WARNING SIGNS OF CERVICAL CANCER

The primary responsibility of the colposcopist is to rule out the presence of cancer. Because the average colposcopist will only rarely view cervical cancer with the coloscope, the skills to diagnose invasive disease must be constantly renewed. The warning signs of invasive cancer should always be kept in mind each time the cervix is examined. The obvious colposcopic impression of a spectacular cervical intraepithelial neoplasia (CIN) may be easier to detect than the subtle signs of invasive cervical cancer.

The cervical intraepithelial lesion transforms into a cancer when the epithelial cells break through the basement membrane and appear in the stromal tissue. This may occur at the base of a glandular crypt replaced by CIN or underneath the squamous epithelium itself. The early signs of cancer viewed with the coloscope may not be obvious to the colposcopist if a high index of suspicion is not present. Each patient must be presumed to have cancer until the absence of invasive lesions has been verified.

The best way to minimize errors in diagnosing invasive cancer is to have a high index of suspicion based on the age and risk factors of the patient and the results of the cytologic smear. The principles of expert colposcopy must be followed when each patient is examined. The entire transformation zone must be viewed. If the squamocolumnar junction (SCJ) is deep in the endocervical canal, it may not be possible to rule out the presence of atypical vessels at the leading edge of the transformation zone. Once the transformation zone is identified, the colposcopic signs of cervical cancer can be appropriately and individually assessed.

There should be good correlation between the cytology, colposcopic impression and the histologic results. If the clinician believes that the cervix exhibits signs of invasive cancer despite reassuring cytologic and histologic results, the diagnosis must be pursued until the cancer is confirmed or excluded. On the other hand, the histology may suggest the presence of cancer but the colposcopic impression does not support this diagnosis. If the histology is confirmed by expert opinion, further evaluation by conization is required.

ATYPICAL VESSEL FORMATION

The hallmark of invasive cancer is the presence of atypical vessel formation. As the intraepithelial neoplasia progresses, the epithelium thickens and the mosaic and punctuation patterns which are characteristic of preinvasive disease may be more difficult to see as the vessels are compressed. Without new vessel formation however, the intraepithelial lesion could
not continue to proliferate. This neovascularization process in stimulated by tumor angiogenic factor (TAF). TAF stimulates new vessels to form under and parallel to the surface epithelium. The difference between the abnormal blood vessels of premalignant disease and the atypical vessels of cancer is the pattern of the vessel formation. The punctation and mosaic patterns become more irregular, wider and display abrupt changes in caliper of the vessels as the cancer progresses. The regular pattern is completely lost as the new vessels take on a non-branching pattern and can be seen running parallel to the surface epithelium. The atypical vessels often form acute angles to the surface. The intercapillary distance is increased as the tumor continues to grow. The tortuous corkscrew and comma-shaped vessels associated with atypical epithelium are coarser and display greater variation in caliper than punctation and mosaic patterns.

Instead of displaying arborization as the benign vessels do, the atypical vessels do not decrease in caliper as they branch but remain straighter and non-branching. The atypical vessels may bleed easily when touched with a cytology sampling device or a cotton-tipped applicator. Use of a green filter will screen out the red color of the vessels and make the vascular pattern appear blacker so they are easier to visualize.

Dilated, bizarre vessels can occur in situations other than cervical cancer. The skill of a colposcopist is tested by the need to differentiate atypical vessels from the normal vessels that occur throughout the transformation zone. Vessels present in exophytic condyoma, granulation or inflammatory tissue and tissue previously irradiated may all exhibit vessels that have bizarre shapes on a surface with irregular contour. A colposcopic directed biopsy may be the only way to reliably differentiate benign from atypical vessels.

The following will illustrate examples of blood vessels seen on the cervix:

1. **Benign blood vessels**
   - regular branching of vessels (arborization)
   - gradual reduction in caliper
   - normal intercapillary distance
   - no abrupt change in direction
   - not usually present in areas of acet whitening
   - usually diffuse

2. **Atypical blood vessels**
   - irregular and haphazard arrangement
   - abrupt acute angles
   - increased intercapillary distance
   - bizarre shapes
     ~ corkscrew
~ hairpins
~ commas
~ star-bursts

COLOR

The colposcopist should be alert for color changes that indicate cervical cancer. Healthy cervical epithelium has a pinkish tint. Any shade of red other than the light red color of the normal transformation zone should be viewed with suspicion. Grayish red tones which give the transformation zone an opaque appearance should also be suspect. If the cervix exhibits a yellow color indicating tissue necrosis, cancer should be suspected.

