Complete Summary

GUIDELINE TITLE

Management of initial abnormal Pap smear.

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Management of initial abnormal Pap smear. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Oct. 28 p. [56 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Institute for Clinical Systems Improvement (ICSI). Management of initial abnormal Pap smear. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2004 Jul. 45 p.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Abnormal Pap smear

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Nursing
Obstetrics and Gynecology
Oncology
Pathology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Health Plans
Hospitals
Managed Care Organizations
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To provide recommendations for appropriate clinical follow-up for women who undergo cervical cytologic analysis and receive an abnormal Pap result
- To provide recommendations regarding colposcopic directed biopsy for women who are diagnosed with a high grade abnormal Pap smear
- To reduce the psychological distress and increase the knowledge of women who are notified of an abnormality on their Pap smear

TARGET POPULATION

Any woman who has undergone cervical cytologic analysis (Pap smear) and has received an abnormal result

INTERVENTIONS AND PRACTICES CONSIDERED

1. Patient education regarding Pap smears and abnormal results
2. Routine Pap smear screening
3. Management based on classification of abnormal Pap smears. Options include repeat Pap smear, treatment of infections, intravaginal estrogen creams, human papillomavirus (HPV) DNA testing, colposcopy, endocervical curettage (ECC), endometrial biopsy, loop electrocautery excision procedure (LEEP), dilation and curettage (D & C), and cone biopsy
4. Consultation with gynecology or gynecologic oncology, when necessary

MAJOR OUTCOMES CONSIDERED

- Incidence of abnormal Pap smear findings
- Risk of cervical and endometrial cancer in women with abnormal Pap smears

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system presented below, and are designated as positive, negative, or neutral to reflect the study quality.

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results

from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Study Quality Designations:

The quality of the primary research reports and systematic reviews are designated in the following ways on the conclusion grading worksheets:

Positive: indicates that the report or review has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.

Negative: indicates that these issues (inclusion/exclusion, bias, generalizability, and data collection and analysis) have not been adequately addressed.

Neutral: indicates that the report or review is neither exceptionally strong nor exceptionally weak.

Not Applicable: indicates that the report is not a primary reference or a systematic review and therefore the quality has not been assessed.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

   Class A:

   - Randomized, controlled trial

   Class B:

   - Cohort study

   Class C:

   - Non-randomized trial with concurrent or historical controls
   - Case-control study
   - Study of sensitivity and specificity of a diagnostic test
   - Population-based descriptive study

   Class D:

   - Cross-sectional study
   - Case series
   - Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

   Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Clinical Validation-Pilot Testing
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Institute Partners: System-Wide Review

The guideline draft, discussion, and measurement specification documents undergo thorough review. Written comments are solicited from clinical, measurement, and management experts from within the member medical groups during an eight-week period of "Critical Review."

Each of the Institute's participating medical groups determines its own process for distributing the guideline and obtaining feedback. Clinicians are asked to suggest modifications based on their understanding of the clinical literature coupled with their clinical expertise. Representatives from all departments involved in implementation and measurement review the guideline to determine its operational impact. Measurement specifications for selected measures are developed by Institute for Clinical Systems Improvement (ICSI) in collaboration with participating medical groups following general implementation of the guideline. The specifications suggest approaches to operationalizing the measure.

Guideline Work Group: Second Draft

Following the completion of the "Critical Review" period, the guideline work group meets 1 to 2 times to review the input received. The original guideline is revised as necessary and a written response is prepared to address each of the suggestions received from medical groups. Two members of the Ob/Gyn Steering Committee carefully review the Critical Review input, the work group responses, and the revised draft of the guideline. They report to the entire committee their assessment of two questions: (1) Have the concerns of the medical groups been adequately addressed? (2) Are the medical groups willing and able to implement the guideline? The committee then either approves the guideline for pilot testing as submitted or negotiates changes with the work group representative present at the meeting.

Pilot Test

Medical groups introduce the guideline at pilot sites, providing training to the clinical staff and incorporating it into the organization's scheduling, computer, and other practice systems. Evaluation and assessment occur throughout the pilot test phase, which usually lasts for three months. Comments and suggestions are solicited in the same manner as used during the "Critical Review" phase.

