

Maine Breast and Cervical Health Program

March 2003
**Cervical Cancer Screening
and Diagnostic
Follow-Up Guidelines**

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ACKNOWLEDGMENTS

This is the third edition of the *Maine Guidelines for Cervical Cancer Screening and Follow-up*. The first edition was issued in 1995 and the second edition in 1997. The members of the Maine Breast and Cervical Health Program's (MBCHP) Clinical Advisory Group have provided invaluable assistance in the development of this document.

The Maine Bureau of Health believes that guidelines for the evaluation and management of breast cancer and its precursors will enhance the quality and effectiveness of patient care. This protocol represents the Bureau's recommendations for all providers in Maine involved in cervical cancer screening. It will serve as the clinical protocol for providers participating in the Bureau of Health's Breast and Cervical Health Program, a program funded by the Centers for Disease Control and Prevention. In addition to professional education and quality assurance, public education, patient tracking, and surveillance are part of this comprehensive statewide screening program.

In 1997 the Oregon Breast and Cervical Cancer Program adapted the *Maine Guidelines for Cervical Cancer Screening and Follow-up*. In 2002, the two states began a collaboration which led to this document. Vivian Hanson, MD, of the University of Washington was the principal author and Laura Ronan, MPH of Maine and Marjorie McGee, MS of Oregon were the editors and project coordinators. Donna Conkling, MD, the Medical Consultant for the MBCHP, provided clinical and editorial guidance.

Any clinician seeking to apply or consult these guidelines is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. The MBCHP makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. Decisions to adopt any particular recommendation must be made by the practitioner in light of their expertise, available resources, and circumstances presented by the patient.

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BACKGROUND

WHAT IS THE MAINE BREAST & CERVICAL HEALTH PROGRAM (MBCHP)?

In 1990, Congress passed the Breast and Cervical Cancer Mortality Prevention Act and authorized the National Centers for Disease Control and Prevention to undertake a screening program for low-income women. In 1994, The Maine Department of Human Services' Bureau of Health received a grant to establish this program in Maine. The MBCHP promotes education and screening for early detection of breast and cervical cancer among Maine women. Since the enactment of the Treatment Act in 2001, the MBCHP can ensure that all uninsured MBCHP women diagnosed with cancer will be covered by Maine Cares. More information about the MBCHP can be found at <http://www.maine.gov/dhs/bohdcfh/bcp>.

MBCHP INDICATORS AND POLICIES

THE MBCHP HAS A SET OF PERFORMANCE INDICATORS TO STRIVE TOWARDS, AS WELL AS POLICIES, MOST OF WHICH HAVE COME FROM THE CDC. POLICIES AFFECTING PROVIDERS IN THE MBCHP ARE BRIEFLY SUMMARIZED IN SIDEBARS THROUGHOUT THE DOCUMENT AND DETAILED IN APPENDIX A. THESE POLICIES ARE NOT TO BE CONFUSED WITH CLINICAL GUIDELINES WHICH ARE THE FOCUS OF THIS DOCUMENT.

WHAT IS THE PURPOSE OF THIS DOCUMENT?

These guidelines are intended to aid primary care providers participating in the Maine Breast and Cervical Health Program. These guidelines are directed towards women of all ages although only women over the age of 40 are eligible to participate in the MBCHP, since these are the women eligible for screening services provided by the MBCHP.

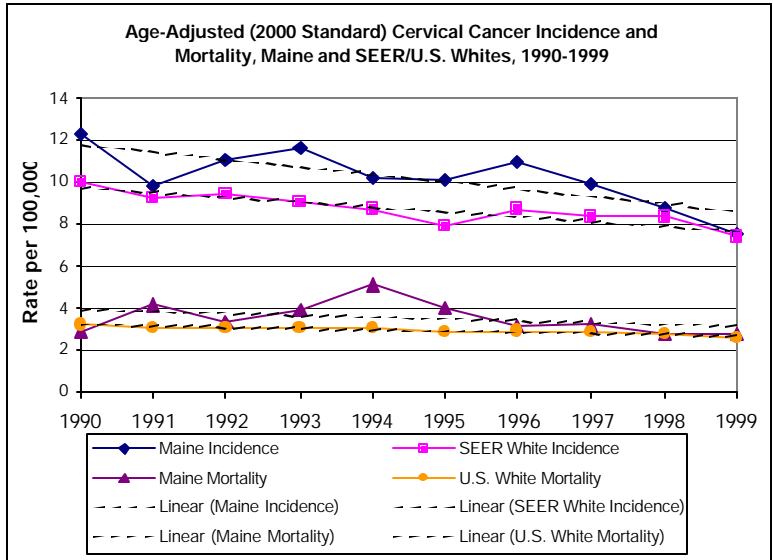
WHAT IS THE IMPACT OF CERVICAL CANCER IN MAINE?

According to data from the Maine Cancer Registry, Maine had 70 new cases of invasive cervical cancer and 26 deaths due to cervical cancer in 1998.

The incidence and mortality from cervical cancer in the United States have been dramatically reduced over the past 45 years, primarily due to the success of population-based screening with the Pap smear. While problems inherent with medical technology preclude total prevention of cervical cancer, it is theoretically possible to nearly eradicate this disease with appropriate sampling, interpretation, and follow-up.

INCIDENCE

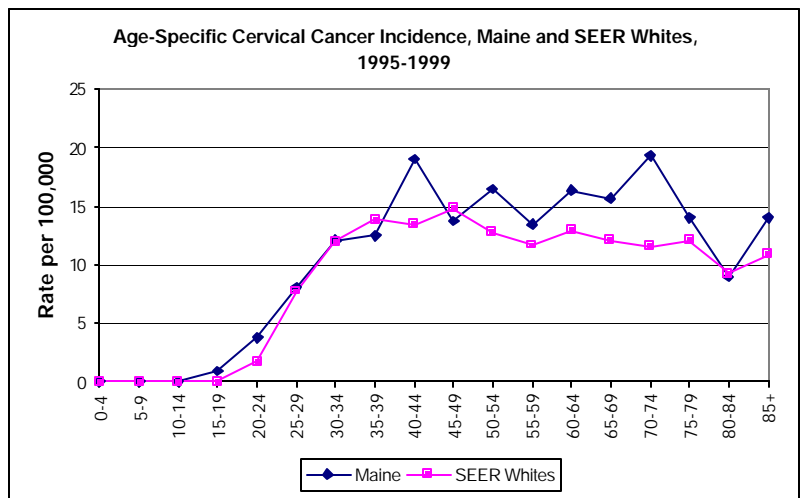
Maine’s average annual age-adjusted cervical cancer incidence rate for 1999 (preliminary) was 7.5 per 100,000. This is the lowest rate of cervical cancer since the inception of the Maine Cancer Registry in 1983. This rate was similar to the ‘SEER’ rate for white females of 7.4 per 100,000 for the same period.



Since the inception of the Maine Cancer Registry in 1983, Maine has always had a higher rate than the SEER white female population. In some years the age-adjusted incidence rates of cervical cancer were significantly higher in Maine than the U.S. The general trend in Maine and the nation since 1990 suggests a gradual overall decrease with the Maine rate showing a trend toward convergence with the national rate.

MORTALITY

Mortality data show trends similar to incidence. Overall, Maine’s cervical cancer mortality rate has declined during the period 1990-1998 as has the national rate. In 1999, Maine’s average annual mortality rate was 2.7 per 100,000, compared to the national rate of 2.6 per 100,000. The difference between Maine and national cervical cancer mortality rates is not statistically significant.



INTERPRETATION

The age-specific incidence rates from 1995-1999 indicate that, with the exception of the 45-49 and 80-84 year old age groups, Maine's rates were higher than SEER's for all women age 40 and older. The highest incidence rates were observed in women age 70-74 (Maine: 19.3 per 100,000; SEER Whites: 11.6 per 100,000) followed by women age 40-44 (Maine: 19.1 per 100,000; SEER Whites: 13.4 per 100,000). These data show that the incidence of invasive cancer increases rapidly between ages 20 and 35.

HOW OFTEN ARE MAINE WOMEN SCREENED?

According to the Maine Behavioral Risk Factor Surveillance System (BRFSS) data, most Maine women have routine Pap tests. However, in 1998 15% of Maine women reported not having had a Pap test in the past three years.

I. Pap Test Screening Guidelines

BACKGROUND

Since the 1980's most public and private professional organizations and healthcare agencies have supported guidelines stating that all women who are or have been sexually active, or who have reached age 18, should have an annual Pap smear and pelvic examination. These recommendations also stated that after a woman has had three or more consecutive, satisfactory, normal annual examinations, the Pap smear may be performed less frequently at the discretion of the woman and her clinician.

In 2002, the American Cancer Society (ACS) published new guidelines. [ACS] The ACS worked closely with representatives of other organizations to develop these new guidelines. These guidelines incorporate new screening tests and clarify the screening interval and other areas previously left to physician discretion. As of November, 2002 the ACS guidelines are supported by: American College of Obstetricians and Gynecologists (ACOG), American Social Health Association, (ASHA), American Society of Colposcopy and Cervical Pathology (ASCCP), Association of Reproductive Health Practitioners (ARHP), Gynecologic Cancer Foundation (GCF), National Association of Nurse Practitioners in Women's Health (NANPWH), and Society of Gynecologic Oncologists (SGO).

The Maine screening recommendations in this document are primarily based upon the 2002 ACS guidelines, supplemented with information from the US Preventive Health Services Task Force (USPHSTF) Guidelines issued in early 2003 and the recent medical literature. (The USPHSTF are available at <http://www.ahrq.gov/clinic/uspstf/uspstfscerv.htm>.)

Cervical Cancer Screening

- “The purpose of screening, in addition to detecting cervical cancers at an early stage, is to detect and remove high-grade lesions and thus prevent potential progression to cervical carcinoma.” [ACS]
- Since 1940 when the Papanicolaou (Pap) smear was developed, cervical cancer in the USA has decreased over 75%, primarily due to Pap smear screening.
- Women with a preinvasive lesion have a five-year survival rate of nearly 100%.

	American Cancer Society (November 2002)	US Preventive Services Task Force
When to begin Pap Screening	Within 3 years after start of vaginal intercourse, but no later than age 21.	Within 3 years after start of sexual activity, but no later than age 21
Routine Pap screening	<ul style="list-style-type: none"> • \leq age 30, annual traditional Pap tests; or • $<$ age 30, every other year liquid-based test; • After age 30, every 2-3 years after 3 consecutive normal test results. 	<ul style="list-style-type: none"> • At least 3 years for women who have a cervix; interval frequency based on risk factors
When to discontinue Pap screening	<ul style="list-style-type: none"> • Age 70 or older, if at least 3 normal test results and no abnormal results in 10 years; • Women who have had a total hysterectomy with removal of the cervix. 	<ul style="list-style-type: none"> • After age 65 for women who have had adequate recent screening with normal Pap tests and are not at high risk; or • Women who have had a total hysterectomy for benign disease

WHEN TO START SCREENING

Experts recommend waiting **approximately three years** following the initiation of vaginal sexual activity because transient HPV infections and cervical cell changes that are not significant are common and it takes years for significant abnormality or cancer to develop. Cervical cancer is extremely rare in women under the age of 25. The term “approximately” is used to assure insurance coverage for teens or young woman if the Pap is done before 3 years. Screening young women results in detection of a large number of atypical and LSIL results, which will usually resolve spontaneously within a year or two, and floods the follow-up system for little benefit. **Exceptions to starting at 3 years post initiation of sexual activity include HIV positive women and other immunocompromised women who should be screened following the US Public Health Services Guidelines that indicate that women who are HIV positive should have a Pap smear soon after diagnosis and, if normal, a repeat Pap in six months. [CDC]**

MBCHP Policy: AFTER 3, CONSECUTIVE, NORMAL PAP TESTS WITHIN A 5-YEAR PERIOD, THE PAP TEST SHALL BE PERFORMED EVERY 3 YEARS.

