

Anal Cancer Screening: What the OBGYN Needs to Know

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Disclosures

- I am the site PI of a Teal Health Study. I receive no direct funding, but funds support our research staff.
- I previously was the site PI for a Pfizer vaccine study. This study has ended.
- I am currently the Secretary of the ASCCP and serve on several committees for the International Anal Neoplasia Society (IANS)

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Objectives

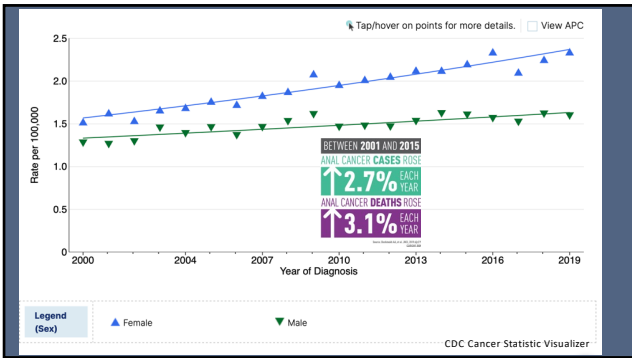
- Define anal cancer and describe the epidemiology
- Associate HPV and anal cancer
- Describe the role of an OBGYN in anal cancer screening
- Identify anal cancer screening strategies

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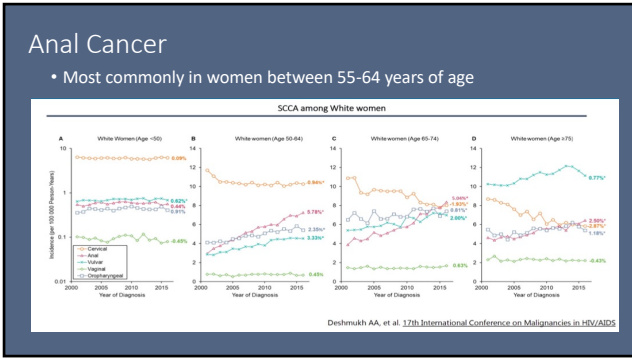
Anal Cancer Epidemiology

- 9440 new cases annually (3150 in men and 6290 in women)
- 1670 deaths annual (930 in women and 740 in men)
- Most common in white women and black men
- Anal cancer rates are rising

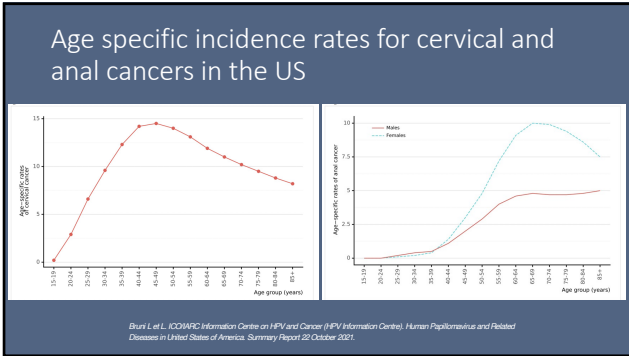
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Anal Cancer

- Predominately squamous cell cancers (perianus and anus)
- Symptoms
 - Rectal bleeding (45%)
 - Feeling of a mass (30%)
 - Asymptomatic (20%)
- Treatments
 - Radiation
 - Chemotherapy
 - May need colostomy due to tumor, cancer, or complications of treatment
 - Colostomy-free 5-year survival rate 65-86%

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Anal Cancer

- 50% of anal cancers are diagnosed at stage II or worse
- 5-year survival (all cases) = 71.1%
- 37% positive LNs at diagnosis

Stage	5- year Survival Rate (%)
T2N0	82
T3N0	74
T4N0	57
T2N+	70
T3N+	57
T4N+	42

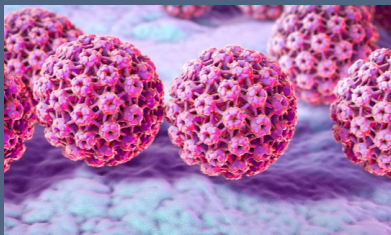
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Risk Factors for Anal Cancer

