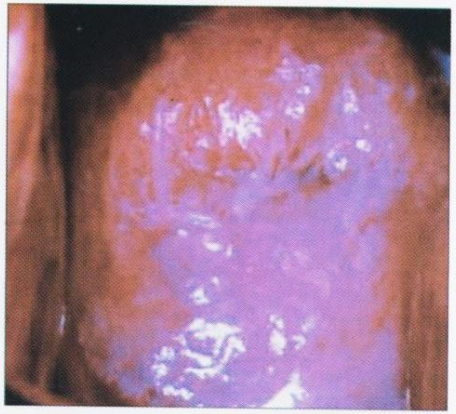


FIGURE 3 .21: A dense acetowhite lesion with regular margin and coarse, irregular punctation in a CIN 3 lesion

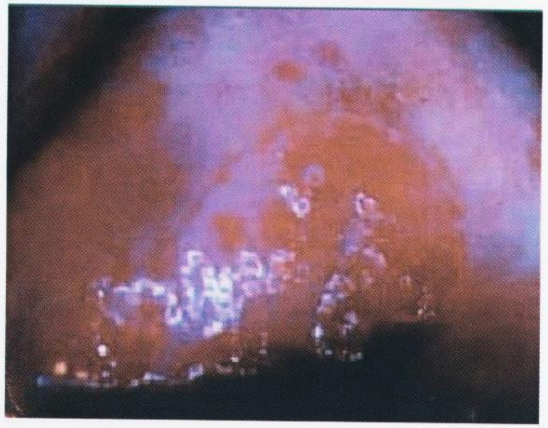


FIGURE 3.22: Coarse mosaics in a CIN 3 lesion

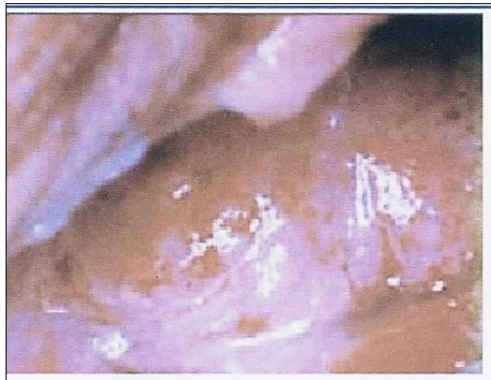


FIGURE 3.23: Note the intensely dense, complex, acetowhite lesion (CIN 3 lesion) with raised and rolled out margins, obliterating the external os

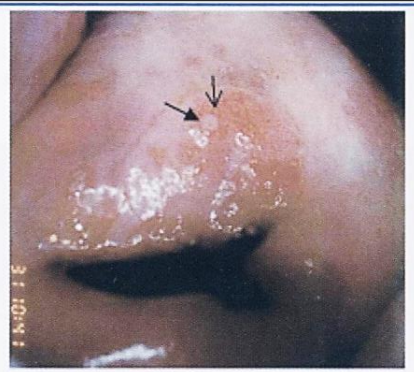


FIGURE 3.24: A dense acetowhite lesion with raised and rolled out margins with a cuffed crypt opening (dense arrow) and coarse mosaics with umblication, suggestive of a CIN 3 lesion

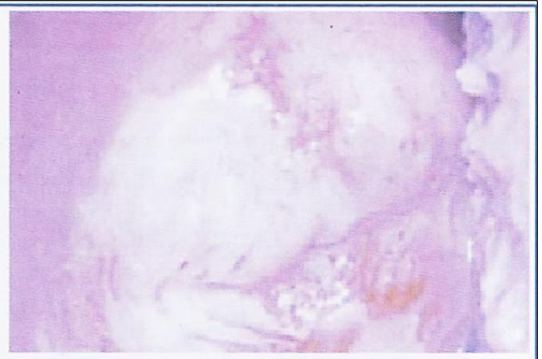


FIGURE 3.25: A dense acetowhite, opaque, complex, circumorificial CIN 3 lesion

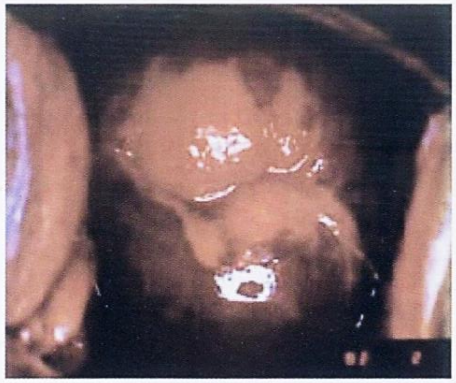


FIGURE 3.26: Satellite lesions do not stain with iodine after the application of Lugol's iodine solution and remain as thin yellow areas

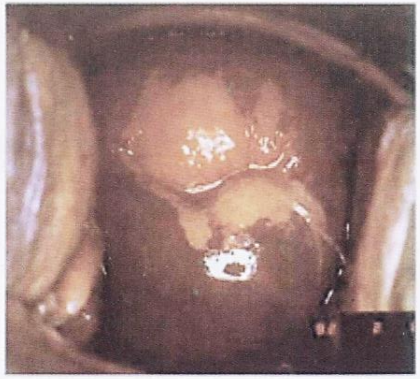


FIGURE 3.27: A CIN 1 lesion with a mustard yellow iodine-negative area with irregular margins (see the appearance after acetic acid application in Figure 3.13)

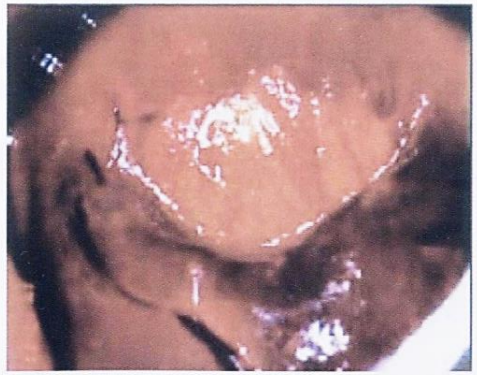


FIGURE 3.28: Mustard yellow iodine-negative area in the anterior lip (CIN 2 lesion) after the application of Lugol's iodine solution

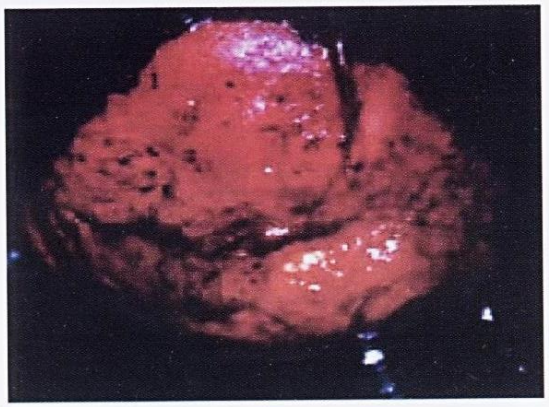


FIGURE 3.29: Dense saffron yellow iodine-negative area of a CIN 3 lesion after the application of Lugol's iodine solution. Note the surface irregularity.

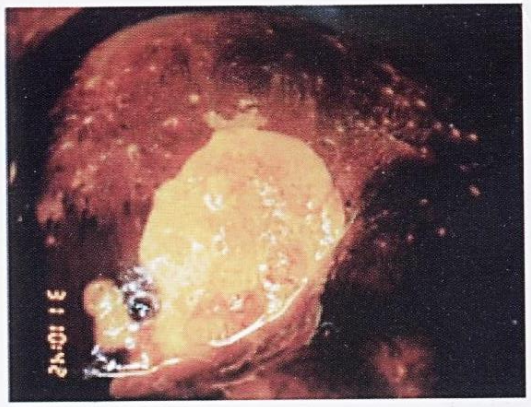


FIGURE 3.30: A dense mustard yellow iodine-negative area in the upper lip suggestive of CIN 3 lesion (see the appearance after acetic acid application in Figure 3.24)

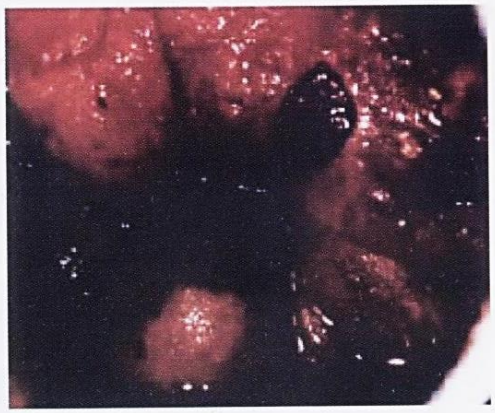


FIGURE 3.31: A condylomatous lesion does not stain with iodine (see the appearance after acetic acid application in Figure 3.8)

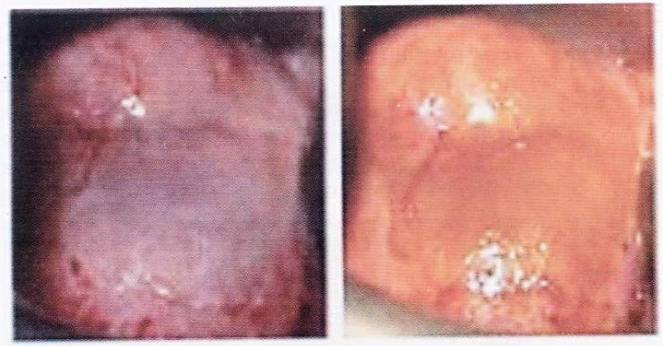


FIGURE 3.32: (a) There is a dense, opaque, thick acetowhite area involving all four quadrants of the cervix and extending into the endocervix, with irregular surface contour and atypical vessels. (b) The lesion is not taking up iodine and remains as a saffron yellow area after the application of Lugol's iodine solution

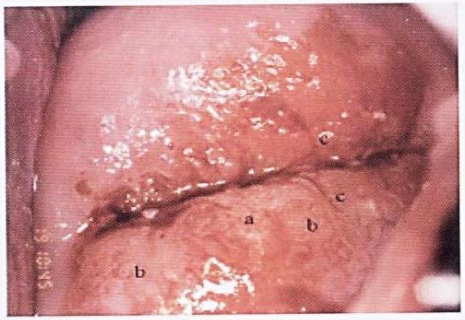
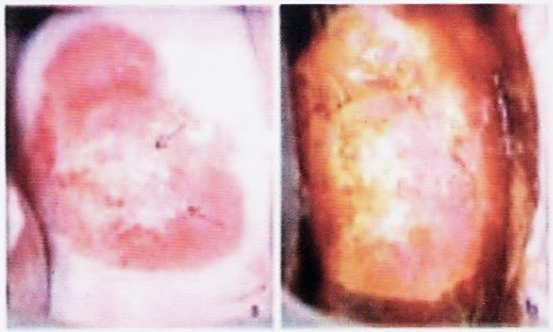


FIGURE 3.33: Early invasive cancer: Note the raised irregular mosaics with umbilication (a), breaking mosaics (b), surface irregularity and the atypical vessels (c) after the application of 5% acetic acid



FUGURE 3.34: Early invasive cancer (a) There is a large, dense, opaque acetowhite area with an irregular surface contour, coarse punctations and atypical vessels, involving all four quadrants of the cervix. There are internal borders within the acetowhite areas (arrows). The are several cuffed crypt openings. (b) The lesion dose not take up iodine and remains as a mustard yellow area after the application of Lugol's iodine.

