What You Should Know About Human Papillomavirus (HPV) in HIV-Infection Robert Dodge, PhD, RN, ANP, AACRN Clinical Associate Professor of Medicine University of North Carolina School of Medicine UNIC SCHOOL OF MEDICINE

Conflict of Interest

- Abbott Laboratories
- Speaker's Bureau
- Boehringer-Ingelheim
 - Speaker's Bureau
- Gilead Sciences
 - Speaker's Bureau
- ViiV Healthcare
 - Speaker's Bureau

Learning Objectives

- 1. Identify the epidemiology and transmission of human papillomavirus (HPV).
- Discuss screening for HPV and management in the HIVinfected population.
- Explain correlation between HPV, genital warts, anogenital & oropharyngeal cancers.
- 4. Describe prevention of HPV through vaccines.

Outline

- 1. HPV epidemiology
- 2. Screening and management of HPV
- 3. Correlation of HPV with anogenital & oropharyngeal cancers.
- 4. Role of vaccines in prevention of HPV

HPV Epidemiology



Incidence and Prevalence of HPV

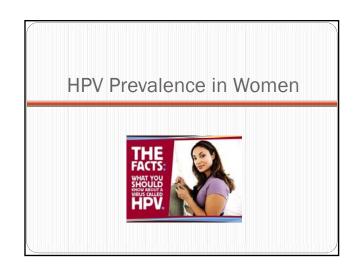
- Incidence estimated around 5 million genital HPV infections annually in United States.
 - $\bullet > 50\%$ of women acquire HPV during first few sexual relationships
 - \bullet Most infections acquired by persons \le 30 years old
- ullet Prevalence estimated at ≥ 25 million infected persons.



- Transmission by direct skin to skin contact
 - Compared to HIV and Herpes (HSV) spread during sex
- Approximately 50% of sexually active persons become infected at least once in their lifetime.
 - $\bullet~90\%$ of infections cleared by immune system within 1 year
- Infection usually asymptomatic, unrecognized, or subclinical Source: cdc.gov

Types of HPV

- DNA virus-double stranded
- Over 100 types of HPV exist
 - 40 HPV types that infect genital areas and oral cavity
- $\bullet \ \ High\mbox{-risk HPV types can lead to an ogenital cancers}$
 - 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68
- Types 16 & 18 (oncogenic)
 - Account for anogenital and oropharyngeal cancers.
- Types 6 & 11 (nononcogenic)
- Account for genital warts



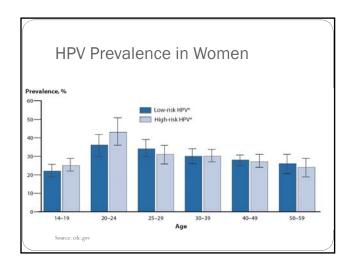
Prevalence of HPV in Women

- Prevalence by age groups:
 - Aged 14-19 years: 35%
 - Aged 20-29 years: 29%
 - Aged 30-39 years: 13%
 - Aged 40-49 years: 11%
 - Aged 50-65 years: 6.3%

females aged 14-59 years is 42.5%.

 National Health and Nutrition Examination Survey (NHANES) revealed the overall prevalence for United States

Source: cdc.gov



HPV Prevalence in Men

HPV Prevalence in Men

- About 1% of sexually active men in the U.S. have genital warts at any one time.
- Cancers of the penis, anus and oropharynx are uncommon
- only a subset of these cancers are actually related to HPV.
- Each year in the U.S. there are about:
 - 400 men who get HPV-related cancer of the penis
 - 1,500 men who get HPV-related cancer of the anus
 - 5,600 men who get cancers of the oropharynx
 - many of these cancers are related to tobacco and alcohol use, not HPV.

HPV & HIV-infection in Men

- Men who have sex with men (MSM) are about 17 times more likely to develop anal cancer than men who only have sex with women.
- Men with HIV-infection are more likely than other men to develop anal cancer.
- Men with HIV-infection are also more likely to get severe cases of genital warts that are harder to treat.

