Protocol for the Reporting of Anal Cytology Specimens

Version: 1.0.0.0
Protocol Posting Date: September 2023
The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

This protocol may be used for the following:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anal cytology</td>
<td>Includes cytobrush, non-cotton swab, broom, and brush collection methods</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP stained anal cytology</td>
<td></td>
</tr>
</tbody>
</table>

The following should NOT be reported using this protocol:

<table>
<thead>
<tr>
<th>Specimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-anal cytology specimens</td>
</tr>
</tbody>
</table>

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With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.
* Denotes primary author.

Accreditation Requirements
The use of this case summary is recommended for clinical care purposes but is not required for accreditation purposes. The core and conditional data elements are routinely reported. Non-core data elements are indicated with a plus sign (+) to allow for reporting information that may be of clinical value.
Summary of Changes
v 1.0.0.0

• New protocol
Reporting Template
Protocol Posting Date: September 2023
Select a single response unless otherwise indicated.

CASE SUMMARY: (ANAL CYTOLOGY)
This case summary may be useful for clinical care purposes but is not required for accreditation purposes. Core data elements are bolded to help identify routinely reported elements. (Note A)

PATIENT INFORMATION

Age: _________________

Gender (Note B)
___ Male
___ Female
___ Other (specify): _________________

Collection Date: _________________

Prescription Drugs (select all that apply)
___ None
___ Unknown
___ Hormone replacement therapy (estrogen / progesterone)
___ Androgen therapy
___ Immunosuppressive therapy (other than chemotherapy)
___ Chemotherapeutic agents
___ Other (specify): _________________

Clinical History (select all that apply)
___ Unknown
___ Pregnant
___ Anal receptive intercourse (including MSM)
___ Genital warts
___ Prior radiation therapy
___ Anorectal bleeding
___ Transplant
Select all that apply
___ Solid organ: _________________
___ Bone marrow
___ Other immunocompromised conditions (specify): _________________
___ Other (specify): _________________

History of Anorectal and Perianal Dysplasia or Malignancy
___ Unknown
___ Negative
___ Positive
Select all that apply
___ Dysplasia, NOS
___ Low-grade squamous intraepithelial lesion (LSIL / AIN1)
___ High-grade squamous intraepithelial lesion (HSIL / AIN2-3)
___ Squamous cell carcinoma
___ Carcinoma, NOS
___ Other (specify): ___________________

**History of Other Lower Urogenital Tract Dysplasia or Malignancy**
___ Unknown
___ Negative
___ Positive (specify site): ___________________

*Select all that apply*
___ Dysplasia, NOS
___ Condyloma acuminatum
___ Low-grade squamous intraepithelial lesion (LSIL)
___ High-grade squamous intraepithelial lesion (HSIL)
___ Squamous cell carcinoma
___ Endocervical adenocarcinoma in situ (AIS)
___ Endocervical adenocarcinoma, invasive
___ Carcinoma, NOS
___ Other (specify): ___________________

**High-Risk Human Papillomavirus (HPV) History (select all that apply)**
___ Not performed
___ Unknown
___ Negative
___ Positive for high risk
___ Positive for genotype 16
___ Positive for genotype 18
___ Positive for genotype 16/18
___ Positive for genotype 18/45
___ Other high-risk types (specify, if known): ___________________
___ Date of first positive (specify, if available): ___________________
___ Date of most recent HPV testing: ___________________

**HPV Vaccination History (Note C)**
___ Unknown
___ Unvaccinated
___ Vaccinated

*Select all that apply*
+ ___ Completed
+ ___ Incomplete
+ ___ Quadravalent
+ ___ Nonavalent
+ ___ Other (specify): ___________________

**Human Immunodeficiency Virus (HIV) Status (Note D)**
___ Unknown
___ Negative
___ Positive
___ Positive but undetected
PREANALYTICAL EXAMINATION OF THE SPECIMEN

Source
___ Anorectal, clinician-collected
___ Anorectal, self-collected
___ Other (specify): _________________

+Sampling Device
___ Broom
___ Brush
___ Spatula
___ Swab
___ Unknown
___ Other (specify): _________________

Test(s) Ordered
___ Anal Pap test only
___ Anal Pap test with concurrent HPV test
___ HPV test following abnormal diagnosis

Gross Description (select all that apply)
___ Number of conventional smear slides: _________________
___ Liquid-based in fixative
___ Color (specify): _________________
   Approximate Volume in Milliliters (ml): _________________ ml
___ Other (specify): _________________

Preparation Type
___ Conventional
___ Liquid-based ThinPrep
___ Liquid-based SurePath
___ Other (specify): _________________

Number of Slides Prepared (specify): _________________

INTERPRETATION

Specimen Adequacy (Note E)
___ Satisfactory for evaluation
___ Unsatisfactory for evaluation
___ Processed and examined
   Select all that apply
     ___ Insufficient nucleated squamous cellularity
     ___ Obscuring blood
     ___ Obscuring inflammation
     ___ Obscuring acellular material
     ___ Other (specify): _________________
     ___ Not processed (explain): _________________
Quality Indicators
___ Transformation zone present
___ Transformation zone absent
___ Not applicable
___ Cannot be determined