- Any factor associated with new HPV acquisition
 - Multiple sexual partners
 - Anal condylomas
 - Anal receptive intercourse
 - PWC: history of cervical, vulvar, vaginal dysplasias and cancer
- Age
- Tobacco
- Defects in cell-mediated immunity
 - HIV
 - Immunosuppression

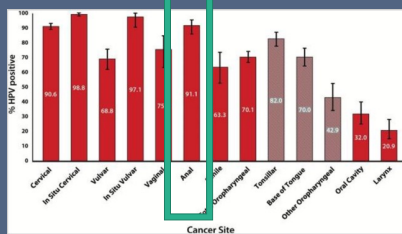
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Epidemiology of Anal HPV & Anal Neoplasias



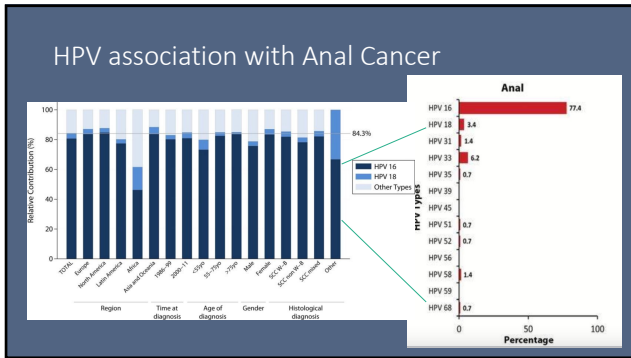
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HPV association with Anal Cancer



<https://www.cdc.gov/cancer/hpv/statistics/cases.htm>

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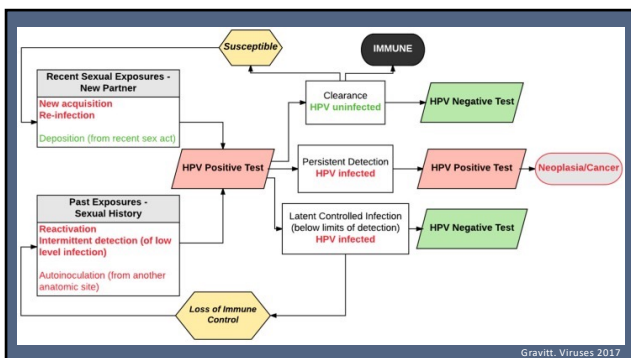


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Lessons from the cervix – anal assumptions

- High Grade Squamous Intraepithelial Lesions (HSIL) is the anal cancer precursor lesion
- Natural history of HPV, HSIL, and anal cancer is similar to cervical HPV, HSIL, and cervical cancer
- Hypothesized that:
 - Screening at risk populations -> Identification of anal HSIL -> treatment of anal HSIL -> prevent progression of anal cancer

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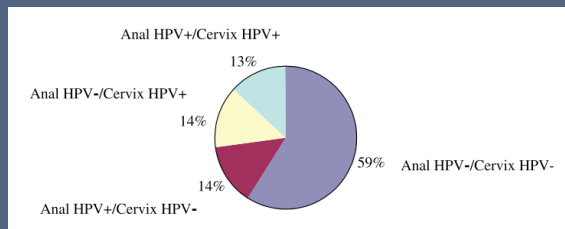
HPV in Women in the General Population – Hawaiian Cohort Study

- 1378 ethnically diverse healthy women > 18 years of age
 - Mean age 38 years
- Underwent cervical and anal sampling for HPV
 - Baseline
 - 29% had cervical HPV
 - 27% had anal HPV
 - 3-fold increased risk of anal infection if cervix positive
- 80% shared at least one HPV type between sites

Hernandez. Cancer Epi Biomarkers Prev 2005

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HPV in Women in the General Population – Hawaiian Cohort Study



Hernandez. Cancer Epi Biomarkers Prev 2005

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HPV in Women in the General Population – Costa Rica Vaccine Trial

- Control of the HPV vaccine trial
 - 2107 women ages 22-29 years
 - Single anal swab provided at year 4
- Anal and cervical HPV prevalence was high
 - Cervical prevalence 31.6% and anal prevalence 36.5%
 - Anal HR HPV prevalence 22.0%
 - Increased risk in women with history of anal intercourse

Castro. JID 2011

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How do Women get anal HPV infections?

