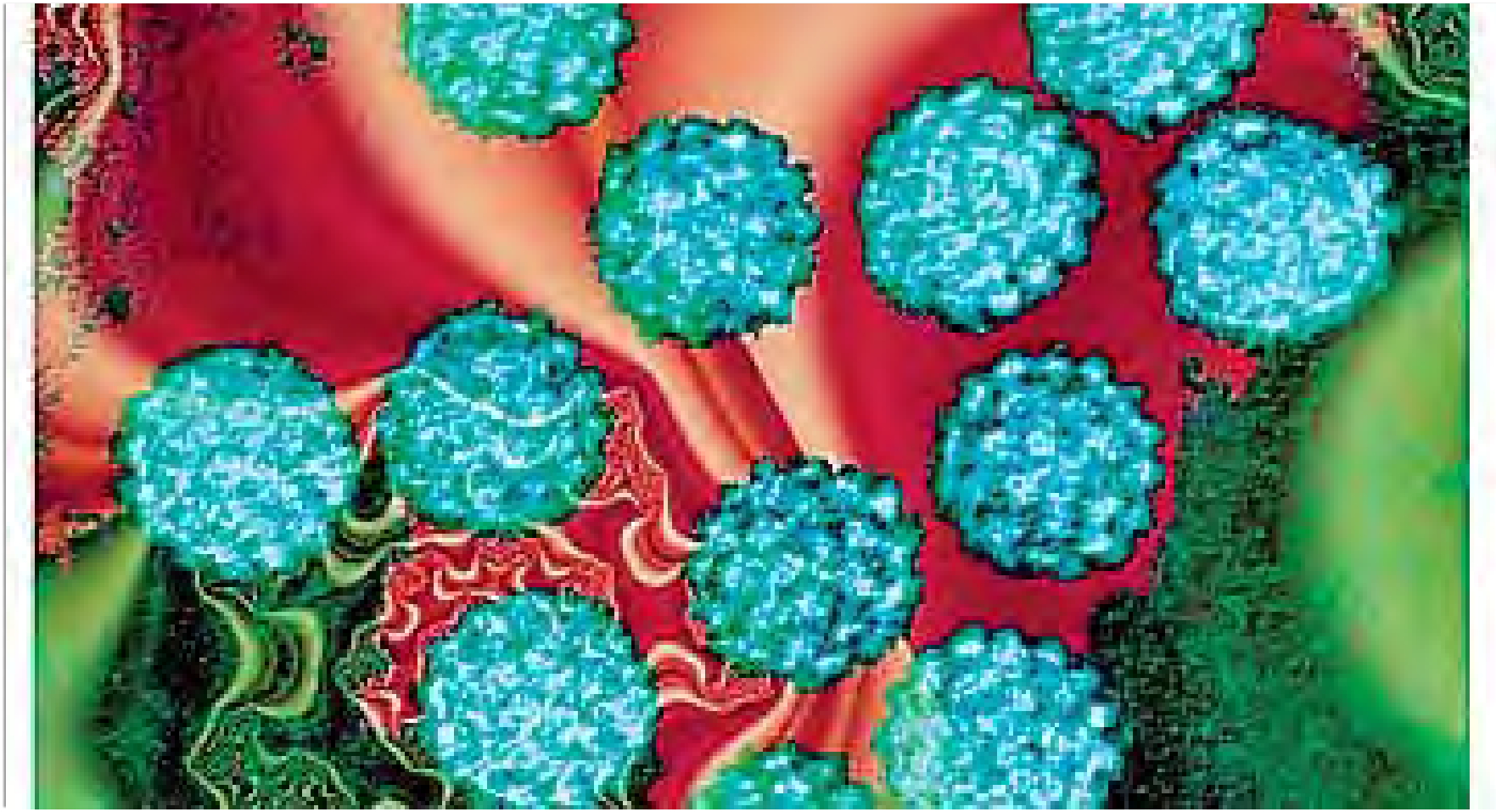
Anogenital Human Papilloma Virus



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

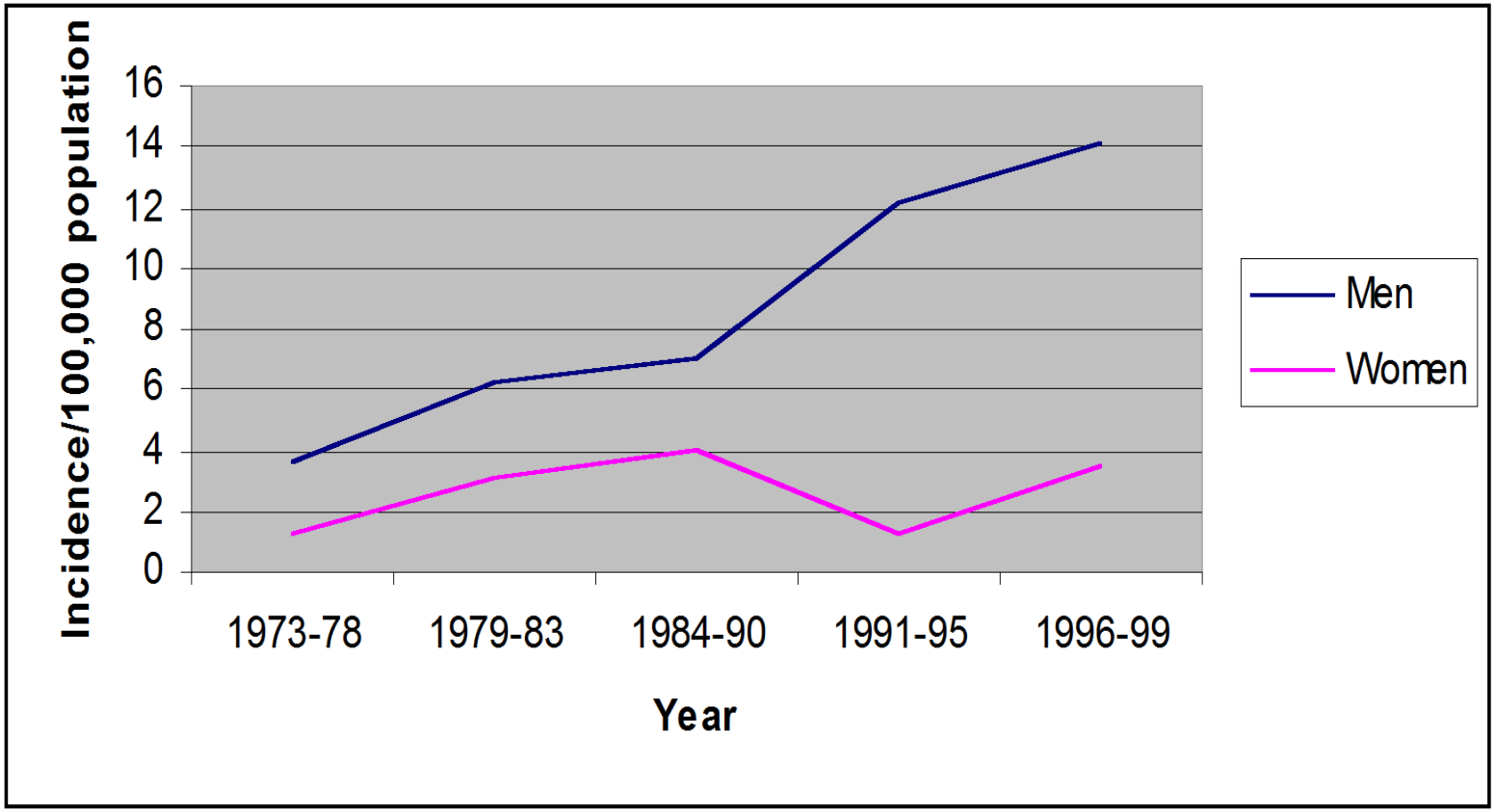
Anal and Perianal Warts

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

Treatment of Anal Warts

- Infrared coagulation
- Electro-cautery
- Trichloroaceitic 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