EROSIONS AND ULCERATIONS

The older colposcopic literature designated the term “true erosion” because it was felt that all visible lesions of the cervix were erosions. In the more recent use of the term, an erosion is used to indicate the presence of columnar epithelium on the ectocervix. The use of the term erosion as it applies to this columnar epithelium which has everted onto the ectocervix implies that this is not part of the normal cervical architecture. The use of the term erosion in this fashion is to be discouraged. The correct use of the term should be restricted to cases of actual epithelial defects. If these defects are deep enough to expose the stroma, the lesion is appropriately called an ulcer.

Erosions do not normally occur in women who are in the reproductive age range. However, the atrophic epithelium of postmenopausal women can be prone to erosions. This atrophic epithelium is vulnerable to erosions because it lacks cohesiveness, being more loosely structured than normal squamous epithelium. The epithelium is also less firmly attached to the underlying stroma so it can detach easier to produce an erosion. An erosion can be recognized by its intense red color, granular base and its punched out margin. If erosions are large and coalesce, whole epithelial fields can be detached. An area of erosion may occur in a field of colposcopic atypia and be associated with high grade CIN. These lesions can be seen with iodine staining because the exposed stroma does not stain at all. Biopsies should be taken from the rim and the base of the erosion. Invasive cancer should always be suspected when an erosion is present and appropriate biopsies should be obtained.

FRIABILITY

Tissue that is friable or bleeds easily on contact should be viewed as possible cancer. Ectocervical tissue that indicates the presence of bleeding areas that are not the result of cervical trauma must be considered suspicious for cancer. If the cancer is exophytic in nature, the lesion will be soft with a surface that is easily abraded. Microcapillary oozing may be present. Columnar epithelium bleeds normally easier than squamous epithelium because the underlying blood vessels are poorly concealed. The presence of contact bleeding when the endocervical
curettage is preformed does not necessarily mean that endocervical cancer is present. However, adenocarcinoma of the endocervix may exhibit none of the characteristic signs of cervical cancer normally present on the ectocervix.

**SURFACE CONTOUR**

An irregular surface contour of the cervix may indicate cervical cancer. The surface may be fissured and have a cauliflower appearance. As the new atypical vessels proliferate, more destruction of the surface architecture occurs. Distortion of the ectocervical contour depends on the growth pattern of the developing tumor. Exophytic tumors may actually extend into the vagina. Cancer may be localized to one area and the remaining surface may appear relatively normal.

Other benign conditions producing irregularity of the surface contour include exophytic condyloma, columnar epithelium on the ectocervix, decidual reaction during pregnancy and DES stigmata. If there is any question that cancer is present, a representative biopsy should be taken.

**SAFEGUARDS AGAINST MISSING AN INVASIVE LESION**

In order to avoid missing an invasive lesion, the following safeguards should be considered. A normal cytology in the face of a clinically apparent invasive lesion should not be overlooked. A high number of invasive cancers are associated with normal cytology. A colposcopic impression of cancer should not be ignored. The diagnosis of cervical cancer most frequently occurs following a cytology report of invasive disease or the presence of a high grade intraepithelial lesion.

Cancer should be suspected in the face of a high grade intraepithelial lesion on the cervix. The presence of a large precancerous lesion may be associated with cancer. The colposcopist should not miss those tiny atypical blood vessels in the same area as the mosaic and punctuation patterns. The larger CIN lesions should be carefully examined for subtle signs of cancer. The lesions that are large and densely acetowhite should raise suspicion. High grade lesions that extend into the endocervical canal have a more significant risk of invasive cancer. The full extent of the transformation zone must be viewed in order to rule out the presence of cancer. Women who are postmenopausal, immunosuppressed or have a history of pelvic irradiation are at high risk for invasive disease of the cervix.

If there is any question about the diagnosis of cancer, conization should be performed.

**Summary of warning signs of cervical cancer**

1. Cytologic prediction of invasive cancer
2. Severe colposcopic atypia
3. Large, high grade cervical lesions
4. Ectocervical lesions extending into the endocervical canal
5. Yellow, friable epithelium
6. Irregular surface contour
7. Ulceration
8. The presence of atypical vessels
9. A histologic suspicion of invasion
10. High risk patient groups such as postmenopausal, previously irradiated or immunosuppressed women