FIGURE 3.36: Atypical vessel patterns

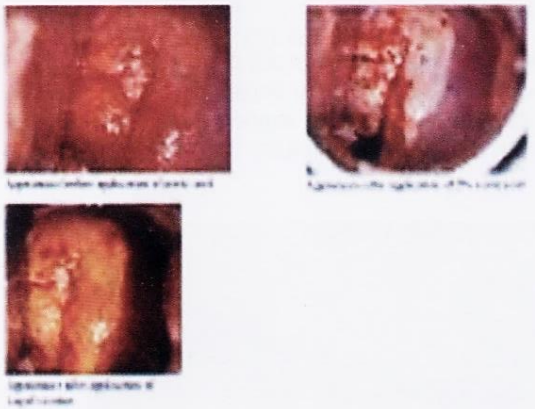


FIGURE 3.35: Early invasive cancer: Note the thick, dense, opaque acetowhite lesions with raised and rolled out margins (a) and atypical vessels (b) which started to bleed after touch. Note the mustard-yellow iodine-negative area corresponding to the extent of the lesion. Irregular surface with "mountains-and-valleys" pattern is evident

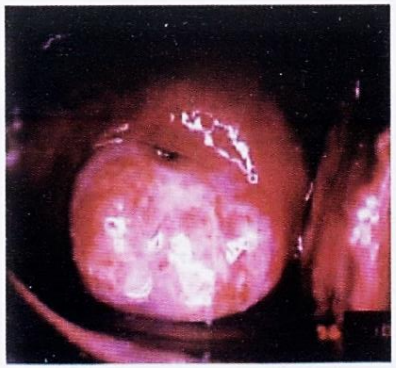


FIGURE 3.37: Dense, chalky white complex acetowhite lesion with raised and rolled out margin and irregular, nodular surface suggestive of early invasive cancer

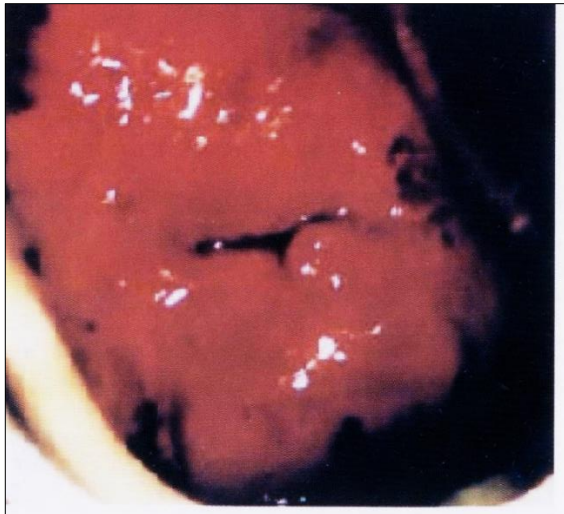


FIGURE 3.38: Invasive cervical cancer: (a) note the irregular surface contour with mountains-and-valleys appearance with atypical blood vessels in the dense acetowhite area; (b) appearance after the application of Lugol's iodine

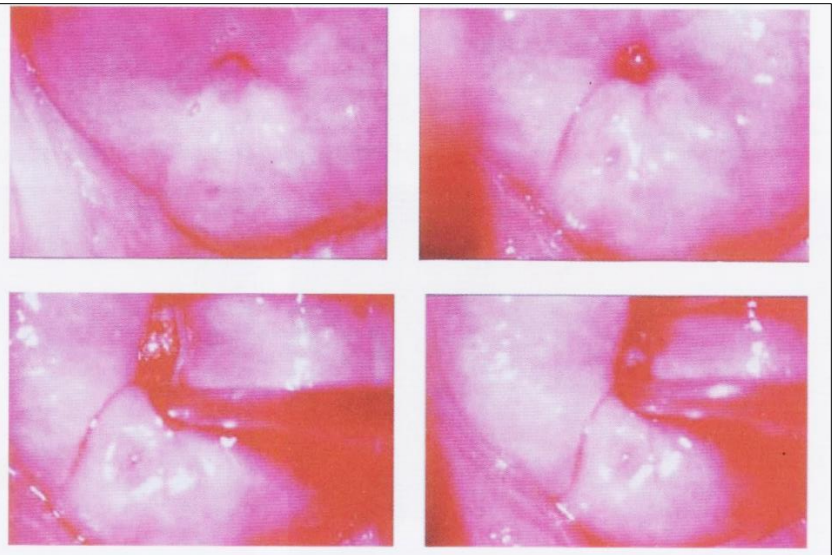


FIGURE 3.39: A dense acetowhite lesion in the endocervical canal visible after stretching the os with a long dissection forceps (adenocarcinoma in situ).

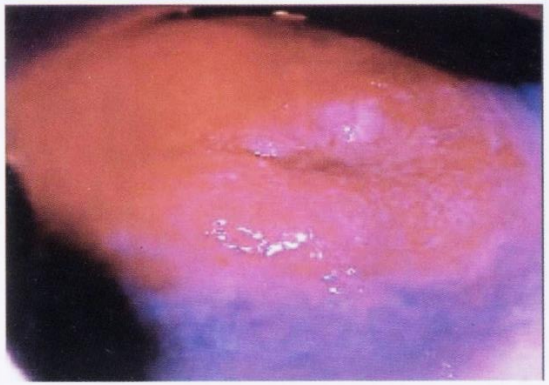
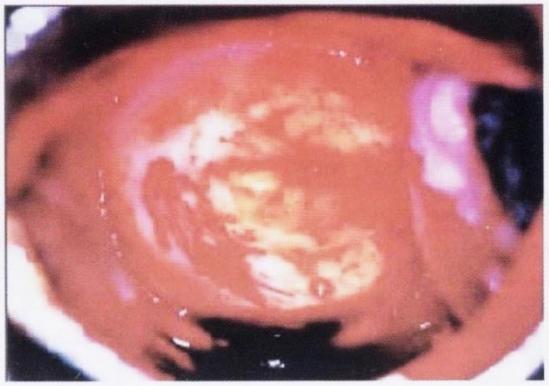


FIGURE 3.40: Adenocarcinoma in situ : The tips of some of the columnar villi turn densely white compared to the surrounding columnar villi after the application of acetic acid. The nabothian cysts turn white after the application of acetic acid



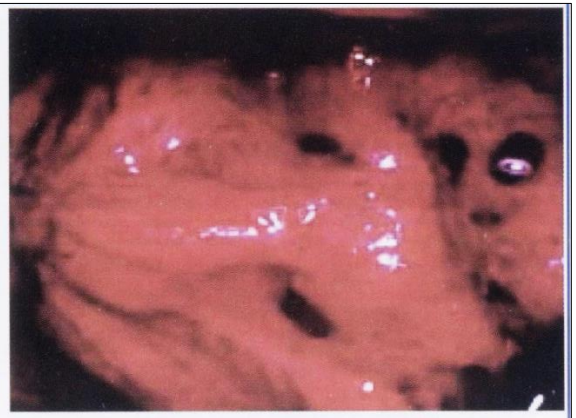


FIGURE 3.41: Adenocarcinoma in situ: Note the elevated lesions with an irregular acetowhite surface, enlarged and hypertrophied villi, papillary patterns and atypical vessels overlying the columnar epithelium

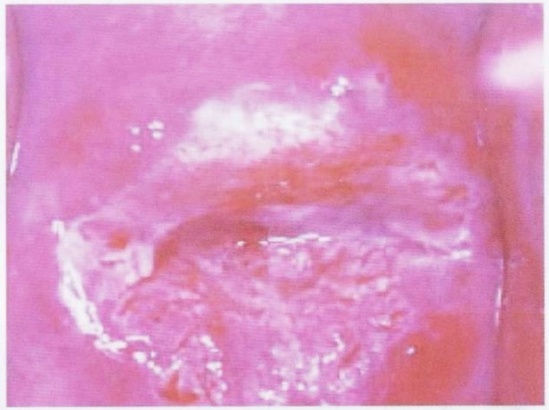


FIGURE 3.42: Adenocarcinoma: Note the greyish-white dense acetowhite lesion with character writing-like atypical blood vessels

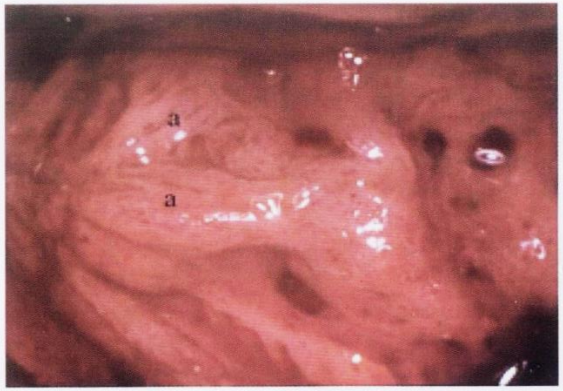


FIGURE 3.43: Adenocarcinoma: Note the elongated, dense acetowhite lesion with irregular surface in the columnar epithelium with atypical blood vessels (a)

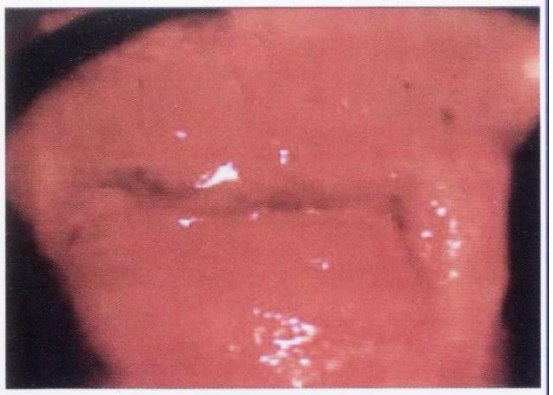


FIGURE 3.44: Adenocarcinoma: Note the multiple cuffed crypt openings (narrow arrow) in a dense acetowhite lesion with irregular surface and the hypertrophied columnar villi (dense arrows) in the columnar epithelium

Chap 4: Inflammatory Lesions of the Uterine Cervix

BEFORE THE APPLICATION OF ACETIC ACID

Examination, before application of acetic acid, reveals moderate to excessive cervical and vaginal secretions, which may sometimes indicate the nature of underlying infection. ln T. vaginalis infection (trichomoniasis), which is very common in tropical areas, there is copious, bubbly, frothy, malodorous, greenish-yellow, mucopurulent discharge. Bacterial infections are associated with thin, liquid, seropurulent discharge. The secretion may be foul-smelling in the case of anaerobic bacterial overgrowth, bacterial vaginosis, and Trichomonas infection. In the case of candidiasis (moniliasis) and other yeast infections, the secretion is thick and curdy (cheesy) white with intense itching resulting in a reddened vulva. Foul-smelling, dark-coloured mucopurulent discharges are associated with inflammatory states due to foreign bodies (e.g., a retained tampon). Gonorrhoea results in purulent vaginal discharge and cervical tenderness. Small vesicles filled with serous fluid may be observed in the cervix and vagina in the vesicular phase of herpes simplex viral infection. Herpetic infections are associated with episodes of painful vulvar, vaginal and cervical ulceration lasting for two weeks. Excoriation marks are evident with trichomoniasis, moniliasis and mixed bacterial infections.

A large coalesced ulcer due to herpes, or other inflammatory conditions, may mimic the appearance of invasive cancer. Chronic inflammation may cause recurrent ulceration and healing of the cervix, resulting in distortion of the cervix due to healing by fibrosis. There may be associated necrotic areas as well. A biopsy should be directed if in doubt. Rare and uncommon cervical infections, due to tuberculosis, schistosomiasis and amoebiasis, cause extensive ulceration and necrosis of the cervix with symptoms and signs mimicking invasive cancer; a biopsy will confirm the diagnosis.

If the infectious process is accompanied by marked ulceration (with or without necrosis), the ulcerated area may be covered with purulent exudate, with marked differences in the surface level of the cervix. There may be exudation of serous droplets.

Longstanding bacterial, fungal or protozoal infection and inflammation may lead to fibrosis, which appears white or pink, depending on the degree of fibrosis. The epithelium covering the connective tissue is fragile, leading to ulceration and bleeding. Appearances following acetic acid and iodine application are variable, depending on the integrity of the surface epithelium.

In the case of cervicitis, the columnar epithelium is intensely red, bleeds on contact and opaque purulent discharge is present. The columnar villous or grape-like appearance may be lost due to flattening of the VILLI, to repeated inflammation and to the fact that there are no clearly defined papillae (Figure 4.1). Extensive areas of the cervix and infected vaginal mucosa appear red due to congestion of the underlying connective tissue.

AFTER APPLICATION OF ACETIC ACID

The liberal application of acetic acid clears the cervix and vagina of secretions, but may cause pain. Cervicovaginitis is associated with oedema, capillary dilatation, enlargement of the stromal papillae, which contain the vascular bundles, and infiltration of the stroma with inflammatory cells. Chronically inflamed cervix may appear reddish, with ill-defined, patchy acetowhite areas scattered in the cervix, not restricted to the transformation zone and may bleed on touch (Figures 4.2,4.3). The enlarged stromal papillae appear as red spots (red punctation) in a pinkish-white background, usually in the case of T. vaginalis infection, after application of acetic acid. An inexperienced colposcopist may confuse the inflammatory punctations with those seen in cervical intraepithelial neoplasia (CIN). However, one can differentiate using the following criteria: inflammatory punctations are fine, with extremely minimal intercapillary distances, and diffusely distributed (not restricted to the transformation zone) and they involve the original squamous epithelium and vagina with intervening inflamed mucosa. As the inflammation persists and becomes chronic, it results in large, focal red punctations due to large collections of capillaries grouped together, which appear as several red spots of different sizes visible in a pinkish-white background, producing the so-called 'strawberry spots' (Figure 4.4). Colposcopically, a chronically inflamed cervix may sometimes resemble invasive cervical cancer (Figure 4.5).