Age 21 was selected as the **upper limit** to start screening based on “expert opinion”. It was felt that an upper age limit for when to initiate screening is needed for providers who don’t ask patients about their sexual history and for adolescents who are unable or unwilling to disclose prior consensual and/or nonconsensual intercourse. Such an upper age limit ensures that young women, including victims of sexual abuse, are protected. Women with a history of sexual abuse should be screened once they are post-puberty and are psychologically ready, by a provider who has experience and sensitivity for working with abused women.

It is noted by the ACS under rationale that “provider discretion and patient choice following counseling should be used to guide the **initiation of cervical cytology** screening in young women who have never had vaginal sexual intercourse and for whom the absence of a history of sexual abuse is certain.” Vaginal intercourse is specified because “the risk of HPV transmission to the cervix is low for other types of sexual activity.” [ACS] Women who have only had sex with women (exclusively lesbian women) are at a lower, but not negligible risk of cervical cancer and do need Pap screening. [Marazzo].

HOW OFTEN TO SCREEN

After initiation of screening, Pap smears should be performed **annually** with **conventional cervical Pap smears OR every two years using liquid-based Paps**. At or after **age 30**, women who have had **three consecutive, technically satisfactory normal/negative cytology results** may be screened **every two to three years**.

Since the 1980s, many providers have continued to screen annually despite the recommendation for a **longer screening interval** for women with a series of normal Pap tests. Some of the **risk factors** that may have led providers to over screen women are no longer considered exceptions for the long screening interval (see sidebar on page 10). The US Preventive Services Task Force recommends screening at least every three years, with the interval frequency based on individual risk factors.

The **exceptions** to the longer screening interval include women who: are under surveillance for prior abnormal cytology, are HIV positive, had DES exposure *in utero*, or are immunocompromised by organ transplantation, chemotherapy, or chronic systemic corticosteroid treatment. The ACS rationale in support of screening yearly for women under 30 years of age is that “preliminary [unpublished] data suggests the most appropriate screening interval is age-dependent and younger women may benefit more from a shorter screening interval.” In support of screening every two years in younger women with LBP, ASC notes that “most studies show improved sensitivity [for LSIL] for liquid-based Pap (LBP)” and the longer screening interval “compensates for the decrease in specificity,” but “there are currently no data to support a particular screening interval for LBP.” [ACS] This recommendation was based on mathematical modeling.

After the age of 30, women who have had three normal tests in a row may get screened every 2 to 3 years. The ACS has eliminated some of the risk factors (see below) that may have led to more frequent screening. ACS and others (e.g., AAFP, ACP, ACPM, ACS, CDC, NBCCEDP, USPHSTF, WHO) have recommended since before 1980 that conventional cytology can be safely performed up to every three years for most women, in the United States. [ACS] This recommendation was based on studies of relative risk and cost-effectiveness. Furthermore, several studies have shown that a history of normal/negative results has a protective effect on cervical cancer incidence. Pelvic exams for STDs or other appropriate reasons should be conducted as needed regardless of the Pap smear screening interval.

Summary of ACS 2002 Screening Guide-

lines: The American Cancer Society’s new guidelines are available at <http://caonline.amcancersoc.org>

- Cervical cancer screening should begin approximately three years after a woman begins having vaginal intercourse, but no later than 21 years of age.
- Cervical screening should be performed every year with regular (“conventional”) Pap tests or every two years using liquid-based tests. Beginning at age 30, women who have had three normal tests results in a row may get screened every two to three years. (See “exceptions” on this page)
- Women 70 years of age who have had at least three normal Pap tests and no abnormal Pap tests in the last 10 years may decide, to stop cervical cancer screening.
- Women who have had a total hysterectomy (removal of the uterus and cervix) do not need to undergo cervical cancer screening, unless the surgery was done as a treatment for cervical precancer or cancer.
- Women who have had a hysterectomy without removal of the cervix should continue cervical cancer screening until age 70.

Exceptions to Standard Screening Guidelines

- HIV Infection
- Women with weakened immune system
- Women exposed to DES in utero
- Adolescents who may have been sexually abused
- Women with a history of cervical cancer or pre cancer

MBCHP POLICY: FUNDS MAY NOT BE USED FOR PAP SMEARS IN WOMAN AFTER A HYSTERECTOMY, INCLUDING THE CERVIX, UNLESS THE HYSTERECTOMY WAS FOR CERVICAL NEOPLASIA. IF A CERVICAL STUMP REMAINS, PAP SMEARS SHOULD BE CONTINUED ON A REGULAR (EVERY 3 YEARS) BASIS.

No longer considered as acceptable rationales for more frequent screenings [Boon et al]

- Early onset of sexual activity
- Multiple sexual partners
- Smokers

ACS states, in the rationale, that the “number of high-grade lesions that might progress [to invasive cancer] during a screening interval longer than three years is considered to be unacceptably high in the United States,” [ASC] and that “while more frequent screening increases sensitivity, it also increases patient harm and cost.” [ASC] The average time for progression from HPV infection to HSIL is 3 (<1-20) years and from HSIL to invasive cancer is 12 (3-40) years. [Alanen et al.]

WOMEN WHO HAVE HAD A TOTAL HYSTERECTOMY

Thirty three to 40% of women in the US have had a hysterectomy. Women often don't know why the hysterectomy was done and almost never have records of previous Paps. However, women usually know if they had an HSIL Pap, as they assume it was “cancer”. Based on the literature, the ACS reinforced the following recommendations:

- No further screening for women after hysterectomy (with removal of cervix) for non cancer indication
- Usual screening for post hysterectomy women who still have a cervix
- Document presence or absence of cervix by careful exam and review any available pathology report from previous surgery to ascertain benign/malignant reasons for hysterectomy
- If unable to be sure of previous cervical pathology or if CIN 2/3, women post hysterectomy should be screened until three documented, consecutive, satisfactory negative Paps every 4-6 months are obtained over 2 years.

Review the history of women who had a hysterectomy:

- History of prior abnormal pap smears
- Date of hysterectomy
- Reason for hysterectomy
- Type of hysterectomy-
 - Abdominal - is there a cervical stump? If unsure, do a speculum examination.
 - Vaginal - cervix is always removed

- Women with diagnosis of DES exposure or cancer in-situ should continue Pap smears indefinitely as long as they do not have other significant life-limiting chronic conditions. (Pap smear frequency is unspecified and left up to discretion of doctor.)
- Screening for vaginal cancer is not worthwhile since incidence is 1-2/100,000. Abnormal vaginal smears are uncommon and rarely significant.

MBCHP Policy: IN ORDER TO REACH THOSE MOST AT RISK, AT LEAST 20% OF THE WOMEN BEING SCREENED FOR CERVICAL CANCER WILL NOT HAVE HAD A PAP SMEAR IN THE LAST 5 YEARS.

WOMEN WHO SHOULD STOP BEING SCREENED

Women who are 70 and older with an intact cervix and who have had three or more documented, consecutive, technically satisfactory normal/negative cervical cytology tests and no abnormal/positive cervical cytology tests within the 10-year period prior to age 70 may elect to cease cervical cancer screening. [ACS]

Exceptions include: women with a history of invasive cervical cancer, DES exposure *in utero*, and/or women who are immunocompromised (including HIV positive), who should continue Paps as long as they are in reasonably good health. Women with severe co-morbid or life-threatening illnesses may forego cervical cancer screening.

Due to maturation of the transformation zone, postmenopausal women have a very low risk of developing new lesions. There is general consensus that the incidence of cervical cancer in older women is almost entirely confined to the unscreened and underscreened. Evidence suggests there is very low risk of cervical cancer for women aged 50 and older in countries with organized screening programs. Since few studies provide data on women over 65, the choice of age 70 is based on the opinion of an expert panel, mathematical modeling and demographic trends. [ACS] The USPSTF recommends stopping Pap smears in well screened women at age 65.

WOMEN WHO ARE NOT WELL SCREENED

Most screening in USA is opportunistic, often related to contraception, pregnancy, hormone replacement therapy, or gynecological problems. Approximately half of the cervical cancers diagnosed in the U.S. are in women who have **never** been screened and an additional 10% of cancers occur in women who have not been screened **within the past five years**. Those who are inadequately screened include women who:

- are low income
- lack insurance coverage or a regular health care provider
- are less educated

- are new immigrants
- are members of racial or ethnic minorities
- are socially or culturally isolated, including homeless women
- live in rural areas
- women who have sex with women (lesbian)
- are physically or mentally disabled
- have completed their families

INTERVENTIONS THAT INCREASE SCREENING

Clinicians and clinics should try to provide screening according to the frequencies described in these guidelines. A recent analysis indicates that the following organizational and system changes are beneficial: [Stone]

- Organizational and systems changes:
 - Elicit and clearly indicate support of top management for prevention
 - Clinical Procedures and protocols
 - .. Include screening as clinic/program policy priority
 - .. Use acute care visits to identify unscreened women and women due for screening
 - .. Reminders to providers: flag charts, flow sheets, etc.
 - .. Standing orders for nurses/clinic assistants
 - Make prevention routine
 - .. Include responsibility for identifying, locating, notifying, and screening persons in need of clinical preventive services in appropriate job descriptions
 - .. Run computer printouts listing persons late for/missing screening

II. Increasing the Accuracy of Pap Tests

OBTAINING THE MEDICAL HISTORY

Careful history taking is essential in order to educate the woman and to indicate to the Pap laboratory that the smear needs extra (double) screening. When taking the patient's history, obtain the following information:

- History of previous routine Pap smears
- History of abnormal Pap smears
- Sexual behavior:
 - Onset of first coitus
 - Multiple partners
 - Male partner with multiple partners
 - Bisexual partners
 - History of sexual abuse and/or molestation
- HIV positive, or other causes of immunodeficiency
- DES exposure
- History of smoking
- History of sexually transmitted diseases, including HPV.
- Previous colposcopy, treatment and follow-up history
- History of cervical cancer or pre-cancer
- Hysterectomy (type and reason)

PATIENT EDUCATION

The following are suggested topics of discussion before, during, and after the appointment for a Pap smear. Women must have the opportunity to ask questions and express concerns, and responses must be conveyed to them as clearly as possible, with a sensitivity to cultural/ethnic diversity and language and sexual preference.

- Educate all women about Pap smear screening. Invite unscreened women to be tested. The Pap smear is one of the most effective tests in medicine. Explain that by the time a woman has had three Pap tests the chance of all three failing to detect that she has a significant problem (false negative) is only about one in 10,000.
- Educate the woman about human papillomavirus (HPV). Discuss HPV with any woman who has an abnormal Pap result (ASC-US or worse), being referred for colposcopy, or if an HPV-DNA test is being done. If using liquid-based cytology women need to be informed about the possibility of a reflex test.

Consumer Resources:

HPV Fact Sheets

- American Social Health Association (ASHA)
www.ashastd.org
- Seattle and King County Public Health
www.metrokc.gov/HEALTH/apu/std/hpv.htm

- The client should not douche, use intravaginal medications, vaginal contraceptives, tampons, or lubricants; or have intercourse or other penetrative sexual activity for at least 48 hours prior to the appointment.
- When the client is scheduling the appointment, she should select a day not likely to coincide with her period. Ideally the Pap should be done one to two weeks after the end of her menses.
- Knowing what will occur during the examination helps the client relax and makes performing the examination easier. Helping the woman keep warm and comfortable also helps her relax.

- If the patient tells you she has not had a Pap smear before, explain the steps in the examination and show her the speculum. Also explain that the examination may be uncomfortable (cause some pressure) and ask her to let the provider know if she experiences any pain. If this occurs make adjustments to the procedure.
- Remind the client that she can decrease her risk for cervical cancer (and associated sexually transmitted diseases such as HPV and HIV) by practicing safer sex using condoms, knowing more about a partner's sexual health history, reducing the number of partners, delaying the onset of sexual intercourse, or remaining abstinent.