Results (select all that apply)
___ Negative for intraepithelial lesion or malignancy (NILM)
___ Squamous cell abnormalities
  ___ Atypical squamous cells - undetermined significance (ASC-US)
  ___ Atypical squamous cells cannot exclude HSIL (ASC-H)
  ___ Low-grade squamous intraepithelial lesion (LSIL)
  ___ High-grade squamous intraepithelial lesion (HSIL)
  ___ High-grade squamous intraepithelial lesion (HSIL) with features suspicious for invasion
  ___ Squamous cell carcinoma
  ___ Other (specify):
___ Glandular cell abnormalities
  ___ Atypical glandular cells
  ___ Adenocarcinoma
  ___ Other (specify):
  ___ Other malignant neoplasms (specify):

+Other Significant Findings (select all that apply)
___ Amoeba species
___ Trichomonas vaginalis
___ Fungal organisms morphologically consistent with Candida species
___ Enterobius vermicularis (pinworm)
___ Cellular changes consistent with herpes simplex virus
___ Cellular changes consistent with cytomegalovirus
___ Inflammation (includes typical repair)
___ Therapy related change (radiation):
___ Other (specify):

ANCILLARY TESTING
Please complete all available test results associated with the current Pap test

HR-HPV (select all that apply)
___ Not performed
___ Negative
___ Positive, NOS
___ Positive for genotype 16
___ Positive for genotype 18
___ Positive for genotype 18/45
___ Positive for other high-risk types (specify):
___ Positive for unknown subtype
___ Pending at the time of cytologic evaluation
HR-HPV Test Platform
___ BD Onclarity TM HPV Assay
___ Hologic Cervista
___ Hologic Aptima
___ Qiagen Digene Hybrid Capture 2 (HC2)
___ Roche cobas 4800
___ Roche cobas 6800/8800
___ Laboratory-developed method
   ___ DNA
   ___ RNA
   ___ Other (specify): _________________
___ Other (specify): _________________

+Neisseria gonorrhoeae
___ Negative
___ Positive

+Chlamydia trachomatis
___ Negative
___ Positive

+Trichomonas vaginalis
___ Negative
___ Positive

+Treponema pallidum
___ Negative
___ Positive

+Herpes Simplex Virus (HSV) (select all that apply)
___ Negative
___ Positive, NOS
___ Positive for HSV-1
___ Positive for HSV-2

+Immunocytochemistry (select all that apply)
___ p16: _________________
___ Ki-67: _________________
___ Other (specify): _________________

Other Tests Performed (specify): _________________

+Concurrent Biopsy
___ Yes
___ No

COMMENTS
Comment(s): _________________
Explanatory Notes

A. Introduction
The aim of this protocol is to improve the completeness, clarity, and portability of Anal Pap test reporting, while being mindful of the wide range of practice settings in which the data in the report is generated and disseminated. This report includes terminology from the Bethesda System for Reporting Cervical Cytology as anal cytology is backed by our knowledge of HPV infection in the cervix.1,2 That terminology is widely used and standardized 3-4. Although there are no well-established screening and management guidelines, this protocol incorporates clinical and ancillary testing results that have been already incorporated in daily practice.5-7. It also takes into consideration the introduction of additional testing modalities in the future.

The protocol is based upon input from present members of the CAP Cytopathology Committee and prepared in conjunction with the CAP Pathology Electronic Reporting Committee.

This reporting format is meant to replace the final report and will be adapted to laboratory information systems to facilitate utilization and provide more easily reproducible and extractable data. The construction of this protocol does allow for the insertion of pertinent additional information when available. It may be used as a guide for trainees and pathologists who may only perform a limited number of Anal Pap tests in their practice. The committee hopes this is a first step in providing a general framework for more standardized quality Anal Pap test reporting practice.

The content of the protocol represents the consensus opinion of the CAP Cytopathology Committee and the CAP Pathology Electronic Reporting Committee. It is the Committees’ recommendation that all available elements be included.

References

B. Gender
In anal cancer screening, it is important to recognize the importance of using inclusive gender terminology within the pathology report. Individuals at risk for anal cancer may identify as women, men, or other non-binary or gender fluid terms. Pathology reports should avoid gendered terminologies unless the patient is known to identify with those terminologies.
Patients at risk of anal cancer include all genders. Evidence specific to anal cancer risks in transgender and non-binary patients is limited given the lack of available information in national databases.1 Men who have sex with men are at increased risk of anal cancer; however, this risk is not uniform to all patients who engage in anal receptive intercourse. In cisgender women with cervical HPV infection, anal receptive intercourse is not associated with an increased risk of anal HPV, and the approach to screening should not be limited to patients with a history of anal receptive intercourse.2

Laboratory information systems should accurately convey the patient’s gender identity on reports. At minimum, a nonbinary option is recommended to be included, ideally allowing the patient to self-describe their gender identity. Laboratory information systems may also record the sex assigned at birth, which would be kept separately from the gender identity.3 Ideally, patients would be offered the opportunity to update this information at any time they choose, such as through an online patient portal or at appointments. If pronouns are used in the pathology report, “they/them/their” pronouns are recommended if patient-identified pronouns are not indicated.