Source: cdc.gov

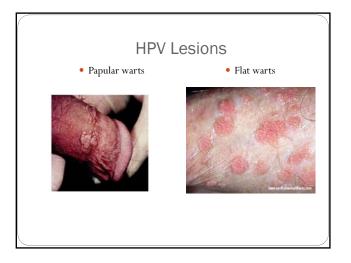
Clinical Symptoms & Diagnostic Screening and Testing

HPV Clinical Symptoms

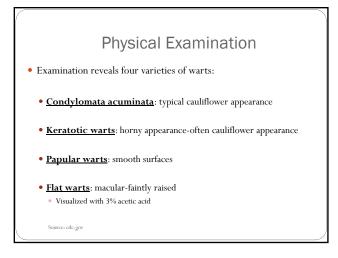
- Usually asymptomatic
- Large or traumatized lesions become ulcerated or infected.
 - Itching
 - Pain
 - Discharge
 - Malodor
- Urethral Lesions
 - Altered urine stream
 - Rarely obstruction

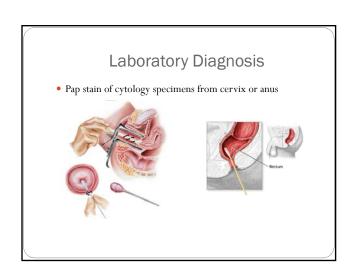
Source: cdc.go

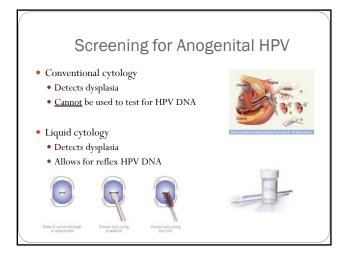
HPV Lesions • Condyloma acuminata • Keratotic warts







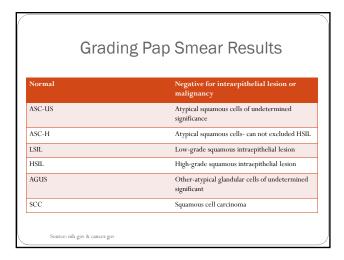


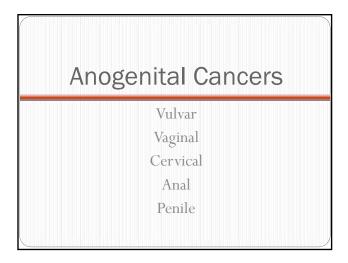


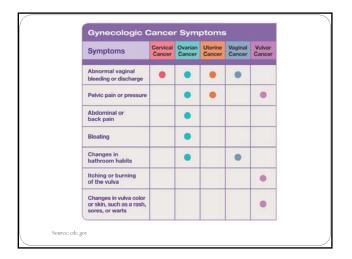
Recommendations for Screening

- Initial cervical Pap smear performed when first diagnosed or present for care for HIV-infection
 - Repeat 6 months
 - \bullet After two (2) consecutive normal Pap smears
 - · Conduct annually
- No national guidelines for anal cancer screening
 - Experts recommend anal Pap smear and digital anal examination as initial evaluation then annual
 - Repeat in 6 months
 - Two (2) consecutive normal anal Pap smears
 - · Conduct annually





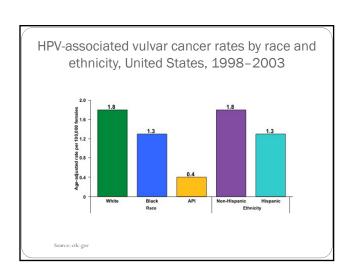






Vulvar Cancer Epidemiology

- Vulvar cancers are rare.
- It is estimated that almost 2,300 new cases of HPV-associated vulvar cancers are diagnosed in the United States each year.
- More white women get vulvar cancer than women of other races or ethnicities.
- In general, HPV is thought to be responsible for about 40% of vulvar cancers.



Risk Factors for Vulvar Cancer

- HIV-Infection
- HPV
- C----1-2--
- History of cervical cancer
- Age
- 50% of invasive vulvar cancer occurs in women over age 70
- Less than 20% of cases are in women younger than age 50
- Vulvar intraepithelial neoplasia (VIN)
 - · Pre-cancerous changes that may last for several years occur first
- Lichen sclerosus et atrophicus (LSA)
 - Vulvar skin becomes very thin and itchy.
 - About 4% of women having LSA later develop vulvar cancer.
- Melanoma or atypical moles
 - Having melanoma or dysplastic nevi (atypical moles) elsewhere on the body increases risk of developing melanoma on the vulva.
 - A family history of melanoma also leads to an increased risk.