The guideline work group meets to review the pilot sites' experiences and makes the necessary revisions to the guideline, and the Ob/Gyn Steering Committee reviews the revised guideline and approves it for implementation.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC) and the Institute for Clinical Systems Improvement (ICSI): In addition to updating their clinical guidance, ICSI has developed a new format for all guidelines. Key additions and changes include: combination of the annotation and discussion section; the addition of "Key Points" at the beginning of most annotations; the inclusion of references supporting the recommendations; and a complete list of references in the Supporting Evidence section of the guideline. For a description of what has changed since the previous version of this guidance, refer to "Summary of Changes -- October 2005."

The recommendations for the management of abnormal Pap smear are presented in the form of five algorithms with a total of 28, accompanied by detailed annotations. Algorithms are provided for: Initial Pap Smear Result; Benign Endometrial Cells (BEC); Atypical Squamous Cells of Undetermined Significance (ASC-US); Atypical Glandular Cells of Uncertain Significance/Atypical Glandular Cells (AGUS/AGC); and Low-Grade Squamous Intraepithelial Lesion (LSIL). Clinical highlights and selected annotations (numbered to correspond with the appropriate algorithm) follow.

Class of evidence (A-D, M, R, X) ratings are defined at the end of the "Major Recommendations" field.

Clinical Highlights

1. Atypical squamous cells of undetermined significance (ASC-US) as an initial Pap result necessitates human papilloma virus (HPV) testing or immediate colposcopy. If results of HPV testing are unknown, a repeat Pap smear in 6 months is recommended. (ASC-US Algorithm; Annotations # 5, 6)
2. Atypical glandular cells of uncertain significance/atypical glandular cells (AGUS/AGC) as an initial Pap result requires a colposcopy and endocervical curettage (ECC) and possible endometrial biopsy. AGUS/AGC Pap results can, in some cases, be indicative of extracervical malignancy. Therefore, aggressive follow-up is highly recommended. If all initial evaluations have normal results, follow-up needs to include Pap smears every 6 months repeat 4 times. (AGUS/AGC Algorithm; Annotations #12, 17, 19, 21)
3. Low-grade squamous intraepithelial lesion (LSIL) as an initial Pap result generally warrants a colposcopy. Special considerations may be made for adolescent and postmenopausal women. (LSIL Algorithm Annotations #22, 23, 24, 26, 28)
4. High-grade squamous intraepithelial lesion (HSIL) as an initial Pap result requires colposcopy with biopsy and/or loop electrocautery excision procedure (LEEP). (Annotations #29)

Introduction

Abnormal Pap

The guideline group recognized the difficulties faced by clinicians who must respond to abnormal Pap smears as reported by the Bethesda system. The group also recognized that there is a significant degree of variability in the approach to various diagnoses within the Bethesda system. Finally, the group realized that many patients are confused and perhaps unnecessarily alarmed when they receive a report of an abnormal Pap smear. It was the intention of the work group to provide a framework, based on objective evidence, that would provide guidance to the clinician and/or the patient facing an abnormal Pap smear result. Group efforts were hindered by the paucity of controlled randomized trials investigating various approaches to the follow-up of various cytologic diagnoses. The guidelines presented herein are recognized to be an interim effort based on critical review of existing data and on work group review consensus. Firm recommendations are anticipated to be available in the not-too-distant future as clinical studies currently underway provide more accurate objective evidence. (See the original guideline document for the 2001 Bethesda System [Abridged] classification.)

Health Education

Receiving the diagnosis of an abnormal Pap smear is a traumatic occurrence for many women. The work group was made aware of this fact repeatedly and felt that education attempts need to be improved if patient anxiety is to be successfully reduced. It was felt that written general information provided at the time of the initial Pap smear could serve to educate patients about the role of Pap smears, as well as provide basic information about some of the potential results, and emphasize the fact that most such findings may require nothing further than repeating the Pap smear or undergoing relatively simple evaluations such as colposcopy. It was felt to be imperative that physicians or health care personnel who provide the initial diagnosis of an abnormal result to a patient have sufficient training to allay most fears and answer basic questions. Finally, it was felt that mailing written material specific to the diagnosis and recommended procedures and follow-up would help prepare the patient for the next phase of evaluation. With a commitment to such education and continued sensitivity to the anxiety produced by the finding of an abnormal Pap smear result, physicians and other health care workers can provide effective and compassionate evaluation and treatment as needed.