References

C. Human Papillomavirus (HPV) Vaccination
Human papillomavirus (HPV) is a common sexually transmitted viral infection that affects multiple sites. For both sexes, it causes cancer of the anus and oropharynx. In females, the virus causes cancer of the cervix, vulva, and vagina. In males, it causes cancer of the penis. Infection also causes benign lesions, such as anogenital warts and respiratory papillomatosis. Although there are many types of HPV, studies have identified key genotypes associated with disease. HPV 16 and 18 are the two most common genotypes associated with HPV-related cancers and are considered high risk types.

Currently, there are three vaccines approved by the United States Food and Drug Administration. 9-Nonavalent, (Gardasil 9, 9vHPV), quadrivalent, (Gardasil, 4vHPV), and bivalent (Cervarix, 2vHPV).1 All three vaccines protect against high-risk HPV types 16 and 18 with specific targets to the L1 protein. Quadrivalent vaccine includes additional targets to HPV 6, and 11. Nonavalent vaccine includes additional targets to HPV 6, 11, 31, 33, 45, 52, and 58. Currently, only nonavalent vaccine is distributed in the United States. Both bivalent and 9-valent vaccines are distributed in Canada and all three are distributed in Europe.2

The recommended dosing for the vaccination is based on the patient’s age at administration and patient’s history.3 Two doses are required for patients who received the first dose before their 15th birthday. Three doses are required for a) patients who received two doses less than 5 months apart when they were between 9-14 years old OR b) patients are between 9-26 years old with weakened immune systems. Vaccination is not recommended for patients older than 26 years old.

References


D. Human Immunodeficiency Virus (HIV)

Human immunodeficiency virus (HIV) is a lentivirus that attacks the immune system. The virus destroys CD4 positive T-cells, a subset of lymphocytes, that are a key component of the immune system. Although there is currently no cure, treatment of HIV with antiretroviral therapy can lead to long term suppression of the virus. Left untreated, viral loads increase over time, and the disease progresses to the most advanced stage, acquired immunodeficiency syndrome (AIDS). AIDS is also the stage during which HIV is most easily transmitted to other people.¹

Because of their weakened immune systems, patients with HIV are at an increased risk of contracting other infections and developing cancers. Opportunistic infections are those infections that occur more easily and progress more rapidly and extensively in immunocompromised individuals compared to those with an intact immune system. A few examples of opportunistic infections in HIV patients are Pneumocystis, Candidiasis, Mycobacterial organisms (tuberculous and atypical Mycobacterial infections), and Coccidiomycosis. HIV patients are at elevated risk for cancers, such as lymphoma and Kaposi sarcoma.²

Human papillomavirus infection (HPV) is the most common sexually transmitted infection. HPV infection in the anal region can cause benign genital warts, precancerous lesions, or anal cancers. Anal screening in HIV patients is strongly recommended due to their increased risk of infection and cancer from HPV.³

References


E. Specimen Adequacy

The criteria for specimen adequacy of anal cytology samples are based on the Bethesda System recommendations.¹ For conventional smears, the minimal cellularity required for an adequate sample is approximately 2,000-3,000 nucleated squamous cells (NSC). For evaluating the adequacy of liquid-based preparations, the average number of NSC per high-power field (HPF) is estimated and varies with the type of preparation and the optical parameters of the microscope. For ThinPrep (Hologic, Marlborough, MA), an average of 1-2 NSC per HPF and for SurePath (Beckton Dickinson, Franklin Lakes, NJ), an average of 3-6 NSC per HPF correspond to the conventional smear requirement and are considered satisfactory. Specimens that are predominantly composed of anucleated squames without the minimal required number of NSC, should be designated as unsatisfactory.

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Similar to cervical cytology, the presence of a transformation zone (TZ) component (i.e., at least ten rectal columnar cells/squamous metaplastic cells in this scenario) is not a requirement for deeming an anal cytology sample adequate. However, the presence of the TZ component does signify sampling of the anal
canal above its keratinized portion and is utilized as a quality indicator. The significance of the presence of the TZ component has been variably reported in literature. In a study involving conventional smears, the absence of rectal columnar cells in the sample did not impact the sensitivity, specificity, or predictive value of anal cytology. However, in a relatively recent study based on the evaluation of ThinPrep, the lack of the TZ component was associated with a significantly higher number of false-negative results. Obscuring factors such as fecal material, lubricant, bacteria and inflammation may interfere with the evaluation of an anal cytology sample and if the majority of the cells are obscured and the required minimal NSC cellularity cannot be well visualized, the specimen should be considered unsatisfactory. It is also important to note that any atypia encountered in the specimen makes it adequate regardless of the number of NSC.

References