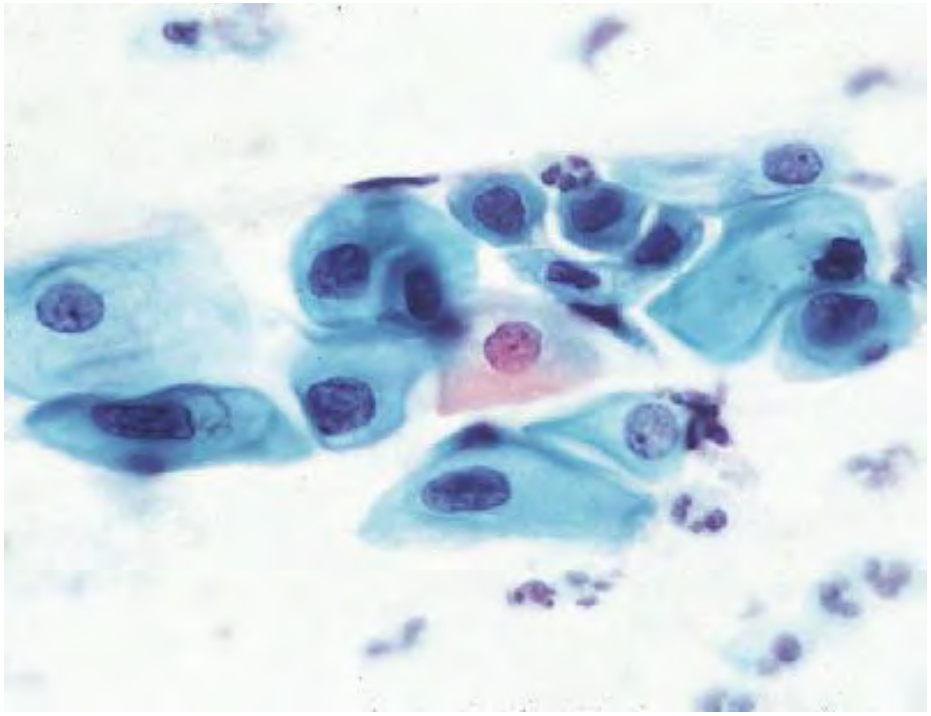
Signs and Symptoms of Anal Cancer

- 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