Evidence supporting this recommendation is of classes: A, C

Benign Endometrial Cells Algorithm Annotations

1. Benign Endometrial Cells Present (BEC)

   Key Points:

   - Benign endometrial cells (BEC) occur in 12% of Pap smears from premenopausal women and less then 1% in postmenopausal women.
   - Laboratories report BEC since they do not have access to menopausal status. Clinicians can determine the significance of the findings for their patient.

   The finding of BEC occurs in 12% of Pap smears from premenopausal women and 0.6 to 0.01% of postmenopausal women. The incidence varies with the phases of the menstrual cycle and the type of contraception used, as well as with the use or non-use of hormone replacement therapy. Bethesda 2001 guidelines recommend that pathologists report the presence of BEC in smears from women over the age of 40. This new reporting recommendation does not imply that it is abnormal to see endometrial cells in all women over 40, but, rather, reflects the fact that cytology laboratories do not reliably have access to accurate information about menopausal status. The clinician is therefore given the information so that he or she can determine the significance of the finding for the patient. No specific guidelines are offered for the management of BEC in postmenopausal women. The reported risk of endometrial cancer in postmenopausal women who underwent histologic evaluation within 24 months of such a Pap smear ranges from 0.8 to 21%. These figures are probably biased because the group of women undergoing endometrial biopsy or dilation and curettage (D&C) have a higher probability of cancer than women who did not have further evaluation. On this basis, the guideline group recommends that clinicians should review the menopausal status of

women with a report of benign endometrial cells in a woman over 40. If the woman is menopausal the guideline group recommends that she be specifically questioned about the presence of endometrial cancer symptoms, especially unexpected bleeding or spotting. If symptoms are present, endometrial tissue should be evaluated using endometrial biopsy or D&C. In the absence of symptoms a clinician might reasonably elect to continue with routine gynecologic care.

Evidence supporting this recommendation is of classes: B, C, D

Atypical Squamous Cells of Undetermined Significance (ASC-US) Algorithm Annotations

5. Atypical Squamous Cells of Undetermined Significance Present (ASC-US)

   Key Points:

   - Atypical Squamous Cells of Undetermined Significance (ASC-US) is used by pathologists to denote cellular changes that are more marked than those attributable to reactive changes, but that are quantitatively or qualitatively short of a definitive diagnosis of Squamous Intraepithelial Lesion (SIL).
   - Exceptions may apply to special circumstances.

   The new Bethesda System has identified criteria for ASC-US on Pap screening. Atypical Squamous Cells of Undetermined Significance (ASC-US) is used by pathologists to denote cellular changes that are more marked than those attributable to reactive changes, but that are quantitatively or qualitatively short of a definitive diagnosis of Squamous Intraepithelial Lesion (SIL).

   Options for evaluation include triage to colposcopy by HPV DNA testing, immediate colposcopy, or repeat cytology tests at 6 and 12 months.

   Special circumstances exist when infection or atrophy are present. It is reasonable to treat the infection and repeat cytology in 4 to 6 months. Vaginal estrogen therapy, applied 1 to 2 times per week can effectively reverse atrophic changes. This should be continued for 6 months and cytology performed within one week of completing estrogen therapy.

   Refer to the original guideline document for more information.

   Evidence supporting this recommendation is of classes: B, C, D, M, R, X

6. High-Risk HPV Isolated?

   Key Points:

- It is now scientifically well established that Human Papilloma Virus (and more specifically, certain DNA subtypes like #16) has an important role in the progress of cervical dysplasia and development of squamous cervical cancer in almost all cases.
- The American Society for Colposcopy and Cervical Pathology (ASCCP) is now advocating follow-up HPV DNA testing for ASC-US Pap smears. It is the consensus of the work group that this is an excellent option.

At this point, testing for HPV is not yet considered "standard of care," but some are advocating its use to help triage patients with ASC-US. It can be cost-effective when done in a setting that includes liquid-based Pap smear collection methods, since the residual fluid can be saved for HPV analysis rather than calling the patient back for sampling. Since HPV testing is another viable option for evaluation of the ASC-US Pap smear, colposcopy could be deferred and performed only for those women who have tested positive for intermediate or high-risk HPV types. Women with evidence of oncogenic HPV DNA should have whatever follow-up they would normally have depending upon their colposcopic diagnosis.

