



Anal squamous intraepithelial lesions: Diagnosis, screening, prevention, and treatment

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INTRODUCTION

The anal and cervical canal share embryologic, histologic, and pathologic characteristics. Both develop from the embryonic cloacal membrane, and are sites of fusions of endodermal and ectodermal tissue to form a squamocolumnar epithelial junction. Both areas may display normal metaplastic change and abnormal dysplastic change related to infection with human papillomavirus (HPV) (figure 1). (See "Virology of human papillomavirus infections and the link to cancer".)

The pathology, risk factors, clinical manifestations, screening, prevention, and treatment of anal SIL are discussed here. Anal cancer is discussed separately. (See "Clinical features, staging, and treatment of anal cancer".)

NOMENCLATURE

The classification of lower genital tract squamous terminology for HPV associated lesions has recently been re-evaluated with consensus reached that there will be a single set of diagnostic terms for the lower anogenital tract (LAT). A two tiered nomenclature is recommended for HPV associated squamous proliferations of the LAT, with low-grade and high-grade squamous intraepithelial lesions (LSIL and HSIL respectively), that may be further classified to intraepithelial neoplasia (IN) of the cervix, vulva, vagina, penis and anus to grade 1, 2, or 3. For example, AIN 1 corresponds to anal LSIL, and AIN 2 and 3 to anal HSIL [1].

The biologic consequences of anal SIL, are considered analogous to those of cervical SIL. Anal HSIL, corresponding to AIN grade 2 or 3, is considered premalignant and may progress to anal cancer, similar to the progression of cervical HSIL to cervical cancer [2]. Anal LSIL, corresponding to AIN 1, is not considered to be a direct precursor of anal cancer, but may progress to HSIL [3]. (See "Invasive cervical cancer: Epidemiology, risk factors, clinical manifestations, and diagnosis".)

PATHOLOGY

Anal SIL and the histopathologic manifestations of HPV infection are most apparent at the anal transition zone (ATZ) where rectal columnar epithelium and anal squamous epithelium meet (figure 2) [2]. Anal SIL and cervical SIL share cytopathologic features, and both anal and cervical cytology are described using the 2001 Bethesda classification system (table 1). Cytologic changes are reported, in increasing severity, as atypical squamous cells of undetermined significance (ASC-US), LSIL, ASC-suggestive of HSIL (ASC-H), and HSIL [4]. A diagnosis of atypical squamous cells cannot rule out the presence of a higher grade lesion. (See "Cervical intraepithelial neoplasia: Terminology, incidence, pathogenesis, and prevention".)

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References

▲ Тор

- Darragh TM, Colgan TJ, Thomas Cox J, et al. The Lower Anogenital Squamous Terminology Standardization project for HPV-associated lesions: background and consensus recommendations from the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology. Int J Gynecol Pathol 2013; 32:76.
- Palefsky JM. Anal human papillomavirus infection and anal cancer in HIV-positive individuals: an emerging problem. AIDS 1994; 8:283.
- 3. Berry JM, Jay N, Cranston RD, et al. Progression of anal high-grade squamous intraepithelial lesions to invasive anal cancer among HIV-infected men who have sex with men. Int J Cancer 2014; 134:1147.
- Solomon D, Davey D, Kurman R, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA 2002; 287:2114.
- 5. Palefsky JM, Holly EA. Molecular virology and epidemiology of human papillomavirus and cervical cancer. Cancer Epidemiol Biomarkers Prev 1995; 4:415.
- 6. Palefsky JM, Holly EA, Ralston ML, et al. High incidence of anal high-grade squamous intra-epithelial lesions among HIV-positive and HIV-negative homosexual and bisexual men. AIDS 1998; 12:495.
- Palefsky JM, Holly EA, Hogeboom CJ, et al. Virologic, immunologic, and clinical parameters in the incidence and progression of anal squamous intraepithelial lesions in HIV-positive and HIV-negative homosexual men. J Acquir Immune Defic Syndr Hum Retrovirol 1998; 17:314.
- Palefsky JM. Cutaneous and genital HPV-associated lesions in HIV-infected patients. Clin Dermatol 1997; 15:439
- 9. Arends MJ, Buckley CH, Wells M. Aetiology, pathogenesis, and pathology of cervical neoplasia. J Clin Pathol 1998; 51:96.
- 10. Palefsky JM, Holly EA, Ralston ML, et al. Anal squamous intraepithelial lesions in HIV-positive and