- Cross sectional study of women with a previous HPV-mediated gynecologic neoplasia in Tasmania, Australia
- Women presenting for follow-up GYN care had anal swab samples taken for anal cytology and HPV genotyping
- Women with abnormal anal cytology were referred for HRA

Simpson. Cancer Epi 2016

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How do Women get anal HPV infections?

- Of the 123 women tested for HR HPV DNA, 48 (39.0%) had anal HR HPV detected
- Front to back wiping was associated with significantly increased prevalence of cytological and histological abnormality and HR HPV carriage/co-carriage (prevalence 1.99-3.6)
- Dabbing post-toilet was significantly associated with decreased prevalence (PR range 0.5-0.62)



Simpson. Cancer Epi 2016

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Why Should Gynecologists Care about Anal Cancer Screening?



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Your patients will ask!

Actress Marcia Cross

Farrah Fawcett Foundation

On Battling Anal Cancer and Breaking the Silence of HPV

Actress Marcia Cross Beat Anal Cancer & She's Made a Point to Give Her Daughters the HPV Vaccine: Here's What You Should Know about the Vaccine and HPV-Linked Cancers

Leading Ladies Affected by Anal Cancer Brings New Awareness to Rare Disease

TODAY

What are the symptoms of anal cancer? Farrah Fawcett put disease in spotlight

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Why Should Gynecologists Care about Anal Cancer Screening?

- You already have most of the tools!!

Liquid Media

Polyester Swab

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Why Should Gynecologists Care about Anal Cancer Screening?

- Experts in HPV-related dysplasias and colposcopy
 - High prevalence of anal HPV in women with cervical and vulvar HPV
 - Anal cancer most commonly diagnosed in women
 - Risk of multi-zonal disease

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Multi-Zonal Disease

- Definition – presence of high-grade squamous intraepithelial lesions (HSIL)/carcinoma concurrently at two or more of the following sites/zones: perianus, anal canal, vulva, vagina, or cervix
- Retrospective study from London (Homerton Anogenital Neoplasia Service)
 - January 2012-March 2017
 - All patients who underwent multizonal anogenital neoplasia (MZN) assessment
 - History of any lower genital tract neoplasia (LSIL, HSIL or cancer)

Albuquerque. BMC Cancer 2021

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Multi-Zonal Disease

- MZN Assessment
 - Vulvar, vaginal and cervical colposcopy
 - Examination of the perianus
 - High resolution anoscopy
 - Biopsy any area suspicious for HSIL
- 253 patients underwent MZN
 - Median age 47 years
 - Median duration of followup 12 months
 - 20% history of anogenital cancer

Table 1 Characteristics of the women with multizonal anogenital neoplasia assessments included in this study (n=253)

Parameter	Descriptive statistics*
Age at first visit (years) median (IQR)	47 (36-56)
Duration of the follow-up (months) median (IQR)	12 (0)
Previous cervical HSIL/cancer, n (%)	94(25) (37)
Previous vulval HSIL/cancer, n (%)	91 (36)
Previous vaginal HSIL/cancer, n (%)	16 (6)
Previous anal HSIL/cancer, n (%)	42 (25)
Previous perianal HSIL/cancer, n (%)	34 (13)
Previous history of anogenital tract HSIL/cancer any site, n (%)	191(75)
One site HSIL/cancer, n (%)	112 (69)
Two sites HSIL/cancer, n (%)	61 (32)
Three sites HSIL/cancer, n (%)	14 (7)
Four sites HSIL/cancer, n (%)	3 (1.5)
Five sites HSIL/cancer, n (%)	1 (0.5)
Previous anogenital cancer/per patient, n (%)	51 (20)
Cervical	9
Vulval	16
Anal	21
Perianal	8
One anogenital cancer site, n (%)	48 (94)
Two anogenital cancer sites, n (%)	9 (18)