Clinicians ordering HPV tests should be aware of the strengths and limitations of the assay. The report that clinicians will receive from the high risk assay will say that the patient tested positive or negative for "one or more of the following high-risk types" followed by a list of the HPV types. The careful wording is intended to convey to clinicians that the assay does not test for all HPV types known to associate with cervical cancer. A positive test for high-risk HPV types should indicate a need to educate the patient about HPV infection. A colposcopic examination should be scheduled. A negative HPV test result tells the clinician that the patient does not have a detectable burden of the high-risk virus types included in the test. The patient may, however, have a high-risk type at a lower titer than that which is reliably tested for or the patient may have an infection with a high-risk HPV type that is not part of the HPV assay. Clinical judgment and knowledge of the patient's health history and lifestyle should determine which women can return to routine screening on the basis of a negative HPV assay and which women might be considered for enhanced surveillance on the basis of the test result.

7. Repeat Pap Smear in 12 Months

Women who test negative for high-risk HPV can be reassured that their risk of having cervical intraepithelial neoplasia (CIN) 2/3+ is less than 2%. They can be scheduled for repeat cytology in 12 months.

8. Colposcopy

Women who test positive for high-risk HPV have a 15 to 27% chance of having CIN 2/3 or worse. They should be scheduled for colposcopy. The exception to this recommendation is the adolescent, for whom the risk of invasive cancer approaches zero and the likelihood of HPV clearance is very high. Adolescents with ASC-US who are HPV positive may be monitored with cytology at 6 and 12 months or with a single HPV test at 12 months. Colposcopy should be performed for any abnormal cytology or positive HPV result.

9. Repeat Pap at 6 and 12 Months or Colposcopy

Key Points:

- Two consecutive negative Pap smears at 6 and 12 months approach the sensitivity of a single HPV test for the detection of CIN 2/3 or greater.
- Immediate colposcopy may be an option for some women who have an initial Pap smear result of ASC-US.

One option for the low-risk reliable patient with an ASC-US result would be to have a follow-up Pap test at 6 and 12 months. Two consecutive negative follow-up Paps will approach the sensitivity of a single HPV test for the detection of CIN 2/3+. Routine testing can be resumed after normal results at 6 and 12 months. If either is ASC-US or higher, colposcopy is recommended.

10. Atypical Squamous Cells: Cannot Exclude High-Grade Squamous Intraepithelial Lesion (ASC-H)

The 2001 Bethesda reporting system recognizes a new category of atypical squamous cells -- cannot rule out high grade dysplasia (ASC-H). In the 1988 system, emphasis was placed on identifying all squamous intraepithelial lesion (SIL) Paps, including LSIL and HSIL. Currently, the emphasis of the 2001 Bethesda system is to identify HSIL and cytology associated with histologically proven high-grade disease.

ASC-H is thought to include 5 to 10% of all atypical squamous cell (ASC) cases and includes mixtures of true HSIL and mimics. The positive predictive value of ASC-H in detecting CIN 2 and CIN 3 lies somewhere between 48 and 56%.

Colposcopic examination is the established appropriate evaluation of women with ASC-H Pap smear reports. ECC should be performed if no lesion can be visualized. Initial evaluation of the ASC-H Pap smear should not routinely include the use of LEEP.

Controversy does exist in the area of management of ASC-US Pap smears. Some favor immediate colposcopy for all ASC-US smears. Some practitioners have in the past favored colposcopy only for women with high-risk factors: teenage sexual activity, multiple sexual partners, intercourse with a male who has HPV, history of sexually transmitted disease or genital warts, tobacco use or history of tobacco use, intrauterine exposure to diethylstilbestrol (DES), poor compliance for follow-up, lack of normal immune response, no history of regular Pap smears, and age less than 30.

Advocates for immediate colposcopy for all ASC-US Pap smear results include:

- Reduces risk of missing a significant lesion
- Reduces risk of being lost to follow-up

- More quickly reassures patient of normalcy; or avoids multiple follow-up Pap smears, resulting poor compliance, potentially overburdened clinics
- Avoids delay in diagnosis of cancer or high-grade CIN

Ongoing clinical prospective trials are expected to have more definite answers for ASC-US follow-up in about five years.

