12/14/2020 bb

ANMC Cervical Cancer Prevention Guideline

Our system for the prevention of cervical cancer in Alaska Native people requires four elements working together.

1. Maximize uptake of HPV vaccine.
2. Regular Pap and HPV screening of people at risk for the disease.
3. Medical evaluation and management of abnormal Pap results.
4. Tracking of Pap results and treatments with patient notification.

After maximizing vaccine uptake, the system that is in place for tracking Pap tests and treatment has worked well. Facilities and providers involved in cervical cancer screening and prevention will need to continue to work together to maintain the integrity of this database that we all rely on to deliver quality care.

HPV Vaccination Recommendations:
Human papilloma virus (HPV) infections, specifically 15 high risk subtypes, are associated with cervical cancer. About 70% of cervical cancers are associated with HPV genotypes 16 and 18 worldwide. ANMC currently offers the 9-valent HPV vaccine, Gardasil 9. Gardasil 9 protects against oncogenic genotypes16, 18, 31, 33, 45, 52, and 58, as well as 6 and 11 which are associated with condyloma. A review of ANMC colposcopy specimens showed that 95% of CIN 3 involved the Gardasil 9 genotypes.

Ideally, HPV vaccination should be given in early adolescence because vaccination is most effective before exposure to HPV through sexual activity. For adults aged 27 through 45 years who are not adequately* vaccinated, clinicians can consider discussing HPV vaccination with persons who are most likely to benefit. HPV vaccination does not need to be discussed with most adults aged >26 years.

• HPV is a very common sexually transmitted infection. Most HPV infections are transient and asymptomatic and cause no clinical problems.
• Although new HPV infections are most commonly acquired in adolescence and young adulthood, some adults are at risk for acquiring new HPV infections. At any age, having a new sex partner is a risk factor for acquiring a new HPV infection.
• Persons who are in a long-term, mutually monogamous sexual partnership are not likely to acquire a new HPV infection.
• Most sexually active adults have been exposed to some HPV types, although not necessarily all of the HPV types targeted by vaccination.
• No clinical antibody test can determine whether a person is already immune or still susceptible to any given HPV type.
• HPV vaccine efficacy is high among persons who have not been exposed to vaccine-type HPV before vaccination.
• Vaccine effectiveness might be low among persons with risk factors for HPV infection or disease (e.g., adults with multiple lifetime sex partners and likely previous infection with vaccine-type HPV), as well as among persons with certain immunocompromising conditions.
• HPV vaccines are prophylactic (i.e., they prevent new HPV infections). They do not prevent progression of HPV infection to disease, decrease time to clearance of HPV infection, or treat HPV-related disease.

CDC Advisory Committee on Immunization Practices

Children and adults aged 9 through 26 years. HPV vaccination is routinely recommended at age 11 or 12 years; vaccination can be given starting at age 9 years. Catch-up HPV vaccination is recommended for all persons through age 26 years who are not adequately vaccinated.†

Adults aged >26 years. Catch-up HPV vaccination is not recommended for all adults aged >26 years. Instead, shared clinical decision-making regarding HPV vaccination is recommended for some adults aged 27 through 45 years who are not adequately vaccinated. (Box). HPV vaccines are not licensed for use in adults aged >45 years.

Administration. Dosing schedules, intervals, and definitions of persons considered adequately vaccinated have not changed (*3*). No prevaccination testing (e.g., Pap or HPV testing) is recommended to establish the appropriateness of HPV vaccination.

Special populations and medical conditions. These recommendations for children and adults aged 9 through 26 years and for adults aged >26 years apply to all persons, regardless of behavioral or medical risk factors for HPV infection or disease. For persons who are pregnant, HPV vaccination should be delayed until after pregnancy; however, pregnancy testing is not needed before vaccination. Persons who are breastfeeding or lactating can receive HPV vaccine. Recommendations regarding HPV vaccination during pregnancy or lactation have not changed.

Two dose Schedule:

For people starting the vaccination series before the 15th birthday, the recommended schedule is 2 doses of HPV vaccine. The second dose should be given 6–12 months after the first dose (0, 6–12-month schedule).