Albuquerque. BMC Cancer 2021

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First Visit

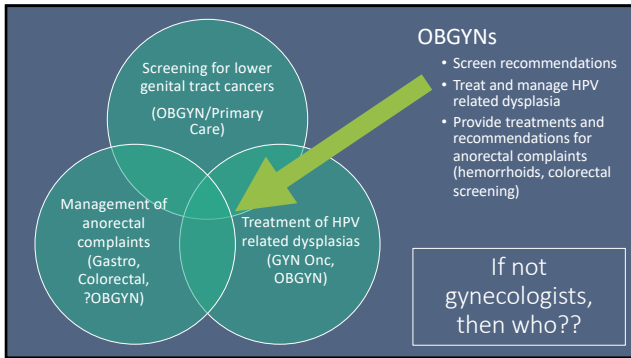
MZN At first visit (n=50)	
Disease location	
Site	Number of cases HSIL/cancer
Cervical	3
Vulval	37
Vagina	14
Anal	34
Perianal	40
Number of sites HSIL/cancer	N (%)
Two sites	27 (54)
Three sites	18 (36)
Four sites	5 (10)
Five sites	0 (0)

Follow-up Visits

MZN at follow-up (n=20)	
Disease location	
Site	Number of cases HSIL/cancer
Cervical	2
Vulval	12
Vagina	8
Anal	13
Perianal	13
Number of sites HSIL/cancer	N (%)
Two sites	13 (65)
Three sites	6 (30)
Four sites	1 (5)
Five sites	0 (0)

- 20% with MZN at first visit
 - Most common sites anal canal or perianus
- Most unsuspected or new zone
- Cancer diagnosed in 9 patients
- 11% with MZN during followup
 - New diagnosis
 - Most common sites anal canal or perianus
- 4 new cancers diagnosed during followup

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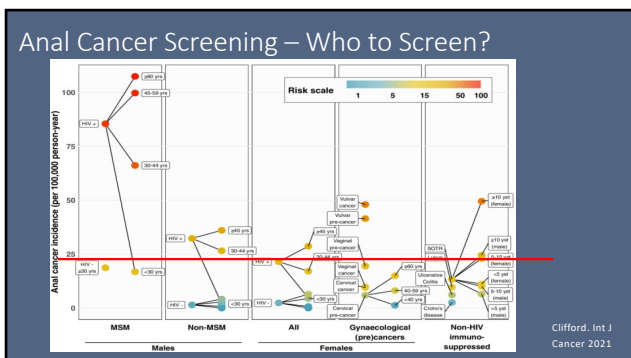


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Anal Cancer Screening – Who to screen?

- HIV positive women (SIR 18-47)
- Women with HPV-associated cancers (SIR 13.6)
- History of vulvar cancer (SIR 45.5)
- History of cervical cancer (SIR 6.3)
- History of CIN 3/HSIL (SIR 5.9-6.7)
- Condyloma (SIR 7.8-9)

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International Anal Neoplasia Society's Consensus Guidelines for ACS

TABLE 1 Populations for screening.

Population—Risk category	When	Anal cancer incidence ^a per 100,000 person-years
Risk Category A (Incidence \geq 10-fold compared to the general population)		
MSM and TW with HIV	Age 35	$>70/100,000$ age 30–44
Women with HIV	Age 45	$>25/100,000$ age 45+
MSM with HIV	Age 45	$>30/100,000$ age 45+
MSM and TW not with HIV	Age 45	$>18/100,000$ age 45–59
History of vulvar HSIL or cancer	Within 1 year of diagnosis	$>40/100,000$
Solid cancer transplant recipient	≥ 10 years post-transplant	$>25/100,000$
Risk Category B (Incidence up to 10-fold higher compared to the general population)		
Cervical/vaginal cancer	Shared decision age 45 ^b	9/100,000
Cervical/vaginal HSIL	Shared decision age 45 ^b	8/100,000
Perianal warts (male or female)	Shared decision age 45 ^b	Unknown
Persistent cervical HPV (16) (> 1 year)	Shared decision age 45 ^b	Unknown
Other immunosuppression (e.g., Rheumatoid arthritis, Lupus, Crohn's, Ulcerative colitis, on systemic steroid therapy)	Shared decision age 45 ^b	6/100,000

Incidence among the general population: 1.7 per 100,000^b

Stier. Int J Cancer 2024

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Screening Strategies for Anal Neoplasia

- Digital Anal Rectal Exam
- High-Risk HPV (HR HPV)
- Cytology
- High Resolution Anoscopy (HRA)

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Summary Recommendations for Anal Cancer Screening in Individuals with Cervixes

