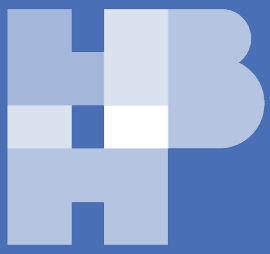

Howard Brown Health

Anal Dysplasia Screening Guidelines

Gary Bucher et al.

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ABOUT HOWARD BROWN HEALTH

Howard Brown Health (Howard Brown) is a national center of excellence for sexual health and HIV/STI treatment and prevention, primary care, research and advocacy. One of the nation's largest lesbian, gay, bisexual, transgender, and queer (LGBTQ) organizations and a Federally Qualified Community Health Center, Howard Brown serves 35,000 adults and youth through its health and social service delivery system located across the diverse neighborhoods of Chicago. The overarching mission of Howard Brown is to eliminate the disparities in healthcare experienced by LGBTQ people through research, education, and the provision of services that promote health and wellness.

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Summary:
Anal cancer incidence has been increasing for several years and disproportionality impacts people living with HIV; people with a history of cancer of the cervix, vagina, or vulva; people who have receptive anal intercourse or play with multiple partners; and people who have chronic HPV. It is estimated that about 4,300 new cases of HPV-associated anal cancers are diagnosed in women and about 2,200 are diagnosed in men each year in the United States. The screening, early detection, and treatment of anal dysplasia and anal cancer has the potential to significantly improve morbidity and mortality as early detection can facilitate a cure. However, the question of who should be screened for anal cancer remains controversial and formal screening guidelines have not been widely adopted. In response to this, Howard Brown has developed these screening guidelines as a tool to identify patients who are more likely to benefit from anal dysplasia screening using the best available evidence. This guideline also includes billing and lab coding considerations as an additional resource for medical providers.

Definitions:

Anal cytology (aCyt) - this test may also be known as anal rectal cytology (ARC) or anal Pap smear. This test detects cellular morphology changes associated with HPV-related lesions and cancers and is usually interpreted by a cytotechnologist or cytopathologist.

Atypical cells of undetermined significance (ASCUS) - inflammatory, reactive, and reparative processes which are atypical and of higher level and insufficient to be classified as cervical intraepithelial lesions (CIN).

Atypical squamous cells, cannot exclude high-grade lesion (ASC-H) - denotes changes suggestive, but inconclusive for, a squamous intraepithelial lesion.

Combined modality therapy (CMT) - the treatment of a disease or condition by several different means simultaneously or sequentially.

Digital anal rectal exam (DARE) - examination by a clinician that includes the following: 1) a perianal visual examination of the skin and external anus and 2) a lubricated finger is inserted into the anus and the clinician palpates for abnormalities such as masses or areas of induration.

Examination under anesthesia (EUA) - examination of a patient while they are under anesthesia.

High resolution anoscopy (HRA) - examination of anorectal tissue under magnification to identify abnormal areas.

High-grade squamous intra-epithelial lesion (HSIL) - a squamous cell abnormality associated with human papillomavirus (HPV).

Low-grade squamous intra-epithelial lesion (LSIL) - a mild squamous cell abnormality associated with human papillomavirus (HPV).

Rectal high-risk HPV (rHRHPV) test - detects the presence of mRNA E6/E7 from 14 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68).

Anal Dysplasia Screening Recommendations:

1. Persons living with HIV who are less than 30 years of age should be screened annually with a Digital Anal Rectal Exam.
2. Persons living with HIV at age 30 and above should be screened annually with anal cytology, DNA test for rectal high-risk HPV, and a Digital Anal Rectal Exam.
3. Persons of any age with a history of cancer of the cervix, vagina, and/or vulva should be screened immediately after diagnosis and then annually. Screening should include anal cytology, DNA test for rectal high-risk HPV, and a Digital Anal Rectal Exam.
4. Persons at age 30 and above with a history of high-grade squamous intra-epithelial lesions (HSIL) of the cervix, vagina, and/or vulva should be screened annually with anal cytology, DNA test for rectal high-risk HPV, and a Digital Anal Rectal Exam.
5. HIV negative persons at 40 years of age and above and who have regular anoreceptive penetrative sex or anoreceptive play with multiple partners should be screened annually. Screening should include anal cytology, DNA test for rectal high-risk HPV, and a Digital Anal Rectal Exam.
6. Persons who are recipients of solid organ transplants should be screened annually starting 2 to 5 years post-transplant. Screening should include anal cytology, DNA test for rectal high-risk HPV, and a Digital Anal Rectal Exam.