Source: American Cancer Society

Vulvar Cancer Clinical Symptoms

- Itching, burning, or bleeding
- Color changes on the skin of the vulva
 - Erythematous or pale
- Skin changes on the vulva
 - Including a rash or warts
- Sores, lumps, or ulcers
- Pain in the pelvis
 - Especially on urination or during sex

Source: cdc.go

Vulvar Cancer Clinical Manifestation

Management of Vulvar Cancer

- Surgery:
 - Laser surgery
 - Excision
 - Vulvectomy
- Radiation therapy
- Chemotherapy

Source: cancer.gov

Prevention and Education for Vulvar Cancer

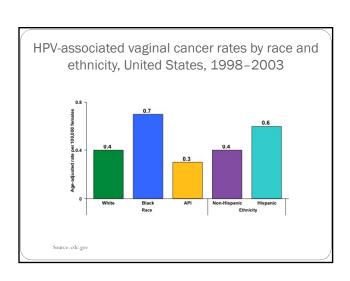
- Delaying first sexual intercourse until the late teens or older
- Avoiding sexual intercourse with multiple partners
- Avoiding sexual intercourse with someone who has had many partners
- Practicing safe sex, including condom use
- Quit smoking
- Gardasil
 - approved to prevent vaginal cancer.
- Annual physical examination
 - STI screening
 - Pelvic exam with Pap smear

Source: cancer.net



Vaginal Cancer Epidemiology

- Vaginal cancers are rare.
- It is estimated that around 600 new cases of HPV-associated vaginal cancers are diagnosed in the United States each year.
- More Black and Hispanic women get vaginal cancer than women of other races and ethnicities, similar to cervical cancer.
- In general, HPV is thought to be responsible for about 40% of vaginal cancers.



Risk Factors for Vaginal Cancer

- Age:
 - almost half of cases are in women age 70 or older
- Exposure to diethylstilbestrol (DES) as a fetus (mother took DES during pregnancy)
- History of cervical cancer
- History of cervical precancerous conditions
- Human papillomavirus (HPV) infection
- HIV infection
- Vaginal irritation
- Smoking

Source: American Cancer Society

Vaginal Cancer Clinical Symptoms

- Bleeding or discharge not related to menstrual periods
- Difficult or painful urination
- Pain during intercourse
- Pain in the pelvic area
- Constipation
- · A mass that can be felt

Source: cdc.go

Vaginal-Vulvar Cancer Clinical Manifestation



Management of Vaginal Cancer

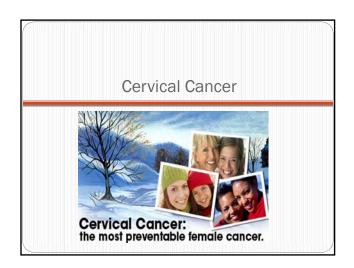
- Surgery:
 - Laser surgery to remove the cancer • LEEP (loop electroexcision procedure)
 - Local excision to remove the cancer
 - (Partial) vaginectomy to remove the vagina
 - $\bullet \ \, \text{Total hysterectomy}$
- Chemotherapy (topical)
- Radiation therapy

Source: cancer.org

Prevention and Education of Vaginal Cancer

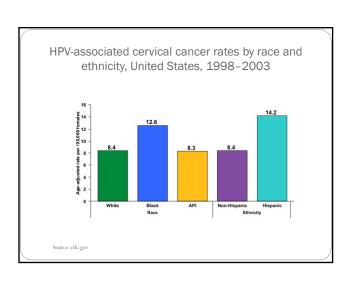
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Source: cancer.net



Cervical Cancer Epidemiology

- It is estimated that about 10,800 new cases of HPV-associated cervical cancers are diagnosed in the United States each year.
- More Black and Hispanic women get cervical cancer
 - diagnosed at later stages of the disease than women of other races or ethnicities
 - possibly because of decreased access to Pap testing or follow-up treatment