Three dose Schedule:

CDC continues to recommend a 3-dose schedule for persons starting the HPV vaccination series on or after the 15th birthday, and for persons with certain immunocompromising conditions. The second dose should be given 1–2 months after the first dose, and the third dose should be given 6 months after the first dose (0, 1–2, 6-month schedule).

> CDC recommends 3 doses of HPV vaccine (0, 1–2, 6 months) for immunocompromised people age 9 through 26 years. People whose immune responses might be lower, for example due to HIV infection, cancer, autoimmune disease, or taking immunosuppressant medications, should receive 3 doses to make sure they get the most benefit. However, children with asthma, diabetes, and other conditions that would not suppress immune response to HPV vaccination can receive a 2-dose schedule.

Please see the CDC FAQ website for further vaccination details.
https://www.cdc.gov/hpv/hcp/2-dose/clinician-faq.html

Pap Screening Recommendations:

The Alaska Native Medical Center has adopted the recommendations from the 2019 American Society for Colposcopy and Cervical Pathology (ASCCP) Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors. By linking our guidelines to the ASCCP, we hope to remain current and to present our process in a familiar

format. We will continue to track our age-specific cervix cancer rates and periodically review our guidelines to be sure that no deviation from the national recommendations is still warranted. The OB/GYN and Pathology Departments have adopted the Lower Anogenital Squamous Terminology (LAST)/World Health Organization (WHO) recommendation for terminology of cervical histopathology reporting Low Grade (LSIL) and High Grade (HSIL) with qualifiers, ie: HSIL (CIN2) and HSIL (CIN 3).

For screening and management recommendations, the ASCCP App will be utilized to determine an individual's risk for CIN3 and recommended plan of care.

The full ASCCP Risk Based Management Consensus can be found at:

https://journals.lww.com/jlgtd/Fulltext/2020/04000/2019_ASCCP_Risk_Based_Management_Consensus.3.aspx

Risk-Based Framework

The new guidelines provide risk thresholds for clinical action (Table 1) and establish risk estimates for the development of cervical intraepithelial neoplasia grade 3 (CIN 3), adenocarcinoma in situ, or cancer (ie, CIN 3+) for different combinations of test results. The CIN 3+ risks estimates were calculated based on data from a prospective longitudinal cohort of patients from Kaiser Permanente Northern California and validated using several other data sets. Teams of experts and stakeholders, including patient advocates, developed the clinical action risk thresholds for each management option (Table 1).

Table 1. CIN 3+ Risk Thresholds for Management

Management Option	Clinical Action Threshold
Expedited treatment preferred*	≥ 60%†
Expedited treatment or colposcopy acceptable*	25% to < 60%†
Colposcopy recommended	4% to < 25%†
Repeat test in 1 year	0.55% to < 4%‡
Repeat test in 3 years	0.15% to < 0.55%‡

Management Option	Clinical Action Threshold
Return to routine screening at 5-year intervals	< 0.15%‡

*For nonpregnant patients 25 years or older.
†Refers to immediate CIN 3+ risk.
‡Refers to 5-year CIN 3+ risk.

Data from Perkins RB, Guido RS, Castle PE, Chelmow D, Einstein MH, Garcia F, et al. 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors. J Low Genit Tract Dis. 2020;24(2):102–131.

In addition to test results, CIN 3+ risk was considered for a number of individual risk factors such as screening history, age, and immunosuppression, which were reviewed by the consensus panels. One of the most important updates to the guidelines is the recognition of the importance of previous human papillomavirus (HPV) test results. New abnormal screening test results after a negative HPV test within the previous 5 years indicate new, as opposed to persistent, HPV infection. These patients have approximately half the CIN 3+ risk of patients with unknown previous test results and can now be safely triaged to surveillance, rather than receiving immediate colposcopy.

Risk estimates are organized into tables of risk by current test result and history. Decision support tools are available to help providers find the CIN 3+ risk estimate for an individual patient from the risk tables and then compare that risk to the clinical action threshold to determine the next step for the patient.