Population at Risk	SIR Per 100,000	PE Symptoms pain/bleeding	DARE	Anal Cytology	HRA
Women with HIV (age over 45 years)	27		X	X	X
Current or hx of vulvar HSIL or vulvar cancer	45-47		X	X	X
Current or history of cervical or vaginal HSIL	10	X	X		
Organ Transplant Recipients (> 10 years ago)	51		X	X	X
Healthy individuals with cervixes with none of the above risk factors	< 25	X	X		

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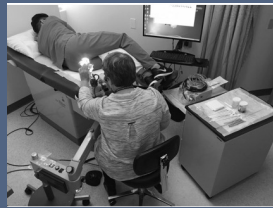
DARE as a Screening Tool for Anal Cancer

- DARE = Digital Anal Rectal Exam
 - Definition: Palpation of the complete anal canal and visual inspection and palpation of the anal margin (5 cm distal to the anal verge)
 - Goal = Identify palpable lesions in the anal canal
 - Sensitive to palpation of lesions as small as 3 mm
 - Found to be acceptable and low cost
- Necessary to perform in women with symptoms (bleeding or pain)

Hillman. J Low Genit Dis. 2019

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DARE Positioning

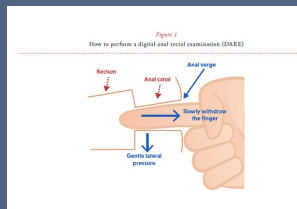


Jay. Sem. Colon Rectal Surg, 2017

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The DARE

- Expose the anus by separating the buttocks
- Use lubricated, gloved index finger to apply gentle pressure on the anal verge and enter the anal canal
- Pull your finger back to the sphincter feeling the circumference of the anal canal; palpate the perianal region
- Sweep the finger 360 in the rectum applying gentle pressure to the lateral walls



Hillman. J Low Genit Dis. 2019

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Anal Cytology as a Screening Strategy for Anal Neoplasia

Studies	Sensitivity	Specificity	PPV	NPV
Moscicki 2016	55-93%	32-81%	26-57%	82-88%
Ramos-Cartagena 2020	85.4%	38.8%	45.6%	81.6%
Chiao 2020	83%	50%	37%	
Sambursky 2018	89%	51%	24%	96%
Heard 2015	82%	76%	22%	98%
Albuquerque 2018	71%	73%	55%	84%

Sensitivity, Specificity, PPV and NPV for Anal Cytology to predict anal HSIL

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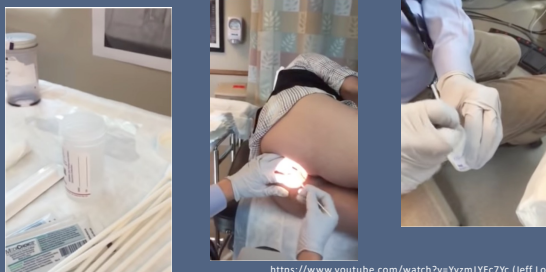
High-Risk HPV as a Screening Strategy for Anal Neoplasia

Studies	Sensitivity	Specificity	PPV	NPV
Moscicki 2016	55-93%	32.81%	26-57%	82-88%
Ramos-Cartagena 2020	95.8%	31.3%	45.5%	92.6%
Chiao 2020	77%	67%	45%	
Sambursky	96%	48%	24%	99%
Heard 2015	91%	44%	12%	98%

Sensitivity, Specificity, PPV and NPV for HR HPV to predict anal HSIL

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Obtaining Anal Cytology/HPV



<https://www.youtube.com/watch?v=Vvzm1VFC7Yc> /Jeff Logan - How to Perform anal Cytology)

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But... should we screen??



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Lessons from the cervix – anal assumptions

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- Natural history of HPV, HSIL, and anal cancer is similar to cervical HPV, HSIL, and cervical cancer
- Hypothesized that:
 - *Screening at risk populations -> Identification of anal HSIL -> treatment of anal HSIL -> prevent progression of anal cancer*

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High Resolution Anoscopy (*Identification*)

- Office-based procedure for examination of the anus, anal canal and perianus using a colposcope with 5% acetic acid and Lugol's solution
- Adapted from cervical colposcopy
- Tools, terminology, lesion descriptions and patterns validated for anal canal
- Differences from cervical colposcopy? Yes
 - Long learning curve