Risk Factors for Cervical Cancer

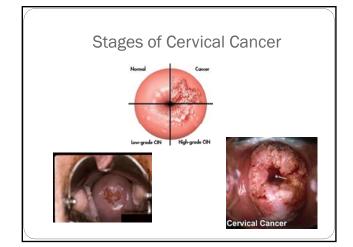
- HIV-infection
- CD4 count < 200
- Oral contraceptives
- Genital warts: previous or current
- Previous abnormal cervical and/or anal Pap smear
- Sexual activity before age 20
- Multiple sexual partners
- Cigarette smoking

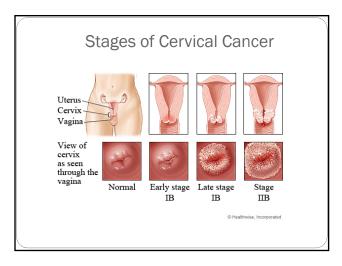
Source: HRSA-Guide for HIV/AIDS Clinical Care

Clinical Symptoms of Cervical Cancer

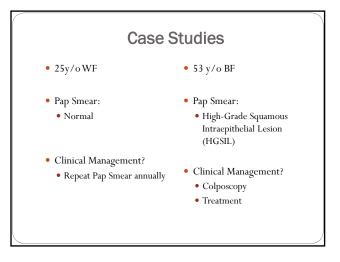
- Vaginal bleeding
- Unusual vaginal discharge
- Pelvic pain
- Pain during sexual intercourse.

Source: cdc.gov & cancer.org

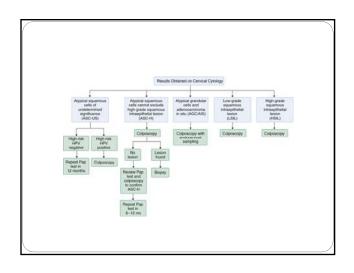


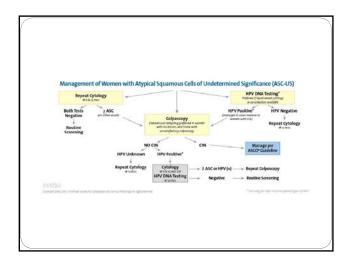


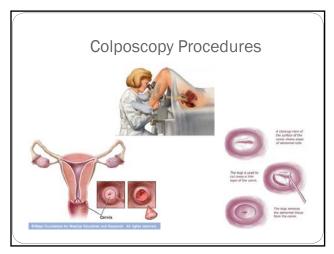
Case Studies • 38 y/o BF • 41y/oWF • Pap Smear: • Pap Smear: • Atypical Squamous Cells of • Atypical Squamous Cells of Undetermined Significance Undetermined Significance (ASCUS) (ASCUS) • Negative Human Papillomavirus • Human Papillomavirus (HPV) Present • Clinical Management? • Clinical Management? • Repeat Pap Smear in 6 Months Colposcopy



Case Studies • 35y/oWF • Pap Smear: • Low-Grade Squamous Intraepithelial Lesion (LGSIL) • Clinical Management? • Colposcopy







Management of Cervical Cancer

Psychosocial care and support

Provision of information to patients and

CD4 count >350 significantly cleared

Decrease in viral load may also have an

Communication methods (written,

• Support services

caregivers

audiotape)

Medical Management

Antiretroviral therapy

ACTG - A5029*

- Surgery
 Radical hysterectomy
 - Laparoscopic-vaginal radical hysterectomy
 - Surgical management in women with subtotal hysterectomy
 - Removal of pelvic lymph nodes
 - Fertility conservation surgery
 - Radical trachelectomy and pelvic lymph node dissection
 - Cold knife conisation or large loop excision of the transformation zone combined with pelvic lymph node dissection
- Non-surgical treatment
 - Concurrent chemoradiotherapy
 - Adjuvant chemoradiotherapy/radiotherapy

ncer.gov and Chang. M & Cu-Uvin. S HIV Med. 2012; 13(6)*

Prevention and Education of Cervical Cancer

- Delaying first sexual intercourse until the late teens or older
- Limiting the number of sex partners
- Avoiding sexual intercourse with people who have had many partners
- Avoiding sexual intercourse with people who are obviously infected with genital warts or show other symptoms
- $\bullet~$ Having safe sex by using condoms will reduce the risk of HPV & HIV -infection.
- Quit Smoking
- Annual physical examination

