Anal cancer in women and men: Never heard of it!

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Disclosure – Dr. Bouchard

- Honorarium received
  - Merck Canada for lectures
  - Roche Diagnostic Canada for lecture

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Disclosures – Dr. Kucharski

I receive a stipend from Cancer Care Ontario, Ontario's provincial cancer agency

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Clinical Case

- A 55-year-old woman presents to your office for her periodic gynecological examination
  - Medical history:
    - G2P2, menopause for 2 years, no hormone therapy, divorced but stable with her new partner for 2 years
    - At age 40, LEEP for cervical HSIL * ; Pap tests always normal since treatment and was released from colposcopy;
    - Otherwise healthy with no complaint; current smoker
  - Gynecological exam:
    - Normal vulva
    - Vagina and cervix normal with naked eye; Pap repeated
    - 1 whitish surelevated and irregular 1 cm x 1 cm lesion detected around the anus

*: HSIL: High Grade Squamous Intraepithelial Lesion

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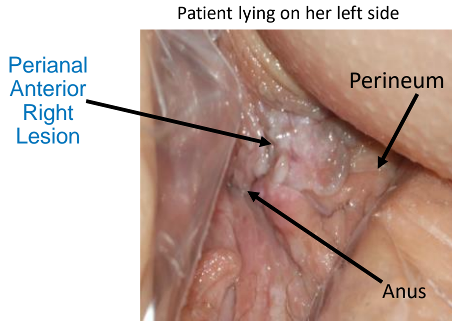
Patient lying on her left side



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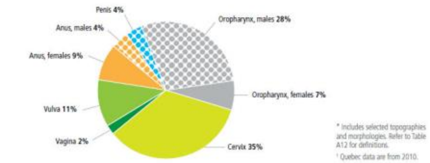
HPV-associated cancers, Canada 2012



Canadian Cancer Statistics 2016

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Anal Cancer in Women

- Risk factors
  - Cervical cancer, CIN 2 (+), VIN2 (+)
  - Smokers
  - Anal condylomas
  - Immunosuppressed women
    - HIV (+) : abnormal anal cytology (26-35%)
    - Transplant (10 times increased risk)
    - Immunosupprive treatments and chronic diseases
- Mean Age
  - 63 years

Ouhoummane N et all. Caner Epidemiology 37 (2013) 807-812

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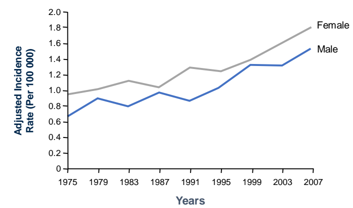
Age-Adjusted Incidence Rate of Anal Cancer by Gender and Year of Diagnosis



Palefsky J. Vaccine 2011

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Anal Cancer = HPV 16 infection 90% of the time

- Contamination of the vulvar and perianal area
- Self-inoculated vaginal or cervical infected secretions
- Anal intercourse
  - Results vary among cohort studied
  - Seems to be less important as MSM * and being receiver

* MSM: Men Having Sex with Men

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Prevalence of HPV anal infection in women

- As high as the cervix
- Hawaiian cohort (healthy women) [1,2,3]
  - 27%+ anal HPV vs 29% + HPV at the cervix
  - Transient infection in 50% of the cohort
    - 87% of the remaining cohort will eliminate infection in the first year
    - Compared to 90% of HPV elimination after 2 years for the cervix

1 Hernandes BY et coll. Cancer Epidemiol Biomarkers Prev 2005;14(11 Pt 1):2550-6
2 Shvetsov YB et coll. Clinic Infect Dis 2009;48(5):536-46
3 Goodman MT et coll. J Infect Dis 2010;201:1331-39

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Screening Recommendations for Anal Cancer in Women: at-risk Groups

- No universal screening but focalised screening
  - All HIV+ women
  - History of genital cancers: cervix, vagina or vulva
  - Women with condyloma
  - Women with history of vulvar intraepithelial neoplasia (VIN) or HSIL
  - Women who engage in anal sex ?
  - Women treated with immunosuppressive drugs after organ transplant

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Anal Cancer Impact of Screening

- Prevention and early detection of anal cancer
  - Precancerous lesions can be detected and treated
  - Study currently undertaken to prove that treatment of precancerous lesions in HIV (+) MSM decrease the progression to cancer (ANCHOR)
- Impact on survival
  - Localized anal cancer: survival rate at 5 years: 80%
  - Metastatic cancer: 30% survival rate at 5 years
- Remember: important to know if you have access to resources in your area to take care of positive results