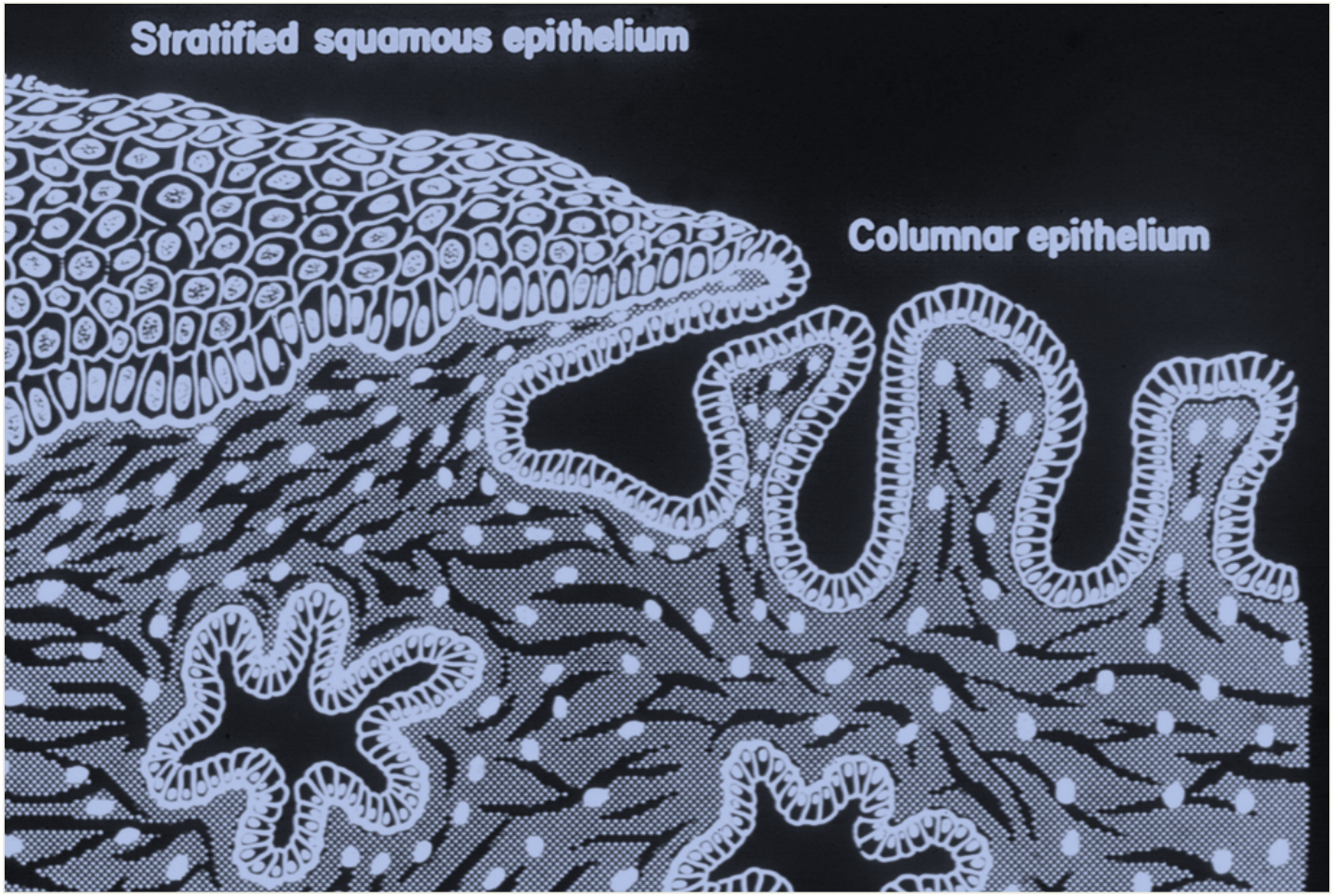
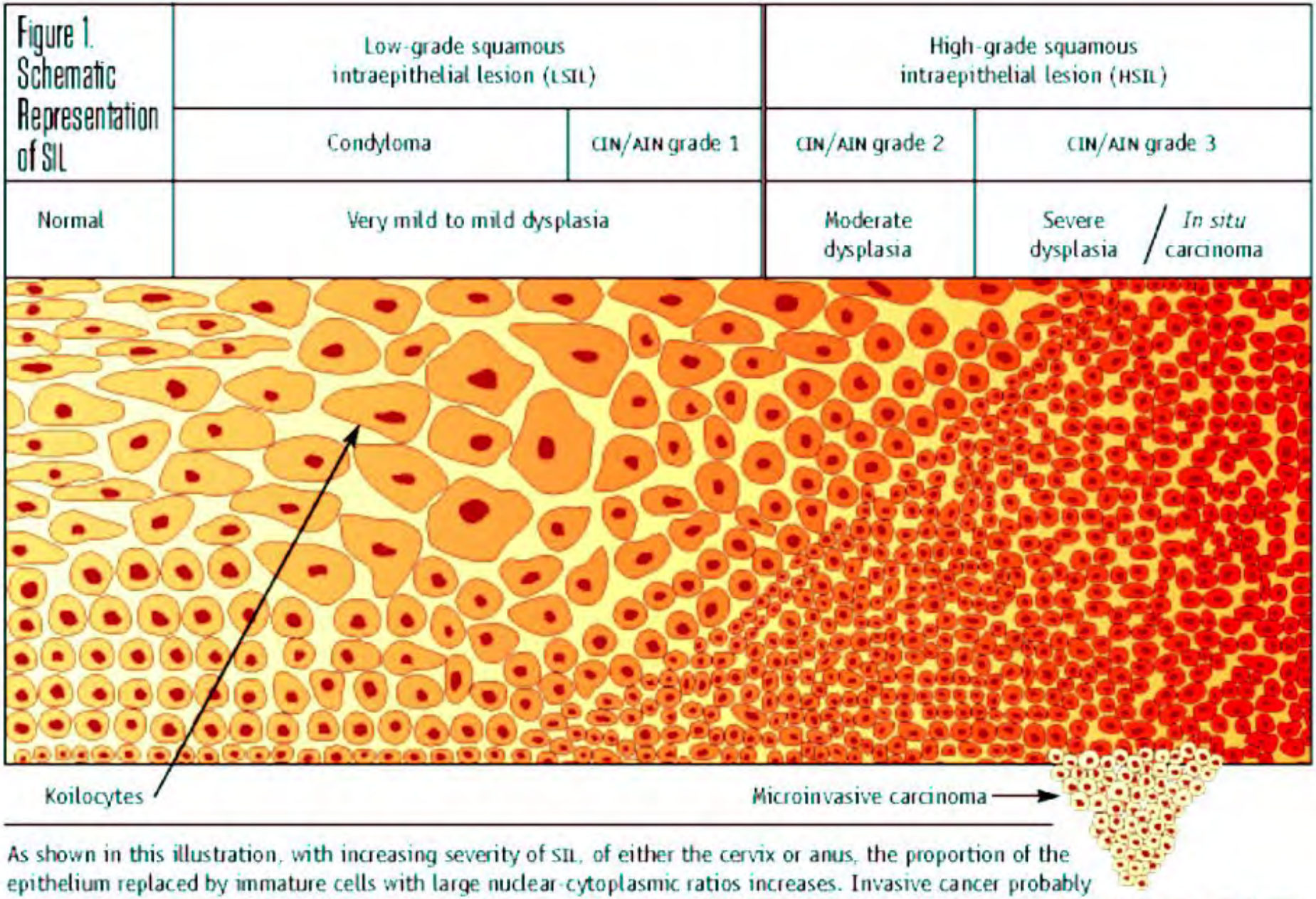