 - Pelvic exam with Pap smear

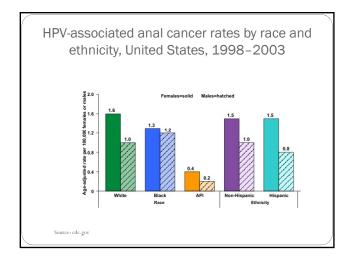
Source: cancer.net



Anal Cancer Epidemiology

- It is estimated that about 1,600 new cases of HPV-associated anal cancers are diagnosed in women in the United States
 - \bullet about 900 are diagnosed in men each year in the United States.
- More white women get anal cancer than women of other races.
- More Black men get anal cancer than men of other races.
- \bullet HPV is thought to be responsible for about 90% of anal cancers.

Source: cdc.gov



Risk Factors for Anal Dysplasia

- HIV-infection
- CD4 count < 200
- Receptive anal intercourse (RAI)
- HPV infection
- Genital warts: previous or current
- Immunosuppression
- High-grade cervical or vulvar dysplasia
- Cigarette smoking
- Multiple sexual partners

Source: HRSA-Guide for HIV/AIDS Clinical Care

Anal Cancer Clinical Symptoms

- Sometimes there are no signs or symptoms.
- Anal bleeding, pain, itching, or discharge.
- Swollen lymph nodes in the anal or groin area.
- Changes in bowel habits or the shape of your stool.

Source: cdc.gov & cancer.org

Case Studies

- 55 y/o BM
- 44 y/oWM
- Pap Smear:
 - Atypical Squamous Cells of Undetermined Significance (ASCUS)
- Clinical Management?
- Repeat anal Pap smear in 6 months
- Pap Smear:
- Low-Grade Squamous Intraepithelial Lesion (LGSIL)
- Human Papillomavirus (HPV) Present
- Clinical Management?
 - High Resolution Anoscopy (HRA)

Case Studies

- 26 y/o BM
- 54 y/o WM
- Pap Smear:
 - Normal
- Clinical Management?
 - Repeat anal Pap smear annually
- Pap Smear:
 - Low-Grade Squamous Intraepithelial Lesion (LGSIL)
- Clinical Management?
 - Repeat anal Pap smear in 6 months

Evaluation of Cytology: Abnormal Anal Pap Smear • All individuals with ASCUS or higher anal dysplasia • Referred for High Resolution Anoscopy (HRA) • Biopsy to grade the lesion Source: HRSA-Guide for HIV/AIDS Clinical Care

Management of Anal Dysplasia

- Focus of treatment is on HSIL
 - Topical 5-fluorouracil
 - Cryotherapy
 - Infrared coagulation
 - Shown to be most effective for HSIL in HIV-infected individuals
 - Laser therapy
 - Surgical excision

Source: HRSA-Guide to HIV/AIDS Clinical Care

Prevention & Education for Anal Dysplasia

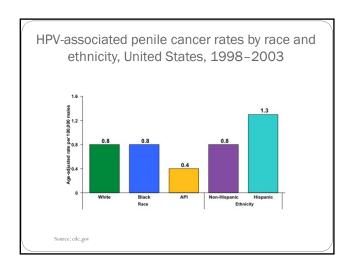
- Latex or plastic barrier
- Blocks HPV transmission in area covered
- Condoms use for vaginal, anal, and oral sex
- HPV vaccines
 - No data on efficacy of HPV vaccines in preventing anal HPV
 - · Studies are under way
 - ACTG -A5298 is a double-blinded, placebo-controlled, phase III trial of the quadrivalent human papillomavirus vaccine (qHPV) in HIV-1-infected men to prevent anal HPV infection.
- Patient Education
 - Avoid having anal sex, douching or using enemas before anal Pap smears.
- Annual physical examination

Source: HRSA-Guide to HIV/AIDS Clinical Care



Penile Cancer Epidemiology

- Penile cancer is another rare cancer.
- Estimated that more than 800 new cases of HPV-associated penile cancers are diagnosed in the United States each year.
- More common among Hispanic men than non-Hispanic men.
 - Uncircumcised
- In general, HPV is thought to be responsible for about 40% of penile cancers.



Penile Cancer Clinical Symptoms

- First signs:
- changes in color
- skin thickening
- Phimosis- foreskin difficult to retract or is constricted



- - a growth or sore on the penis
 - It is usually painless.
 - In some cases, the sore may be painful and bleed.