- Avoid medical terminology and language that may have a sexual connotation:

- Tighten the knob on the speculum, avoiding the word screw.
- Examine, rather than feel or palpate.
- Insert or place, rather than stick in or put in
- Remove rather than withdraw or pull out.
- Table, not bed
- Relax your legs open, not spread your legs

- After the examination, explain that spotting may occur as a result of the Pap smear, but this is usually transient, self-limiting, and not an indication of a medical problem.

- Let the client know when and how she will obtain her Pap smear results

TIMING OF THE PAP SMEAR

The Pap Smear should be obtained under the following circumstances:

- Mid-cycle
- No douching at least within the past 48 hours

Increasing the Accuracy of Pap Tests

- No intercourse at least within the past 48 hours
- No intravaginal medication within the past 72 hours

Instructions regarding the timing of the Pap smear should be given to women at the time the appointment is made. If, however, a woman presents for her appointment in less than “optimal” circumstances, the Pap smear may be obtained anyway. Women should be informed that the Pap smear is being obtained under less than ideal circumstances and that a return visit and repeat Pap smear may be necessary. If the Pap smear results indicate that the specimen is inadequate, a repeat Pap smear should be obtained under more optimal circumstances, and the woman educated about proper preparations for her next screening. Also, educate the woman about how to best prepare for her next regular Pap smear.

OBTAINING THE OPTIMUM PAP SMEAR SAMPLE

A major cause of false negative smears is sampling error, hence obtaining a representative sample is critical. Sampling devices, spatula and endocervical brush, are recommended. The wooden spatula is better for conventional Paps but the plastic is preferred for liquid-based Paps. To obtain a reliable sample, first, scrape the portio (exposed portion of the cervix about the cervical os) with the spatula to include the entire transformation zone (TZ). Then sample the endocervical canal with the endocervical brush. If the brush is used in pregnancy, it is important that the patient be informed that slight spotting may occur immediately after the procedure but that this does not appear to jeopardize the pregnancy.

Sampling with a broom obtains endocervical and squamous cells with one instrument. If the broom is used it must be rotated a minimum of five 360 degree turns. [Ferris] Several studies (Ferenczy et al) indicate that the broom is less effective than the brush/spatula at collecting endocervical cells although this remains controversial. The USPSTF 2003 cites the results of a 1999 meta-analysis of randomized clinical trials to support the combined use of an extended tip spatula and the cytobrush. [USPSTF]

A single slide combining both the endocervical and ectocervical samples is usually used. Two separate slides from the ectocervix and endocervix can also be used, but is higher in cost. Use a separate slide if a vaginal smear/scrape is done (sometimes indicated for women exposed to DES *in utero*, but is very poor as a hormone assay). **A most important consideration is rapid fixation.** It should be appreciated that cellular samples, particularly those from the endocervical canal, can be damaged by air drying in a matter of seconds, underscoring the need for prompt fixation. Important steps in obtaining an adequate sample include: [McClatchey]

- When making the appointment, woman should be educated about preparation and about the examination.

Sampling with Liquid-Based Cytology

- If liquid based cytology is done, collect as for a conventional Pap but immediately (before collecting the endocervical sample) place the spatula into the transport fluid and agitate and scrape it to remove all the cells. (The plastic spatula is preferred to the wooden spatula for liquid-based cytology as plastic sheds the cells better.)
- Similarly, immediately after collecting the endocervical material, put the endocervical brush into the transport fluid, agitate the brush and scrape the brush with the spatula, to remove all the cells from the brush. Any delay will fix the cells onto the collection instrument. A broom is provided with some liquid based cytology kits and may also be used.
- Some liquid-based cytology systems recommend cutting off the end of the brush instead and leaving it in the transport fluid, so the material on the brush is removed at the laboratory.

- Prepare the woman for a pelvic examination, with attention to her comfort and privacy.
- Cells should be collected prior to the bimanual examination.
- No lubricant should be used before collecting the sample.
- If testing for sexually transmitted diseases is indicated, the Pap smear should be taken first, followed by tests for gonococcus and chlamydia. A vaginal specimen for wet mount and pH may be taken before the Pap smear.
- The entire portio (exposed portion of the cervix about the cervical os) should be visible when the smear is obtained.
- The cervix should not be wiped before obtaining the smear. If vaginal discharge is present in excessive amounts, it may be carefully removed so as not to disturb the epithelium or remove endocervical mucus before obtaining the smear. To remove excess discharge, gently place a gauze pad on the surface and lift it off. This is rarely necessary.

- Small amounts of blood will not interfere with cytologic evaluation, but large amounts, as occurring during menses, preclude cytologic sampling. If the patient has signs or symptoms of cervicitis or vaginitis, consideration may be given to treating the infection first. It is important to not delay the Pap test too long because cancer can look like cervicitis or cause bleeding.
- First take a 360° portio sample with the spatula. For the conventional Pap hold the spatula until the endocervical sample is taken.
- Take the endocervical sample second because of the frequency of bleeding from the endocervix when the brush is used. The endocervical canal is best sampled by gently rotating a brush 90° to 180°. Turning more should be avoided to prevent excessive bleeding and discomfort.
- To avoid air drying promptly spread the spatula and brush specimens thinly and uniformly on to the slide (first the spatula by sweeping and then the brush by rolling

on the slide), without clumping. Samples may overlap but don't attempt to mix them. Fix within 1-2 seconds (maximum 5 seconds).

- If spray fixatives are used, the spray should be held at least 10 inches away from the slide to prevent dispersal and destruction of the cells by the propellant.
- For diethylstilbestrol-exposed patients, some providers take one or more additional smears from the fornices or upper two thirds of the vagina. The material collected is placed on separate slides (Don't use liquid-based cytology).

CAUSES OF FALSE NEGATIVE AND FALSE POSITIVE PAP SMEARS

All tests have false negative and false positive results. False negative results cause women who have significant dysplasia to be missed. False positive results cause women to be labeled as having dysplasia when there is no disease. Since the Pap smear has been successful in preventing most cervical cancer the prevalence of the disease is now very low. Thus, when evaluating for significant disease (CIN 3 of which about one third would progress to invasive cancer if left untreated) there are more women with false positive results than false negative results. Both of these groups of women are of concern. The women with false negative results, if not detected on further testing, could progress to cancer. The women with false positive results, by contrast are subjected to multiple tests searching for the disease (colposcopy, conization, etc.). They are sometimes subjected to treatments (conization, hysterectomy, etc.) that are unnecessary. The woman and the clinician are often frustrated and stressed in the fruitless search for the non-existent disease.

Common Causes of False Positives:

- Client preparation and timing
 - Recent sex
 - Smear before 8 weeks postpartum
 - Smear before 4 months post treatment (cryocautery, laser, LEEP, cone, etc.)
 - Recent use of podophyllin to treat warts
 - Severe atrophy
 - Previous irradiation or chemotherapy
 - Infection/inflammation/repair
- Sampling technique
- Vigorous use of the cytobrush
- Air-drying artifact
- Over-reading of the specimen in the Pap laboratory

Common Causes of False Negatives:

- Smears lacking diagnostic cells
- Inadequate client preparation: e.g. recent sex, douching, vaginal medication, etc.
- Lesion characteristics that affect specimen quality: e.g. non-shedding, overlying leukoplakia, very small HPV infection with minimal dysplasia
- Sampling error (inadequate technique)
 - Repeating Pap too soon (under two months)
 - Cleaning cervix before taking sample
 - Failure to obtain an adequate number of cells
 - Failure to sample the whole transformation zone including endocervical cells or transformation zone component (EC/TZ) and squamous cells
 - Spreading cells too thick on slide
 - Delay in fixation of cells
- Smears in which diagnostic cells are masked by inflammatory cells, blood, or mucus.
- Smears in which diagnostic cells are overlooked or misinterpreted (screening or interpretive errors).

Methods to Minimize False Positives and False Negatives:

- Proper timing of Pap Smears
- Client preparation and education
- Appropriate management of atrophic changes and infection.
- Appropriate sampling technique and fixation of smear.
- Inclusion of appropriate clinical information on Pap smear requisition.

SPECIAL CIRCUMSTANCES

Stenosed Cervical OS

Stenosis may occur from atrophy after menopause or from prior conization. If the woman is postmenopausal, use a course of vaginal estrogen. If stenosis is a complication after treatment for HSIL, it is essential to get a good Pap smears to ensure adequate treatment. Attempt to sample the endocervix with an endocervical brush, a male chlamydia swab, or Calgiswab. Attempt to obtain endocervical component. Sometimes you may need to dilate cervix. Indicate on the Pap smear requisition that cervical stenosis exists. If the Pap smear is unsatisfactory and the woman is high risk (history of cervical dysplasia/treatment) consider colposcopy and ECC or referral to a gynecologist.

Atrophic Vagina/Cervix

Attempts should be made to obtain an adequate Pap smear. It is important to be able to visualize the cervix. Frequently vaginal estrogen will be helpful. Use 0.3 to 0.625 milligrams

of vaginal estrogen in the vagina at bedtime for three weeks or use an estrogen vaginal ring for about three weeks. Stop the vaginal medication about 5 to 7 days before the repeat Pap smear. If the cervix cannot be visualized or the Pap smear is unsatisfactory, then the woman should be referred for possible vaginoscopy. Vaginal estrogen may be needed for adequate colposcopy for post menopausal women.

Physically Impaired Women

Women who are disabled, frail, or elderly may have difficulty getting on the exam table or be unable to use conventional stirrups. Special accommodations or equipment, or different approaches may be necessary to permit obtaining the Pap smear. A table that can be raised or lowered facilitates transfer of women with mobility problems. A wide table, side rails or safety straps, and pelvic tilt may make the examination easier. Obstetric stirrups with knee supports or surgical boot stirrups can support weak or unstable legs. Some women need to be examined in alternate positions. Using a proctoscope table or a foam wedge permits use of the knee-chest position. Sometimes a lateral approach is indicated. Use of an assistant or use of other support or positions may be necessary. Often the disabled woman can make suggestions to help the clinician perform the examination and accommodate the disability. See *Table Manners* in the references for some alternate approaches to examining a woman with a physical disability. [Ferreyra]

Difficult Pelvic Examination

It may be difficult to visualize the cervix in obese women, pregnant women, or women with many prior pregnancies. Use a large, and especially an extra long, speculum (Pederson, Graves). Vaginal retractors may be used, if available. Place an unlubricated condom on the speculum and cut off the tip of the condom before insertion of the speculum. The condom holds the vaginal mucosa laterally and frequently permits adequate visualization.

Unable to Perform the Pelvic Examination

If an adequate bimanual exam cannot be performed refer for vaginal ultrasound, vaginoscopy or exam under anesthesia if the woman is high risk and/or has significant gynecologic symptoms. If the examination is unsuccessful consider referral to a gynecologist or a clinic skilled in management of women with access or special problems.

III. NEW TECHNOLOGIES

INTRODUCTION

The Pap smear is a very good screening test. However, it is not perfect. Thus, to improve the detection of significant cervical disease, compensate for the subjectivity of cytology, decrease the false negative rate of Pap smears, and further decrease cervical cancer, different screening methods have been developed and studied. Some of these techniques are heavily marketed to clinicians and advertised directly to women with messages like: “A blink of an eye, a moments inattention, and a cancer missed” and imply the message of “Use this test or else get sick and die.” This section is limited to a review of liquid-based technology and HPV testing.

EVALUATING THE EFFECTIVENESS OF NEW TESTS:

Use of new or special tests requires careful studies on the value of the information or results of the test, and then education of clinicians of the implications of the results and ways to communicate this information to the woman. Furthermore, independent studies, not supported by the companies developing or marketing the techniques are imperative. Many tests are cost-effective only if they permit less frequent screening. A good (better) screening test must:

- Be evaluated by one or more randomized controlled trials compared with the conventional Pap.
- Be more sensitive **and** more specific than the conventional Pap smear.
- Decrease colposcopy and other expensive or invasive tests.
- Be cost-effective with a reasonable risk benefit ratio.
- Be clinically significant, i.e. increase detection of biopsy proven CIN 3 and/or early cancer.
- Impact morbidity and mortality.