Darragh TM et al. Cancer (Cancer Cyto Pathol) 2011;119:5-19

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DARE

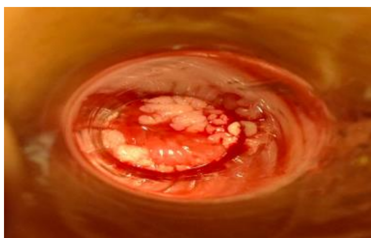
- A DARE is a development of digital rectal examination (DRE)
- DARE also includes palpation of the entire anal canal and inspection of the perianal skin (defined as 5cm distal to the anal margin)
- Who may potentially benefit from DARE:
  - Women with a history of cervical, vulvar or vaginal intraepithelial neoplasia or cancer
- DARE frequency for women :
  - Yearly for women with precancerous anal lesion
  - Every two to five years with others sites HPV precancerous lesions

Hilman RJ et al. J Low Genit Tract Dis. 2019;23(2):138-146

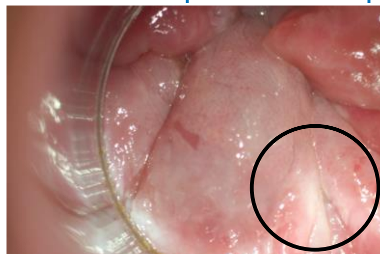
Anal Cancer and Screening

- Anal cytology: Dacron Q-tips with tap water
  - Slide or liquid cytology
- HRA : High Resolution Anoscopy
  - More specific and sensitive technique
  - Needs human and hospital resources ++
  - Evaluation of anal canal when we suspect lesion in the canal
    - PAIN 2+, perianal warts
  - Best technique to treat intra-anal lesion (HGAIN)
  - Usually reserve as screening method for MSM with HIV +
  - Not done everywhere in Canada

Anal Condylomatous Lesions



Anal Intraepithelial Neoplasia



Conclusion for Women at risk

- Women with HPV infection are at risk for anal cancer
- Examination of perianal area is an important part of the gynecological evaluation
- DARE is recommended for women at risk of anal cancer
- Anal cytology can be performed with DARE as a screening method for women at risk of anal cancer
  - Do not offer it if you don't have resources to take care of it
- HRA may be indicated for women with perianal and/or anal disease but resources in Canada are limited

HPV Infection and Anal Cancer in MSM and MSM with HIV

Ed Kucharski, MD, CCFP, FCFP

www.g-o-c.org

Objectives

- Compare the burden of anal cancer in MSM and MSM with HIV (MSM+) to that in the general population
- Describe the evidence around screening for HPV, anal dysplasia in these men
- Implement an approach to screening

Burden of anal cancer in MSM/MSM+

- Incidence of anal cancer in Canada:
  2.1 per 100 000 population in 2016[1]
- Incidence of anal cancer in MSM:
  Estimated 37 per 100 000 person-years*,[2]
- Incidence of anal cancer in MSM+
  131 per 100 000 person-years[3]

*Thought to be similar to cervical cancer prior to introduction of Pap tests
1. Statistics Canada, 2016; 2. Daling et al, 1987; 3. Silverberg et al, 2012.

Case 1: Adil

- Adil, age 34 years comes to your office for a routine STI screen. He is on PrEP (pre-exposure prophylaxis for HIV). He has approximately 7 male partners a month and has been treated for gonorrhea and chlamydia a year ago.
- His q3/12 screen for STIs (HIV, VDRL, syphilis, Hep C, gonorrhea, chlamydia) are negative.
- Adil is wants to know if there is anything else he can do to prevent STIs and promote his health?

Case 1: Adil (cont'd)

PMHx: gonorrhea, chlamydia treated

Medications: Truvada (for HIV prevention)

Allergies: none

Vaccines: Adacel in 2016

Substances: quit cigarette smoking in 2017, occasional cocaine (1-2X year)

What prevention steps might you suggest to Adil for his sexual health?

Steps for prevention

- Condom use
  - 2014 systematic review, 4 studies with statistically significant protective effect of consistent condom use, 4 studies with protective effect[1]
- Vaccinations
  - HPV: Gardasil recommended in males between 9 and 26 years old, may be administered to men over 26 years[3]
  - Hepatitis A and hepatitis B[4,5]
- Limit sexual partners?
- Debatable evidence for circumcision[6-9]

1. Lam et al, 2014; 2. Winer et al, 2006; 3-5. Health Canada, Canadian Immunization Guide; 6. Zhu et al, 2017; 7. Larke et al, 2011; 8. Tobian et al, 2009; 9. Van Howe and Storms, 2009.

Case 1: Adil (cont'd)

Adil returns for his final HPV 9-valent vaccine and is concerned about anal cancer. He volunteers at the local HIV hospice and says that he see quite a few patients dying of anal cancer who are gay. He's done some of his own research and wonders whether or not he should be screened?