Source: cdc.gov

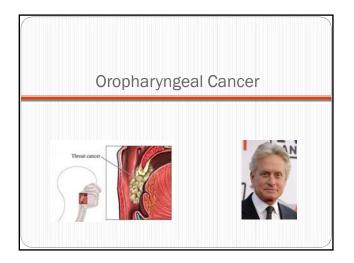
Management of Penile Cancer

- - Circumcision:
 - Partial penectomy: Surgeons try to spare as much of the glans (head) and shaft as possible to keep urinary and sexual function.
 - Total penectomy: Penile reconstruction surgery using a flap of skin from the forearm to create a new penis has been done, but the procedure is rare.
 - Mohs surgery (microscopically-controlled surgery): The surgeon surgically removes a thin layer of skin
 and looks at it right away under a microscope. This process is repeated until the cells are free of cancer.
- Laser surgery: Light from a laser vaporizes penile cancer cells.
- Radiation Therapy
- Chemotherapy
 - Topical chemotherapy: 5-fluorouracil or 5-FU, is applied as a cream for several weeks.
 - Systemic chemotherapy: Medicine injected into a vein or given by mouth.
 Imiquimod: A drug in a cream form that boosts the body's immune system

Source: cdc.gov & cancer.org

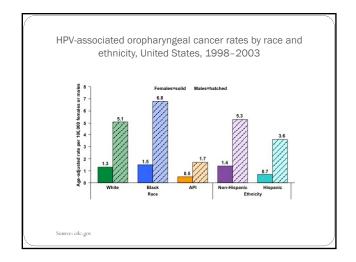
Prevention and Education of Penile Cancer

- Genital hygiene
 - Perhaps the most important factor in preventing penile cancer in uncircumcised men is good genital hygiene.
- Voiding HPV infection
 - Condoms use
 - Limit sexual partners
- Smoking cessation
- Annual physical exam
 - STI screening



Oropharyngeal HPV Epidemiology

- It is estimated that more than 1,700 new cases of HPV-associated oropharyngeal cancers are diagnosed in women.
 - nearly 5,700 are diagnosed in men each year in the United States.
- Black people get these cancers more often than people of other races and
 - Non-Hispanics and men get these cancers more often than Hispanics and women.
- Cancers in this area of the body are usually caused by tobacco and alcohol, but recent studies show that about 63% of oropharyngeal cancers are caused by HPV.



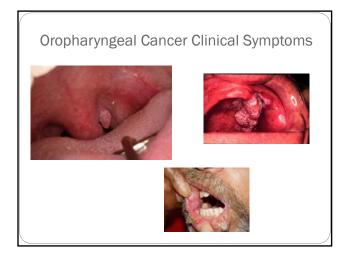
Oropharyngeal Cancer Risk Factors

- Tobacco use
- Alcohol use
- Sunlight
- Chronic irritation
- Lack of fruits and vegetables in diet
- Human papillomavirus (HPV) infection

Males
 Source: cdc.gov & cancer.org

Oropharyngeal Cancer Clinical Symptoms

- Sore throat or ear pain that doesn't go away
- Constant coughing
- Pain or trouble swallowing or breathing
- Weight loss
- Hoarseness or voice changes that last more than 2 weeks
- Lump or mass in the neck



Management of Oropharyngeal Cancer

- Surgery
 - Primary tumor resection –
- Maxillectomy removal of the tumor, including part or all of the hard palate (roof of the mouth), if bone is involved
- $\bullet \;\; Glossectomy$ removal of the tongue
- Mohs' micrographic surgery removal of the tumor in "slices" to minimize amount of normal tissue removed (may be considered when the cancer involves the lip)
- Laryngectomy removal of a large tumor of the tongue or oropharynx, which may involve removing
 the larynx (voice box)
- \bullet $\;$ Neck dissection if cancer has spread to the lymph nodes in the neck
- Radiation therapy
- Chemotherapy
- Targeted therapy drugs that target specific cancer cells

Prevention and Education of Oropharyngeal Cancer

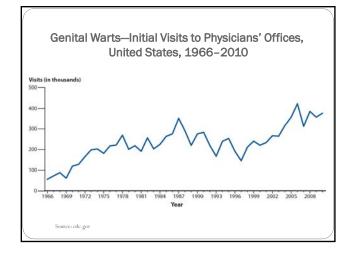
- Stopping the use of tobacco products is the most important thing a
 person can do, even for people who have been smoking for many years.
- To reduce your risk of lip cancer, reduce your exposure to sunlight and other sources of ultraviolent (UV) light.
- To reduce your risk of HPV infection, limit the number of sex partners.
- Regular dental examinations by a dentist are helpful in finding oral cavity cancer and some oropharyngeal cancers at an earlier stage.