The risk database will continue to be updated as new testing methods and follow-up data emerge, and the new framework will allow management to be adjusted accordingly and consistently. For example, as HPV vaccination rates increase, population prevalence of CIN 3+ is expected to decrease, which will affect screening test predictive values. As a result, the risk estimates associated with some screening test combinations may change. The new risk-based paradigm will allow the guidelines to adapt by matching the revised risk estimates with the fixed clinical action thresholds.

HPV Genotyping
Persistent infection with human papillomavirus (HPV) is the principal cause of cervical cancer and its precursor cervical intraepithelial neoplasia (CIN).(1-3) The presence of HPV has been implicated in >99% of cervical cancers worldwide. HPV is a small, nonenveloped, double-stranded DNA virus, with a genome of approximately 8,000 nucleotides. There are more than 118 different types of HPV and approximately 40 different HPVs that can infect the human anogenital mucosa. However, data suggest that 14 of these types (HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) are considered high risk (HR) for the development of cervical cancer and its precursor lesions. Furthermore, HPV types 16 and 18 have been regarded as the genotypes most closely associated with progression to cervical cancer. HPV-16 is the most carcinogenic and is associated with approximately 60% of all cervical cancers, while HPV-18 accounts for approximately 10% to 15% of cervical cancers.

Although persistent infection with HR-HPV is necessary for the development of cervical cancer and its precursor lesions, only a very small percentage of infections progress to these disease states. Sexually transmitted infection with HPV is extremely common, with estimates of up to 75% of all women being exposed to HPV at some point. However, almost all infected women will mount an effective immune response and clear the infection within 2 years without any long-term health consequences. An infection with any HPV type can produce CIN although this also usually resolves once the HPV infection has been cleared.

Data suggest that individual genotyping for HPV types 16 and 18 can assist in determining appropriate follow-up testing and triaging women at risk for progression to cervical cancer. Studies have shown that the absolute risk of CIN-2 or worse in HPV-16 and/or HPV-18 positive women is 11.4% (95% confidence interval [CI] 8.4%-14.8%) compared with 6.1% (95% CI, 4.9%-7.2%) of women positive for "other" HR-HPV genotypes and 0.8% (95% CI, 0.3%-1.5%) in HR-HPV negative women.

Based in part on these data, the American Society for Colposcopy and Cervical Pathology (ASCCP) now recommends that HPV 16/18 genotyping be performed on women who are positive for HR-HPV, but negative by routine cytology. Women who are found to be positive for HPV-16 and/or -18 may be referred to colposcopy, while women who are negative for genotypes 16 and/or 18 may have repeat cytology and HR-HPV testing in 12 months.

The codes for the HPV genotype test that can be ordered up to 21 days post collection of liquid-based cytology are:

91414 PAP and HPV (reflexes to genotype 16,18, 18/45 when PAP -/HPV +)
91826 HPV genotypes 16, 18/45.

Special Circumstance: Ambiguous Results
It is not uncommon to have results where there is no specific guideline or evidence-based resource to direct care. In these circumstances, it is best to consult a gynecologist for a plan of care, since that plan may involve an excisional procedure for diagnosis, a continuity-based follow up plan, or a complex discussion of options with the patient.
Common examples include:

- An ECC shows dysplasia but the grade is not specified.
- A LEEP procedure has positive margins.

Special circumstances: Young people

- At ANMC, this will refer to those less than 25 years old. According to ASCCP the term "young women" also can indicate those who need to be counseled concerning the risk of excisional procedures to pregnancy outcomes, and therefore, no specific age threshold has to be placed on customer owners considering future childbearing. Any deviation from recommended guidelines, should be documented under the provider's **colposcopy** note and a detailed follow up plan should be included.
- Young people are at virtually no risk for developing cervical cancer and have a very high incidence of transient HPV infection that presents as an abnormal Pap.
- Aggressive management with colposcopy and possible excision or ablative therapy is unlikely to have any benefit and can cause significant harm. Dysplasia when found in a young person is both less likely to progress and more likely to regress than similar lesions found in an adult.
- Any Pap visit with a young person should include a review of vaccination history and an offer to start or complete the HPV vaccine series.

