Anogenital Human Papilloma Virus
The Anus is a Sex Organ

• The anus is used for sexual stimulation by people of all sexual persuasions
• Anal sex includes but is not limited to intercourse
• Anal intercourse is not the most common sexual activity among GMSM
• Anal sex is safe if appropriate care is taken to avoid injury and STDs
Prevalence of Anal HPV Infection

Any HPV Type
- GMSM  53%
- Women  31%
- MSW  14%

Low Risk HPV
- GMSM  32%
- Women  17%
- MSW  9%
Prevalence of Anal High Risk HPV

Any High Risk HPV Type
  GMSM  35%
  Women 13%
  MSW  5%

HPV Type 16
  GMSM  12%
  Women  4%
  MSW  2%
Anophobia in Health Care

• Lack of knowledge among health care providers
• Failure to take appropriate history
• Failure to examine the patient
• Failure to follow up on patient complaints of anal problems
Anal and Perianal Warts

- Emotional impact
- Cosmetic concerns
- Hygiene problems
- Impact sexual function
- Pain, bleeding, itch
- Incontinence of stool
Treatment of Anal Warts

• Infrared coagulation
• Electro-cautery
• Trichloroacetetic acid
• Topical 5-Fluorouracil
• Topical Imiquimod
• Cryoablation
• Local excision
Incidence of Anal Cancer, All Men and Women Aged 40-64, San Francisco County 1973-1999
Anal Cancer Incidence

• Increased rates in all racial/ethnic groups
• Increased rates in all adult age groups
• Risk increases with age
• Only 1% of anal cancers occur before age 35
• Anal cancer is a rare cancer
• Higher rates in female general population than males
• Disproportionately affects men with HIV
Anal Cancer Incidence

• Anal cancer currently: 1/100,000
• Anal cancer among HIV- GMSM: 13-35/100,000
• Anal cancer may be three times as high among HIV+ GMSM vs. HIV- GMSM: ~100/100,000
Anal Cancer Risk Factors

- History of cervical cancer or cervical dysplasia
- History of receptive anal intercourse
- Organ transplant
- Long-term steroid therapy
- Congenital immune deficiency
- Smoking tobacco
- **HIV infection**
Relative Risk for Anal Cancer

• 52 fold elevation in HIV-infected GMSM
• 32 fold elevation in HIV-infected MSW
• 24 fold elevation in HIV-infected women
Signs and Symptoms of Anal Cancer

- Bleeding from the anus or rectum.
- Pain or pressure in the area around the anus.
- Itching or discharge from the anus.
- A lump near the anus.
Treatment Options for Anal SCC

• Chemoradiation

• Abdominoperineal resection with permanent colostomy
Squamous Intraepithelial Lesions (SIL)
Squamocolumnar Junction

- Stratified squamous epithelium
- Columnar epithelium
As shown in this illustration, with increasing severity of SIL of either the cervix or anus, the proportion of the epithelium replaced by immature cells with large nuclear-cytoplasmic ratios increases. Invasive cancer probably arises from one or more foci of high-grade SIL (HSIL), as depicted in the drawing by epithelial cells crossing the basement membrane below the region of HSIL.
Abnormal Anal Pap Smear Findings

• Atypical squamous cells of uncertain significance (ASCUS)
• Low-grade squamous intraepithelial lesion (LSIL)
• High-grade squamous intraepithelial lesion (HSIL)
• Atypical squamous cells – cannot rule out high-grade lesion (ASC-H)
GMSM with Abnormal Anal Cytology

HIV-  HIV+  HIV+  HIV+
CD4>500  200-500  <200
Invasive Anal Cancer Rates in Denver Health ID Clinic Patients

- 0 Cases per year from 1995-7
- 1 Cases per year from 1998-2000
- 3.3 Cases per year from 2001-3
Cervical Cancer Incidence

- Cervical cancer prior to cervical cytology screening: 40-50/100,000
- Cervical cancer currently: 8/100,000
- Rates of cervical cancer have fallen by approximately 75% since the introduction of Pap screening programs
Elements of an Anal Cancer Prevention Program

- Anal Pap smear screening of high risk individuals
- Referral of patients with abnormal pap smear results for High Resolution Anoscopy (HRA) and biopsy
- Ablative treatment of HSIL
- Regular follow up
Normal Anorectal Transformation Zone
Anal Histopathology

• Atypical/HPV changes
• Anal Intraepithelial Neoplasia (AIN)
  – AIN I/mild dysplasia
  – AIN II/moderate dysplasia
  – AIN III/severe dysplasia
Anal Histopathology

- Squamous Cell Carcinoma In-Situ (SCCIC)
- Microinvasive SCC (anal cancer)
Treatment of high-grade anal dysplasia

- Infrared coagulation
- Electro-cautery
- Trichloroacetic acid
- Topical 5-Fluorouracil
- Topical Imiquimod
- Cryoablation
- Local excision
Who Should Receive Anal Pap Smear Screening?

- No one
- No one for whom follow up diagnostic and treatment services are not available
- People with HIV
- Women with a history of cervical cancer
- Gay men and other men who have sex with men
- Symptomatic persons with risk factors
ANAL CANCER/HSIL OUTCOMES RESEARCH STUDY
Primary Objective

To determine the effectiveness of treating anal high-grade intraepithelial neoplasia (HSIL) to reduce the incidence of anal cancer in HIV infected men and women.
Enrollment

• 17,385 participants screened
• Accrual target of 5,058 found to have HSIL
Duration

- 3 year accrual period
- 5 years follow up for each participant
- Participants will be followed every 6 months at least at a minimum
Eligibility

- Men and women with HIV infection
- 35 years of age and older
- Previously untreated HSIL
Treatment vs. Observation

• Treatment will be one of the ablative techniques now commonly being used to treat HSIL

• Follow up schedule will depend on treatment modality employed

• Observation will include HRA every 6 months with biopsies as indicated by exam findings
Hypothesis

Treatment of anal high-grade dysplasia will lead to a reduction of 75% of incident anal cancer compared with a population with anal HSIL that is observed without treatment.
Secondary Objectives

- Determine the safety of ablative methods
- Evaluate quality of life measures in both study arms
Exploratory Objectives

Create a bank of well-annotated specimens that will allow the identification of biomarkers and other viral and host factors in HSIL progression to cancer.