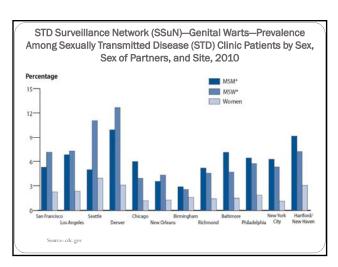
Source: cancer.net



Genital Warts Epidemiology

- National Health and Nutrition Examination Survey (NHANES) data 1999-2004
 - \bullet 5.6 % Sexually adults aged 18-59 years self reported history of genital warts
- National Disease and Therapeutic Index (NDTI) suggests that incidence of genital warts is increasing.





Clinical Symptoms of Genital Warts

- Lesions usually appear as a small to large bump or group of bumps
 - Raised or flat
 - Shaped like a cauliflower
- Occur within weeks to months after exposure
- One or more growths on the penis, testicles, groin, thighs, or in/around the anus.
- Warts may be single, grouped, raised, flat, or cauliflower-shaped. They usually do not hurt.
- Warts may appear within weeks or months after sexual contact with an infected person.

Genital Warts Clinical Symptoms







Management of Anogenital Warts Patient-Applied Treatment Provider-Applied Treatment

Patient-Applied Treatments

- Imiquimod 5% cream (Aldara)
 - · Apply three (3) times per week at bedtime
 - Wash off after 6-10 hours
 - Repeat for up to 16 weeks
 - Side Effects:
 - o Local irritation but mild
 - Safety in pregnancy unknown
- Podofilox 0.5% solution or gel (Condylox)
 - · Apply twice (2) daily for three (3) consecutive days
 - Followed by four (4) treatment free days
 - Repeat weekly up to four (4) cycles
 - Side Effects:
 - o Local irritation common
 - Safety in pregnancy unknown



Patient-Applied Treatments

- Sinecatechins 15% Ointment (Veregen)
 - First botanical drug approved for prescription use in the United States for immunocompetent patients.
 - It is made from the extract of green tea leaves.
 - Apply three (3) times per day
- Side Effects:
 - Local skin irritation



- Not Evaluated
 - Urethral, Intra-vaginal, Cervical, Rectal, Intra-anal
 - Patients under 18 years of age
- Treatment beyond 16 weeks

Provider-Applied Treatment

- Cyrotherapy with liquid nitrogen
 - Apply for approximately 10 -20 seconds
 - Repeat every 1-2 weeks
 - Side Effects:
 - o Local irritation
 - o Ulceration

• Podophyllin resin 10-25% in compound tincture of benzoin

- Apply small amount to external warts
- Instruct client to wash off in 1-4 hours
- · Repeat weekly as needed
 - Side Effects:
 - Local irritation
 - Ulceration
 - Contraindicated in pregnancy

• Local irritation

· Apply small amount to external wart

· Avoid contact with uninvolved tissue

Allow to dry-White "Frosting" develops

Apply oil based ointment around wart

- Side Effects:
- Ulcerations

· Repeat weekly as needed



- Surgical excision
- Laser surgery
- Intralesional interferon

Source: cdc.gov



Provider-Applied Treatment



Prevention & Education for Anogenital Warts

- Advise clients:
 - Most HPV infections are subclinical
 - \bullet Cancer and other complications are rare
 - Most sexually active persons have been infected
 - Condoms may help prevent some infections



Source: cdc.gov

HPV Vaccines Gardasil (Quadrivalent HPV) Cervarix (Bivalent HPV) Supports correct vaccination for girls and young women.

