Management of Histologic Abnormalities of the Cervix

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The American Society for Colposcopy and Cervical Pathology sponsored a consensus conference in 2001 to develop evidence-based guidelines for women with histologic abnormalities of the cervix. The options for management of cervical intraepithelial neoplasia 1, 2, and 3 are ranked according to the strength of the recommendation and the quality of the evidence. Follow-up with repeat cytology at six and 12 months or DNA testing for high-risk types of human papillomavirus at 12 months is the preferred management approach for women with cervical intraepithelial neoplasia 1 and satisfactory initial colposcopy. If results from repeat cytology are reported as atypical squamous cells of undetermined significance or greater, or if DNA human papillomavirus testing is positive for oncogenic types of the virus, repeat colposcopy is preferred. When the initial colposcopy is unsatisfactory, a diagnostic excisional procedure is preferred. Follow-up without treatment is acceptable only in women who are pregnant and adolescents with cervical intraepithelial neoplasia 1 who had unsatisfactory colposcopy. Biopsy-confirmed cervical intraepithelial neoplasia 2 and 3 requires treatment except during pregnancy and in compliant adolescents with cervical intraepithelial neoplasia 2 and negative endocervical curettage. When colposcopy is satisfactory, treatment includes ablative or excisional procedures. A diagnostic excisional procedure is recommended in women with biopsy-confirmed cervical intraepithelial neoplasia 2 or 3 and unsatisfactory colposcopy. (Am Fam Physician 2006;73:105-12.

At approximately the same time that results from the National Cancer Institute's atypical squamous cells of undetermined significance (ASC-US) low-grade squamous intraepithelial lesion triage study (ALTS)[1] were published, the American Society for Colposcopy and Cervical Pathology (ASCCP)[2-4] sponsored a consensus conference to develop comprehensive, evidence-based guidelines for women with cytologic and histologic abnormalities of the cervix. The ASCCP developed new options for management of cervical intraepithelial neoplasia (CIN) and ranked them according to the strength of the recommendation and quality of the evidence *(Table 1[2])*.[3] The terminology used in the guidelines is detailed in *Table 2*.[2]

CIN 1: Overview

There is a high level of intraobserver and interobserver variability in the histologic diagnosis of CIN 1.[5,6] In ALTS, an expert pathology review committee downgraded 41 percent of CIN 1 diagnoses to normal and upgraded 13 percent of CIN 1 diagnoses to CIN 2-3.[5] Studies[7,8] of women with histologic CIN 1 have found that 23 to 55 percent of patients undergoing loop electrosurgical excision procedures (LEEP) actually have CIN 2-3.

A literature review,[9] meta-analysis,[10] and two-year follow-up data from ALTS[11] found that 10 to 15 percent of CIN 1 lesions progress to CIN 2-3, and that 0.3 percent progress to cancer. It was impossible to ascertain whether CIN 2-3 was present at the beginning of the observation period and discovered later, or whether CIN 1 lesions had progressed. It is difficult to develop management protocols that treat only those women with CIN 1 who have or will develop CIN 2-3 because it is not known which CIN 1 lesions will regress or progress. The consensus guidelines attempt to strike a balance between overtreatment of a nonprogressive human papillomavirus

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
The preferred treatment for women with CIN 1 and satisfactory colposcopy is repeat cytology at six and 12 months or DNA testing for HPV types at 12 months.	C	3, 4, 18
Endocervical sampling is recommended before any ablative treatment.	C	3, 4
Observation without treatment is acceptable in pregnant women and adolescents with CIN 1 and unsatisfactory colposcopy.	C	3, 4
Observation is unacceptable in women with CIN 2 except during pregnancy and in compliant adolescents with satisfactory colposcopy and negative results on endocervical curettage.	C	3, 4
After treatment for CIN 2-3, acceptable management methods include cytology with or without colposcopy at four- to six-month intervals until three negative evaluations have been obtained, or HPV DNA testing no sooner than six months after treatment.	C	3, 4
The preferred management for CIN identified at the margin of a diagnostic excisional procedure or in postprocedure endocervical sampling is colposcopy and endocervical sampling at the four- to six-month follow-up evaluation.	C	3, 4

CIN = cervical intraepithelial neoplasia; HPV = human papillomavirus.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 17 or http://www.aafp.org/afpsort.xml.