AFTER APPLICATION OF LUGOIIS IODINE

The test outcome after application of Lugol's iodine solution depends upon the desquamation and the loss of cell layers containing glycogen. If desquamation is limited to the summit of the stromal papillae where the squamous epithelium is thinnest, a series of thin yellow spots are seen on a mahogany-brown background, giving a stippled appearance (Figure 4.6). When the inflammation persists and the infection becomes chronic, the small desquamated areas become confluent to form large desquamated areas leading to the so-called leopard-skin appearance (Figure 4.7). These features are often found with Trichomonas infection, but also may be seen with fungal and bacterial infections. If there is marked desquamation, the cervix appears yellowish-red in colour, with involvement of vagina (Figure 4.8).

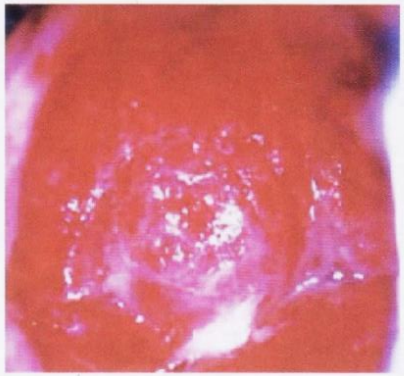


FIGURE 4.1: Reddish "angry-looking", inflamed columnar epithelium with loss of the villous structure and with inflammatory exudate (before application of 5% acetic acid)

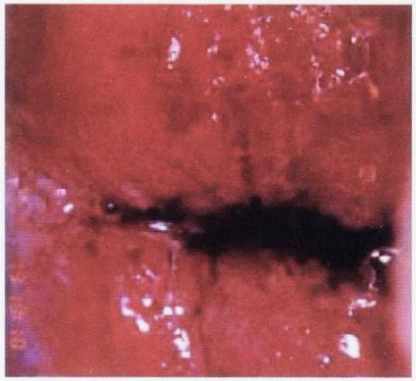


FIGURE 4.2: Chronic cervicitis: this cervix is extensively inflamed with a reddish appearance and bleeding on touch; there are ill-defined, patchy acetowhite areas scattered all over the cervix after the application of acetic acid

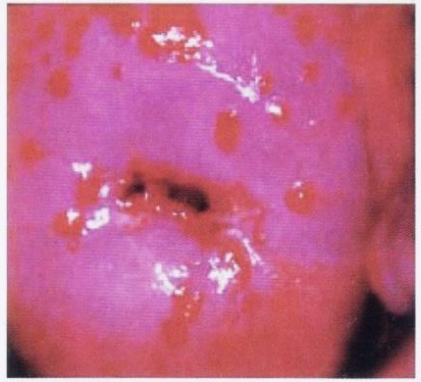


FIGURE 4.3: Chronic cervicitis: the cervix is highly inflamed and eroded with ill-defined, patchy acetowhite areas scattered all over

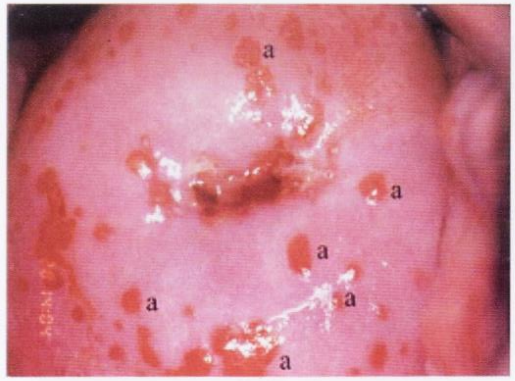


FIGURE 4.4: Multiple red spots (a) suggestive of Trichomonas vaginalis colpitis (strawberry appearance) (after application of 5% acetic acid)

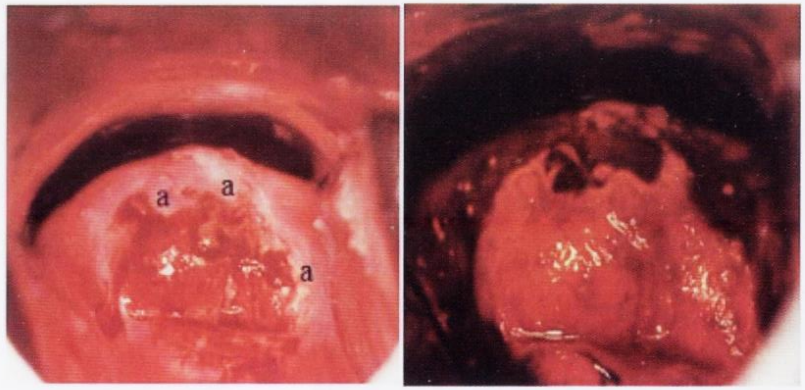


FIGURE 4.5: Colposcopic appearance of a chronically inflamed cervix showing areas of ulceration, necrosis and healing. The regenerating areas turn somewhat white (a) after application of acetic acid. The inflamed areas do not take up

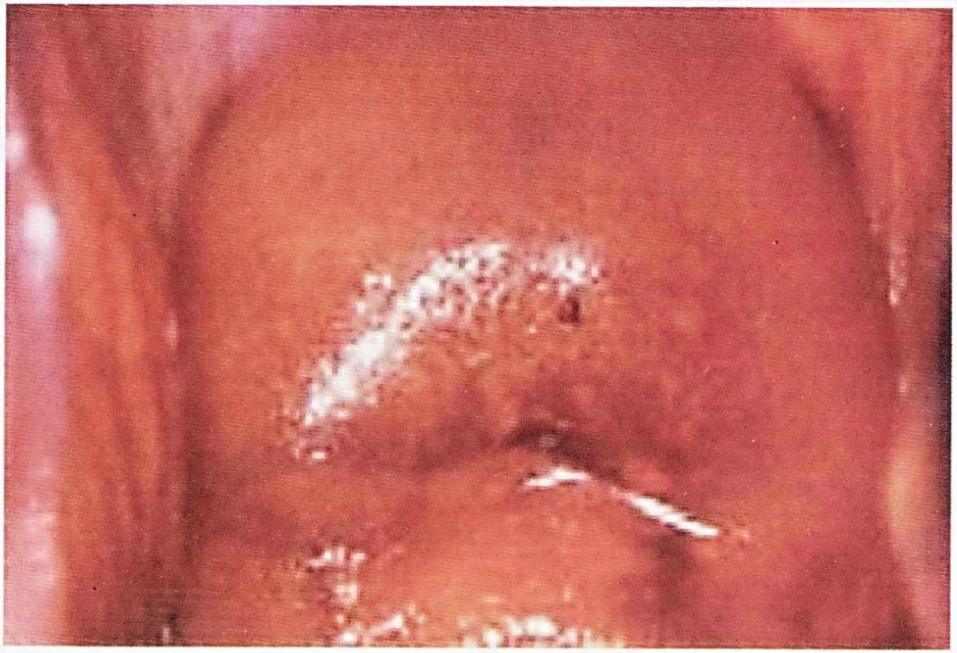


FIGURE 4.6: tippled appearance (a) due to Trichomonas vaginalis colpitis after application of Lugol's iodine

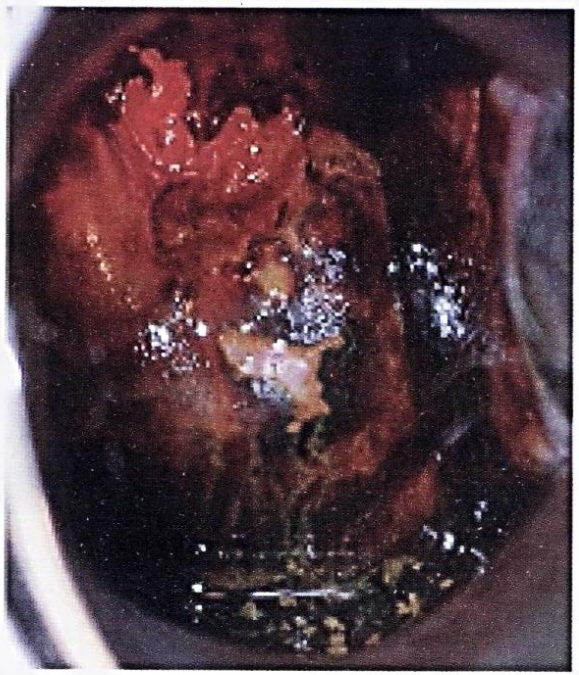


FIGURE 4.7: Chronic cervicitis: there are scattered, ill-defined, patchy iodine non-uptake areas on the cervix and vagina. Also, the cervix appears yellowish red in colour

Chap 5: Avoiding Errors in the Colposcopic Assessment Of The Cervix And Colposcopic Provisional Diagnosis

COMMON SOURCES OF COLPOSCOPIC ERRORS

- Inadequate training and experience
- Inadequate understanding of the natural history of disease
- Failure to use an established diagnostic protocol or deviation from the protocol
- Failure to use the largest speculum possible False squamocolumnar junction caused by abrasion
- Failure to choose appropriate biopsy sites and failure to take enough biopsies
- Failure to take a biopsy when in doubt
- Using a blunt, non-sharp biopsy punch to obtain tissue specimens
- Failure to take a colposcopically directed biopsy Failure to perform biopsies from condylomata or leukoplakia
- Failure to wait for the full effect of acetic acid Failure to apply Lugol's iodine solution and examine
- Failure to examine the endocervical canal adequately when the lesion limit or squamocolumnar junction is not seen
- Failure to do endocervical curettage (ECC) when the lesion limit is not seen
- Failure to perform excision when the lesion limit is not seen with an endocervical speculum or when ECC is equivocal or positive
- Failure to perform excision when microinvasion is suspected
- Failure to inspect the vagina and vulva
- Failure to properly and legibly record colposcopic findings
- Failure to communicate with the pathologist Failure to correlate histological and colposcopic findings
- Failure to consult experts in difficult cases Failure to keep up with continuing education Failure to self-audit.

Table 5.1: A summary of colposcopic features guiding provisional diagnosis											
Diagnosis	**Acetowhitening**						**Vascular features**	**Iodine uptake**	**Bleeding on touch**	**Ulceration**	**Discharge**
	Colour tone	**Demarcation**	**Margin**	**Surface**	**Relation to TZ and SCJ**	**Duration of effect**					
Normal	-	-	-	-	-	-	Normal vascular pattern	Squamous epithelium black in colour; columnar epithelium, no change in colour	Nil	Nil	Clear secretion from the columnar epithelium
Normal, immature metaplasia	Pinkish white, or snow white, translucent, patchy acetowhite areas	Nil	Indistinct, blends with the rest of the epithelium	Smooth; crypt openings, islands of columnar epithelium seen	Restricted to TZ; prominent near the SCJ	< 1 minute	Normal vascular pattern	No or partial uptake	Nil	Nil	Clear secretion from the columnar epithelium
Normal, mature metaplasia	Light pinkish white hue. No confluent acetowhite area	Nil	Blends with the rest of the epithelium	Smooth, reveals crypt openings, nabothian follicles	Restricted to TZ	-	Normal vascular pattern	Takes up iodine, turns black or brown	Nil	Nil	Clear secretion from the columnar epithelium
Inflammation	Pale, patchy areas, with intervening red areas and/or necrotic areas	Nil	Indistinct, blends with the rest of the epithelium	Irregular, variegated appearance	Not restricted to TZ, may be widely disseminated	< 2 minutes	Diffusely distributed, fine red punctation involving cervix and vagina	Partial iodine uptake	May be present	May be present	Malodorous, profuse, mucopurulent or seropurulent or non-odorous thick, sticky, white discharge
Low-grade CIN	Moderately dense, shiny, opaque, thin lesions	Well demarcated confluent lesions	Irregular, feathery, jagged, digitating, angular or geographic	Flat, smooth or microcondylomatous or micropapillary	Mostly seen in the TZ, abuts the SCJ. Very early lesions may be outside TZ as satellite lesions	1-2 minutes	Fine punctation and/or mosaic with in the AW lesion may be seen	No uptake	Nil	Nil	Nil

Table 5 . 1 (cont.): A summary of colposcopic features guiding provisional diagnosis											
Diagnosis	**Acetowhitening**						**Vascular features**	**Iodine uptake**	**Bleeding on touch**	**Ulceration**	**Discharge**
	Colour tone	**Demarcation**	**Margin**	**Surface**	**Relation to TZ and SCJ**	**Duration of effe**					
High-grade CIN	Dull, dense, greyish-white or oyster-white opaque lesion	Well demarcated confluent lesions; internal demarcations and borders may be present	Regular, smooth outlines; occasionally may be raised and rolled out	Less smooth, more irregular and/or occasionally nodular surface	Restricted to TZ, abutting the SCJ	2-4 minutes	Coarse punctation and/or coarse mosaic within the AW lesion may be seen; atypical vessels may be seen (+)	No iodine uptake	May be present in severe lesions	Nil	Nil
Preclinical invasive cancer	Chalky white, thick, dense, opaque lesions	Well demarcated	Raised and rolled out margins	Irregular, nodular or mountains-and- valley pattern	May involve the entire cervix, large complex lesions obliterating the os	> 3 minutes	Coarse raised mosaics and/or breaking mosaics and/or, coarse punctations; atypical vessels always present (+++++)	No iodine uptake	Surface bleeding/-oozing common	May be seen	May be present due to secondary infection
Overt invasive cancer	Dense white areas, may be obliterated by profuse bleeding	Entire cervix replaced by growth	Entire cervix replaced by growth	Ulceropro-liferative growth	Entire cervix replaced by growth extending to adjacent tissues	Whiteness usually obliterated by bleeding	Atypical vessels always present (++++++)	No uptake, but bleeding obliterates iodine uptake patterns	Profuse bleeding	Always present	Malodorous, blood stained, purulent discharge due to secondary infection

Chap 6: Treatment of Cervical Intraepithelial Neoplasia by Cryotherapy

Cryotherapy is a suitable and effective out patient treatment option for CIN in both low- and high-resource settings, as it requires less financial investment for equipment and maintenance, and can be learnt in a short period of time.