Figure 1. Schematic Representation of SIL



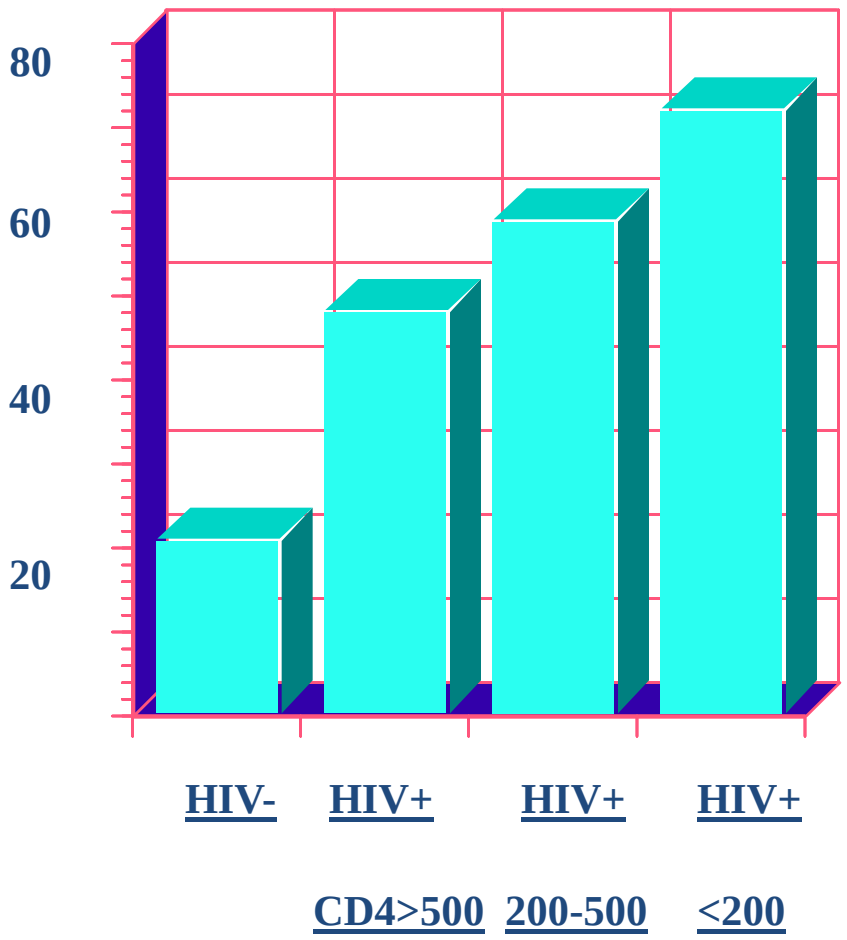
As shown in this illustration, with increasing severity of SIL, of either the cervix or anus, the proportion of the epithelium replaced by immature cells with large nuclear-cytoplasmic ratios increases. Invasive cancer probably arises from one or more foci of high-grade SIL (HSIL), as depicted in the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

Source: Joel Palefsky, MD, FRCP(C)

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



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

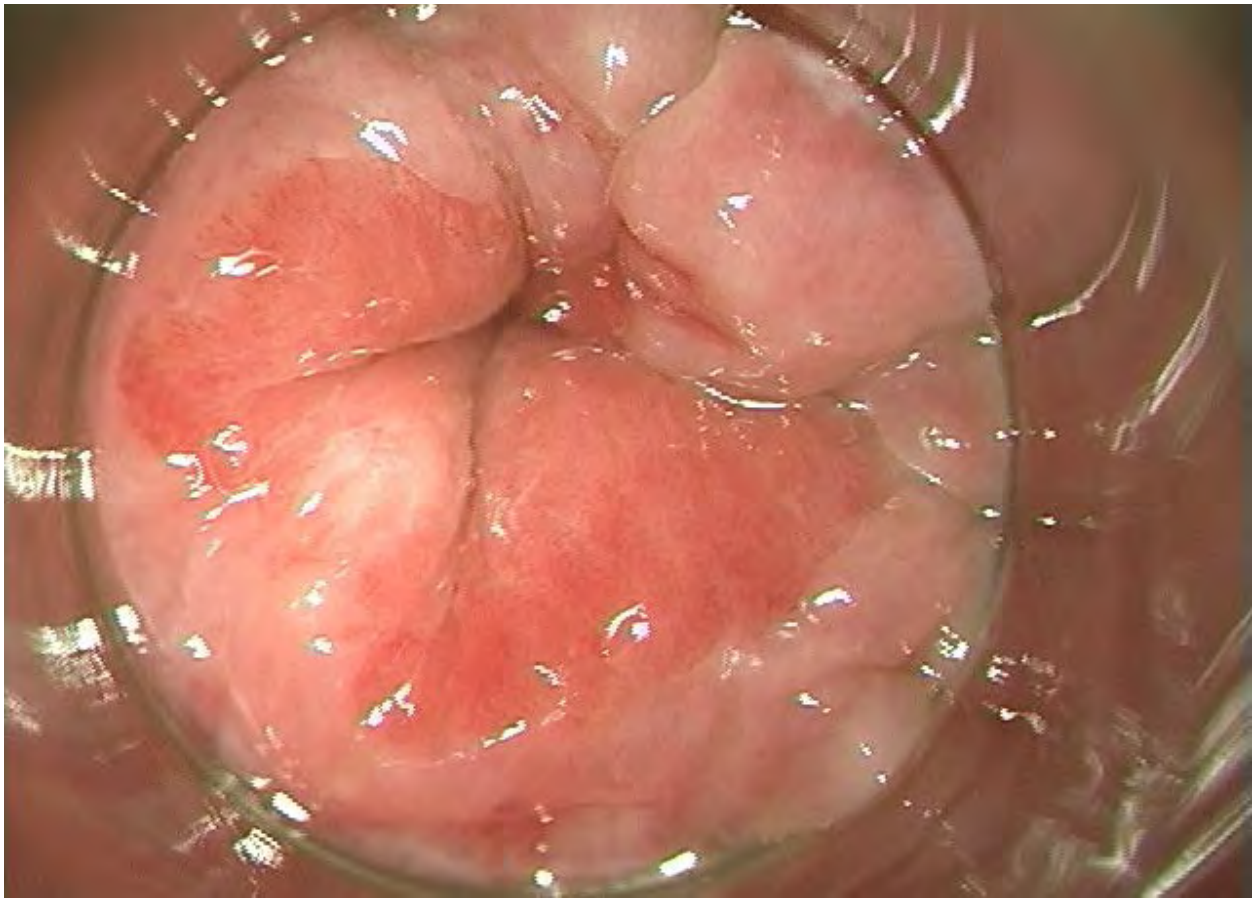
- Cervical cancer prior to cervical cytology screening: 40-50/100,000
- Cervical cancer currently: 8/100,000
- Rates of cervical cancer have fallen by approximately 75% since the introduction of Pap screening programs