Special Circumstance: Menopause/ Atrophy

- ASC-US or LSIL in a postmenopausal person is often due to the effect of estrogen loss on the epithelium (atrophy), rather than HPV infection.
- If the HPV testing is negative, it is recommended that the LSIL or ASC-US Pap result be attributed to the cytologic effect of atrophy and no further diagnostic testing (ie colposcopy) for dysplasia is needed. The Pap and HPV should be repeated in 1 year.
- A diagnosis of atrophic vaginitis should be made by history and exam, including a visual exam of the vagina and a wet mount looking for squamous maturation (parabasal cells). Treatment should be offered, based on symptom relief goals.
- A short course of vaginal estrogen to treat vaginal atrophy prior to follow up co-testing is a practical option to rule out true dysplasia for patients who have no contraindication to estrogen therapy. Rx: Conjugated estrogen cream (Premarin)1gm vaginally qHS X 3wks then repeat cytology (Pap) in 1wk. If the Pap doesn't normalize with this treatment, then colposcopy should be scheduled.

Special circumstances: HIV, people who are immunocompromised, DES

- While cervical cancer is a diagnostic criterion for AIDS and cervical cancer is more common in HIV-positive people, it is rarely a cause of death for these patients.
- People who are younger than 30 living with HIV should have Pap testing (cytology only) at the time of initial diagnosis with HIV. Co-testing is not recommended for HIV-infected people younger than 30. If the initial cytology screening result is normal, the next screening should be in 12 months. If three consecutive annual screenings are normal, follow-up cervical cytology should be every 3 years.
- People who are 30 years and older should be screened with co-testing. People infected with HIV who have one negative co-test result (normal cytology and negative HPV) can have their next cervical cancer screening in 3 years.
- People with HIV infection are managed as per the ASCCP guidelines.
- No studies or major society recommendations exist to guide cervical cancer screening in people who are not HIV-infected but have other reasons to be immunocompromised. It is reasonable to use the HIV recommendations for people in this group and to start screening at age 21 or at the time of initial penetrative sexual activity.

- People who have been exposed to diethylstilbestrol should have cytology screening annually.

Special circumstances: Pregnancy

- The indications for colposcopy are not changed by pregnancy.
- Cervical biopsies are safe in pregnancy and should be done for lesions suspicious for high-grade disease or invasion. Endocervical sampling or curettage should not be done.
- Since unsatisfactory colposcopy may become satisfactory as the pregnancy progresses, it is recommended that pregnant people with an unsatisfactory colposcopy undergo a repeat exam in 6-12 weeks.
- The increased vascularity of the cervix in pregnancy may accentuate colposcopic findings.
- For Pap results including ASC-US and LSIL, a single colposcopic exam that does not suggest a high grade lesion is sufficient evaluation during pregnancy.
- For patients with HSIL cytology or colposcopic findings of high-grade dysplasia found early in pregnancy, a second evaluation can be done later in pregnancy.
- If the abnormal Pap was not completely evaluated during the pregnancy or high grade dysplasia was suspected on exam, a colposcopy should be planned for the 6 wk post-partum visit. Otherwise the patient can follow up at normal intervals.

Who Should Evaluate the Abnormal Pap Test:

Basic colposcopy privileges

Granted to providers recently trained in colposcopy, and not expert in treatment of gynecologic disease. These providers could see patients with ASC-US HPV(+) and LSIL. These two results comprise more than 90% of the patients needing colposcopy. While finding high grade dysplasia in any one of these patients is unlikely, most of the significant dysplasia will come from this group because it is so much larger than the remaining groups. The risk of CIN2/3+ for this group is 6-12%. If the provider recommends a treatment outside the guidelines, then consultation with a provider who has full colposcopy privileges is required.

Full colposcopy privileges

This is limited to providers with training and at least two years of experience in colposcopy and the management of dysplasia AND with the recommendation of the Medical Director. All colposcopies for cytology results other than ASC-US and LSIL should optimally be with a provider in this group. If the provider recommends a treatment outside the guidelines, then it is required that the provider document the reasons for the plan in the customer owner's record.