Additional Considerations

Patient history of anogenital warts or cigarette smoking may help with identifying risk but in and of itself is not an indication for anal dysplasia screening.

There must be a reliable provider that performs HRAs that accepts referrals from your institution before rCyt or rHRHPV is offered to patients.

When to Refer to High Resolution Anoscopy (HRA) Provider

If any anal cytology result is abnormal (ASCUS, ASC-H, LSIL, or HSIL), the DNA test result for rectal high-risk HPV is positive, or the Digital Anal Rectal Exam is abnormal, the patient should be referred to a HRA provider for high-resolution anoscopy (HRA) and subsequent screening.

If the result states that “Specimen is adequate for evaluation,” even if the transformation zone is not present, that is a good result. If it does not say that, then the collection must be repeated.

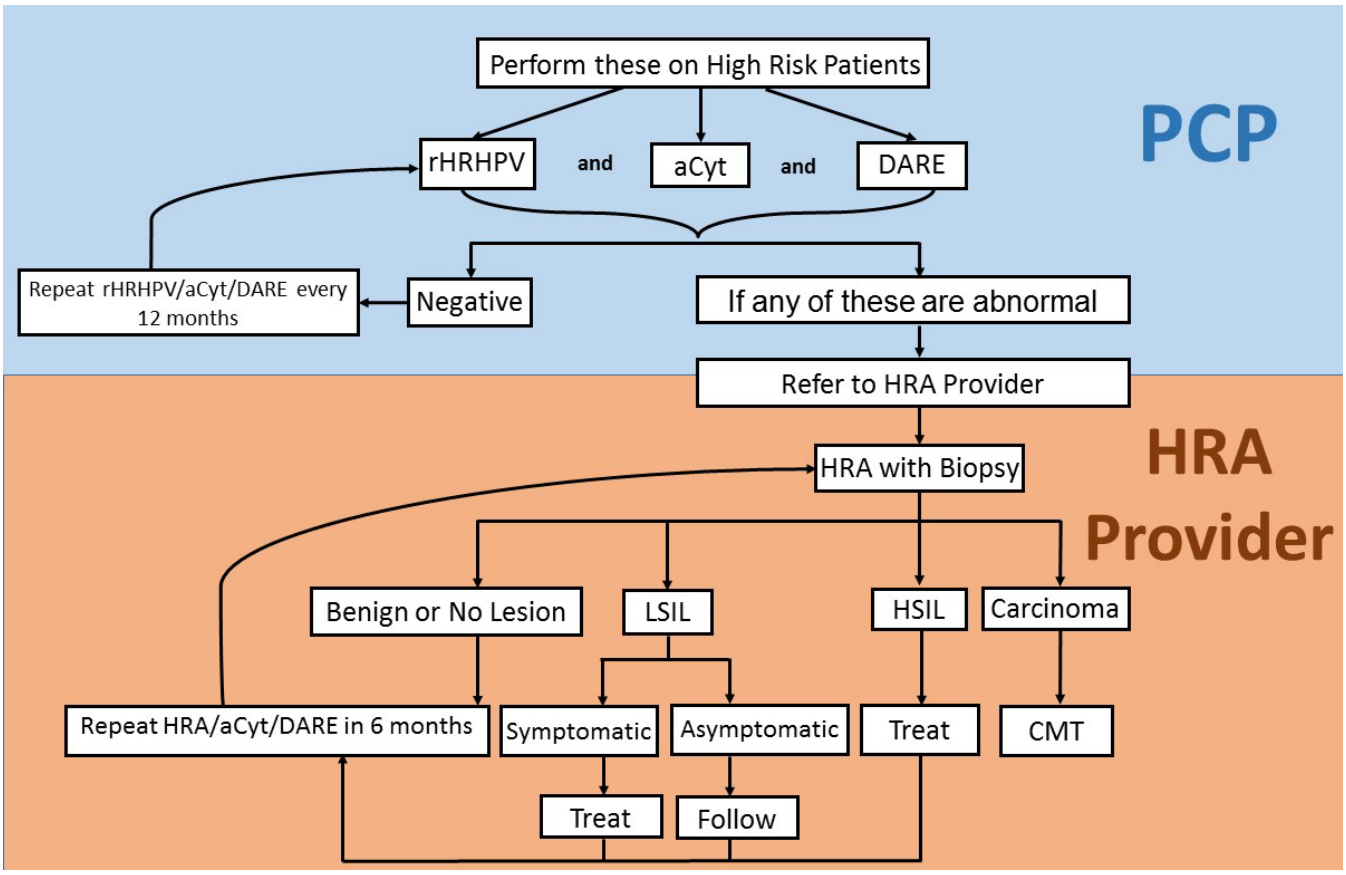
Anal Dysplasia Screening Guidelines

Anal Dysplasia Screening Guidelines by High Risk Group		
Age	**Recommended Screening**	**Frequency**
HIV Positive		
Under 30	DARE	Annually
30 and above	aCyt, rHRHPV, DARE	Annually
HIV Negative, Having Anoreceptive Sex or Play with Multiple Partners		
40 and above	aCyt, rHRHPV, DARE	Annually
History of cancer of the Cervix, Vagina, or Vulva		
Any	aCyt, rHRHPV, DARE	At time of diagnosis and annually
History of HSIL of the Cervix, Vagina, or Vulva		
30 and above	aCyt, rHRHPV, DARE	At time of diagnosis and annually
Solid Organ Transplant Recipients		
Any	aCyt, rHRHPV, DARE	2-5 years post-transplant and annually

Abbreviation Key

aCyt: Anal cytology testing
DARE: Digital anal rectal exam
rHRHPV: Rectal high-risk HPV testing

Anal Dysplasia Screening Workflow



Abbreviation Key

aCyt: Anal cytology testing
DARE: Digital anal rectal exam