Atypical Glandular Cells of Uncertain Significance/Atypical Glandular Cells (AGUS/AGC) Algorithm Annotations

11. Atypical Glandular Cells of Uncertain Significance Present (AGUS/AGC)

    Key Points:

    - A report of atypical glandular cells on a Pap smear could be a result of inflammation, hyperplasia, dysplasia, endometrial or cervical adenocarcinoma and rarely signals the presence of distant cancer (e.g., pancreatic).

    Atypical glandular cells (which can be either uterine or cervical in origin) have enlarged nuclei, decreased cytoplasmic volume, and a variety of other unusual characteristics. In the new Bethesda system, "favor reactive change" has been dropped. AGUS/AGC becomes AGC (atypical glandular cells) with one of the following subheadings: NOS (not otherwise specified), FN (favor neoplasia) and favor either endocervical or endometrial origin.

    A report of atypical glandular cells on a Pap smear could be a result of inflammation, hyperplasia, dysplasia, endometrial or cervical adenocarcinoma and rarely signals the presence of distant cancer (e.g., pancreatic).

    Evidence supporting this recommendation is of classes: C, D

12. Perform Colposcopy and Endocervical Curettage/Perform Endometrial Biopsy if: $\geq$35 Years of Age or if Abnormal Bleeding

    Key Points:

    - Women over the age of 35 or women who have abnormal bleeding should have an endometrial biopsy performed if AGUS/AGC is present.

    An AGUS/AGC Pap smear may be indicative of a precancerous change or a frank malignancy. Approximately one half of the patients will have a normal exam including colposcopy and ECC; however, 21 to 57% will have a clinically significant lesion. Results of two recent studies showed that 57% of patients had histological diagnoses, 37% had a significant lesion, and that the closer a practitioner looked for an abnormality, the more likely one would be found. Further, those patients having a previous diagnosis of CIN had an almost three-fold increase in findings of significant lesions in the current study. These numbers warrant a vigorous approach to evaluating these Pap smears. Some

laboratories qualify AGUS/AGC abnormalities as favor reactive or favor neoplasm. Perform an endometrial biopsy to rule out endometrial cancer or hyperplasia in patients with abnormal bleeding or if 35 years of age and older. (A recent study showed correlation with significant lesions [60%] in postmenopausal women with only a 6% chance of significant lesions in premenopausal women.) Referral is appropriate for the portions of the evaluation the primary practitioner cannot complete.

Evidence supporting this recommendation is of classes: C, D

14. Treat Findings Appropriately

An abnormal Pap smear is not the only concern with an AGUS/AGC result. The same considerations for underlying abnormalities noted in the AGUS/AGC Algorithm Annotation #19 "Repeat Evaluation Every 6 Months x4" also pertain here.

17. Diagnostic Excisional Procedure

Because of the increased chance of HSIL or a glandular endocervical neoplasia, the practitioner should perform a procedure to obtain a specimen from the transformation zone and endocervical canal. Although cold-knife cone has historically been performed, laser conization, LEEP, and loop electrosurgical conization are acceptable sampling procedures.

19. Repeat Evaluation Every 6 Months x4

Key Points:

- Repeat Paps are designed to pick up any undetected disease process before two years lapse.
- If the Pap smear does not revert to normal on the follow-up Paps, further aggressive evaluation is indicated.

The minimum follow-up for "normal" evaluations should be a Pap smear every 6 months until four consecutive normal results are recorded. When unable to demonstrate a colposcopic/biopsy abnormality after ACG Pap result, it may be helpful to consult with the pathologist to better define the nature of the lesion. Repeat Paps are designed to pick up any undetected disease process before two years lapse. It is clear from continuing studies that these patients are at significant risk, especially when they have other predisposing findings such as a history of CIN, for having abnormality ranging from CIN to adenosquamous carcinoma to extracervical adenocarcinoma (including uterine, cervical, fallopian, ovarian, and even nongynecologic malignancies). AGUS/AGC or AGC findings in premenopausal women are ultimately much more likely to result in the diagnosis of SIL or adenocarcinoma than the same Pap smear result in a postmenopausal patient. If the Pap smear does not revert to normal on the follow-up Paps, further aggressive evaluation is indicated. The extensiveness of this evaluation is the subject of debate, and is left to the discretion of the provider.