- HIV-negative homosexual and bisexual men: prevalence and risk factors. J Acquir Immune Defic Syndr Hum Retrovirol 1998; 17:320.
- 11. Palefsky JM, Shiboski S, Moss A. Risk factors for anal human papillomavirus infection and anal cytologic abnormalities in HIV-positive and HIV-negative homosexual men. J Acquir Immune Defic Syndr 1994; 7:599.
- 12. Moscicki AB, Hills NK, Shiboski S, et al. Risk factors for abnormal anal cytology in young heterosexual women. Cancer Epidemiol Biomarkers Prev 1999; 8:173.
- 13. Jay N, Berry JM, Hogeboom CJ, et al. Colposcopic appearance of anal squamous intraepithelial lesions: relationship to histopathology. Dis Colon Rectum 1997; 40:919.
- **14.** Chin-Hong PV, Vittinghoff E, Cranston RD, et al. Age-related prevalence of anal cancer precursors in homosexual men: the EXPLORE study. J Natl Cancer Inst 2005; 97:896.
- 15. Kiviat NB, Critchlow CW, Holmes KK, et al. Association of anal dysplasia and human papillomavirus with immunosuppression and HIV infection among homosexual men. AIDS 1993; 7:43.
- 16. Palefsky JM. Anal squamous intraepithelial lesions in human immunodeficiency virus-positive men and women. Semin Oncol 2000; 27:471.
- Palefsky JM, Holly EA, Ralston ML, Jay N. Prevalence and risk factors for human papillomavirus infection
 of the anal canal in human immunodeficiency virus (HIV)-positive and HIV-negative homosexual men. J
 Infect Dis 1998; 177:361.
- Chin-Hong PV, Vittinghoff E, Cranston RD, et al. Age-Specific prevalence of anal human papillomavirus infection in HIV-negative sexually active men who have sex with men: the EXPLORE study. J Infect Dis 2004; 190:2070.
- 19. Holly EA, Ralston ML, Darragh TM, et al. Prevalence and risk factors for anal squamous intraepithelial lesions in women. J Natl Cancer Inst 2001; 93:843.
- 20. Williams AB, Darragh TM, Vranizan K, et al. Anal and cervical human papillomavirus infection and risk of anal and cervical epithelial abnormalities in human immunodeficiency virus-infected women. Obstet Gynecol 1994; 83:205.
- 21. Machalek DA, Poynten M, Jin F, et al.. Anal human papillomavirus infection and assoicated neoplastic lesions in men who have sex with men: a systematic review and meta-analysis. Lancet Oncol 2012.
- 22. Palefsky JM, Holly EA, Efirdc JT, et al. Anal intraepithelial neoplasia in the highly active antiretroviral therapy era among HIV-positive men who have sex with men. AIDS 2005; 19:1407.
- 23. Silverberg MJ, Lau B, Justice AC, et al. Risk of anal cancer in HIV-infected and HIV-uninfected individuals in North America. Clin Infect Dis 2012; 54:1026.
- 24. Bower M, Powles T, Newsom-Davis T, et al. HIV-associated anal cancer: has highly active antiretroviral therapy reduced the incidence or improved the outcome? J Acquir Immune Defic Syndr 2004; 37:1563.
- 25. Crum-Cianflone NF, Hullsiek KH, Marconi VC, et al. Anal cancers among HIV-infected persons: HAART is not slowing rising incidence. AIDS 2010; 24:535.
- 26. Hessol NA, Holly EA, Efird JT, et al. Anal intraepithelial neoplasia in a multisite study of HIV-infected and high-risk HIV-uninfected women. AIDS 2009; 23:59.
- 27. Palefsky JM, Holly EA, Ralston ML, et al. Anal cytological abnormalities and anal HPV infection in men with Centers for Disease Control group IV HIV disease. Genitourin Med 1997; 73:174.
- 28. Melbye M, Sprøgel P. Aetiological parallel between anal cancer and cervical cancer. Lancet 1991; 338:657.
- 29. Ogunbiyi OA, Scholefield JH, Raftery AT, et al. Prevalence of anal human papillomavirus infection and intraepithelial neoplasia in renal allograft recipients. Br J Surg 1994; 81:365.
- **30**. Lammé J, Pattaratornkosohn T, Mercado-Abadie J, et al. Concurrent anal human papillomavirus and abnormal anal cytology in women with known cervical dysplasia. Obstet Gynecol 2014; 124:242.
- 31. Tramujas da Costa e Silva I, de Lima Ferreira LC, Santos Gimenez F, et al. High-resolution anoscopy in the diagnosis of anal cancer precursor lesions in renal graft recipients. Ann Surg Oncol 2008; 15:1470.
- 32. Palefsky JM, Barrasso R. HPV infection and disease in men. Obstet Gynecol Clin North Am 1996; 23:895.
- 33. Burgos J, Curran A, Tallada N, et al. Risk of progression to high-grade anal intraepithelial neoplasia in