CRYOTHERAPY EQUIPMENT (FIGURE 6.1)

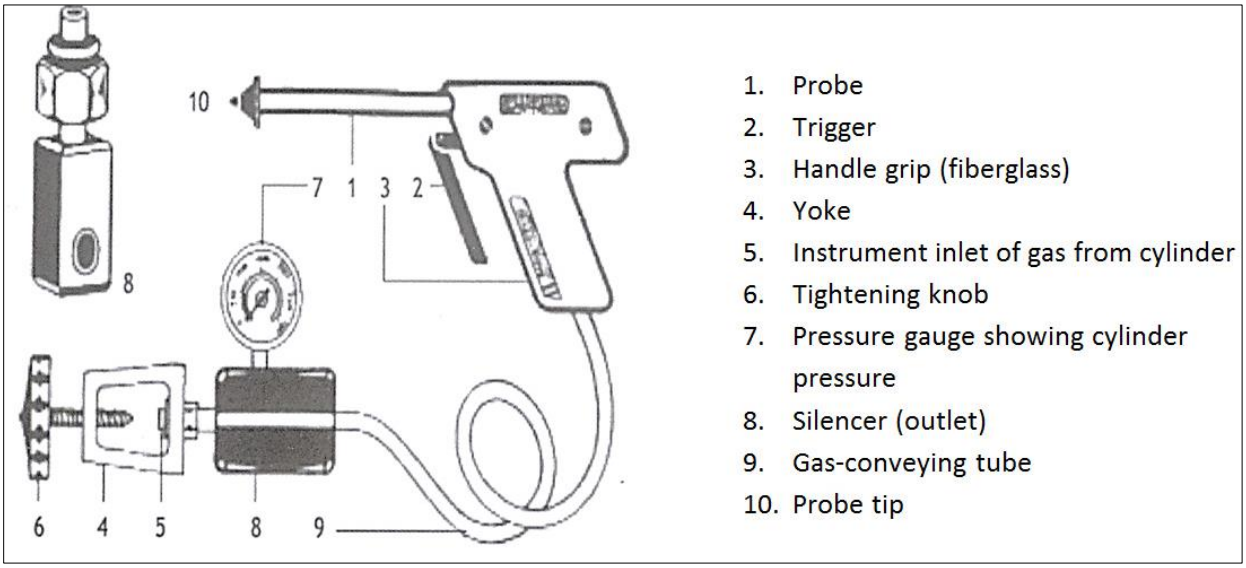


FIGURE 6.1: Components of cryotherapy equipment

The cryotherapy unit consists of a compressed gas cylinder (tank), a yoke with a tightening knob and an inlet of gas to connect the gas cylinder to the cryotherapy gun through a flexible gas-conveying tube, a pressure gauge showing the cylinder gas pressure, an outlet silencer, a cryotherapy gun with handle grip, a gas trigger to allow the gas to be released to the cryotherapy probe at high pressure and the cryotherapy probe. In most equipment, the pressure gauge shows three colour zones: yellow, green and red. When the gas cylinder is opened, if the pressure indicator in the gauge moves to the green zone, there is adequate gas pressure for treatment; if the needle remains in the yellow zone, the pressure is too low and the gas cylinder should be changed before commencing treatment; if the needle moves to the red zone, excess pressure is indicated and this excess pressure should be released. One should consult the manual provided by the manufacturer thoroughly for operational instructions.

CRYOTHERAPY FOR ECTOCERVICAL LESIONS

Eligibility criteria that must be met for cryotherapy are given in Table 6.1. If the woman is suffering from cervicitis, trichomoniasis or bacterial vaginosis, she may be offered a choice of having either cryotherapy immediately with simultaneous antimicrobial treatment or

antimicrobial treatment and returning two to three weeks later for cryotherapy. If there is evidence of pelvic inflammatory disease (PID), it is advisable to delay cryotherapy until the infection has been treated and resolved. If there is marked atrophy due to estrogen deficiency in an older woman and staining of the outer margin of a lesion is indistinct, cryotherapy may be carried out after a course of topical estrogen treatment and colposcopic reassessment. The woman must give written consent to have the treatment, after being thoroughly informed as to how it will be performed and the probabilities of its effectiveness, adverse effects, complications, long-term sequelae, and alternative ways that can be used to manage her problem.

It is advisable to use the largest cylinder of refrigerant gas possible, so that a sufficient amount of refrigerant is available to complete the treatment and the pressure forcing the refrigerant through the probe tip is maintained at a high level so that the effectiveness of the procedure is maintained. Standard-size tanks only allow adequate pressure to treat three women. A large tank has the advantage of treating more women, but transport from clinic to clinic may pose a problem.

Table 6.1: Eligibility Criteria for Cryotherapy

- The entire lesion is located in the ectocervix without extension to the vagina and/or endocervix
- The lesion is visible in its entire extent and does not extend more than 2 to 3 mm into the canal
- The lesion can be adequately covered by the largest available cryotherapy probe (2.5 cm); the lesion extends less than 2 mm beyond the cryotherapy probe
- CIN is confirmed by cervical biopsy/colposcopy
- There is no evidence of invasive cancer
- The endocervical canal is normal and there is no suggestion of glandular dysplasia
- The woman is not pregnant
- If the woman has recently delivered, she is at least three months post-partum
- There is no evidence of pelvic inflammatory disease
- The woman has given informed written consent to have the treatment

If excellent contact is achieved between the probe tip and the ectocervix (Figures 6.2 and 6.3b), a nitrous oxide-based cryotherapy will achieve temperatures of about -89°C and the carbon dioxide-based system will achieve -68° C at the core of the tissue ice ball. The temperature at the edges of the frozen tissue may be around - 2O°C. Cells held at -20°C for one minute or more will undergo cryonecrosis. The minimum temperature at the probe tip for effective freezing

should be -60° C. It is critical to establish and maintain good contact throughout the procedure between the probe tip and the tissue - poor contact means a relatively large variation in the temperatures achieved within the ice ball and therefore variable effectiveness in the target tissue.

STEP-BY-STEP APPROACH TO CRYOTHERAPY (FIGURES 6.2 AND 6.3):

A woman should meet the eligibility criteria in Table 6.1. Generally, it is preferable to have the diagnosis of CIN firmly established before cryotherapy is performed. However, there may be exceptions to this general rule, and women may be offered treatment at their first colposcopy visit to maximize treatment coverage (otherwise patients lost to follow-up would not receive treatment for lesions) on the basis of a colposcopy diagnosis. However, directed biopsy may be carried out before instituting cryotherapy, so that a histological diagnosis will be available to establish the nature of the lesion treated a posteriori. The consequences of such an approach in terms of possible over-treatment or unnecessary treatment, as well as the side-effects and complications of the treatment procedure, should be explained and informed consent obtained.

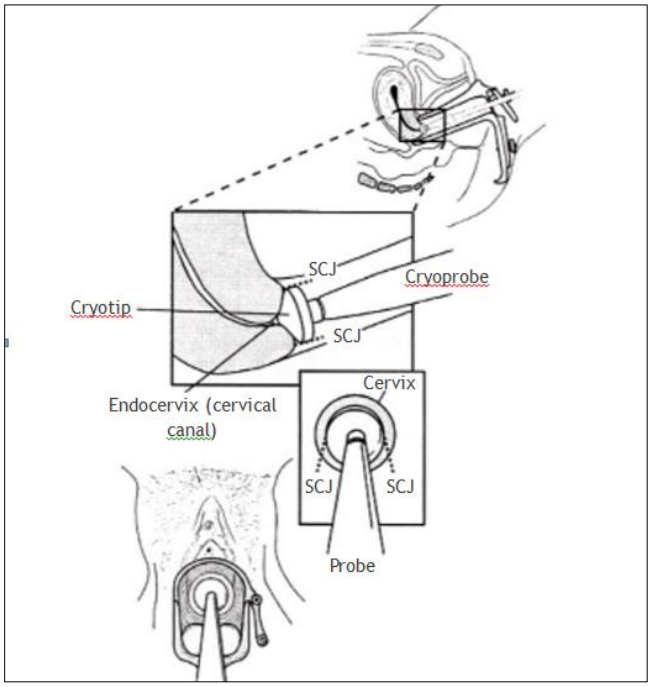


Figure 6.2: Positioning of the cryoprobe tip on the lesion.

The provider should be familiar with the cryotherapy equipment and its different components (Figure 6.1) that will be used in a given setting. The instructions for operational use and safety provided by the manufacturer should be read carefully. The safety regulations should be strictly followed. Before cryotherapy is initiated, the gas tank pressure should be checked to ensure that it is sufficient to provide an effective flow of the refrigerant through the probe tip for the required duration of treatment. One should follow the instruction of the manufacturer in this regard. In most models of cryotherapy equipment, a green zone in the pressure gauge indicates adequate pressure (40-70 kg per cm2) and a yellow zone indicates low pressure (less than 40 kg/cm2). If there is adequate gas pressure in the cylinder, the indicator moves to the green zone in the gauge, after the cylinder is opened to release the gas. If the pressure is low, there will be insufficient freezing to give the required extent of cryonecrosis. The minimum working pressure shown on the gauge should be 40 kg/cm2, and the freezing will be inadequate if the pressure falls below this level. In such an event, the gas cylinder should be changed before continuing treatment.

lf the woman is returning to the clinic on a second visit (after histological confirmation) for treatment, colposcopic assessment should be done immediately before cryotherapy to confirm that the location and linear extent of the lesion are amenable to effective cryotherapy.

The physician or the nurse should explain the treatment procedure to the woman and reassure her. This is important to help the woman to relax during the procedure. After ensuring she has emptied her bladder, she should be placed in a modified lithotomy position and the cervix should be exposed with the largest speculum that can be introduced comfortably. The secretions are removed with a cotton swab soaked in saline. Then 5% acetic acid is applied and the cervix is examined with the colposcope. Following this, Lugol's iodine is applied to delineate the limits of the lesion. There is no need for local anaesthesia when performing cryotherapy.

The cryoprobe surface is wiped with saline to ensure adequate thermal contact with the cervix and optimal lowering of the tissue temperature. The cryotherapy probe tip is then firmly applied, with the centre of the tip on the os. It is obligatory to ensure that the vaginal walls are not in contact with the cryoprobe tip. The timer is then set and the gas trigger in the cryogun is released or squeezed to cool the cryoprobe in contact with the cervix. The gas escapes through the pressure gauge with a hissing noise. One should be able to observe ice being formed on the tip of the cryoprobe and on the cervix as freezing progresses. Make sure that the probe adequately covers the lesion and the tip does not inadvertently contact and d freeze any part of the vagina during the procedure.