LIQUID BASED CYTOLOGY

All collection devices leave a large percentage of the collected material on the instrument. There are several new liquid based collection techniques (ThinPrep, SurePath) available or being developed that should, increase the number of cells submitted to the laboratory and decrease air drying. The cells are collected with the usual instruments but instead of spreading some of the material collected from the cervix on a slide, they are washed into a bottle of fixative. The laboratory filters the material to remove blood, mucus, WBC and debris and to disperse thick cell clumps. Reportedly, diagnostic cell clusters are still kept together. A

representative sample of the cells is then transferred to a slide in a monolayer (one cell thick). The process avoids over-thick smears, smudged or disrupted cells, obscuring by blood or WBC, air drying, and some of the other problems with Pap smear preparation and interpretation. The specimen quality (except for presence of endocervical material) is usually better in liquid-based Paps than conventional Pap slides. Fewer slides are unsatisfactory or limited by blood and inflammation, since fresh red cells and white cells are filtered out in the process. However, liquid cytology slides have more unsatisfactory specimens due to scanty cells.

Cost Effectiveness

The cost of using liquid based technology is about \$14 to \$26 more than the conventional Pap smear. A recent review concluded that there is insufficient evidence to evaluate cost-effectiveness. [Hartmann] The Agency for Healthcare Research and Quality (AHRQ) concluded that LBP would only be cost effective if screening were done every three to four years instead of yearly. [McCrorry] One cost-effectiveness study determined that liquid-based cytology costs more than other approved enhancements to screening and produces less health benefits. In some studies, liquid-based Paps detected more HSIL than conventional Pap tests. Liquid-based cytology also detects more ASC-US/LSIL which may only indicate the presence of transient HPV infections that will usually resolve. Several studies found more liquid-based smears lacked glandular cells, endometrial cells, or especially endocervical material. There is evidence that detection of endocervical in-situ cancer or invasive adenocarcinoma is deficient.

Disadvantages

- Costs of equipment and supplies is high.
- The laboratory spends more time and effort on processing. The cells appear different and diagnostic criteria are different.
- Cytotechnologists need considerable retraining in the use of monolayers.
- Unsatisfactory results may occur due to a low cell count in the vial or clumping preventing slide preparation.
- Scanty specimens are particularly difficult to read, but use of accurate counts of the number of cells applied to the slide should obviate this problem.
- About 5% of specimen bottles lack sufficient material to do HR-HPV testing.

Advantages

- The material remaining in the vial could be used to obtain more cells for additional Pap smears for questionable results or for the required 10% rescreen.
- The material can also be used for other screening techniques such as “reflex” HR-HPV testing when the Pap smear is ASC-US.
- The same specimen can be used for screening for STD such as gonorrhea and chlamydia. Future uses include: aneuploidy probes, nuclear grading, monoclonal antibodies for E6 and E7, or other probes and tests that may be developed.
- Many computer-based automated screening devices require a monolayer and this has been an impetus for development and promotion of these technologies.

Conclusion

Currently, available data suggest that while liquid-based technologies may have advantages over conventional Papanicolaou (Pap) tests in identifying cervical cancer precursors squamous cells in some situations, the net benefit is small compared to the significantly increased costs of the newer technology. According to many organizations and reviews it is premature to determine if the new technologies actually increase detection of significant disease, can decrease the rate of invasive cancer, are cost effective, or can be endorsed or recommended. [ACOG] The technology needs more testing and evaluation especially for detection of HSIL and AGC. “ For the purposes of guiding decision making about choice of screening tools, the current evidence is inadequate to gauge whether new technologies are ‘better’ than conventional cytology.” [Hartmann] With the addition of reflex HR-HPV testing after an ASC-US Pap and other new uses for the cells left in the vial (e.g., chlamydia, gonorrhea), the liquid based Pap may become cost effective. New automated cytology systems may require liquid based specimens in the laboratory.

HUMAN PAPILLOMAVIRUS (HPV) AND HPV DNA TESTING

Background

High risk types of HPV (HR-HPV) are recognized as the initiator of cervical carcinogenesis. Now studies are underway to determine the utility of HPV tests . HPV is rarely, if ever, found in women who have never had sexual intercourse. Infection with HPV occurs in most women soon after onset of sexual intercourse, with about a 20% chance of infection with each new sexual partner. At least 75% to 80% of women and men who have had sex have been infected with HPV. Although more common in heterosexual women, HPV can be spread sexually between women. The risk of genital infection from perinatal exposure (usually with low risk HPV) appears to be low and transitory. Infection with low risk HPV may be clinical, with visible warts in about 1% to 2% of persons. Some women have transient LSIL, which appears within one to two years after contracting the infection. Most persons have asymptomatic, latent infection with no signs or symptoms.

MBCHP Policy:
CDC DOES NOT PERMIT MBCHP FUNDS TO BE USED TO REIMBURSE FOR LIQUID-BASED CYTOLOGY AT A REIMBURSEMENT RATE ABOVE THE MEDICARE RATE FOR A CONVENTIONAL PAP TEST.

HPV Infection

The incubation period for clinical warts (thus presumably for LSIL Paps) usually is about nine months but may take years. High risk HPV infection lasts an average of 13.5 months while low-risk infection last about 8.2 months. Then, although the virus persists in the basal cells (subclinical or latent infection), the Pap smear becomes normal in most women. Subsequently, the only marker for infection is serology which persists for years. It is unknown if the virus is cleared from the body or only suppressed.

High Risk (HR) / Low Risk HPV Viral Types

There are over 200 HPV types known with probably an equal number yet unknown. Various types infect different areas of the body, and over 40 infect the genitals. About 25% of women with HPV have evidence of infection with multiple types. The types vary in carcinogenic risk and are separated into “low risk” and “high risk” types. Low risk types include HPV 6, HPV 11 and closely related types. Low risk types are less prevalent, transient, unable to integrate into cellular DNA, and are not found in cancers. Low risk types cause visible genital warts and may cause LSIL. Higher risk types include HPV 16 and 18, and related types, are found in over 50% of women, and cause most SIL and cervical cancer. Over 99% of invasive cervical cancer contains high risk HPV. [Walboomers] Most infection, even with “high risk” HPV causes only a transitory LSIL or is unrecognized.

Treatment of HPV

It is not possible to eradicate HPV with any known treatment. Use of condoms for all sexual contacts, cryocautery, laser surgery, electrocautery, application of 5-FU, vaginal washes with trichloroacetic acid, hysterectomy, or other modalities have all been recommended for therapy for subclinical HPV infection, though all have high failure rates. Thus, most experts do not treat LSIL since it is just Pap smear evidence of HPV infection. Prophylactic vaccines are under study to prevent HPV infection or development of LSIL or HSIL.

Indications for HPV Testing and Screening

Hybrid Capture (HC-II) testing for HR types is useful for triage of women with ASC-US and increases the detection of small, early HSIL lesions. [Manos, Soloman] Trials show HPV testing by HC-II is not useful for the initial management of reproductive age women who have LSIL or HSIL since almost all tests are positive. [ALTS, Manos] Limited data suggest other possible future uses of HPV testing for management of women who have an

HPV AND GENITAL WARTS

- Patients with genital warts need routine Paps; they do not need HPV testing unless warranted by certain Pap test results (i.e., AS-CUS)
- Genital warts are caused by low risk HPV types 6 & 11
- Genital warts are diagnosed clinically by visual inspection. Women with genital warts may be asymptomatic or have pruritis, bleeding, burning, or tenderness. Larger clumps of genital warts can interfere with sexual intercourse, defecation, and vaginal delivery. Any suspicious, ulcerated lesion should be biopsied to rule out squamous cells cancer.
- Incubation period ranges from 3 weeks to eight months post exposure. Most infections are transient and clear spontaneously within 2 years. If patient is immuno compromised (e.g. HIV, chemotherapy) then infection with HPV 6 & 11 can be associated with squamous cell carcinoma. Genital warts are sexually transmitted and increased incidence is found in women with 5 or more sexual partners over preceding 5 years.
- Treatment of genital warts include; chemical agents, surgery, cryotherapy and laser therapy. All therapies are less than satisfactory with recurrence rates of 30 - 70% within 6 months.

Consequences of HPV Infections

High Risk (HR) HPV is thought to be a key step in the development of cervical cancer, but the consequences of HPV infection may be multiple:

- At least 80% of women have subclinical HPV at some time during their lives
- About 1 % of women have visible genital warts
- Many (most) women will have transient ASC-US or LSIL changes soon after contracting HPV
- Regression to asymptomatic, subclinical disease is usual; complete cure is uncertain
- Development of HSIL may not have intervening LSIL
- Progression of HSIL to cancer occurs, about 30% of the time if HSIL is not diagnosed and treated

More Points about HPV:

- Testing for low-risk HPV types is worthless
- Prevalence of HPV in the sexually active population is high (50-90%)
- LSIL usually indicates acute infection with one or more types of HPV
- Women need education as they may feel a stigma associated with a “cancer causing STD”

It is reassuring to note that most HR-HPV positive women will not have abnormal Pap smears much less cervical cancer. Progression from HSIL to cancer is a slow process (takes over 10 years) and most cancer can be prevented by treatment of the HSIL.

AGC Pap, management of postmenopausal women who have an LSIL Pap, and post-treatment follow-up.

Types of HPV Tests

Hybrid Capture (HC-II) is a commercially available DNA detection test. HC-II require 5,000-50,000 HPV DNA copies for detection of the presence of one or more high-risk (HR) HPV types. There may be false negative results in some women due to fluctuating or very low levels of virus. HSIL and especially cancer sometimes have low levels of virus, explaining older reports of many cancers without HPV. PCR (DNA amplification test) can detect very low levels of virus (10-100 copies) and identify specific types, and is only available for research.

HPV Testing and Screening

Although often suggested for routine screening, testing for the presence of HPV DNA is currently not recommended. Since HPV infection is very common in young sexually active women, primary screening of young women for “high risk” HPV types should be limited to research purposes. **Screening for “low risk” HPV types is of no clinical value.** Older women (over age 35 years or especially after menopause) have much lower rates of HPV infection and future studies may show benefit of screening. As with any new technology, most of the research available is sponsored and/or paid for by the manufacturers of the tests and will need independent confirmation. “At present HPV testing simply represents greater use of resources and increases in medical costs.” [Shingleton]

MBCHP Policy: HPV TESTING (HC-II) IS ALLOWABLE ACCORDING TO MAINE ALGORITHMS FOR WOMEN WITH ASC-US TEST RESULTS. IT IS ALSO ALLOWABLE IN THE CASE OF LOW-RISK POST-MENOPAUSAL WOMEN WITH LSIL. ONLY HIGH-RISK VIRAL TYPING IS REIMBURSABLE.

HPV Testing: Methods of Collection

- Reflex testing refers to automatic testing for HPV by the laboratory if the Pap smear shows ASC-US or LSIL. This is possible if liquid based cytology was used for the Pap smear and the clinician has made the appropriate arrangements with their laboratory.
- Co-collection refers to the collection of material from the cervix at the same time as the Pap smear. A liquid-based cytology test may be used or an HPV test kit.
- An HPV kit includes a swab and transport material. The material collected from the cervix is stored in the transport material until the Pap result is known. If appropriate, the specimen is sent to the laboratory for testing for high-risk HPV viral types. Due to shelf-life, the specimen must be sent to the laboratory within 3 weeks after collection. All other specimens are discarded.

The indications for HPV testing as follow-up for Pap smear findings are discussed in Section IV.

IV. Management of Bethesda (TBS-3) Diagnoses

BACKGROUND

TBS was designed to be flexible and modified over time. In April 1991, TBS-2 made a few modifications of the terminology. TBS became the standard for Pap smear reports throughout the United States and has been used in many other countries. In April, 2001, TBS-3 was convened with over 150 experts in cytology and cervical dysplasia. The result was a further modification of the classification system which is described in this section, along with management guidelines of those results. [Solomon2]

OVERVIEW OF MANAGEMENT

Additional Information on the Pap Report

Automated review, ancillary testing, and other information: If the slide is scanned by a computer, the report should include the automated report and indicate the instrument used. If ancillary tests are done, such as HPV testing, this should also be included on the report. In addition, the report should indicate if the specimen was a conventional Pap slide or liquid-based. If liquid-based, the type of process should be specified.

