Cervical Intraepithelial Neoplasia (Cervical Dysplasia): Therapy

Description/Etiology

Cervical intraepithelial neoplasia (CIN; also called cervical dysplasia) is a precancerous condition that is characterized by abnormal growth in the epithelial lining of the cervix. Over time, CIN can develop into cervical cancer (for more information, see series of Quick Lessons and Evidence Based Care Sheets about cervical cancer). CIN is identified based on results of a Papanicolaou (Pap) smear test, and cell abnormalities can range from mild to severe. Colposcopy is widely used to aid in the diagnosis and treatment of CIN and cervical cancer. It involves the use of a colposcope (i.e., a specialized lighted microscope) to provide high-powered magnified visual examination of the cervix that ideally allows for complete visualization of the extent and borders of all CIN lesions and allows the clinician to obtain histologic samples by punch biopsy or endocervical curettage (ECC). Indications for colposcopy include a positive Pap smear.

The Bethesda system grades Pap smear findings as either negative for intraepithelial lesions and malignancy or as positive for epithelial cells abnormalities, which can include atypical squamous cells, low-grade squamous intraepithelial neoplasia, high-grade squamous intraepithelial neoplasia, or cancerous lesions. The CIN system, which is a classification system that is based on the degree of abnormality and the depth of the dysplasia found on histopathology evaluation of cervical specimens, grades lesions as follows: CIN 1 is cellular dysplasia that is confined to the basal third of the epithelium (formerly called mild dysplasia), CIN 2 is cellular dysplasia confined to the basal two-thirds of the epithelium (formerly called moderate dysplasia), and CIN 3 is cellular dysplasia that involves more than two-thirds of the epithelial thickness, including full-thickness lesions (formerly called severe dysplasia and carcinoma in situ).

Management of CIN will vary according to Pap smear results; colposcopy, biopsy, and/or ECC findings; and patient characteristics and history. Treatment options include ablative or excisional techniques; excisional modalities include the options of loop electrosurgical excision procedure (LEEP) or large loop excision of the transformation zone (LLETZ) using an electrified wire loop, cold-knife conization (CKC; generally used to remove deeper lesions), laser conization, and hysterec tom. Ablative techniques include cryotherapy with liquid nitrogen, laser ablation using a laser beam, radical electrocoagulation diathermy, and cold coagulation. Ablative techniques can only destroy abnormal cells to a depth of 5 mm. Excisional techniques can reach deeper lesions and preserve the integrity of specimens for histopathology analysis.

Untreated CIN 1 is more likely to resolve spontaneously (in 57% of cases) than to progress to cervical cancer (in 11% of cases). Management depends on physician and patient preference and patient history, and may include diagnostic excisional procedures, clinical follow-up in 6–12 months with colposcopy and cytology, or treatment with ablation or excision. CIN 2 and CIN 3 are likely to persist or progress to cervical cancer and require prompt treatment; with a satisfactory colposcopy (i.e., in which the entire area of CIN can be visualized), either ablation or excision is acceptable and follow up is scheduled at six month intervals for cytology or cytology/colposcopy. In cases of an unsatisfactory colposcopy (i.e., in which the extent of CIN lesions is not visualized), one of the diagnostic excisional methods (e.g., cervical cone biopsy, conization with a cold knife cone, laser cone,
or LEEP conization) is performed in order to obtain further diagnostic information, followed by human papillomavirus (HPV; i.e., a virus that is necessary for the development of CIN 3 and cervical cancer) DNA testing in 6–12 months, and performing colposcopy if HPV testing is positive. If CIN is persistent or recurrent, treatment with repeat colposcopy, tissue sampling, and excision is considered acceptable. Hysterectomy is considered in patients who have recurrent CIN and do not desire future fertility.

Management of CIN in adolescent females includes follow-up with cytology in 12 months, and colposcopy if there is evidence of a high-grade squamous intraepithelial lesion or atypical squamous cells. CIN 2 or CIN 3 in adolescents and young women can be managed either with ablative or excisional procedures or conservatively with observation, colposcopy and cytology due to lower risk of progression to cervical cancer. Local treatment should be considered for women who are of reproductive age with CIN to preserve fertility, but without compromising treatment efficacy. Treatment of CIN in pregnant women is usually delayed until after delivery unless cervical cancer is suspected. Immunosuppressed females, including those with HIV infection, have higher rates of CIN persistence and recurrence and require more aggressive treatment.