Elements of an Anal Cancer Prevention Program

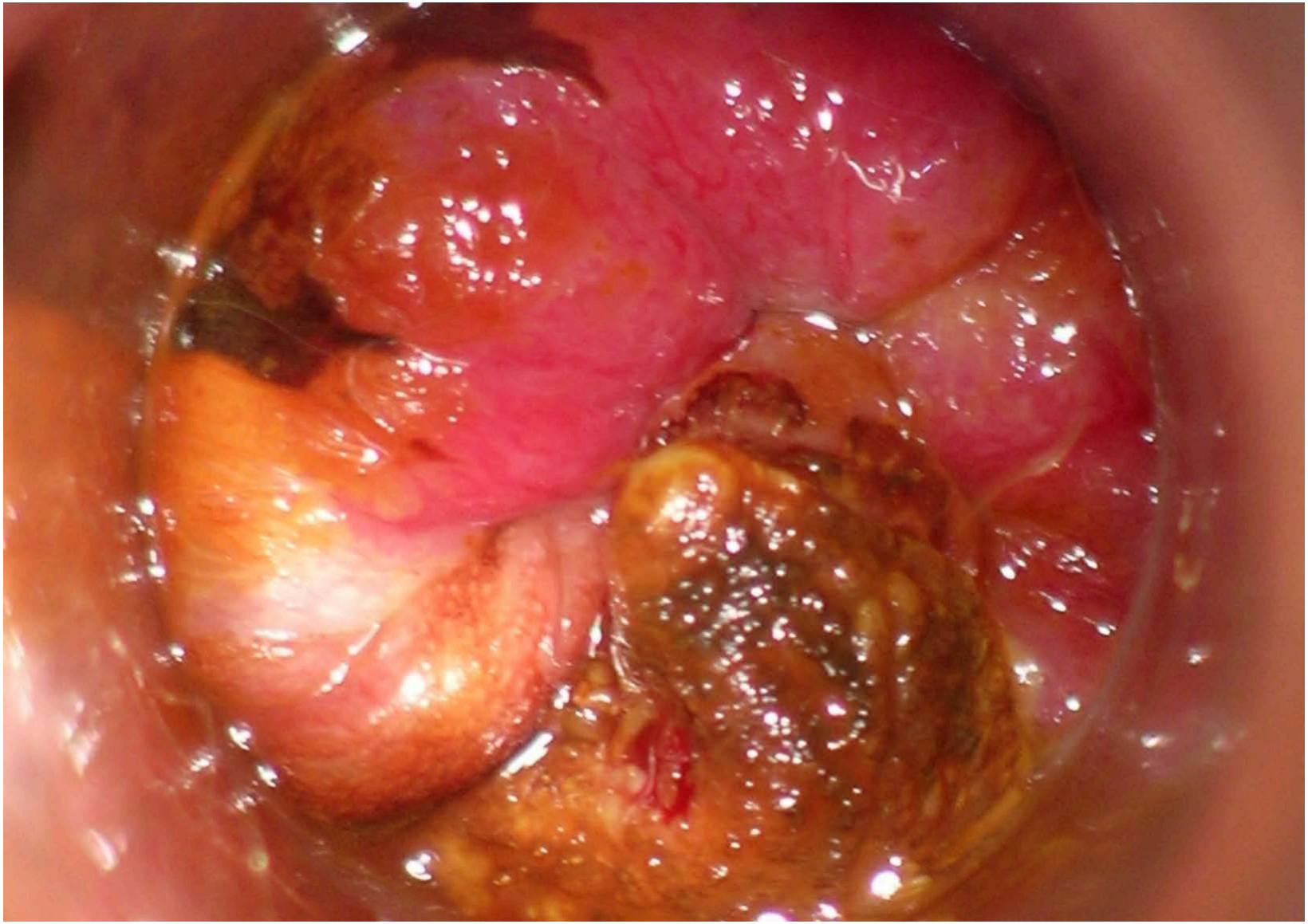
- Anal Pap smear screening of high risk individuals
- Referral of patients with abnormal pap smear results for High Resolution Anoscopy (HRA) and biopsy
- Ablative treatment of HSIL
- Regular follow up