Educational notes and suggestions: Educational notes and suggestions are optional. They should be concise, phrased as suggestions, and consistent with published clinical guidelines.

The follow-up of abnormal smears depends upon the severity of the findings, and are based upon the TBS-3 revised nomenclature [Solomon2] and management guidelines developed by various ASCCP committees and at the ASCCP Consensus Conference for the Management of Cytological Abnormalities and Cervical Cancer Precursors. [Davey, Wright] There are several ways to manage benign and neoplastic findings. The method selected is based upon the advantages and disadvantages of these modalities and the severity of the Pap findings. See the algorithms in this section on page 42, 43 and 44 for a summary of MBCHP recommended follow-up. Timely follow-up is critical to ensuring appropriate care and the number of days between an abnormal result and a diagnostic test should be kept to a minimum.

There is general agreement on the management of some findings but controversy regarding some benign and borderline findings (lack of endocervical cells, ASC-US, and LSIL). The goal is to find the true cancer precursor disease that can be treated to prevent cancer, while limiting the risks and costs (stress, time, dollars) of more complicated and invasive procedures.

MBCHP Guidelines for Timely Follow-up Recommendations for Cervical Cancer Screening Follow-Up Schedule	
Date of Pap smear to test results	≤ 2 weeks
Abnormal Pap smear report (≥HSIL) to Dx procedure	≤ 2 weeks
Date of Dx procedure to final diagnosis	≤ 1 week
Final diagnosis of cancer to date Tx initiated	≤ 6 weeks

SPECIMEN ADEQUACY:

Unsatisfactory Pap Smears

Pap smears are considered unsatisfactory for evaluation if:

- The Pap specimen cannot be evaluated due to:
 - Inappropriate labeling,
 - Lack of identifying information accompanying the specimen,
 - Slide was broken so it could not be processed or was otherwise unreadable.
- The slide was processed and examined but unsatisfactory for evaluation of epithelial abnormalities because:
 - Slide lacks an adequate number of well preserved and well-visualized squamous epithelial cells (minimum of 8,000-12,000 for conventional Pap or 5,000 for liquid-based Pap).
 - Blood, inflammation, thick areas, poor fixation, air drying artifact, or contaminants obscure over 75% of the epithelial cells.

In general, in laboratories employing TBS, the rates of unsatisfactory specimens are about 0.2% to 1%. Rates significantly higher than this may imply either overuse of the unsatisfactory designation or poor Pap smear technique on the part of the provider.

All these smears will also include the reason why the specimen was reported as unsatisfactory (e.g., obscuring inflammation or atrophic changes) and this may alter the approach in the subsequent smear. Some unsatisfactory smears cannot be processed or read because of lack of proper identification or if the slide is broken. Most unsatisfactory smears are read but can not be reported because of poor quality of the material. The problem should be corrected, if appropriate (see table on page 29), and the Pap smear should be repeated in two to four months. If repeat smears are unsatisfactory arrange/refer for colposcopy.

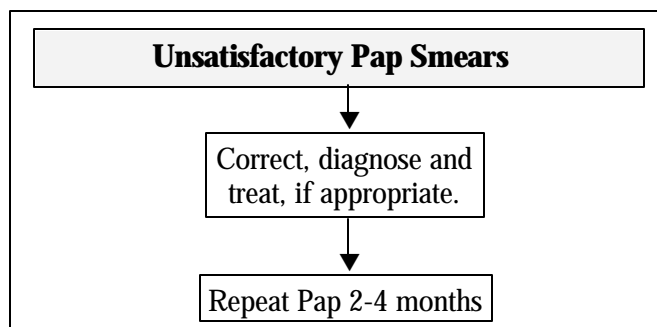
Overview of Specimen Adequacy

- Unsatisfactory
- Satisfactory
 - Without qualification
 - Satisfactory but include information about a quality indicators
 - History may be inadequate
 - Satisfactory smears may lack EC/TZ component
 - Partial obscuring by blood or inflammation

Note:

- The “SBLB” category has been eliminated.
- If a specimen was satisfactory for evaluation but the quality was less than perfect, quality limitations will be noted in the comments section of the report.

Repeating Paps
Repeating Pap tests too soon (less than six to eight weeks) may cause a false negative result.



Management of Unsatisfactory Paps Smears	
Causes of Unsatisfactory Paps	Appropriate Response
Lack of identification and clinical information on slide and/or requisition.	Include client's name on the slide and name and clinical information on the requisition.
Broken slide	Use care in packaging and transport.
Obscuring blood (excess red blood cells)	Repeat Pap when not bleeding. Use endocervical brush gently. If persists, refer for colposcopy.
Obscuring inflammation (excess white blood cells)	Diagnose and treat any identified infection. Don't use nonspecific creams. [Ferrante]
Poor fixation or air dried	Fix slide within two seconds. Use care with spray fixative.
Cells are cytolysed	Avoid water from douching or over-moist speculum. Have the client avoid lubricants or vaginal medications.
Scanty cellular material	Scrape more firmly to obtain more cellular material. Have the client avoid anything in the vagina for two days. Don't clean the cervix before taking the Pap.
Cellular material too thick	Spread more evenly over the slide or use two slides for heavy material.
Cells too atrophic	Prescribe vaginal estrogen for three to four weeks. Stop the estrogen for one week before the repeat Pap smear.
Foreign material or obscuring contaminants	Avoid medications and lubricants. Have the client avoid sex for two days before the Pap.

Table [Hanson]

SATISFACTORY PAP SMEARS

Pap Smears that are Satisfactory without qualification

Satisfactory Pap smears indicate that the specimens may be interpreted by the laboratory. Each specimen has proper client identification, so the laboratory can locate prior Pap smears and reports for comparison. The requisition form should include pertinent clinical information including age and last menses, previous diagnosis or therapy, or other risk factors for correlation. Presence of significant risk factors indicate the need for increased review and these slides will be evaluated twice. The slide contains adequate numbers of well-preserved and clearly visible squamous epithelial cells, so a diagnosis can be made. A satisfactory smear does not imply whether the results are normal or abnormal.

Pap Smears that are Satisfactory but include information about quality indicators

TBS-3 eliminated the “Satisfactory but limited by . . .” category (TBS-2) and “Less than optimal” category (TBS-1). The category was originally created as an education tool so clinicians would improve collection techniques but created confusion. Descriptions do not determine adequacy. Unless the Pap smear is abnormal the woman should have regular follow-up. **There is no need for an early repeat smear.** Quality limiting factors include obscuring inflammation or blood cells, air-drying artifact, and other examples are:

- ***The history provided may be inadequate.*** At a minimum the client’s age and last menstrual period must be included. Client’s clinical history should include contraceptive methods, hormones, pregnancy, menopause, infections, prior surgery or radiation, prior Pap smear results, prior abnormal Pap smears, results of prior colposcopy, prior treatment of the cervix, and DES exposure *in utero*. Since many of these factors change the appearance of the cells, the pathologist may give an incorrect reading if the information is lacking. A history of prior abnormalities requires that the slide gets closer scrutiny.
- ***Satisfactory smears may lack EC/TZ component.*** Endocervical cells and metaplastic cells constitute the EC/TZ component. Endocervical cells (EC) in a Pap smear are a normal finding that documents sampling above the squamocolumnar junction in women with a cervix. Metaplastic cells are the cells that, if infected with HPV, may become HSIL. The presence of either EC or metaplastic cells suggests, but does not prove, that the cervix was adequately sampled. Clinicians should expect EC/TZ on over 90% of slides. However, their absence does not prove that the cervix was inadequately sampled.

Absence of endocervical cells may be due to inadequate sampling of the endocervical area (cervix not visualized, no cervical brush, etc.) characteristics of the woman (pregnant, on oral contraceptives, postmenopausal, hysterectomy), or interpretation in the laboratory (on review EC/TZ cells are found in nearly 50% of these slides). Most

studies show no increase of SIL in smears lacking EC/TZ and follow-up of women who lack EC/TZ finds they continue to have less SIL. The presence of an endocervical component may correlate with a higher detection of endocervical glandular abnormalities, since glandular abnormalities are part of the endocervical component.

NEGATIVE FOR INTRAEPITHELIAL LESION OR MALIGNANCY

If there are no significant (neoplastic) abnormalities, the report must clearly state “**Negative for intraepithelial lesion or malignancy**” (formerly called “Within Normal Limits”) either in an optional general categorization and/or as the first finding in the “Interpretation/Result” section of the report. The interpretation and results section also includes all non-neoplastic (benign) and any epithelial abnormalities (neoplastic or cancer precursors).

- **Negative findings with infections and reactive changes.** The various additional diagnoses within the “Negative for intraepithelial lesion or malignancy” category include cytological changes related to the presence of various infectious organisms, atrophy, reaction to an IUD or radiation, or nonspecific inflammation. This is considered a benign condition in which follow-up Pap smears should be done in one year. Obviously, the presence of a specific infectious organism, such as Trichomonas or Candida, can be correlated with the clinical findings and treated, if appropriate.
- **Other: includes endometrial cells in a woman over age 40 years.** The presence of normal endometrial cells in a menstrual age woman or in a postmenopausal woman on cyclic hormone replacement therapy is usually of no clinical significance. Endometrial cells in postmenopausal women are often related to a benign process but can indicate endometrial hyperplasia or even endometrial cancer.

Since the menopausal status of women is often not clearly indicated on the Pap requisition, laboratories will report the presence of benign appearing endometrial cells on all women over the age of 40.

Overview of Negative Pap Results:

- Negative for intraepithelial lesion
 - Negative findings with infections and reactive changes
 - Other: includes endometrial cells in a woman over age 40

Pap Smears that are Negative for Intraepithelial Lesion or Malignancy, without any quality indicators. Most smears have normal/negative results without any quality indications or benign conditions present. Review the history to assure that the woman does not need closer follow-up due to prior abnormal (neoplastic) results. If the previous smear was ASC-US or worse, manage as indicated for the previous finding. Otherwise, these women should have the Pap smear repeated in

one year. After a woman has had three, documented, consecutive, normal Pap tests within a 5-year (60-month) period, the Pap test shall be performed every 3 years. Notify the woman of the results and assure that systems are in place so she will be recalled for rescreening at the appropriate interval.

Pap Smears that are Negative for Intraepithelial Lesion or Malignancy, but include information about quality indicators. *Formerly called Less Than Optimal (TBS-1) or Satisfactory but limited by . . . (TBS-2).* This includes smears that lack endocervical cells or other evidence of sampling the transformation zone as well as infections, atrophy, or collection problems such as scanty slides, air-drying, poorly preserved cells, and obscuring blood or inflammation. The clinician should note the factors and correct as appropriate. It is prudent to repeat the Pap smear in one year instead of the recommended three year follow-up for satisfactory specimens that do not note any quality indicators.