TABLE 1
Rating System for Consensus Guideline Recommendations

Rating	*Criteria*
Strength of recommendation	
A	Good evidence for efficacy and substantial clinical benefit support recommendation for use
B	Moderate evidence for efficacy or only limited clinical benefit supports recommendation for use
C	Evidence for efficacy is insufficient to support a recommendation for or against use, but recommendation may be made on other grounds
D	Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use
E	Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use
Quality of evidence	
I	Evidence from at least one randomized controlled trial
II	Evidence from at least one clinical trial without randomization, cohort or case-controlled analytic studies (preferably from more than one center), multiple time-series studies, or dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees
Terminology	
Acceptable	One of multiple options when data indicate another approach is superior or when no data favor any single option
Preferred	Best option (or one of the best) when multiple options are available
Recommended	Good data to support use when only one option is available
Unacceptable	Good data against use

Adapted with permission from Wright TC Jr, Cox JT, Massad LS, Twiggs LB, Wilkinson EJ; ASCCP-Sponsored Consensus Conference. 2001 Consensus guidelines for the management of women with cervical cytological abnormalities. JAMA 2002;287:2121.

(HPV) infection (i.e., CIN 1) and failure to identify and treat lesions with true malignancy potential (i.e., CIN 2-3).

The degree of certainty that the most advanced lesion has been recognized and sampled is an important consideration. When the transformation zone is visualized completely (i.e., satisfactory colposcopy) and endocervical curettage is negative, physicians can be reasonably certain that the histology represents the most serious lesion. However, if the colposcopy is unsatisfactory or the endocervical curettage is positive, unrecognized CIN 2-3 or cancer may be present, and further diagnostic testing is indicated.

Most experts advocate observation without treatment when colposcopy is satisfactory[12] because most cases of CIN 1 spontaneously regress and because most cases of invasive cancer occur in women who are lost to follow-up.[13] The risk of a woman with histologic CIN 1 subsequently developing CIN 2-3 is 9 to 16 percent,[11,13,14] similar to the risk of finding CIN 2-3 in women with ASC-US.[1,11,15,16] This statistic suggests that women with CIN 1 can be followed safely with protocols similar to those for women with ASC-US.[2,3]

In ALTS, repeat cytology at six and 12 months cumulatively detected 85 percent of CIN 3 lesions in women with ASC-US, whereas HPV DNA testing detected 95 percent of CIN 3 lesions over

Figure 6[4]).[3,4] Excisional modalities are preferred in women with recurrent CIN 2-3 (AII recommendation).[3,4] A diagnostic excisional procedure is recommended in women with biopsy-confirmed CIN 2-3 and unsatisfactory colposcopy (AII recommendation).[3,4] Observation of CIN 2-3 without treatment is unacceptable except in special circumstances (EII recommendation).[3,4] Hysterectomy is unacceptable as a primary therapy for women with CIN 2-3 (EII recommendation).[3,4]

Follow-Up After Treatment for Biopsy-Confirmed CIN 2-3

Acceptable follow-up protocols after treatment of CIN 2-3 include cytology or a combination of cytology and colposcopy at four- to six-month intervals until three negative evaluations have been performed (AII recommendation, *Figure 6*[4]).[3,4] Annual cytologic follow-up is recommended thereafter (AII recommendation).[3,4] A cytologic result of ASC is the recommended threshold for referral to colposcopy during follow-up (AII recommendation).[3,4] Surveillance with HPV DNA testing performed no sooner than six months after treatment also is acceptable (BII recommendation).[3,4] A positive test for high-risk HPV types is the recommended threshold for referral to colposcopy (BIII recommendation).[3,4] If HPV testing is negative, annual cytologic screening is recommended (BIII recommendation).[3,4] Repeat conization or hysterectomy based on a single positive HPV test that is not corroborated by other findings (e.g., cytology, colposcopy, histology) is unacceptable (DIII recommendation).[3,4]

If CIN is identified at the margin of a diagnostic excisional procedure or on a postprocedure endocervical curettage, it is preferred that endocervical sampling be added to one of the previous follow-up protocols (BII recommendation).[3,4] When CIN 2-3 is identified at the endocervical margin or in the endocervical sampling obtained after the diagnostic excisional procedure, a repeat diagnostic excisional procedure is acceptable (AII recommendation).[3,4] Hysterectomy is acceptable when repeat diagnostic excision is not feasible (BII recommendation)[3,4] or for women with recurrent or persistent CIN 2-3 (BII recommendation).[3,4]

Follow-Up After Treatment for Biopsy-Confirmed CIN 2-3: Special Circumstances

In compliant adolescents with histologic CIN 2, satisfactory colposcopy, and negative endocervical curettage, observation with colposcopy and cytology at four- to six-month intervals for one year is acceptable (BII recommendation).[3] Ablation or excision is required for adolescents with CIN 3 (BIII recommendation).[3,4]

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