TriScope

Normal Anorectal Transformation Zone



UCSF Anal Neoplasia Study



Anal Histopathology

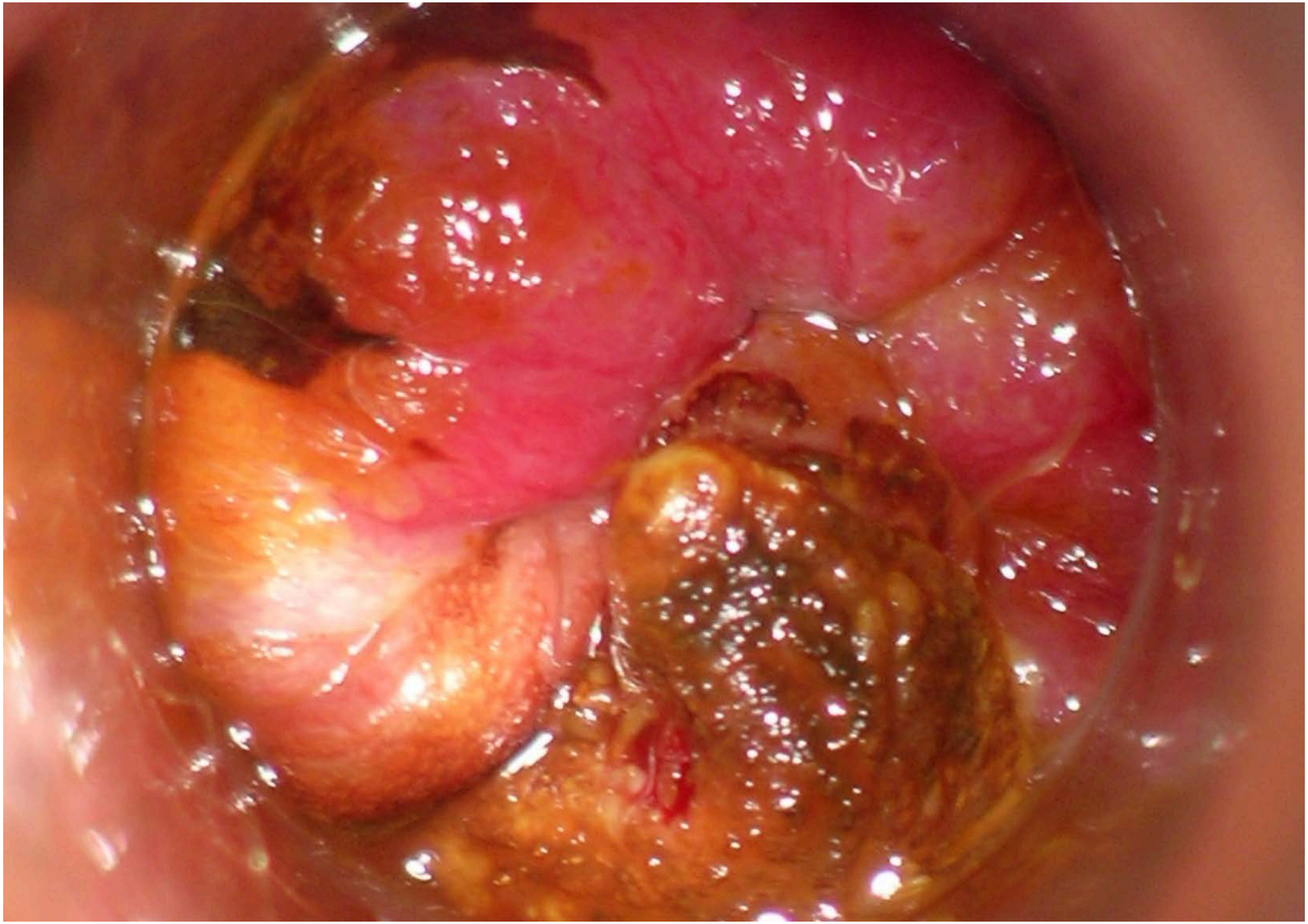
- Atypical/HPV changes
- Anal Intraepithelial Neoplasia (AIN)
  - AIN I/mild dysplasia
  - AIN II/moderate dysplasia
  - AIN III/severe dysplasia