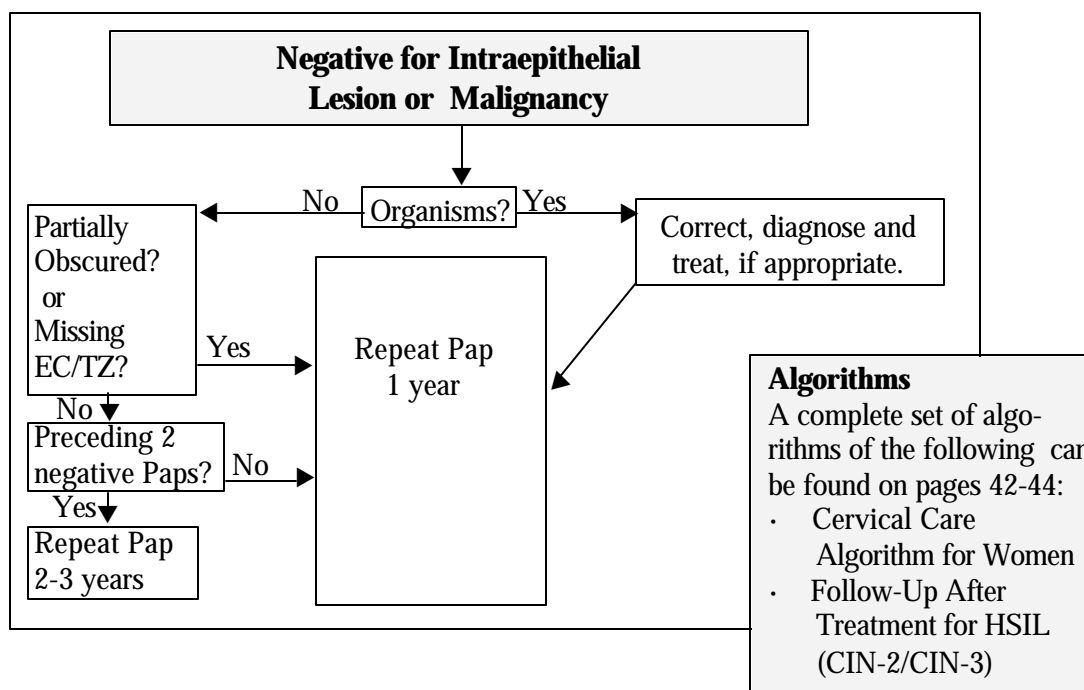
TBS-3 Changes:

- “WNL” is now “Negative for Intraepithelial lesion or malignancy”
- Benign cellular changes (BCC) has been deleted as a category. These cases are classified as “Negative for Intraepithelial lesion or malignancy”
- A new general category of “other findings” has been added.

Pap Smears that are Negative for Intraepithelial Lesion or Malignancy, but include information about inflammation or a specific infection. *Formerly called benign cellular changes.* If signs or symptoms are noted at the time of the examination or indicated by the findings on the Pap report review the history and take appropriate laboratory specimens including vaginal wet mount, amine odor and pH, tests for gonorrhea or chlamydia, or other diagnostic tests. If a specific vaginal or cervical infection is identified, either on the Pap report or diagnostic tests, manage the infection. Nonspecific inflammation will clear as rapidly with time as with nonspecific medications or remedies.

Pap Smears that include information about atrophy. Atrophy or atrophic vaginitis is common in postmenopausal women not using hormone replacement therapy. If the Pap is otherwise negative and the woman lacks symptoms or sexual problems, no therapy is indicated. Sometimes the Pap smear will need to be repeated because it is unsatisfactory or shows atypical cells (ASC-US or LSIL). Treatment with vaginal estrogen will frequently make the subsequent Pap normal. Vaginal estrogen is also indicated before colposcopy for evidence of more serious abnormalities (HSIL). Review the woman’s history for contraindications for estrogen (breast cancer, endometrial cancer, etc.). If estrogen is NOT contraindicated, the woman should be treated with vaginal estrogen for three to four weeks, starting about a month before the repeat Pap or colposcopy is planned. If using estrogen cream, stop the medication about one week before the return visit. If using a vaginal ring, it should be removed about three days before the return visit.

MBCHP POLICIES:
MBCHP FUNDS CANNOT
BE USED FOR VAGINAL
ESTROGEN.



All epithelial abnormalities are grouped as either:

- Squamous cell
- Glandular

Squamous cell abnormalities include:

- ASC-US or atypical squamous cells of undetermined significance
- Atypical cells, cannot exclude HSIL (ASC-H)
- LSIL (encompassing HPV and CIN-1)
- HSIL encompassing moderate [CIN-2] and severe dysplasia [CIN-3], CIS); and,
- Squamous Cell Carcinoma

EPITHELIAL CELL ABNORMALITIES (ASC-US)

These follow-up instructions DO NOT apply to women with prior abnormalities. See Appendix A, for management of these women. Women who are HIV positive should all have colposcopy.

Pap Smears that show atypical cells of undetermined significance (ASC-US)

This category indicates Pap smears in which the cytologic changes exceed those attributable to benign or reactive processes but do not meet definitive criteria for the diagnosis of a squamous intraepithelial lesion. The diagnosis should not include mild atypical changes favoring a benign reactive process since the rate of significant lesions with this report is very low. These very mild cell changes should be omitted or reported as non-neoplastic reactive changes. When a low-grade squamous intraepithelial lesion is suspected, the report should be ASC-US. A few of these women will be found to have high grade disease with follow-up. This diagnosis should be used sparingly by the laboratory. In general, this category should not account for more than 5% of the total volume of smears and should not exceed two times the laboratory’s usual squamous intraepithelial lesion rate.

The authors of the ASCCP consensus statement point out that women whose Pap test results yield findings of ASC have a 5% to 17% chance of having CIN 2, 3 confirming biopsy and those with ASC-H, 24% to 99%. Yet the risk of invasive cancer is 0.1% to

0.2%. While follow-up is warranted, unnecessary inconvenience, anxiety, cost, and discomfort should be avoided.

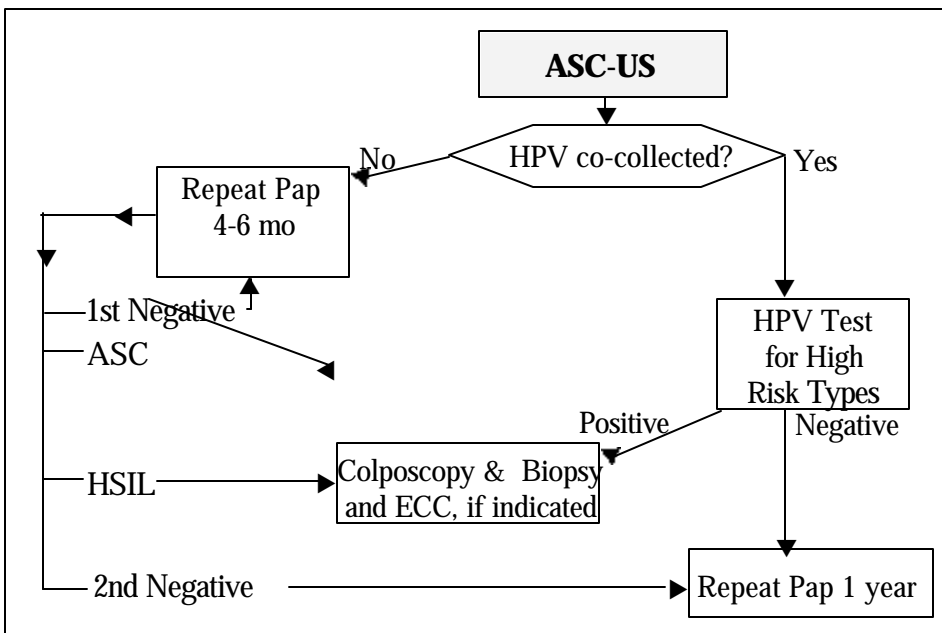
If material for HPV testing was collected at the time of the Pap smear (liquid based cytology or with an HPV collection kit), the preferred management is to do a reflex HPV test (for high risk types only) for Paps with ASC-US results. If the HPV test is positive, arrange for colposcopy. If the HPV test is negative, repeat the Pap smear in one year. If either Pap is read as HSIL or AGC or worse, arrange for colposcopy and discard the HPV specimen. HPV testing will not be needed when the Pap is HSIL or AGC or worse.

When NOT to do HPV Testing: Doing HPV testing when the Pap is worse than ASC-US. Low-Risk viral typing is not useful.

If material for HPV testing was **not** collected at the time of the initial Pap smear, there are a variety of options:

- return within 1 to two weeks for HPV sampling (and arrange for colposcopy if positive)
- return in 4 to 6 months for repeat Pap tests and, if negative, repeat Pap again in 4 to 6 months (see algorithm below)
- for women over age 40, repeat Pap smear and co-collect HPV sample in 4-6 months and again in 12 months. If either the 4/6 month or 12 month Pap is ASC-US or LSIL then the HPV sample is sent for testing. If the HPV test is positive arrange for colposcopy.

If either of the repeat Pap smears is read as ASC-US or LSIL (see next page) in low-risk postmenopausal women, then arrange for colposcopy. If either Pap is read as HSIL or AGC or worse, arrange for colposcopy.



MBCHP Reimbursement Policies: HPV testing (HC-II) has become a part of management of the ASC-US Pap test. MBCHP funds can be used for the HPV test (HPV kit or LBC). However, the liquid based cytology Pap test itself is only reimbursable at the same amount (Medicare rate) as the conventional Pap test. A return visit for HPV sampling is also reimbursable.

ASCUS = ASC

ASCUS is now ASC, and includes two distinct categories:

- ASC-US
- ASC-H

ASC-H includes atypical squamous cells of undetermined significance where high grade changes cannot be excluded.

This category indicates Pap smears in which the cytologic changes exceed those attributable to benign or reactive processes but have atypical metaplastic cells and a significant possibility of a high grade squamous intraepithelial lesion. In general, this category should not account for more than 5% to 10% of the ASC smears. This is a serious diagnosis, although less so than HSIL. These women need colposcopy.

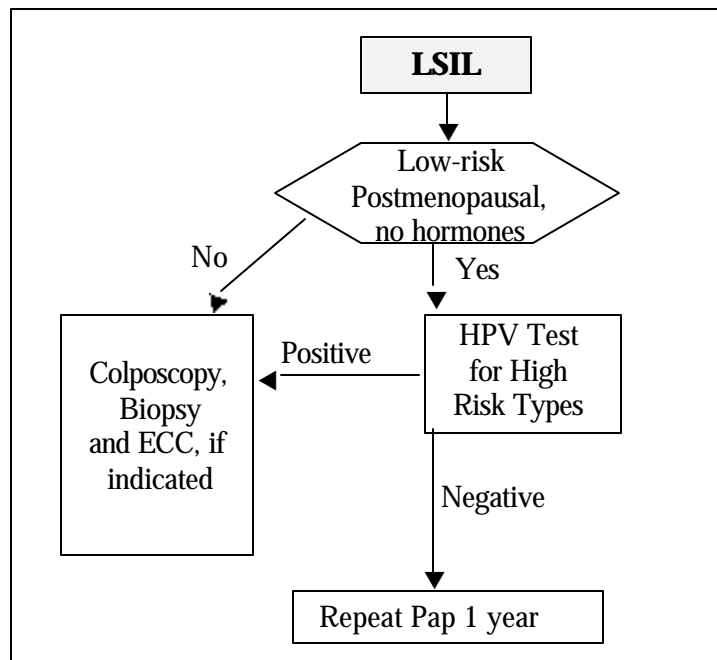
LSIL includes all low grade squamous intraepithelial lesions

This category includes mainly transient acute human papillomavirus (HPV) infections in young women. Most of these women will, if tested, have high risk types of HPV. These lesions typically persist for about one year, until the immune system suppresses the infection.