Screening MSM without HIV for HPV

- No consensus about use of anal Pap or high-resolution anoscopy for MSM and other high-risk groups[1,2]
- Anal Pap sensitivity, 47-90%: specificity, 16-92% (lower when compared with biopsy)[3]
- Expert opinion suggests some may benefit from screening; one study reported anal Pap testing may be cost-effective[1,4]
- Anal Pap testing to be guided by local practice and availability[1]
- Retrospective study showed regular anoscopy and "watch and wait" both effective at stopping progression to anal cancer if treatment was followed[5]

1. PHAC, 2014; 2. Siddharthan et al, 2019; 3. Long et al, 2016; 4. Goldie et al, 2000; 5. Crawshaw et al, 2015.

Case 2: Clark

Clark is a 52 year-old male patient who moved to Canada from the USA. Clark is a MSM with HIV. His HIV is well controlled (viral load undetectable, CD4 count 800). Clark's partner is a high-profile malpractice lawyer in your city.

Clark is in for a periodic health exam. He has all his appropriate screening (and HPV vaccine) and at the end of his encounter asks when he should get his next anal Pap test, as he had been getting them in the US at his annual physicals.

How HPV infection differs in people with HIV

- 2X ↑ risk of HPV infection
  (pooled aRR = 2.46 (95%CI, 1.86-3.26))[1]
- 2X ↓ rate of HPV clearance
  (pooled aRR = 0.50 (95% CI, 0.38-0.66))[1]
- Incidence of anal cancer higher than in general population
  SRR 42.9 (95% CI, 34.1-53.3)[2]
- Conflicting evidence on efficacy of HPV treatments in patients with HIV on HAART compared with general population[3]
- HAART has not decreased prevalence of HPV infection in MSM+;[4] may delay progress to anal cancer[5]

aRR, adjusted relative risk; HAART, highly active antiretroviral therapy; RR, relative risk; SRR, standardized rate ratio
1. Looker et al, 2018; 2. Patel et al, 2008; 3. Wang et al, 2017; 4. Palefsky et al, 2005; 5. Duncan et al, 2015.

What do we recommend in Canada?

From the BC CfE HIV Primary Care Guidelines:

- Anal cytological screening (anal Pap test) in HIV-positive individuals is not considered standard of care at this time but is being performed in some health care centres in Canada.
- A few US guidelines have recommended routine anal Pap tests for some populations.
- The rationale behind screening for anal cancer is based on the similarities between anal dysplasia and cervical dysplasia, and the success of the cervical Pap screening program.
- However, there are currently no randomized clinical trials to corroborate the benefits of anal Pap smear in decreasing anal cancer incidence or mortality.

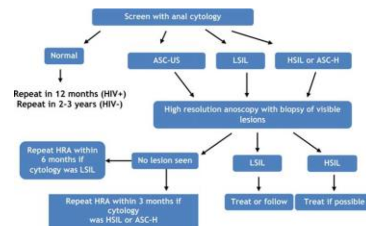
BC Centre for Excellence in HIV/AIDS, August 2015.

US IDSA primary care recommendations

- HIV-infected men and women with human papillomavirus (HPV) infection are at increased risk for anal dysplasia and cancer.
- MSM, women with a history of receptive anal intercourse or abnormal cervical Pap test results, and all HIV-infected persons with genital warts should have anal Pap tests (*weak recommendation, moderate quality evidence*).

HIV Medicine Association of the Infectious Diseases Society of America, January 2014.

Some follow this, but not endorsed as a guideline



Palefsky, 2015.

Ed Weiss's (UHN) approach (expert opinion):

If you have access to HRA and patients are willing to undergo regular exams:

- Learn how to do a proper anal cytology collection and digital anorectal exam
- Do a thorough digital anorectal exam, feel for induration/pain (refer to surgery if +)
- Offer HPV-DNA testing (if available and affordable)

If HR-HPV present, do anal cytology.

Refer for HRA if:

- HR-HPV present and any abnormal cytology, or if HPV-16 positive with any cytology result
- Unable to do HPV-DNA and cytology shows HSIL/ASC-H

Note: For ASCUS/LSIL, repeat in 6 months, and then check with HRA provider if accepting referrals for persistent ASCUS/LSIL

If no HR-HPV present, repeat q2-3 years

If no access to HRA or patients not willing to under regular exams:

- Learn how to do a proper anal cytology collection and digital anorectal exam(DARE), feel for induration/pain (refer to surgery if +), repeat yearly
- If patients are well-informed and **not likely to be anxious**, offer HPV-DNA testing (if available and affordable) or cytology
- If HR-HPV present, or any cytological abnormalities, yearly DARE
- If no HR-HPV and normal cytology, repeat in 2-3 years

Ed Weiss's pearls

- If there's external dysplasia, there's likely internal dysplasia
- External high grade dysplasia is usually visible, internal is not
- External dysplasia responds well to imiquimod but is not well tolerated
- Warts should not be painful. If they are, consider cancer
- Don't dismiss symptoms as hemorrhoids, unless you've ruled out dysplasia
- Dare to DARE!

Likely at the end of the day, it will be a case of shared decision making...

GOC