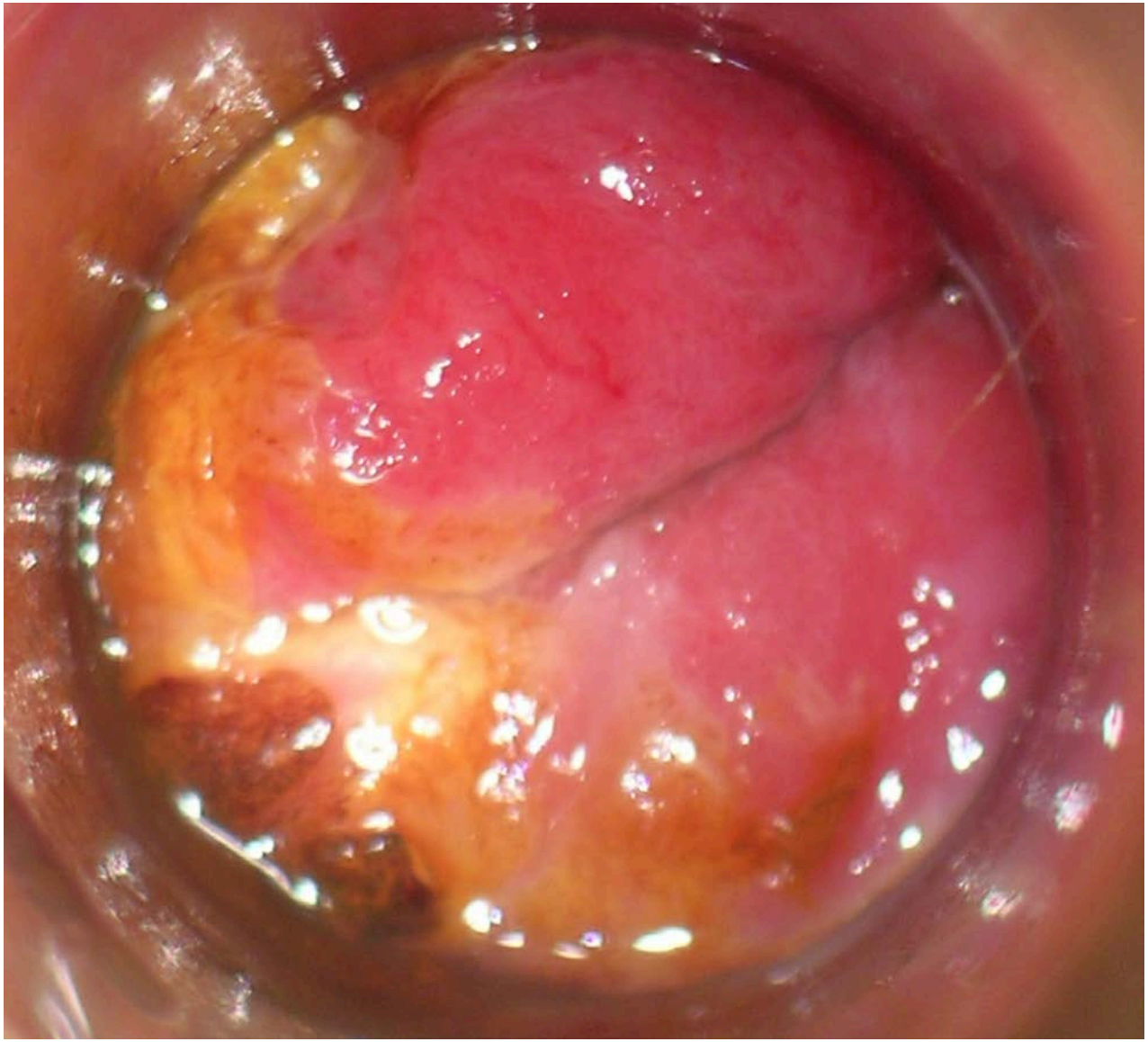
Anal Histopathology

- Squamous Cell Carcinoma In-Situ (SCCIC)
- Microinvasive SCC (anal cancer)

Treatment of high-grade anal dysplasia

- Infrared coagulation
- Electro-cautery
- Trichloroaceitic 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. Obsevation

- 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