This category includes:

- Changes associated with HPV infection
- Koilocytotic atypia
- CIN-I (mild dysplasia)

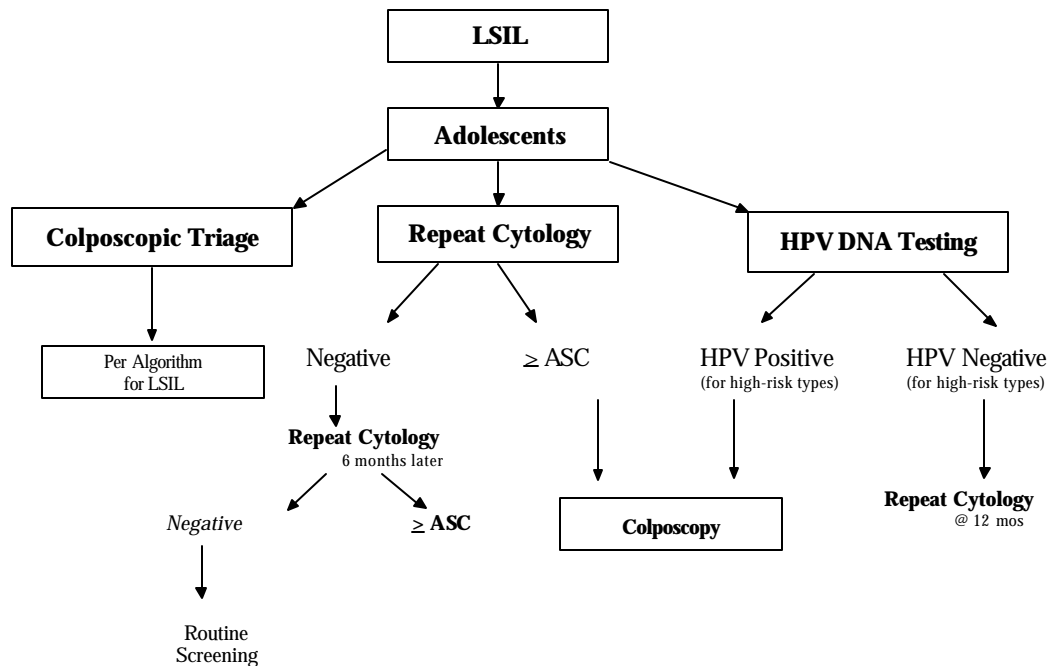
For women of reproductive age, the recommended management is to arrange for colposcopy low-risk, postmenopausal women, who are not using hormone replacement therapy, often have atrophic changes on the cervix and also need to be treated with vaginal estrogen before colposcopy. True LSIL and HPV infection is relatively low in these women. Thus, Maine MBCHP recommends having postmenopausal women return for an HPV test soon after the LSIL Pap is reported. If the HPV test is positive, arrange for colposcopy. If the HPV test is negative, repeat the Pap smear in one year. The ASCCP also gives the option of repeat cytology in 4 to 6 months after the initial Pap.



Notes: MBCHP funds may be used to do high-risk HPV testing for LSIL results in postmenopausal low risk women.

Special Considerations: Adolescents

If teenage women have regular Pap smears they have greater than 70% chance of being referred for colposcopy. Teenage women have very low risk of invasive disease and very high risk of recent acquisition of a transient HPV infection. The stress, expense, compliance, and confidentiality issues in these women may make colposcopy a less acceptable alternative. Thus, Pap smear follow-up at six and twelve months may be a better management. If both Paps are negative she may resume routine screening. If either Pap is ASC-US or worse arrange for colposcopy. Alternatively, an HPV test can be done at one year after the LSIL Pap, with colposcopy if the HPV test is positive.



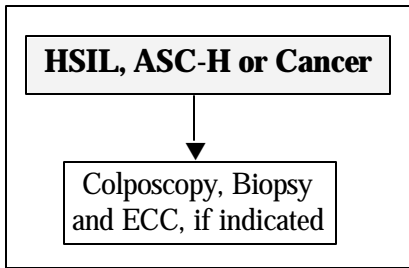
HSIL includes all high grade squamous intraepithelial lesions

This category includes evidence of significant cellular changes that indicate a possible cancer precursor or, in a few cases, early invasive cancer. Some of these lesions will regress but progression to invasive cancer is significant and, if confirmed, these women need treatment to prevent development of cancer.

This category includes:

- CIN 2 (moderate dysplasia)
- CIN-3 (severe dysplasia)
- CIS (carcinoma in situ)

2001 TBS / ASCCP Consensus Guidelines
 LSIL = CIN-1
 HSIL = CIN-2, CIN-3



AGC cells should be identified as to origin, if possible, and reported as:

- Endocervical cells
- Endometrial cells
- Glandular cells (unspecified as to origin)

Glandular cell abnormalities include:

- AGC or atypical glandular cells, specifying endocervical, endometrial, or not otherwise specified cell types
- Atypical glandular cells, favor neoplasia, specifying endocervical or NOS cell types
- Endocervical adenocarcinoma in situ (AIS)
- Adenocarcinoma (may be specified as endocervical, endometrial, extrauterine, or NOS)

Patients with the diagnosis of HSIL should undergo colposcopy and directed biopsy with endocervical curettage, if indicated. Review of the Pap, colposcopic impression, and biopsy specimens should be considered to resolve any discrepancy. If no lesion is found or the colposcopy is unsatisfactory a LEEP or cone biopsy is frequently necessary. High grade lesions require treatment.

Squamous Cell Carcinoma

This category includes findings suspicious for or diagnostic of invasive squamous cervical cancer. **Pap Smears that are one of the following: (1) High Grade Squamous Intraepithelial Lesions (HSIL), (2) Atypical cells of undetermined significance, cannot exclude HSIL (ASC-H), or (3) Squamous cell carcinoma.**

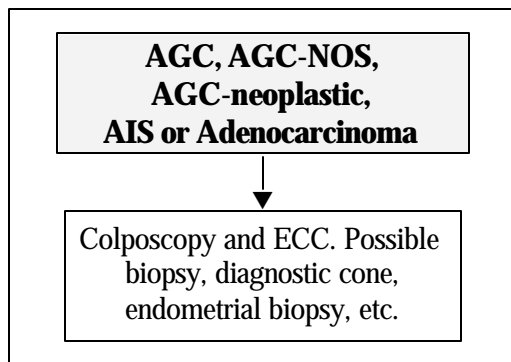
AGC includes atypical or abnormal glandular cells AGC-NOS includes atypical glandular cells, not otherwise specified. AGC-neoplastic includes atypical glandular cells, when a serious lesion is suspected.

In the past, these reports were confused with ASCUS and was prone to mismanagement. Atypical glandular cells are less common than abnormal squamous cells. These categories are important because high grade squamous or glandular disease will be found in 10% to 39% of women with AGC-NOS.

AGUS=AGC
AGUS is now AGC, the subcategories have been expanded:

- Atypical (NOS)
- Atypical (favor neoplastic)

The category of AGC includes a spectrum of abnormalities ranging from benign reactive atypias to endocervical or endometrial adenocarcinoma. Follow-up studies in most labs have demonstrated that this is a highly significant diagnosis which includes a large number of high grade squamous lesions as well as glandular lesions. This is also a category in which communications with the laboratory is



important. Laboratories should qualify the diagnosis further, if possible, as favoring an endocervical adenocarcinoma or AIS, endometrial adenocarcinoma, a high grade squamous lesion, or a benign reactive process, such as microglandular hyperplasia. The latter interpretation should help guide management.

Colposcopy is indicated and the endocervical canal needs evaluation, with a good endocervical curettage. If an endometrial origin for the atypical glandular cells is suspected, endometrial sampling is required to resolve the abnormality. All women with AGC who are over age 40 years or have other risk factors for endometrial hyperplasia (diabetes, polycystic ovary syndrome, etc.) should have an endometrial sampling. Cone biopsy should be considered if no explanation for the atypical cells are found, especially if the report is AGC-neoplastic or worse. Sometimes hysteroscopy, laparoscopy and other procedures are indicated.

Adenocarcinoma-in-situ (AIS) is now distinct.

AGC-neoplastic is suggestive, but not diagnostic for AIS and is more worrisome. Often, endometrial cells can be distinguished from endocervical cells but sometimes the disease is from another area.

AIS includes carcinoma in situ or glandular preinvasive changes

Since TBS-2 cytological criteria for AIS have been clearly defined. Some of these women will have well-differentiated invasive adenocarcinoma.

Adenocarcinoma includes suspicion of invasive glandular cancer

- Invasive adenocarcinoma of cervix
- Endometrial carcinoma
- Extrauterine carcinoma
- Not otherwise specified (NOS)

Other Malignant Neoplasms (specify) This is a new category.

V. Follow-Up After Treatment for HSIL (CIN-2/CIN-3)

Algorithms

A complete set of algorithms for the following listed below can be found on pages 41-43:

- Cervical Care Algorithm for Women
- Follow-Up After Treatment for HSIL (CIN-2/CIN-3)

All treatments cure about 90% of lesions. Most recurrences are treatment failures and appear within the first year. If margins are positive for disease close follow-up is necessary with possible re-treatment if subsequent Pap smears are abnormal. Repeat Pap smears after treatment will detect treatment failures.

Long term follow-up is necessary, since recurrences may occur years later, probably as the result of new SIL developing from the same factors that caused the original disease. New lesions (true recurrence) may occur from new HPV infection or incorporation of HPV into the healing tissue. The probability of developing invasive cancer in women with treated CIN 3 is about 85/100,000 women years. This is about 5 times the risk in the general population.

Thus, close follow-up is essential to detect treatment failures and long-term follow-up is prudent to detect new abnormalities. Unfortunately, many women do not return for follow-up Pap smears after treatment. One study found 43% of women treated for SIL failed to return for Pap smears. The following actions should be taken in long-term follow-up care of HSIL and cervical cancer after treatment (see second algorithm in Appendix -specifically for Pap smears after treatment of biopsy-proven HSIL (CIN 2/3).)

- **Repeat Pap smears after treatment every 4 to 6 months** for 1 to 2 years, or perhaps longer for invasive cancer. After three normal Pap smears the woman can return to annual screening. The first Pap smear may be ASC-US due to the extensive reparative process, especially if done in less than six months after treatment. LSIL due to persistent HPV infection is not uncommon. If any Pap smear shows SIL, colposcopy is indicated to rule out treatment failure.
- **Women with biopsy results of HSIL (CIN 3) or cancer need regular Pap smears for life** for detection of recurrent disease or development of vaginal intraepithelial lesions. Women with HSIL who have had more than three normal Pap smears after treatment and subsequent hysterectomy, probably do not need further screening.
- **Women with biopsy results less severe than CIN 3 may return to regular Pap smear screening** after three normal Pap smears post treatment.
- **Perform prompt colposcopy, biopsy, and therapy for any evidence of SIL or cancer** because of a high risk of invasive disease in women with failed treatment and a significant risk of new disease with cancer even as long as 18 years later.