HRA: High resolution anoscopy
HSIL: High-grade squamous intra-epithelial lesion
LSIL: Low-grade squamous intra-epithelial lesion
CMT: Combined modality therapy
rHRHPV: Rectal high-risk HPV testing

Additional Notes

If the result states that “Specimen is adequate for evaluation” even if the transformation zone is not present, that is a good result. If it does not say that then the collection must be repeated.

There must be a reliable provider that performs HRAs that accepts referrals from your institution before rCyt or rHRHPV is offered to patients.

Summary of Current Anal Dysplasia Screening Recommendations

American Society of Colon and Rectal Surgeons

- Consider screening with anal cytology (or anal Pap) in high-risk populations as part of a comprehensive screening program (Grade 2B: Weak recommendation based on moderate-quality evidence).
- HPV testing may be used as an adjunct to screening for anal cancer (Grade 2B: Weak recommendation based on moderate-quality evidence).
- HRA may be considered as a screening option for patients at high risk for anal cancer when performed by clinicians with appropriate training in the procedure (Grade 2B: Weak recommendation based on moderate-quality evidence).
- Persons with anal dysplasia should be followed at regular intervals with a history, physical exam, and a discussion of screening/testing options (Grade 2B; Weak recommendation based on moderate-quality evidence).
- Topical imiquimod, 5-fluorouracil, trichloroacetic acid and cidofovir with close long-term follow-up are all options for the treatment of LSIL or HSIL (Grade 2B: Weak recommendation based on moderate-quality evidence).
- Ablative treatments with conventional anoscopy or HRA are also appropriate therapies for HSIL (Grade 2B: Weak recommendation based on moderate-quality evidence). [1]