HGSIL results

The cytological HGSIL (CIN II/CIN III) result will be reviewed by a provider and management options (treatment versus colposcopy) will be discussed with the customer owner. For patients traveling to Anchorage for management of a HGSIL, an appt for a LEEP should be scheduled in the event the patient opts for treatment after in-person consultation with provider.

Colposcopy Documentation Responsibilities

Evaluate and document the following:

- Indications for colposcopy
- Past history of cervical cytology, colposcopy, treatment
- Parity
- Contraception
- Pregnancy status
- Menopausal status
- Hysterectomy status
- Smoking history
- HIV status
- HPV vaccination status

Obtain informed consent.

Examination

- Examine vulva and vagina grossly.
- Examine the cervix with multiple magnifications after application of 3%–5% acetic acid.
- Examine cervix with both white light and a red-free (blue or green) filter.
- Examine upper vagina with magnification.

Documentation

- Document findings using a diagram, photograph, or annotation if possible.
- Document:
    - cervix visibility (fully/not fully visualized)
    - SCJ visibility (fully/not fully visualized)
    - whether cervical manipulation is needed, to completely visualize the SCJ, e.g., using an applicator stick or endocervical speculum
    - colposcopic findings.
        - Aceto-whitening present (yes/no)
        - Lesion(s) present (yes/no)
        - If lesion(s) present, document extent of lesion(s) visualized (fully/not fully), lesion size and location, description (color, contour, borders, vascular changes).
    - colposcopic impression (benign–normal/LSIL/HSIL/cancer).
    - Location of biopsies if biopsies indicated,
    - Whether ECS performed and method: curettes brush or both

- Post-procedure: Document how customer owner will be notified of results and management plan. Once results are available, the customer owner will be notified and recommendations for plan of care discussed. Documentation of notification should be included as an addendum in the **colposcopy** note from that visit. A copy of this note should be forwarded to Screening and Prevention for coordination of follow up.

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APPENDIX A
Dot Phrase Examples

Colpo Visit History

Here for colposcopy

Pap/HPV/Colpo Hx:

Social Hx:
Tobacco:
Contraception:

Gyn Hx:

HPV Vaccine:

Colposcopy Exam

CONSENTS:
Consented for: exam, colposcopy, biopsies and endocervical curettage.
Discussed risks of discomfort, infection, bleeding and failure to diagnose.
Specific concern for the need for further evaluation/treatment addressed.
Benefits: diagnosis of abnormal cells or cervical cancer in an early stage.

Description of procedure:
A speculum was placed and complete visualization of the cervix and vagina was undertaken without complication. The cervix was visualized completely.
The squamocolumnar junction was _ visualized completely with manipulation. Acetic acid was placed on the cervix as well as the vagina. The green filter was utilized to view any lesions/vessels. Translucent/Dense acetowhite areas with geographic/straight borders were noted at _, _ and _ o'clock. No AV, mosaicism, or punctation noted. Biopsies were taken using the Tischler biopsy forceps at these locations. A vigorous endocervical curetting was performed in the standard manner using a Kevorkian curette, as well as the endocervical cytobrush. Silver Nitrate/Monsels was used to achieve hemostasis and the patient tolerated the procedure well.

IMP:

Colposcopy Plan:
Discussed Impression and HPV infection. Encouraged healthy lifestyle exercise, daily multivitamins and avoiding excessive ETOH, drugs or tobacco.

Will call with pathology results, follow-up to be coordinated at that time.
Post-procedure instructions given. Nothing in vagina for next 2-3 days. Brownish/black discharge is common following the use of Monsel's solution. Call if fever, pelvic pain, or significant bleeding or discharge occurs and will call if any symptoms persist
Patient given opportunity to ask questions and all questions answered. She verbalized understanding and is agreeable to the above plan of care.

Follow up one year
Discussed results with CO who agrees with recommended plan to repeat cotest in one year.

Treatment

Discussed diagnosis with CO with options and recommendations. For HSIL lesions, LEEP is preferred option. Alternatives include expectant management with colpo and cotests q 6 months. Risks and benefits of LEEP reviewed and CO agrees with this plan. Will forward to Screening and Prevention to schedule CO for next available LEEP appt.

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