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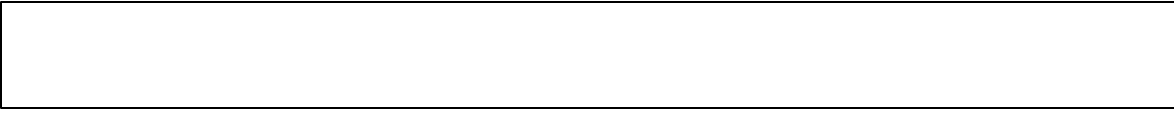
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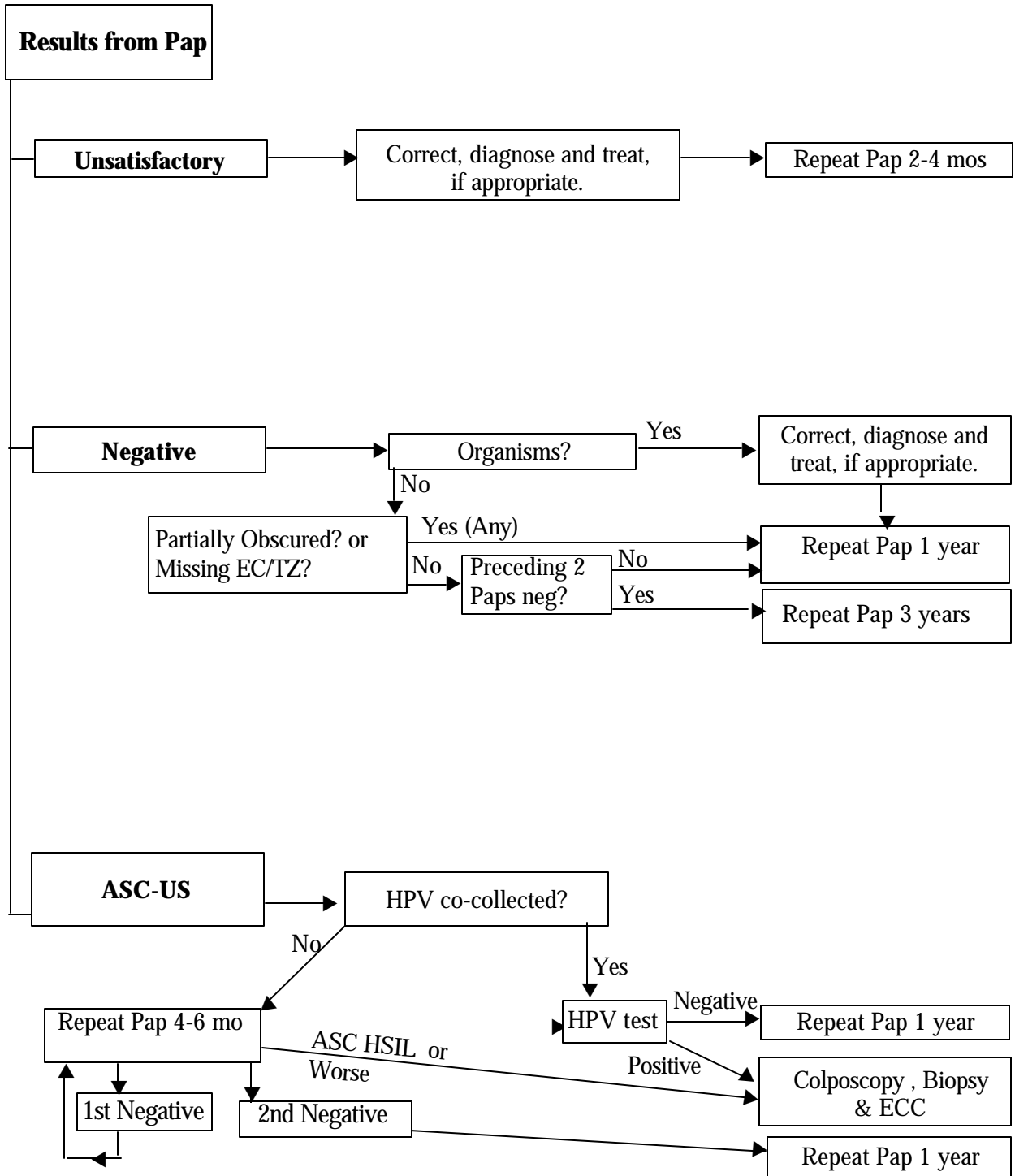
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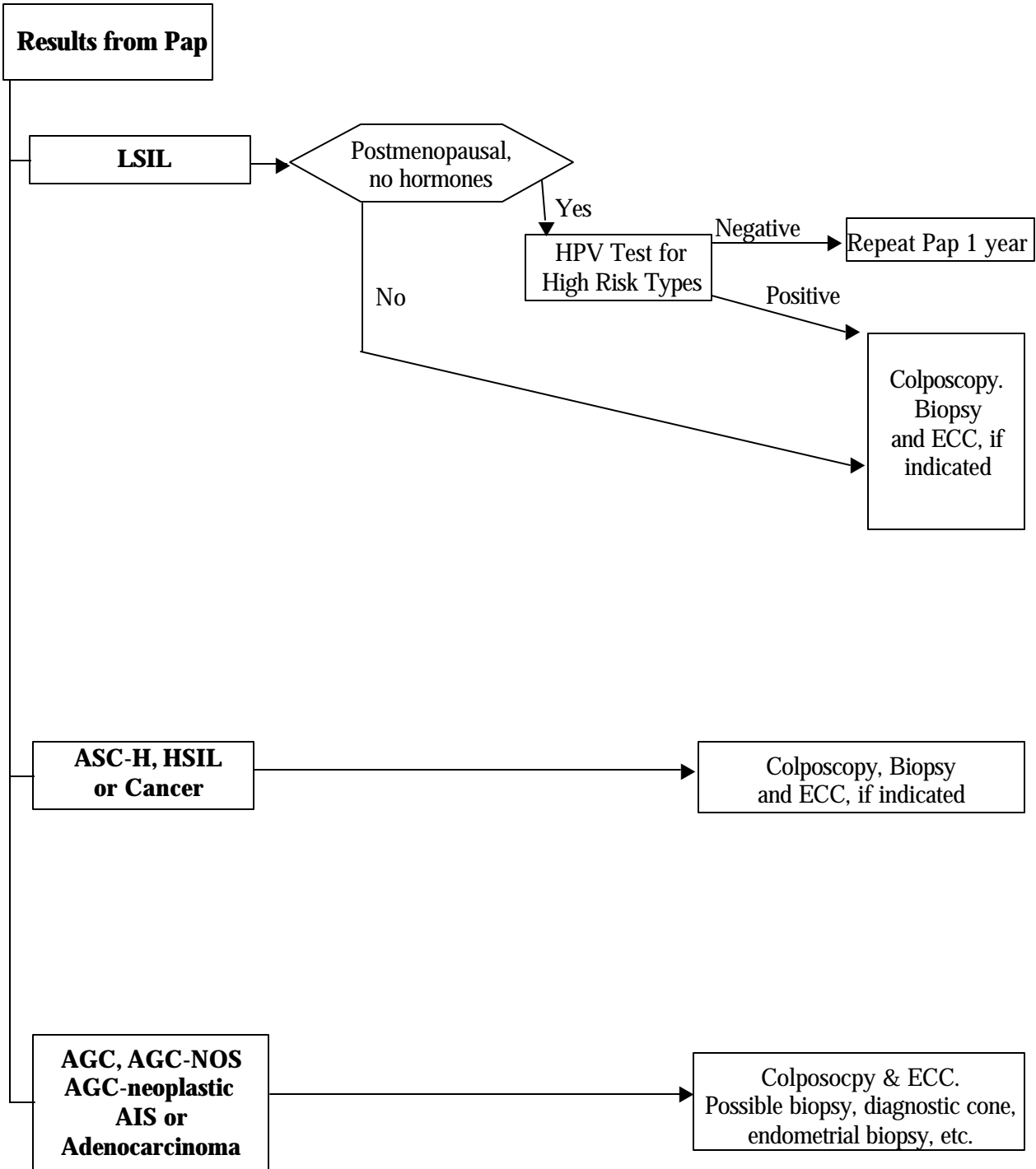
Appendix A



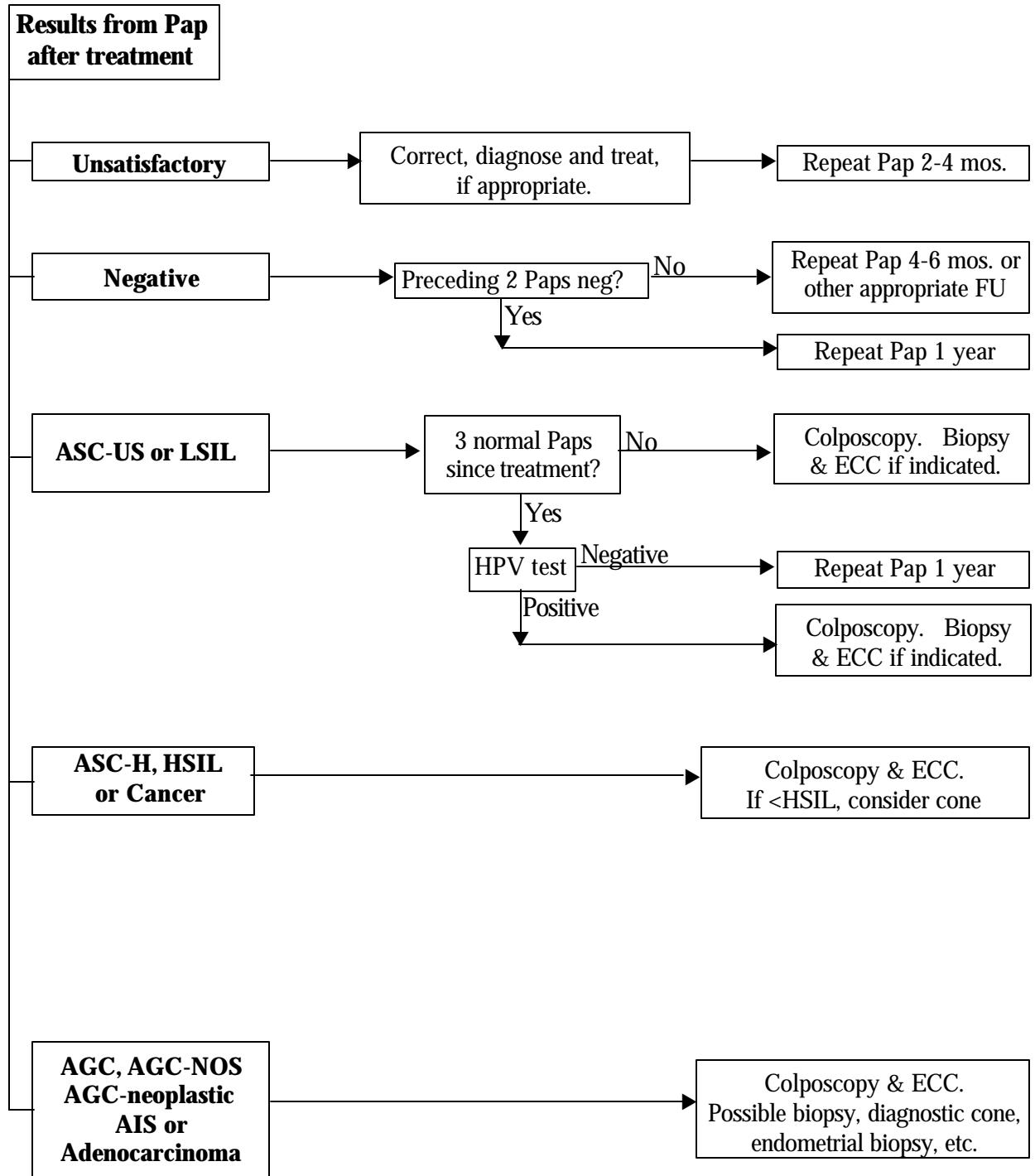
Cervical Care Algorithm for Women



Cervical Care Algorithm for Women -page 2



Cervical Care Algorithm for Women with history of biopsy proven HSIL (CIN-2/CIN-3)



MBCHP Program Indicators and Policies

PROGRAM INDICATORS :

The MBCHP Program strives to meet CDC's Timeliness and Adequacy Performance Indicators. The indicators are:

1. Median days between abnormal Pap result and final diagnosis is less than 60 days with not more than 25% of cases over 60 days.
2. Median days between final diagnosis of CIN II, CIN III/CIS or invasive cancer of the cervix and treatment started is less than 60 days with not more than 20% of cases over 90 days.
3. Percent of abnormal Pap smears that have a complete workup with a diagnostic procedure and final diagnosis recorded is 100% (10% may be comprised of lost-to-follow-up, refused, or pending).
4. After diagnosis of CIN II, CIN III/CIS or invasive cervical cancer, the 100% of records will show treatment initiated (10% may be comprised of lost-to-follow-up, refused, or pending).

PROGRAM POLICIES :

Pap every 3 years: After a woman has had three, consecutive, normal/negative Pap tests within a 5-year (60-month) period documented in the program's MDE's (required minimum data elements collected for CDC), the Pap test shall be performed every 3 years.

Hysterectomy: funds may not be used for Pap smears in woman after a hysterectomy, including the cervix, unless the hysterectomy was for cervical neoplasia. Women who have had a hysterectomy for benign conditions are at very low risk for vaginal cancer and do not need further Pap smears. If a cervical stump remains, Pap smears should be continued on a regular (every 3 years) basis.

Never/rarely screened: at least 20% of the women enrolling in the program will not have had a Pap Smear in the last 5 years.

Liquid-Based Cytology: CDC does not permit NBCCEDP funds to be used to reimburse for liquid-based cytology above the Medicare reimbursement rate for the conventional Pap.

HPV testing: HPV testing (HC-11) has become a part of management of the ASC-US Pap test. MBHCP funds can be used for the HPV test (HPV kit or LBC) however, the liquid based cytology Pap test itself is only reimbursable at the same amount (Medicare rate) as the conventional Pap test. A return visit for HPV sampling is also reimbursable.