The Department of Health and Human Services (DHHS) Panel Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents 2018:

- Some specialists recommend anal cytology screening or HRA for HIV-positive men and women (CIII i.e. optional recommendation for the statement and expert opinion).
- An annual anal digital rectal examination may be useful to detect masses on palpation that could be anal cancer (BIII i.e. Moderate recommendation for the statement and expert opinion).
- Screening for anal cancer should not be done without the availability of referral for HRA.
- If anal cytology is performed and indicates ASCUS, ASC-H, LSIL or HSIL, then it should be followed by HRA (BIII recommendation i.e. Moderate recommendation for the statement and expert opinion).
- Visible lesions should be biopsied to determine the level of histologic changes and to rule out invasive cancer (BIII recommendation i.e. Moderate recommendation for the statement and expert opinion).
- They state no adequate randomized controlled trials have been reported in the treatment of HSIL to prevent anal cancer. Treatment decisions are based on assessment of the size and location of the lesion and its histologic grade. They state all treatment modalities are associated with high rates of recurrence.

In addition to these two national organizations recommendations, the clinical guidelines published in October 2011 by the Veterans Administration, “Primary Care of Veterans with HIV,” recommends all patients with abnormal anal cytology of any degree be referred for HRA and biopsy.

Also, the New York State AIDS Institute in July 2007 incorporated HRA evaluation and treatment of HSIL. It recommends patients receive posttreatment serial monitoring with HRA.

An expert panel recently published anal cancer screening recommendations for women in the Journal of Lower Genital Tract Disease (J Lower Gen Tract Dis 2015; 19:S27-S42).[2]

Women living with HIV:

- Screening for anal cancer with DARE and routine assessment for the development or change in anal cancer symptoms such as pain or bleeding that might suggest cancer, with prompt referrals if positive for either.
- Given this population's high incidence of anal cancer, some experts recommend routine screening for, and treatment of, AIN2/3 in this population in an effort to reduce their risk of anal cancer.
- Screening may include anal cytology with referral for HRA-guided biopsies, followed by treatment of biopsy-proven AIN2/3.

Women with organ transplants, systemic lupus erythematosus or Crohn disease
AFAB with vulvar cancer or high-grade VIN and/or AFAB persons with cervical or vaginal cancer or high-grade CIN or VaIN:

- Screening for anal cancer with DARE and routine assessment for the development or change in anal cancer symptoms such as pain or bleeding that might suggest cancer, with prompt referrals, if positive, for either.
- Further research is recommended on screening for, and treating, AIN2/3 to reduce the risk of anal cancer in this population.

Women with none of the risk factors above:

- No screening for anal cancer or AIN2/3 is recommended at this time. Prompt referral for further diagnostic work-up if symptoms of anal cancer (pain and bleeding) are present.

[2] These recommendations are likely inclusive of cisgender women and people assigned female at birth (AFAB), it is unclear if TGNC patients were considered in the design of the recommendation. These recommendations on screening are predicated that HRA and HRA-guided treatment are available.

Coding Considerations for Screening Anal Cytology and/or Rectal HR HPV

Tests for screening purposes that are performed in the absence of signs, symptoms, complaints, or personal history of disease or injury may not be covered by payors except as explicitly authorized by statute. A claim for a diagnostic laboratory service must include a valid ICD-10 diagnosis code. When a diagnosis has not been established by a provider, ICD-10 codes that describe symptoms and signs, as opposed to diagnosis, can be considered. The following ICD-10 codes should be considered for aCyt and rHRHPV:

ICD-10 Signs/Symptoms/Complaints Codes

- K62.5- Anal bleeding (Hemorrhage of anus and rectum)
- K62.89- Anal pain (i.e. in general or with BM or with anoreceptive sex), Anal irritation, Anal burning (other specified diseases of anus and rectum)
- L29.0- Anal itching (Anal Pruritus)
- K62.9- Disease of anus and rectum, unspecified
- K59.4- Anal spasm
- D48.5- Neoplasm of uncertain behavior of skin