Facts and Figures
Worldwide each year, 1–2% of women overall and 10% of women with HIV infection have CIN 2 or CIN 3. Cryotherapy results in a cure rate of 95% in women with CIN1 or CIN2 and a cure rate of 85–90% in women with CIN 3; the cure rate decreases with increasing lesion size. In women with CIN 2 or CIN 3, LEEP is successful in 94% of cases with clear margins and 83% of cases with positive margins. Up to 26% of patients with CIN 2 or CIN 3 who undergo excisional therapy or ablation develop recurrence despite clear margins.

Risk Factors
The primary risk factor for CIN is HPV infection. Other risk factors are multiple sex partners, intercourse before 18 years of age, history of a sexually transmitted disease (STD), multiparity, long-term oral contraceptive use, a compromised immune system, and cigarette smoking. Factors associated with recurrence of high-grade CIN following surgical treatment include positive margins, HIV infection, and smoking.

Signs and Symptoms/Clinical Presentation
There are no known signs and symptoms of CIN. An abnormal Pap smear test result is the clearest clinical indication of CIN.

Assessment
› Patient History
  • Assess patient’s sexual history and obtain results of her physical examination and past Pap smears. If a woman is sexually active or is 18 years of age or older, cervical cancer screening should be initiated
› Laboratory Tests That May Be Ordered
  • The Pap smear for cytology is the primary screening tool
  • Liquid-based Pap testing may be ordered to allow for HPV DNA typing
  • Histologic analysis of biopsy samples will identify the severity of CIN
  • HPV test may be positive, indicating infection
› Other Diagnostic Tests/Studies
  • Colposcopy will be performed to visually examine the cervix for lesions

Treatment Goals
› Promote Optimum Cervical Status and Reduce Risk of Complications
  • Monitor vital signs, assess for pain, assess all physiologic systems, review laboratory/other diagnostic study results, and review results of CIN classification
  • Assess anxiety level and coping ability regarding having CIN, the potential for cervical cancer and impaired reproductive ability, and changes in body image or perception of body function. Provide emotional support and educate about CIN, potential complications, risk factors, treatment risks and benefits, and individualized prognosis
  • Encourage active participation in making decisions about the treatment plan, including educating the patient to take the time to discuss treatment option risks and benefits with spouse/family, feel comfortable asking additional questions, and discuss personal choice for treatment with the treating clinician
  • Request referral, if appropriate, to a mental health clinician for supportive counseling on strategies for coping and to a social worker for identification of support groups and Internet sources of educational information
• Follow facility pre- and posttreatment protocols if patient becomes a candidate for surgery or other treatment for CIN; reinforce pre- and posttreatment education and verify completion of facility informed consent documents
  – Monitor after treatment for common adverse effects, including uterine cramping, vaginal discharge, bleeding, infection, cervical stenosis, and cervical incompetence; report abnormalities and treat, as ordered
  – Emphasize the importance of continued medical surveillance and seeking immediate medical attention for new or worsening signs and symptoms

**Food for Thought**

› Cryotherapy is considered a safe and inexpensive treatment for CIN
  • For women with CIN2 or 3, the World Health Organization (WHO) recommends cryotherapy, LEEP, or CKC over no treatment; cryotherapy over CKC when both are appropriate; and LEEP over CKC when both are appropriate
  › Risk for preterm birth is increased in pregnant women with untreated CIN or a history of excisional therapy for CIN
  • Topical chemotherapy may be an alternative to excisional therapy in women with CIN. Researchers in a study of 60 women with CIN who were 18–29 years of age found that patients who were treated with topical 5-fluorouracil were 62% more likely to have disease regression compared with women who were observed but did not undergo treatment (Rahangdale et al., 2014)
  › Laser treatment for CIN results in faster tissue healing compared with other methods of treatment

**Red Flags**

› Potential complications of cone biopsy in pregnant women include hemorrhage, infection, an incompetent cervix, and spontaneous abortion. For this reason, existing clinical guidelines recommend delay of cone biopsy in pregnant women until after the postpartum period

**What Do I Need to Tell the Patient?**

› Educate about the importance of carefully reviewing all treatment options with the treating clinician and assessing all factors associated with each treatment before making a decision, including the effect of each treatment on future fertility
  › Emphasize the importance of keeping scheduled appointments for follow-up Pap smears, treatment, and continued medical surveillance
  › Encourage asking the treating clinician about referral to a fertility clinician if the patient is concerned about reproductive options

**References**