- HIV-infected MSM. AIDS 2015; 29:695.
- **34.** Tong WW, Jin F, McHugh LC, et al. Progression to and spontaneous regression of high-grade anal squamous intraepithelial lesions in HIV-infected and uninfected men. AIDS 2013; 27:2233.
- 35. Scholefield JH, Castle MT, Watson NF. Malignant transformation of high-grade anal intraepithelial neoplasia. Br J Surg 2005; 92:1133.
- 36. Kreuter A, Potthoff A, Brockmeyer NH, et al. Anal carcinoma in human immunodeficiency virus-positive men: results of a prospective study from Germany. Br J Dermatol 2010; 162:1269.
- 37. Chiao EY, Giordano TP, Palefsky JM, et al. Screening HIV-infected individuals for anal cancer precursor lesions: a systematic review. Clin Infect Dis 2006; 43:223.
- 38. Machalek DA, Poynten M, Jin F, et al. Anal human papillomavirus infection and associated neoplastic lesions in men who have sex with men: a systematic review and meta-analysis. Lancet Oncol 2012; 13:487.
- 39. Piketty C, Darragh TM, Da Costa M, et al. High prevalence of anal human papillomavirus infection and anal cancer precursors among HIV-infected persons in the absence of anal intercourse. Ann Intern Med 2003; 138:453
- **40**. Gaisa M, Sigel K, Hand J, Goldstone S. High rates of anal dysplasia in HIV-infected men who have sex with men, women, and heterosexual men. AIDS 2014; 28:215.
- **41.** Scholefield JH, Sonnex C, Talbot IC, et al. Anal and cervical intraepithelial neoplasia: possible parallel. Lancet 1989; 2:765.
- **42**. Sillman FH, Sentovich S, Shaffer D. Ano-genital neoplasia in renal transplant patients. Ann Transplant 1997; 2:59.
- **43.** Sonnex C, Scholefield JH, Kocjan G, et al. Anal human papillomavirus infection: a comparative study of cytology, colposcopy and DNA hybridisation as methods of detection. Genitourin Med 1991; 67:21.
- **44.** Palefsky JM, Holly EA, Hogeboom CJ, et al. Anal cytology as a screening tool for anal squamous intraepithelial lesions. J Acquir Immune Defic Syndr Hum Retrovirol 1997; 14:415.
- 45. Nathan M, Singh N, Garrett N, et al. Performance of anal cytology in a clinical setting when measured against histology and high-resolution anoscopy findings. AIDS 2010; 24:373.
- 46. Cranston RD, Darragh TM, Holly EA, et al. Self-collected versus clinician-collected anal cytology specimens to diagnose anal intraepithelial neoplasia in HIV-positive men. J Acquir Immune Defic Syndr 2004; 36:915.
- 47. Lampinen TM, Miller ML, Chan K, et al. Randomized clinical evaluation of self-screening for anal cancer precursors in men who have sex with men. Cytojournal 2006; 3:4.
- **48**. Chin-Hong PV, Berry JM, Cheng SC, et al. Comparison of patient- and clinician-collected anal cytology samples to screen for human papillomavirus-associated anal intraepithelial neoplasia in men who have sex with men. Ann Intern Med 2008; 149:300.
- **49**. Panther LA, Wagner K, Proper J, et al. High resolution anoscopy findings for men who have sex with men: inaccuracy of anal cytology as a predictor of histologic high-grade anal intraepithelial neoplasia and the impact of HIV serostatus. Clin Infect Dis 2004; 38:1490.
- 50. Palefsky JM, Gonzales J, Greenblatt RM, et al. Anal intraepithelial neoplasia and anal papillomavirus infection among homosexual males with group IV HIV disease. JAMA 1990; 263:2911.
- **51.** Goldie SJ, Kuntz KM, Weinstein MC, et al. Cost-effectiveness of screening for anal squamous intraepithelial lesions and anal cancer in human immunodeficiency virus-negative homosexual and bisexual men. Am J Med 2000; 108:634.
- Goldie SJ, Kuntz KM, Weinstein MC, et al. The clinical effectiveness and cost-effectiveness of screening for anal squamous intraepithelial lesions in homosexual and bisexual HIV-positive men. JAMA 1999; 281:1822.
- **53**. Giuliano AR, Palefsky JM, Goldstone S, et al. Efficacy of quadrivalent HPV vaccine against HPV Infection and disease in males. N Engl J Med 2011; 364:401.
- 54. Palefsky JM, Giuliano AR, Goldstone S, et al. HPV vaccine against anal HPV infection and anal