21. Dilation and Curettage (D & C) or Endometrial Biopsy if Not Already Performed

Endometrial sampling should be done to obtain a specimen for histologic evaluation. This should be correlated with the abnormal endometrial cells on the cytology specimen so as to explain the original abnormality. Sampling can be done as an office endometrial biopsy or fractional D&C; either of which can be preceded by hysteroscopy to enhance the evaluation. Referral to GYN or GYN Oncology can be made for initial sampling. Referral to GYN or GYN Oncology should be made if the sampling does not explain the original abnormality or if the sampling identifies an endometrial abnormality. Follow-up will be dependent on the findings of this evaluation.

Low-Grade Squamous Intraepithelial Lesion (LSIL) Algorithm Annotations

22. Low-Grade Squamous Intraepithelial Lesion Present (LSIL)

The Bethesda system combines mild dysplasia/CIN I with HPV into a single category of LSIL. Previously, it had been noted that approximately 60% of specimens with a diagnosis of LSIL represent processes that will regress spontaneously without treatment. However, more recent follow-up cytology studies have demonstrated both a high rate of loss to follow-up and a 53 to 76% likelihood of abnormal cytology and a small risk of delaying diagnosis of invasive cancer. Current recommended clinical practice is to perform a colposcopy unless special circumstances exist. An alternative is to repeat the Pap smear.

Evidence supporting this recommendation is of class: R

24. Perform HPV Testing and/or Repeat Pap Smear at 6 and 12 Months

Most LSIL in adolescents is felt to be secondary to self-limited HPV infection. One research study suggests that HPV infection and subsequently mild cervical dysplasia will often resolve spontaneously. A repeat Pap smear at 6 and 12 months is recommended. Persistence of abnormality on Pap smear, however, warrants further colposcopic evaluation.

Evidence supporting this recommendation is of classes: B, C, R

26. Colposcopy

The most common management option is to perform a colposcopy. One must be cautious about over-aggressive biopsy and treatment. Specifically, routine LEEP of the transformation zone as a method for evaluating a LSIL Pap smear is not recommended.

Evidence supporting this recommendation is of classes: C, R

28. Consider Vaginal Estrogen/Repeat Pap Smear in 6 Months

Some women, such as those with estrogen receptor + breast cancer, may not be able to safely use intravaginal estrogen. The clinician and patient must review the risks and benefits of intravaginal estrogen use.

Effective vaginal estrogen therapy should include a six-month treatment period and repeat Pap smear should be done within one week of cessation of therapy.

Postmenopausal women or women with cervical atrophy who have had previous regular and normal cytology have a higher likelihood of spontaneous regression than the general population.

Evidence supporting this recommendation is of class: R

29. High-Grade Squamous Intraepithelial Lesion Present (HSIL)

The Bethesda system combines moderate dysplasia with severe dysplasia and carcinoma-in-situ (CIS) into a single category of high-grade intraepithelial lesion (HSIL). Up to 95% of patients with high-grade Pap smears have been found to have high-grade lesions.

Of all the categories in current nomenclature for Pap smear results, perhaps the least ambiguity and the least controversy in management is with HSIL. Histologic evaluation of directed cervical biopsies from women with HSIL will commonly show moderate or severe dysplasia or even carcinoma in situ. Thus the standard of practice for management is clearly to perform colposcopy and directed biopsy.

Further management of the patient will then be guided by the biopsy results.

Colposcopy with Biopsy and/or LEEP

Colposcopic examination with directed biopsies or LEEP is the appropriate management for women with HSIL Pap smears. When a LEEP is performed immediately it is not necessary to automatically do an ECC. But if endocervical disease is suspected as a result of the colposcopy and LEEP is not done, an ECC should still be performed.