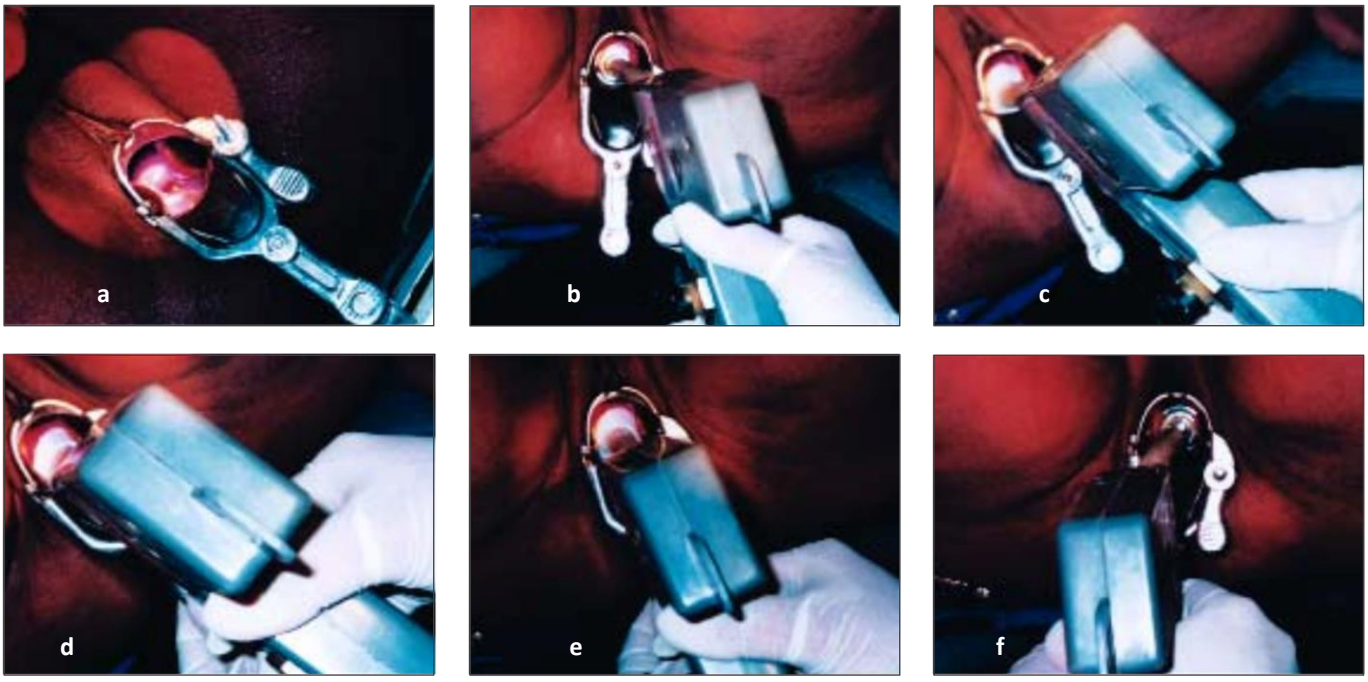
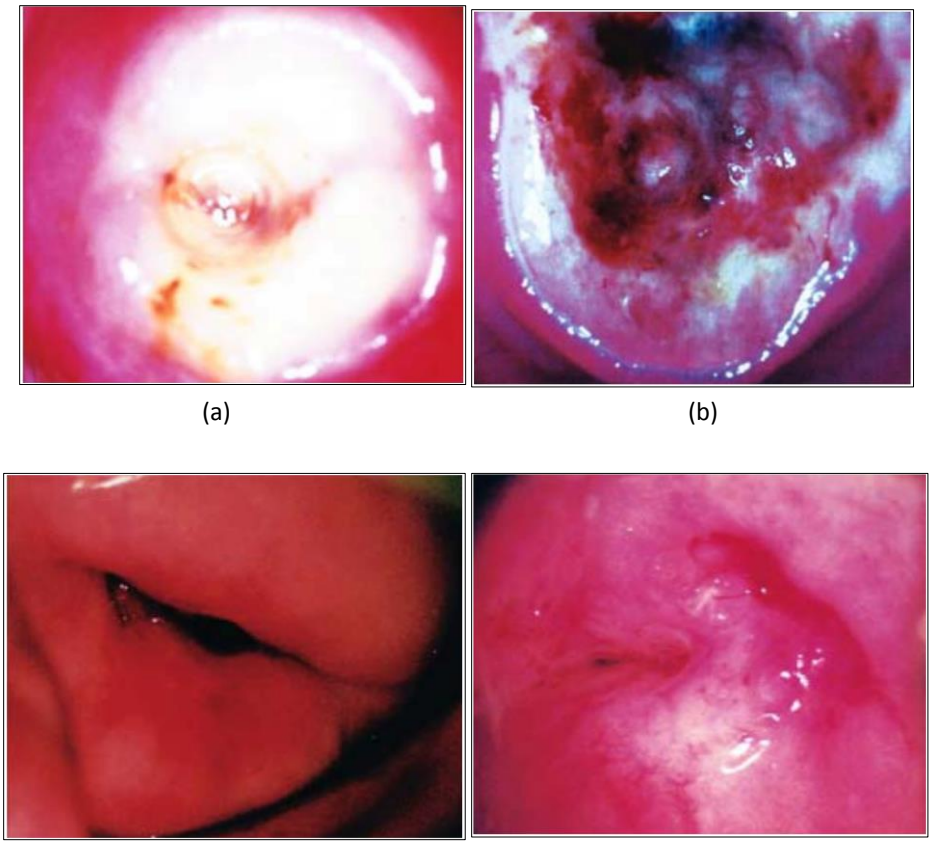


FIGURE 6.3: Cryofreezing in progress. Note the cryoprobe covers the lesion well (a, b). Note the iceball formation in c, d and e. Note the appearance after thawing in (f).

Cryotherapy should consist of two sequential freeze-thaw cycles, each cycle consisting of 3 minutes of freezing followed by 5 minutes of thawing (3 minutes freeze-5 minutes thaw-3 minutes freeze-thaw). The treatment time should be monitored using a stop watch. Adequate freezing has been achieved when the margin of the ice ball extends 4-5 mm past the outer edge of the cryotip. This will ensure that cryonecrosis occurs down to at least 5 mm depth. To achieve this effect evenly throughout the treatment field, it is extremely important to establish and maintain excellent contact between the probe tip and the ectocervical surface. Once the second freeze for 3 minutes is completed, allow time for adequate thawing before removing the probe from the cervix. When thawing is completed, the ice formation on the cryoprobe tip is totally cleared and the probe is removed by gently rotating on the cervix. Do not attempt to remove the probe tip from the cervix until complete thawing has occurred. After removing the probe, examine the cervix for any bleeding. The appearance of the cervix immediately after cryotherapy is shown in Figure 6.4a. Note the iceball formed in the cervix. The vagina should not be packed with gauze or cotton after cryotherapy to allow the secretions to escape. Women may be provided with a supply of sanitary pads to prevent the secretions staining their clothes. After use, the probe tip should be wiped with 60-90% ethyl or isopropyl alcohol and then cleaned well with boiled water and disinfected with 2% glutaradehyde and kept dry. After the procedure is completed, the cryogun, tubing, pressure gauge and gas tank should be de-contaminated by wiping with cotton soaked with 60-90% ethyl or isopropyl alcohol.



(a) (b)

(c) (d)

FIGURE 6.4: (a) The iceball on the cervix immediately after cryotherapy, (b) Appearance 2 weeks after cryotherapy. (c) 3 months after cryotherapy. (d) 1 year after cryotherapy

FOLLOW-UP AFTER CRYOTHERAPY

Women should receive instructions on self-care and what symptoms to expect after treatment. They should be informed that they may experience some mild cramps and a clear or lightly blood-stained watery discharge for up to 4-6 weeks after treatment. Women should be advised not to use a vaginal douche or tampons or to have sexual intercourse for one month after treatment. They should be instructed to report if they have any one of the following symptoms in the six weeks after treatment: fever for more than two days, severe lower abdominal pain, foul-smelling- pus coloured discharge, bleeding with clots or bleeding for over two days. It is preferable to give written instructions on the above aspects and on follow-up.

Healing takes place during the first six weeks after cryotherapy. Granulation tissue is present in the wound during the first 2-3 weeks after cryotherapy (Figure 6.4b), which is followed by re-epithelialization of the surface. Normally, the wound is totally healed within 6- 8 weeks of treatment. The appearance of the cervix 3 months and 12 months after cryotherapy is shown in figures 6.4c and 6.4d.

The effect of cryotherapy on the potential transmissibility of human immunodeficiency virus (HIV) infection (to or from women) during the healing phase is not known. HIV-1 shedding in the vaginal secretions after treatment of CIN in HIV- positive women has been demonstrated (Wright *et al.*, 2001). Therefore, the authors suggest advising all women that cryotherapy may increase the transmissibility of HIV and that using condoms is an effective means of prevention. Condoms should be used for a period of at least four but preferably six weeks. Ideally, a supply of condoms should be available free of charge at colposcopy clinics in settings where HIV infection is endemic.

Appointments should be made for a follow-up visit 6-12 months after treatment. During the follow-up, cytology and/or VIA should be performed, followed by colposcopy and directed biopsy depending upon the colposcopy findings, to assess the regression or persistence of lesions. Retreatment is carried out if lesions persist. Women who are negative for neoplasia may be referred back to a screening programme (if one exists) or advised to undergo follow-up after three or five years.

MANAGEMENT OF WOMEN FOR WHOM CRYOTHERAPY FAILS

Treatment failure is detected in about 5-10% of women during the follow-up in the first year. These persistent, local or multifocal lesions are more likely to occur if the original lesion was large. To rule out the presence of unsuspected invasive carcinoma, it is advisable to biopsy all persistent lesions and then re-treat with cryotherapy, LEEP, or cold-knife conization, as appropriate. Follow-up evaluation may be carried out after 9-12 months in which screening examinations such as cytology and/or VIA and colposcopy should be carried out. Those negative for neoplasia may be referred back to a screening programme (if one exists in the region) or advised to undergo follow-up after three or five years.

ADVERSE EFFECTS, COMPLICATIONS, AND LONG-TERM SEQUELAE

Cryotherapy is usually a painless procedure, if women have been properly reassured, their co-operation is obtained, and the procedure is carried out properly. Some women may experience some lower abdominal pain or cramps during and after cryotherapy. Once in a while, a woman may faint due to a vasovagal reaction. In such a situation, there is no need for panic and the women may be revived easily. Bleeding is extremely rare after cryotherapy.

Treated women experience a watery vaginal discharge for about 3-4 weeks after treatment. Vaginal bleeding is extremely unusual; it may be more likely to occur if freezing has been too aggressive and the ice ball has extended well past 5 mm in depth. The risk of post-operative infection is very slight and can probably be reduced further by delaying cryotherapy until any woman with a likely diagnosis of pelvic inflammatory disease (PID), sexually transmitted cervicitis (e.g., chlamydia or gonorrhea), vaginal trichomoniasis or bacterial vaginosis has been adequately treated and recovered. If a woman presents post-operatively with a malodorous discharge, pelvic pain and fever, the discharge may be cultured if possible, and empirical treatment should be prescribed with antibiotics that are effective for PID. Sexual partners

should also be treated if the woman is diagnosed with PID, sexually transmitted cervicitis, or trichomoniasis. In developing countries, one may consider providing presumptive treatment with antibiotics routinely after cryotherapy (doxycycline 100 mg orally, two times a day, for seven days and metronidazole 400 mg orally, three times a day, for seven days).

Cervical stenosis occurs in less than 1% of women; reduced mucus production occurs in 5-10% of women. Cryotherapy has no known adverse effect on fertility and pregnancy. Invasive cancer has rarely been reported after cryotherapy, it is usually due to missed diagnosis as a result of poor diagnostic workup before cryotherapy.

Chap 7: Treatment of cervical intraepithelial neoplasia by loop electrosurgical excision procedure (LEEP)

Points to remember:

- Electrosurgical current applied to tissues can have one of three effects on the tissue, depending on the power setting and the waveform of the current used: desiccation, cutting, and fulguration.
- Loop electrosurgical excision procedure (LEEP) is a relatively simple procedure that can be readily learnt.
- The key advantage of LEEP over cryotherapy is that it removes rather than destroying the affected epithelium, allowing histological examination of the excised tissue.
- A loop wider than the lesion(s) and the transformation zone to be removed should be used; otherwise, the lesion should be removed with multiple passes.
- If the lesion involves the endocervical canal, a two-layer excisional method should be used.
- Women will have a brown or black discharge for up to two weeks after LEEP.
- Women should be advised not to use a vaginal douche, tampon, or have sexual intercourse for one month after LEEP.
- Moderate to severe post-operative bleeding occurs in less than 2% of treated women and they should be seen promptly.

Electro-surgery is the use of radiofrequency electric current to cut tissue or achieve haemostasis. A loop electrosurgical excision procedure (LEEP) operator needs to keep in mind that electricity flows to ground along the path of the least electrical resistance. The electrical energy used in electro-surgery is transformed into heat and light energy. The heat from a high-voltage electrical arc between the operating electrode and tissue allows the practitioner to cut by vaporizing tissue (at 100^0C) or to coagulate by dehydrating tissue (above 100^0C). The cutting

electrodes are loops of very fine (0.2 mm) stainless steel or tungsten wire to achieve different widths, depths, and configurations of cut (Figure 7.1).