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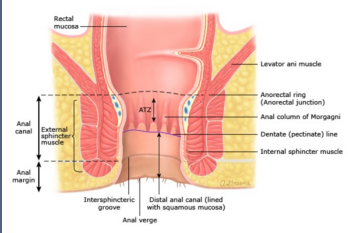
HRA	Cervical Colposcopy
<ul style="list-style-type: none"> • Synthetic polyester swab • Anoscopes – flat end 15mm • Forceps < 3mm <ul style="list-style-type: none"> Flat-end baby Tischler • Colposcope <ul style="list-style-type: none"> Focal length 250-300mm Direct view Magnification (>) Angled eyepieces Side-arm or overhead 	<ul style="list-style-type: none"> • Cytobrush & spatula • Specula • Forceps – large & small <ul style="list-style-type: none"> Variety of sizes and cups • Colposcope <ul style="list-style-type: none"> Focal length 300-350mm Direct or videoscope Magnification (low field ok) Straight-on eyepieces Center, side-arm, overhead

Slide from N. Jay

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Anal Cancer – Transformation Zone

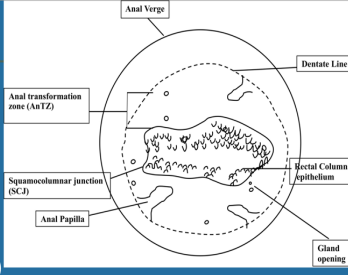
- Morphologically analogous to the cervical transformation zone
- Region of squamous metaplasia
- "Immature" squamous metaplasia
 - Leading edge at SCJ
 - Most susceptible to HPV



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Terminology

- Rectal/columnar (larger view)
- SCJ (harder to find)
- AnTZ (less features)
- Dentate Line
- Verge
- Perianus = anal margin
- 5 cm (anterior midway to introitus)



Slide from N. Jay

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HRA View of the SCJ

- Anal squamous epithelium abuts the rectal columnar epithelium
- Thin white line of metaplasia
- Only seen with acetic acid and metaplasia
- Need manipulation to see in its entirety
- There is always an SCJ
- Close to the verge in women

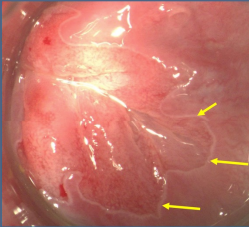






Photo from N. Jay

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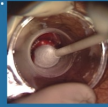
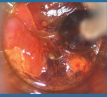
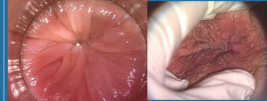
HRA Exam Steps

- 1) Position – lateral or prone. 
- 2) Insert Q-tip wrapped in gauze soaked in 5% acetic acid through anoscope. 
- 3) Remove anoscope leaving swab & gauze inside. Soak for 1-2 minutes. 
- 3a) inspect perianus
- 4) Remove gauze and re-insert anoscope. 
- 5) Observe through colposcope slowly withdrawing the anoscope until the SCJ is seen.

Slide from N. Jay

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HRA Exam (con't)

- 5) Examine entire SCJ 
- 6) Reapply acetic acid liberally throughout exam. 
- 7) Apply Lugol's solution after acetic acid w/cotton swabs 
- 8) Observe distal canal & verge as anoscope is withdrawn, then perianus. 

Slides N. Jay

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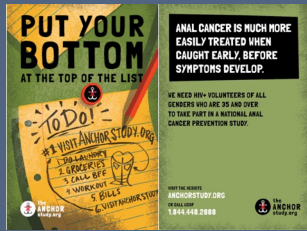
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- Natural history of HPV, HSIL, and anal cancer is similar to HPV, HSIL, and cancer
- Hypothesized that:
 - Screening at risk individuals -> Identification of anal HSIL -> *treatment of anal HSIL* -> *prevent progression of anal cancer*

Does treatment work to prevent cancer??