ICD-10 Diagnosis Codes

- K62.82- Dysplasia of anus
- A63.0- Anogenital warts
- D01.3- Carcinoma in situ (CIS) of anus and anal canal
- D04.5- Carcinoma in situ (CIS) of perianus and anal margin
- R85610- ASCUS
- R85.611- ASC-H
- R85.612- LSIL
- R85.613- HSIL
- R85.614- Cytologic evidence of malignancy on smear of anus
- R85.81- Anal HR HPV DNA test positive
- B97.7- HR HPV and/or LR HPV of the anal canal
- C21.1- Malignant neoplasm of the anal canal
- C44.529- SCCA of perianus and anal margin
- D12.9- Benign neoplasm of anus and anal canal
- K62.0- Anal polyp
- K60.0- Acute anal fissure
- K60.2- Anal fissure, unspecified
- K60.3- Anal fistula

Instructions Regarding Anal Dysplasia Screening

The order of collection and procedures should be as follows:

1. Anal cytology screening collection
2. Rectal high-risk HPV screening collection
3. Gonorrhea /chlamydia RNA swab collection if STI screening is indicated
4. Digital anal rectal examination

Please counsel patient that several swabs will be collected.

The anal cytology test swab should be collected first with the rectal high-risk HPV swap collected second. These need to be collected separately and the cells dispersed into separate ThinPrEP vials. If screening for gonorrhea and chlamydia, this should be done after the collection of anal cytology and rectal high-risk HPV. A digital rectal examination is performed last.

Anal Cytology & Rectal High-Risk HPV Collection Instructions

To collect anal-rectal samples, a wet non-lubricated Dacron swab is used.

1. The Dacron swab is inserted about 3 cm (or until resistance is met) into the anal canal past the anal verge, into the rectal vault. This is done without visualization of the anal canal.

2. Firm lateral pressure is applied to the swab handle as it is rotated and slowly withdrawn from the anal canal, inscribing a cone- shaped arc. The collection should be approximately 20 seconds for each swab.

3. Swish the swab vigorously in PreservCyt® fluid in the ThinPrep® vial for 15 to 20 seconds.

4. Discard the swab.

5. Cap and tighten the ThinPrep® vial.

6. This first collection will be labeled as aCyt, anal collection.

7. If an rHRHPV is being collected as well, the procedure is repeated from step 1 through 5 in a second ThinPrep® vial and labelled rHRHPV anal sample

Additional Collection Notes:

- DO NOT USE a brush to collect anal-rectal samples.
- DO NOT USE ANY cotton swabs for aCyt or rHRHPV testing.
- A swab that is excessively contaminated with feces can be used.

Digital Anal Rectal Exam Instructions

Possible Positions

Standing: patient standing with toes pointing in, then leans over a table.
Knee to chest: patient with lying on table facing down with knees up to chest bent forward.

Perianal Visual Exam

Visual examine the skin and external anus. Look for external hemorrhoids, fissures, skin tags, warts, or discharge.

Palpate Rectum and Prostate

1. Use a small amount of lubricant on the index finger and place your finger at the anus and wait for reflex sphincter relaxation.

2. Ask the patient to take a deep breath and gently insert your finger facing down.

3. Evaluate the external sphincter tone then ask the patient to bear down and feel for tightening of the sphincter.

4. If the patient has a prostate, palpate the prostate gland. Note the following:
    - Approximate size, shape, and consistency of the prostate
    - Tenderness
    - Nodules or masses

5. Palpate the rectal wall starting from the 6 o'clock position clockwise to the 12 o'clock position. Then return to the 6 o'clock position and palpate the other half of the rectal wall feeling for masses, nodules and tenderness.

6. Note rectal contents.

7. Remove finger and evaluate the feces on the gloved finger.

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