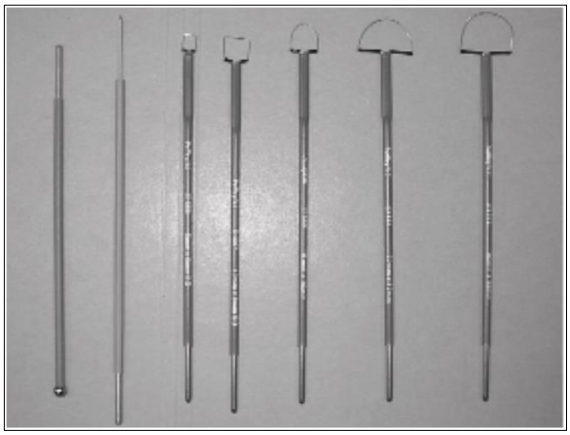


FIGURE 7.1: Ball electrode, macro-needle style electrode, loops.

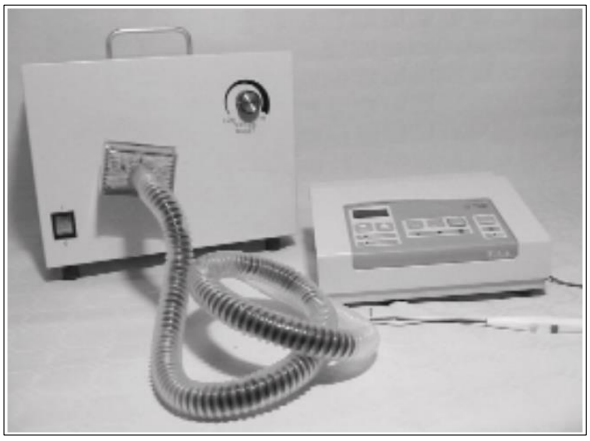


FIGURE 7.2: Electrosurgical generator (1) and the smoke evacuator (2)

Manufacturers of modern electrosurgical generators (Figure 7.2) are aware of the need to control bleeding. They offer electrosurgical cutting settings that lead to some coagulation by blending electrical currents, one with a cutting waveform and another with a coagulation waveform. This combination is called a blended cutting waveform, and is the type of waveform that will be referred to in this manual when electrosurgical cutting is discussed.

Coagulation using the fulguration setting and a 3- to 5- mm ball electrode is the type of coagulation that is normally referred to in this manual (one exception is be the use of a needle electrode to fulgurate a stubborn area of bleeding).

Electro-surgery must not be performed in the presence of flammable gases, flammable anesthetics, flammable liquids (e.g., alcohol-containing skin- preparation solutions or tinctures), flammable objects, oxidizing agents, or an oxygen-enriched atmosphere.

PRACTICING LEEP AND DEMONSTRATING COMPETENCE BEFORE USE ON PATIENTS

It is mandatory that every colposcopist has practiced and demonstrated the ability to perform LEEP adequately by simulating the excision of cervical lesions on meat (beef, pork etc.) or fruits on which mock lesions have been painted to scale. Typewriter correction fluid or trichloroacetic acid work well for painting mock lesions. LEEP should always be practiced using the colposcope, as is done in actual practice. If possible, colposcopists should have experience and demonstrated competence with cryotherapy before learning LEEP.

Table 7.1: The eligibility criteria that must be met before LEEP is performed

- CIN is confirmed by cervical biopsy, when possible
- If the lesion involves or extends into the endocervical canal, the distal or cranial limit of the lesion should be seen; the furthest (distal) extent is no more than 1 cm in depth
- There is no evidence of invasive cancer or glandular dysplasia
- There is no evidence of pelvic inflammatory disease (PID), cervicitis, vaginal trichomoniasis, bacterial vaginosis, anogenital ulcer or bleeding disorder
- If the woman has recently delivered, she should be at least three months post-partum
- Women with hypertension should have their blood pressure well controlled
- The woman must give written consent to have the treatment after being thoroughly informed as to how it is performed and the probabilities of its effectiveness, adverse effects, complications, long-term sequelae, and alternative ways that are available to manage her problem

THE STEP-BY-STEP APPROACH TO LEEP

First, it must be confirmed that the woman meets the eligibility criteria in Table 7.1. If there is evidence of pelvic inflammatory disease (PID), cervicitis, vaginal trichomoniasis, bacterial vaginosis or anogenital ulcer, it is advisable to delay LEEP until that condition has been treated and resolved. If there is marked atrophy due to estrogen deficiency in an older woman and staining of the outer margin of a lesion is indistinct, it is advisable to delay LEEP until after a course of topical estrogen treatment.

It is generally preferable to have the diagnosis of CIN firmly established before LEEP is performed. However, there may be exceptions to this general rule, for example, in the context of developing country settings, women may be offered treatment at their first colposcopy visit to maximize treatment coverage (otherwise patients lost to follow-up would not receive treatment for lesions). Expert colposcopists also may use this approach to maximize treatment coverage and to minimize the number of clinic visits in some clinical settings.

The instruments needed for LEEP should be placed on an instrument trolley or tray (Figure 7.3). If the woman is returning to the clinic on a second visit for treatment, colposcopic assessment should be carried out immediately before LEEP to confirm that the location and linear extent of the lesion are amenable to effective LEEP. The application of Lugol's iodine solution is helpful to outline lesion margins before the start of treatment. An insulated vaginal speculum (Figure 7.3) with an electrically insulating coating or a speculum covered with a latex condom should be used to avoid an electrical shock to the woman in the event that the activated electrode inadvertently touches the speculum (though this type of event usually does not cause any tissue damage because of the relatively large area of contact). Similarly, care must be taken to avoid causing pain by inadvertently touching the vaginal walls with the activated electrode. The later possibility may be avoided by using an insulated vaginal sidewall retractor in addition to an insulated vaginal speculum (Figure 7.3) or by using a speculum covered by a condom.

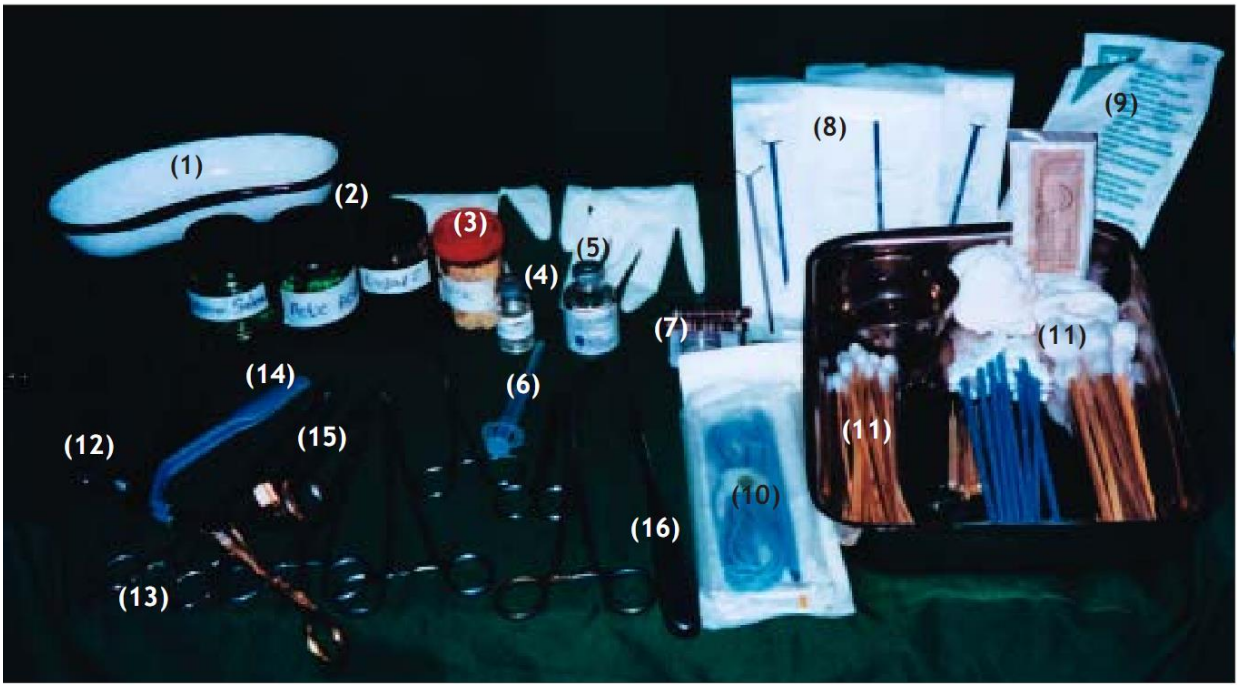


FIGURE 7.3: Instrument tray for LEEP

1. Kidney tray
2. Bottles with normal saline, 5% acetic acid and Lugol's iodine
3. Monsel's solution
4. Bottle containing formalin
5. Bottle containing local anaesthetic agent
6. Syringe for local anaesthesia
7. Needle and suture material
8. Loops and ball electrode
9. Patient return electrode or dispersive plate
10. Pencil with the hand switch
11. Cotton swabs
12. Insulated vaginal speculum
13. Sponge-holding forceps
14. Insulated vaginal side-wall retractor
15. Dissecting forceps
16. Endocervical curett

It is ideal if the vaginal speculum used has a smoke evacuator tube attached to the luminal surface of the anterior blade so that a source of suction can be attached. If this type of speculum is not available, a simple suction tube (preferably made of non-conductive and non-flammable material) may be used, and the open tip should be positioned as near as possible to the cervix. A smoke evacuation system with a high rate of flow and a means of filtering out the smoke particles and odour is mandatory.

Local anesthesia is achieved 30 seconds after multiple injections of a total of 5ml or less of 1% xylocaine (or a similar agent) into the stromal tissue of the ectocervix. The injections are given in a ring pattern 1-2 mm deep (at 3, 6, 9 and 12 o'clock positions) at the periphery of the lesion and transformation zone using a 5ml syringe and 25- to 27- gauge needle.

The aim of the LEEP procedure is to remove the lesions and the transformation zone in their entirety and send the affected tissue to the histo-pathological laboratory for examination.

EXCISION OF AN ECTOCERVICAL LESION WITH ONE PASS (FIGURES 7.4 AND 7.5).

The operator should use a loop that is wider than the lesion(s) and the transformation zone to be removed.

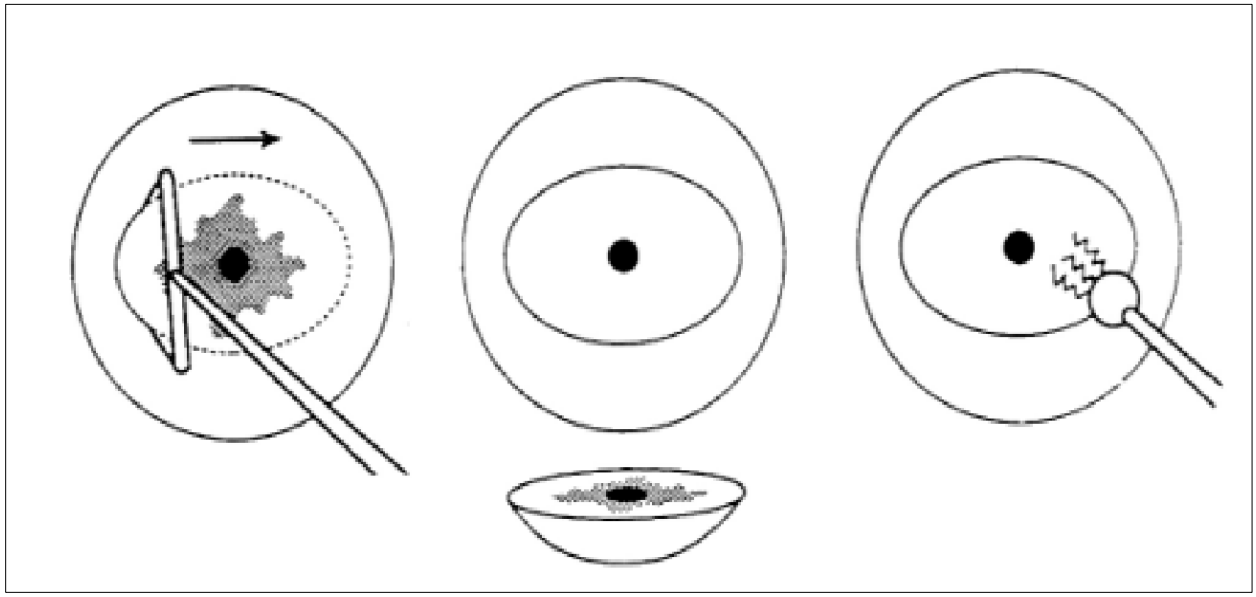


Figure 7.4: Excision of an ectocervical lesion with one pass

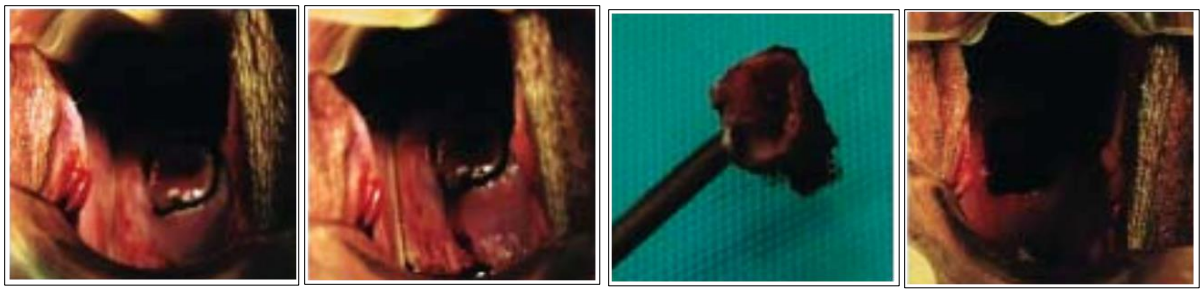


Figure 7.5: Excision of an ectocervical lesion with one pass. Note the excised specimen in place; the excised specimen is removed and the appearance of the cervix after the removal of the excised specimen.