HPV Vaccines General Information

- No therapeutic effect on HPV existing diseases or conditions
- $\bullet~$ HPV vaccines $\underline{\mathrm{CAN}}$ be administered to:
- Lactating women
- Clients with minor acute illnesses-such as diarrhea or URI with or without a fever
- Women who have had an equivocal or abnormal Pap smears, + HPV or genital warts
- Clients who are immunocompromised either from disease or medication
- $\bullet~$ HPV vaccines should \underline{NOT} be given to:
 - Clients with a history of immediate hypersensitivity to any vaccine component
 - Quadrivalent HPV contraindicated for persons with hypersensitivity to yeast
 - \bullet Bivalent HPV in prefilled syringes contraindicated for persons with an aphylactic latex allergy
 - Clients with moderate to severe acute illnesses.
 - Pregnant women

Source: cdc.gov

HPV Vaccines Safety

- Pain at injection site
 - Ice the injection site prior to administration
- Fever
- Dizziness
- Nausea
- Syncope
 - $\bullet\,$ Client should be sitting or lying down during injection
 - Observe client in seated or lying position for 15 minutes

Education for HPV Vaccines

- Importance of receiving all 3 doses of HPV vaccine
- Vaccinated females still need regular cervical cancer screeningbeginning at age 21
- All vaccinated clients should continue to practice abstinence or protective sexual behaviors

Source: cdc.gov

HVP Vaccine: Gardasil

- Approved June 2006/October 2009
- HPV quadrivalent
- Targets: HPV types 6, 11, 16, 18
 - HPV types cause 90% of genital warts
 - Protects against anus, vagina & vulvar cancer





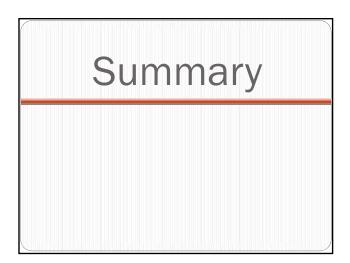
- First dose 0 month
- Second dose- 2 months after first dose
- Third dose- 6 months after first dose
- Shake vial before administration



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HPV Vaccine: Cervarix

- Approved October 2009
- HPV Bivalent
- Targets: HPV types 16 & 18
 - HPV types cause 70% of cervical cancers
- Approved for females aged 10-25 years
- Administered intramuscular: 3 dose series
 - First dose 0 month
 - Second dose- 1 month after first dose
 - Third dose 6 months after first dose



Comparison of Cervical and Anal Cancer		
	Cervical Cancer	Anal Cancer
Issues	Decreasing	Increasing
Prevalence in general population	8.1/100,000	1.6/100,000
Prevalence in HIV population	5.6/100,000	34.6/100,000
Median CD4 at diagnosis	287	276
Duration of HIV (median)	8.2 years	12.4 years
HPV Types	16 (50%) & 18 (20%)	16 (66%) & 18 (5%)
Median age diagnosis	48 years	60 years
National guidelines	Yes	No
Palpation useful	No	Yes
Cytology useful	Yes	Probably
HPV Testing useful in screening	Yes	No
Management	Colposcopy	High resolution anoscopy
Availability of well trained cytologists	Extensive	Limited
Treatment: High grade lesions Source: Darragh and Winkler, Co	Laser, LEEP meer-Cytopath 2011; 119:5	Infrared coagulation, excision

Role of the HIV Nurse Clinician

- Client Behavioral Modifications:
 - Avoid tobacco use
 - Avoid alcohol use
 - Condom use
 - Limit number of sexual partners
- Provides Interventions:
 - Annual physical examination
 - Annual or regular screenings
 - Cervical and anal Pap smears
 - Appropriate management of HPV lesions
 - Patient –Applied vs. Provider-Applied
 - Education & Counseling
 - Vaccination

Thank You Questions & Answers

References

- cdc.gov: Centers for Disease Control and Prevention
- cancer.gov: National Cancer Institute
- cancer.net: American Society of Clinical Cancer
- cancer.org: American Cancer Society
- hab.hrsa.gov: Health Resources and Services Administration-HIV/AIDS Program
- nih.gov: National Institutes of Health

Robert Dodge, PhD, RN, ANP, AACRN

Wake County Human Services Clinic A 10 Sunnybrook Road Raleigh, NC 27610

Office: 919-250-3078
Fax: 919-250-4429
Email: Robert_Dodge@med.unc.edu