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The ANCHOR Study



- Anal Cancer HSIL Outcomes Research
- Enrolled patients over 35 years of age with HIV and confirmed anal HSIL
- Randomized to treatment versus expectant management

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The ANCHOR Study - Results



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The ANCHOR Study - Results

- Patients enrolled September 24, 2014 through August 5, 2021
 - Screened 10,723 total patients
 - HSIL confirmed
 - 4257/7729 men (55.1%)
 - 860/1822 women (47.2%)
 - 188/280 transgender persons (67.1%)
 - 17 patients received an anal cancer diagnosis at baseline
- 4459 enrolled patients
 - Median followup of 25.8 months

Palefsky, NEJM 2022

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Types of Treatment

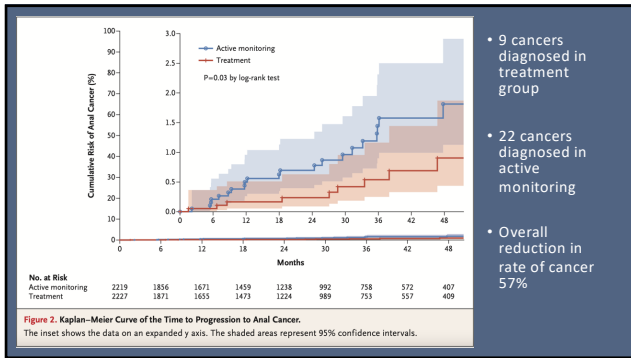
- No specific treatment for HPV
 - Patient-applied topical: imiquimod and 5% fluorouracil cream
 - Clinician-applied topical: 85% trichloroacetic acid, cryotherapy
 - Clinician-applied ablation: infrared coagulation (4.8%), electrocautery (86.2%), laser
 - Surgical excision

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Progression to Cancer

- Cumulative progression to cancer at 48 months was 0.9% in the treatment arm and 1.8% in the monitoring arm
 - 57% reduction in anal cancer (95% CI 6% to 80%, p=0.029)
- Cancer incidence in the treatment arm was 173/100,000 PY of follow-up compared to 402/100,000 PY in the AM monitoring arm
 - 185/100,000 PY (95% CI: 115-298) for lesions less than or equal to 50% size
 - 1047/100,000 PY (95% CI: 608-1803) >50 size
 - Hazard ratio 5.26, 95% CI: 2.54-10.87

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- 9 cancers diagnosed in treatment group
- 22 cancers diagnosed in active monitoring
- Overall reduction in rate of cancer 57%

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Take home points from the ANCHOR study

- Treating anal HSIL can prevent invasive anal cancer
- Almost all participants had office-based electrocautery, primarily hyfrecation
- Operating room for extensive biopsying, disease too bulky to treat in office
- Treatment for HSIL is improving but even better treatments are needed
- Careful follow-up critical as patients tend to recur despite method of treatment

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Should we screen?

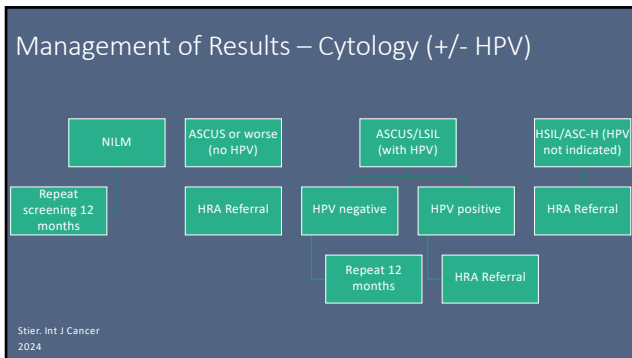
- High risk patient populations
- Able to identify precancerous lesions
- Effective treatment
- Reduction of anal cancer...

OBGYNs – YES YOU SHOULD!

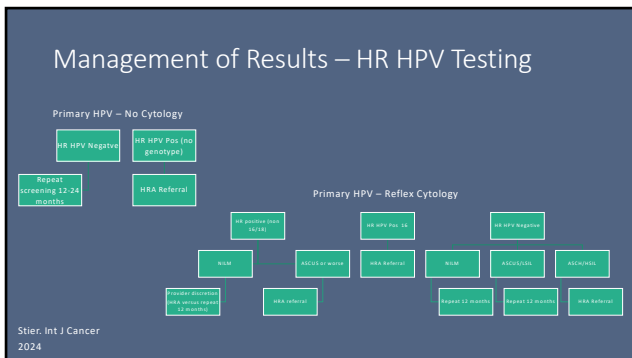
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Objectives

- Define anal cancer and describe the epidemiology
- Associate HPV and anal cancer
- Describe the role of an OBGYN in anal cancer screening
- Identify anal cancer screening strategies

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DARE to CARE..
BACK THERE!



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