- intraepithelial neoplasia. N Engl J Med 2011; 365:1576.
- 55. Chin-Hong PV, Palefsky JM. Natural history and clinical management of anal human papillomavirus disease in men and women infected with human immunodeficiency virus. Clin Infect Dis 2002; 35:1127.
- 56. Kreuter A, Potthoff A, Brockmeyer NH, et al. Imiquimod leads to a decrease of human papillomavirus DNA and to a sustained clearance of anal intraepithelial neoplasia in HIV-infected men. J Invest Dermatol 2008; 128:2078.
- 57. Fox PA, Nathan M, Francis N, et al. A double-blind, randomized controlled trial of the use of imiquimod cream for the treatment of anal canal high-grade anal intraepithelial neoplasia in HIV-positive MSM on HAART, with long-term follow-up data including the use of open-label imiquimod. AIDS 2010; 24:2331.
- 58. Richel O, de Vries HJ, van Noesel CJ, et al. Comparison of imiquimod, topical fluorouracil, and electrocautery for the treatment of anal intraepithelial neoplasia in HIV-positive men who have sex with men: an open-label, randomised controlled trial. Lancet Oncol 2013; 14:346.
- 59. Cranston RD, Baker JR, Liu Y, et al. Topical application of trichloroacetic acid is efficacious for the treatment of internal anal high-grade squamous intraepithelial lesions in HIV-positive men. Sex Transm Dis 2014; 41:420.
- Singh JC, Kuohung V, Palefsky JM. Efficacy of trichloroacetic acid in the treatment of anal intraepithelial neoplasia in HIV-positive and HIV-negative men who have sex with men. J Acquir Immune Defic Syndr 2009; 52:474.
- **61.** Richel O, Wieland U, de Vries HJ, et al. Topical 5-fluorouracil treatment of anal intraepithelial neoplasia in human immunodeficiency virus-positive men. Br J Dermatol 2010; 163:1301.
- **62.** Halasz CL. Treatment of common warts using the infrared coagulator. J Dermatol Surg Oncol 1994; 20:252.
- 63. Goldstone S, personal communication.
- **64.** Cranston RD, Hirschowitz SL, Cortina G, Moe AA. A retrospective clinical study of the treatment of high-grade anal dysplasia by infrared coagulation in a population of HIV-positive men who have sex with men. Int J STD AIDS 2008; 19:118.
- 65. Pineda CE, Berry JM, Jay N, et al. High-resolution anoscopy targeted surgical destruction of anal high-grade squamous intraepithelial lesions: a ten-year experience. Dis Colon Rectum 2008; 51:829.
- **66**. Weis SE, Vecino I, Pogoda JM, Susa JS. Treatment of high-grade anal intraepithelial neoplasia with infrared coagulation in a primary care population of HIV-infected men and women. Dis Colon Rectum 2012; 55:1236.
- 67. Goldstone RN, Goldstone AB, Russ J, Goldstone SE. Long-term follow-up of infrared coagulator ablation of anal high-grade dysplasia in men who have sex with men. Dis Colon Rectum 2011; 54:1284.
- 68. Marks DK, Goldstone SE. Electrocautery ablation of high-grade anal squamous intraepithelial lesions in HIV-negative and HIV-positive men who have sex with men. J Acquir Immune Defic Syndr 2012; 59:259.
- **69**. Bowen JT. Centennial paper. May 1912 (J Cutan Dis Syph 1912;30:241-255). Precancerous dermatoses: a study of two cases of chronic atypical epithelial proliferation. By John T. Bowen, M.D., Boston. Arch Dermatol 1983; 119:243.
- 70. Frisch M, Fenger C, van den Brule AJ, et al. Variants of squamous cell carcinoma of the anal canal and perianal skin and their relation to human papillomaviruses. Cancer Res 1999; 59:753.
- 71. Fenger C, Nielsen VT. Precancerous changes in the anal canal epithelium in resection specimens. Acta Pathol Microbiol Immunol Scand A 1986; 94:63.
- **72**. Marfing TE, Abel ME, Gallagher DM. Perianal Bowen's disease and associated malignancies. Results of a survey. Dis Colon Rectum 1987; 30:782.
- **73.** Jaeger AB, Gramkow A, Hjalgrim H, et al. Bowen disease and risk of subsequent malignant neoplasms: a population-based cohort study of 1147 patients. Arch Dermatol 1999; 135:790.
- 74. Cleary RK, Schaldenbrand JD, Fowler JJ, et al. Perianal Bowen's disease and anal intraepithelial neoplasia: review of the literature. Dis Colon Rectum 1999; 42:945.