The depth of the loop should be at least 5 mm (height from the cross bar to the farthest part of the wire arc). Often one may use a 2.0 x 0.8 cm oval loop. To maintain the ideal geometry and depth of cut, it is desirable to orient the surface of the ectocervix at right angles to the handle of the cutting electrode holder - that is, to keep the cross bar parallel to the ectocervix. To begin, local anaesthesia is administered, the electrosurgical generator is set to the appropriate power and blended cutting setting, and the smoke evacuation system is turned on. When the loop is poised just above the starting point, but not touching the cervical surface, the operator activates the current with a foot pedal or finger switch on the electrode holder. The loop is introduced into the tissue 5 mm outside the outer boundary of the lesion. It is important not to push the electrode in, but to let it cut its own way; the operator should simply provide directional guidance. The loop is directed gradually into the cervix until the cross bar nearly comes in contact with the epithelial surface. Then the loop is guided along parallel to the surface (horizontally or vertically, depending on the orientation of the direction of cutting) until the point is reached just outside the opposite border of the lesion. The loop is then withdrawn slowly, still keeping it at right angles to the surface. The current is switched off as soon as the loop exits the tissue. It does not matter whether the direction of excision is right to left or vice versa. It also is acceptable to pass the loop from the posterior to the anterior. However, it is not acceptable to pass the loop from the anterior to the posterior, since bleeding or excised tissue curling downward may obscure the visual field.

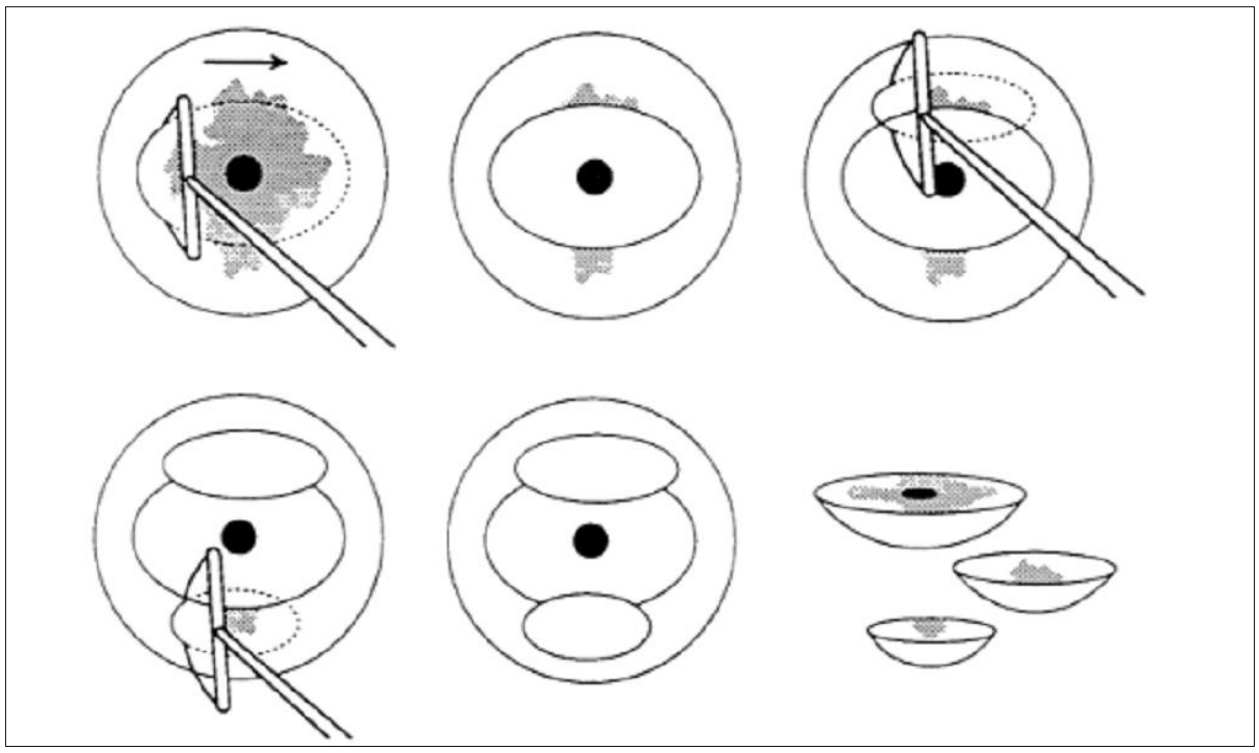
Once the specimen has been removed and placed in formalin, the setting on the electrosurgical generator is changed to fulguration and the appropriate power is selected. The surface of the excisional crater is fulgurated using 3 or 5 mm ball electrode, in the coagulation mode. The edges of the crater should also be fulgurated to preserve the squamocolumnar junction in the visible ectocervix. If active bleeding occurs and is difficult to control using the ball electrode, a macro-needle style electrode can be effectively used to apply the fulguration current in a much more concentrated (higher current density) and localized fashion to a bleeding site. If satisfactory haemostasis has been obtained, the surface of the crater is then coated with

Monsel's paste and the speculum is removed. It is a general observation that an extremely nervous patient tends to bleed more than a relaxed one - another good reason to communicate with the patient throughout the procedure and to try to calm her fears.

If bleeding is difficult to stop despite use of the methods outlined above, the base of the excisional crater should be liberally coated with Monsel's paste and the vagina packed with gauze. The woman should be asked to wait for several hours before removing the pack. This complication appears to occur more frequently in women with cervicitis.

EXCISION OF AN ECTOCERVICAL LESION WITH MULTIPLE PASSES (FIGURE 7.6)

If the diameter of a lesion exceeds the width of the largest loop (usually 2 cm), the lesion must be removed with multiple passes using one or more sizes of loop. Using the basic method described above (Figure 7.3), the central part of the lesion usually is removed first. The remaining parts of the lesion in the periphery are then removed by one or more separate passes. All specimens are preserved for pathological examination.



Cancer 7.6: Excision of an ectocervical lesion with multiple passes

EXCISION OF ECTOCERVICAL PLUS ENDOCERVICAL LESIONS (FIGURES 7.7 AND 7.8)

If a lesion involves the endocervical canal and is not likely to be removed with the depth of the usual single-layer pass as described above and shown in figures 7.4 and 7.5, a two-layer excisional method can be used. When lesions involve the canal, most of them extend for a linear length of 1 cm or less into the endocervical canal. Older women and women with CIN 3 are likely to have longer lesions and require a second layer - composed wholly of the endocervical canal - to be excised.

Usually the ectocervical portion of this type of lesion that extends into the canal can be excised by one pass of a large oval (2.0 x 0.8 cm) loop. The remaining tissue in the endocervical canal can be excised using a smaller loop - usually a square loop with a 1.0 x 1.0 cm configuration - but care must be taken not to go any deeper than is necessary to completely excise the lesion and a margin of normal tissue. This type of excision can reach a maximum of 1.6 cm into the endocervical canal (Figure 7.7). Excision of this depth should be attempted only when absolutely necessary, due to increased risk of bleeding and stenosis as the depth of excision increases. LEEP should not be used if the distal or upper extent of the lesion in the canal cannot be seen and if the distal end of the lesion extends more than 1 cm into the canal. Such patients should undergo cold-knife conization. Since this two- step method requires adequate performance of the basic LEEP procedure, it is recommended that it should not be attempted until the operator is comfortable and competent with the basic LEEP. Women with lesions that extend further up into the canal need cold-knife conization to properly assess the endocervical canal.

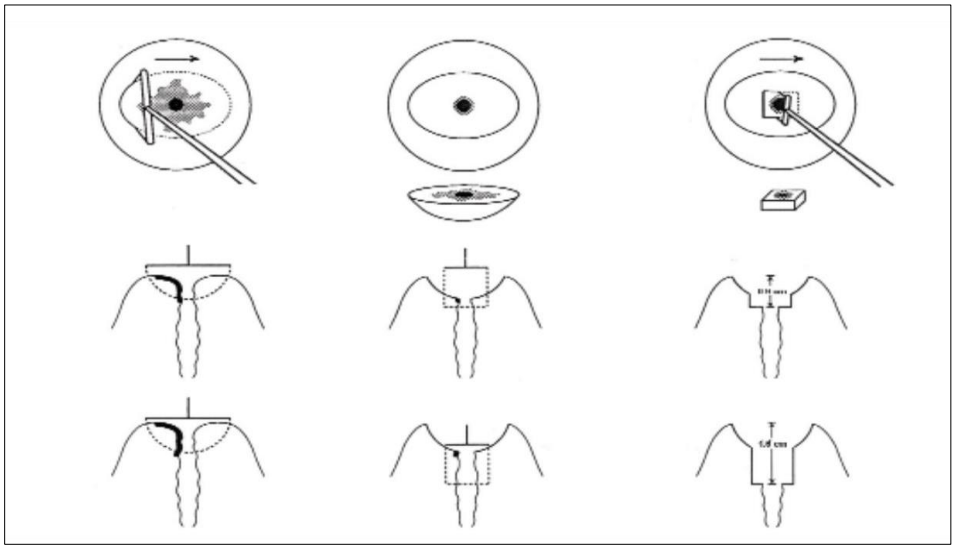


FIGURE 7.7: Excision of ectocervical plus endocervical lesions

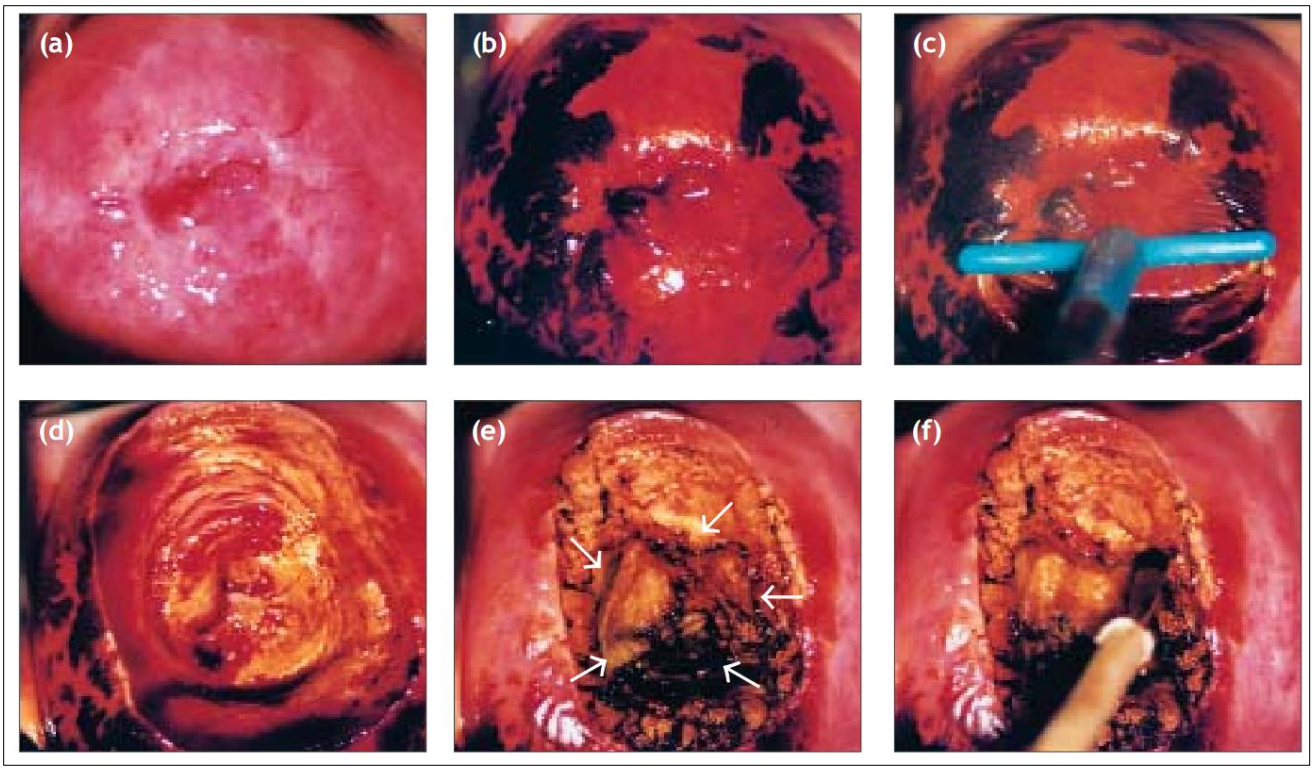


FIGURE 7.8: Excision of an ectocervical lesion extending into the endocervical canal by a two-layer excisional method; (a) appearance of the CIN 3 lesion after 5% acetic acid application; (b) appearance after Lugol's iodine application; (c) excision of the ectocervical lesion in progress; (d) ectocervical cut completed; (e) endocervical cut completed and the specimen in place (narrow arrows); (f) endocervical cut specimen removed and the bleeding points in the floor of the crater are being fulgurated to achieve haemostasis