Evidence supporting this recommendation is of classes: C, M, R

Definitions:

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Non-randomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

CLINICAL ALGORITHM(S)

Detailed and annotated clinical algorithms are provided for:

- Initial Pap Smear Result
- Benign Endometrial Cells (BEC)
- Atypical Squamous Cells of Undetermined Significance (ASC-US)
- Atypical Glandular Cells of Uncertain Significance/Atypical Glandular Cells (AGUS/AGC)
- Low-Grade Squamous Intraepithelial Lesion (LSIL)

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved clinical follow-up of women who receive an abnormal Pap smear

POTENTIAL HARMS

Not stated

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindication to Intravaginal Estrogen

Some women, such as those with estrogen receptor + breast cancer, may not be able to safely use intravaginal estrogen. The clinician and patient must review the risks and benefits of intravaginal estrogen use.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
- This medical guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for general implementation, a medical group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they may form an action group.

In the action group, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action

group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

Detailed measurement strategies are presented in the original guideline document to help close the gap between clinical practice and the guideline recommendations. Summaries of the measures are provided in the National Quality Measures Clearinghouse (NQMC).

IMPLEMENTATION TOOLS

Clinical Algorithm
Pocket Guide/Reference Cards
Quality Measures

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

RELATED NQMC MEASURES

- Management of initial abnormal Pap smear: percentage of women diagnosed with an initial abnormal Pap smear of atypical squamous cells of undetermined significance (ASC-US) with high-risk human papillomavirus (HPV) type who have follow-up colposcopy within six months of abnormality identified.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Management of initial abnormal Pap smear. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Oct. 28 p. [56 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 May (revised 2005 Oct)

GUIDELINE DEVELOPER(S)

Institute for Clinical Systems Improvement - Private Nonprofit Organization

GUIDELINE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health System, Aspen Medical Group, Avera Health, CentraCare, Columbia Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT Specialty Care, Fairview Health Services, Family HealthServices Minnesota, Family Practice Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and Clinics, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic, Mayo Clinic, Mercy Hospital and Health Care Center, MeritCare, Mille Lacs Health System, Minnesota Gastroenterology, Montevideo Clinic, North Clinic, North Memorial Care System, North Suburban Family Physicians, Northwest Family Physicians, Olmsted Medical Center, Park Nicollet Health Services, Pilot City Health Center, Quello Clinic, Ridgeview Medical Center, River Falls Medical Clinic, Saint Mary's/Duluth Clinic Health System, St. Paul Heart Clinic, Sioux Valley Hospitals and Health System, Southside Community Health Services, Stillwater Medical Group, SuperiorHealth Medical Group, University of Minnesota Physicians, Winona Clinic, Ltd., Winona Health

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GUIDELINE COMMITTEE

Ob/Gyn Steering Committee

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Work Group Members: Lynne Lillie, MD (HealthEast Clinics) (Work Group Leader) (Family Medicine); Lynn Stottler, MD (Gateway Family Health Clinic) (Family Medicine); Lachlan Smith, MD, (Affiliated Community Medical Center) (Ob/Gyn); R. Paul Weatherby, MD (Park Nicollet Health Services) (Pathology); Corrine Esch, RN (HealthPartners Medical Group) (Nursing); Jane Suska, CNP (CentraCare) (Nursing); Sylvia Robinson, BSN, MBA (ICSI) (Measurement and Implementation Advisor); Brent Metfessel, MD, MPH (ICSI) (Evidence Analyst); Linda Setterlund, MA (ICSI) (Facilitator)

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In the interest of full disclosure, Institute for Clinical Systems Improvement (ICSI) has adopted the policy of revealing relationships work group members have with companies that sell products or services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline, but they are noted here to fully inform readers. Readers of the guideline may assume that only work group members listed below have potential conflicts of interest to disclose.

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GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Institute for Clinical Systems Improvement (ICSI). Management of initial abnormal Pap smear. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2004 Jul. 45 p.

GUIDELINE AVAILABILITY

Electronic copies of the revised guideline: Available from the Institute for Clinical Systems Improvement (ICSI) Web site.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Management of initial abnormal Pap smear. Executive summary. Bloomington (MN): Institute for Clinical Systems Improvement, 2005 Oct. 1 p. Electronic copies: Available from the Institute for Clinical Systems Improvement (ICSI) Web site
- ICSI pocket guidelines. May 2005 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2005. 362 p.

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PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 23, 2001. The information was verified by the guideline developer as of September 14, 2001. This summary was updated by ECRI on January 28, 2004 and October 8, 2004, and most recently on December 15, 2005.

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