LESIONS WITH VAGINAL EXTENSION

If the lesion extends onto the vagina, it is preferable to use the ball electrode for electro-fulguration on the peripheral, vaginal part of the lesion and LEEP on the central, cervical part of the lesion. The treatment of these vaginal lesions is beyond the scope of this manual and the LEEP treatment referred to here deals only with the type of lesions shown in Figures 7.4, 7.6, 7.7 and 7.8 and described above. Interested readers may refer to standard text books (Wright *et al.*, 1992; Wright *et al.*, 1995).

FOLLOW-UP CARE AFTER LEEP

Women should receive instructions on self-care and what symptoms to expect after treatment. If appropriate, written instructions should be provided. Women should be advised that they will have a brown or black discharge lasting between a few days and two weeks. They should be advised to promptly report back if the discharge persists for more than two weeks, if

discharge becomes malodorous and/or is associated with lower abdominal pain or if profuse bleeding develops. Women should be advised not to use a vaginal douche or tampons, or to have sexual intercourse for one month. The appearance of cervix three months and one year after LEEP is shown in Figures 7.9 and 7.10.

The effect of LEEP treatment on the potential transmissibility of HIV (to or from women) during the healing phase is not known. HIV-1 shedding in the vaginal secretions after treatment of CIN in HIV-positive women has been demonstrated (Wright *et al.*, 2001). Therefore, the authors suggest advising all women that LEEP treatment may increase the transmissibility of HIV and that using condoms is an effective means of prevention. Condoms should be used for period of 6-8 weeks. Ideally, a supply of condoms should be available, free of charge, at colposcopy clinics in settings where HIV infection is endemic.

A follow-up appointment should be made for review at 9-12 months after treatment. Management of women who have persistent disease at the follow-up visit(s) is discussed in the next section.

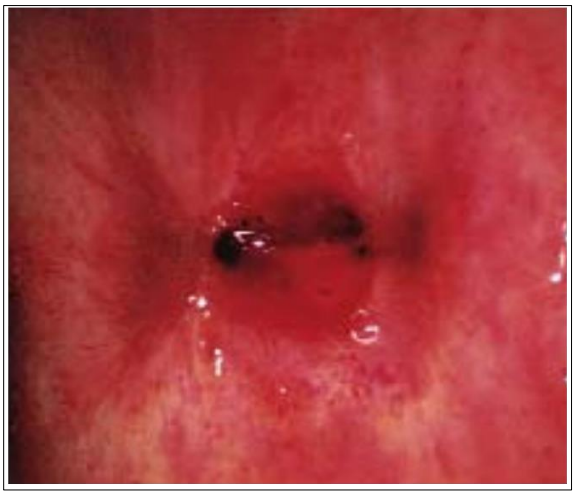


FIGURE 7.9: Appearance of the cervix three months after LEEP; note the parallel blood vessels in the healed cervix (arrow)

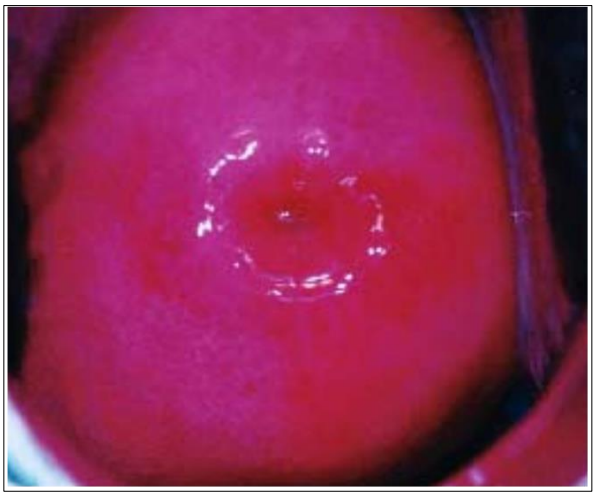


FIGURE 7.10: Appearance of the cervix one year after LEEP

ADVERSE EFFECTS, COMPLICATIONS, AND LONG – TERM SEQUELAE OF LEEP

Most women experience some transitory pain from the injection of local anaesthetic into the cervix. Severe perioperative bleeding occurs after 2% or less of LEEP procedures. Women should be advised to contact the clinic if they have any concerns during the post- operative period. It is advisable to give written post-operative instructions that outline the following points. Few women complain of post-operative pain. If post-operative pain occurs, it usually is similar to cramps; women should be instructed to use oral analgesics such as acetaminophen or ibuprofen, if necessary. A blood-tinged, dark brown (from the Monsel's paste) mucus discharge usually lasts for one or two weeks after treatment. Severe and moderate post- operative bleeding occurs in a few women, who should be seen promptly. Healing after LEEP usually takes place within a month.

When post-operative bleeding occurs, it usually appears 4-6 days after treatment and often from the posterior lip of cervix. This bleeding can usually be controlled by fulguration, applying Monsel's paste, or using a silver nitrate applicator stick. Rarely, placement of a suture at the bleeding site is necessary. The risk of post-operative infection is very small and can probably be reduced even more by delaying surgical treatment until any woman with a likely diagnosis of PID, cervicitis, vaginal trichomoniasis or bacterial vaginosis has been adequately treated and recovered. If a woman presents post-operatively with a malodorous discharge, it should be cultured if possible and empirical treatment prescribed with antibiotics that are effective for PID (see Table 11.1). In developing countries, it may be preferable to institute routine presumptive treatment with antibiotics after LEEP (doxycycline 100 mg orally, two times a day, for seven days and metronidazole 400 mg orally, three times a day, for seven days).

The squamocolumnar junction is in the endocervical canal at the follow-up evaluation in approximately 2% of women. This presents a challenge for adequate colposcopic examination and cytological sampling. Women should be warned that cervical stenosis, partial or complete, is rarely encountered (probably less than 1%), but is more common in menopausal women.

Management of women with persistent lesions at follow-up

All women, regardless of whether or not the pathology report states that the excisional margins are clear, should be followed up at 9 - 12 months from treatment to evaluate regression or persistence of lesions and complications. Treatment failures (persistent lesion(s) at follow-up) are detected in less than 10% of women when they are checked at the follow-up appointment. It is advisable to biopsy all persistent lesions to rule out the presence of unsuspected invasive carcinoma. Persistent lesions should be re-treated with cryotherapy or LEEP or cold-knife conization, as appropriate.

Chap 8: Cleaning of Instruments and Materials Used for Early Detection and Treatment of Cervical Neoplasia

A guide to the processing instruments and materials used for early detection and treatment of cervical neoplasia

Instrument / material	Suggested procedures
Vaginal speculam, vaginal retractors, biopsy forceps, endocervical curette, endocervical speculum, needle holder, toothed forceps, insulated speculum and vaginal side-wall retractor	Autoclaving or disinfection with boiling water
Gloves	Autoclaving as wrapped packs
Cryoprobes	Disinfection with 0.1% chlorine or 2% glutaral dehyde or 6% hydrogen peroxide
Colposcope head, Stand LEEP equipment, cryogen and regulator, cryo gas cylinder, examination table, hand lens, aviscope, torch lights, halogen lamp, instrument trolley, trays	Wipe with 60-90% ethyl, isopropyl alcohol

The instruments should not be left in dilute bleach for more than 10 minutes and should be cleaned in boilewater immediately after decontamination to prevent discolouration and corrosion of metal.

DECONTAMINATION OF THE FLOOR OF THE SCREENING CLINIC

Procedure tables, trolleys, equipment (Colposcope, cryosurgical equipment, electrosurgical generator, smoke evacuator, halogen lamp, etc.) in the screening clinic may be contaminated with body fluids such as vaginal secretions, purulent discharge, blood, etc. While the surface of the procedure table should be decontaminated after each patient procedure, the other surfaces should be decontaminated on a daily basis by wiping with 0.5% chlorine solution, 60-90% ethyl or isopropyl alcohol or other chemical disinfectants such as iodophors. The floor of the screening clinic should also be decontaminated on a daily basis.

Chap 9: Modified Reid Colposcopic Index (RCI)

Feature	0 points	1 point	2 points
Colour of acetowhite (AW) area	Low-intensity acetowhitening; snow-white, shiny AW; indistinct AW; transparent AW; AW beyond the transformation zone	Grey-white AW with shiny surface	Dull, oyster-white; Grey
AW lesion with margin and surface configuaration	Feathered margins; angular, jagged lesions, flat lesions with indistinct margins; micro condylomatous or micropapillary surface	Regular lesion smooth, straight outlines	Rolled, peeling edges; internal demarcations (a central area of high- grade change and peripheral area of low- grade change)
Vessels	Fine/uniform vessels; poorly formed patterns of fine punctuations and/or fine mosaic; vessels beyond the margin of transformation zone; fine vessels within microcondylomatous or micropapillary lesions	Absent vessels	Well defined coarse punctation or coarse mosaic
Iodine staining	Positive iodine uptake giving mahogany brown colour; negative uptake of lesions scoring 3 points or less on above three categories	Partial iodine up-take by a lesion scoring 4 or more points on above three categories – variegated, speckled appearance	Negative iodine uptake by a lesion scoring 4 or more points on the above three criteria

Colposcopic grading performed with 5% aqueous acid and Lugol's iodine solution.

1. Microexophytic surface contour indicative of colposcopically overt cancer is not included in this scheme.
2. Epithelial edges tend to detach from underlying stroma and curl back on themselves. Note: Prominent low-grade lesions often are over-interpreted, while subtle avascular patches of HSIL can easily be overlooked.
3. Score zero even if part ofthe peripheral margin does have a straight course.
4. At times, mosaic patterns containing central vessels are characteristic of low-grade histological abnormalities. These low-grade-lesion capillary patterns can be quite pronounced. Until the physician can differentiate fine vascular patterns from coarse, overdiagnosis is the rule.
5. Branching atypical vessels indicative of colposcopically overt cancer are not included in this scheme.
6. Generally, the more microcondylomatous the lesion, the l_ower the score. However, cancer also can present as a condyloma, although this is a rare occurrence.
7. Parakeratosis: a superficial zone of cornified cells with retained nuclei.

Colposcopic prediction of histologic diagnosis using the Reid Colposcopic Index (RCI)

Overall RCI = Histology

0 to 2 points = Likely to be CIN 1;
3 to 4 points = Overlapping lesion: likely to be CIN 1 - 2;
5 to 8 points = Likely to be CIN 2 - 3 lesions.

Grading abnormal colposcopic findings using two categories

Grade	Findings
1. Insignificant	The acetowhite epithelium is usually shiny or semitransparent. The borders are not sharp, with or without fine-calibre vessels (fine punctation and/or fine mosaic), which have ill-defined patterns and short intercapillary distances. There is an absence of atypical vessels.
2. Significant	Dense acetowhite or grey opaque epithelium is sharply bordered. There are dilated calibre, irregular shaped or coiled vessels (coarse punctation and/or mosaic). Atypical vessels and sometimes irregular surface contour indicate either imminent or invasive cancer.

Adapted from Coppleson *et al.*, 1993 b

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