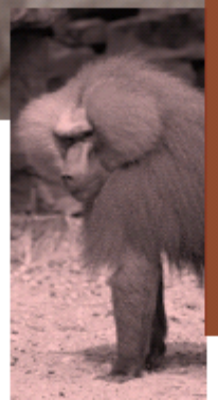
Joep Bartelsman
Paul Drillenburg



(potentiële) belangenverstrengeling	**Geen**
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Bedrijfsnamen
• Sponsoring of onderzoeksgeld • Honorarium of andere (financiële) vergoeding • Aandeelhouder • Andere relatie, namelijk …	• • • •

Joep Bartelsman
Paul Drillenburg

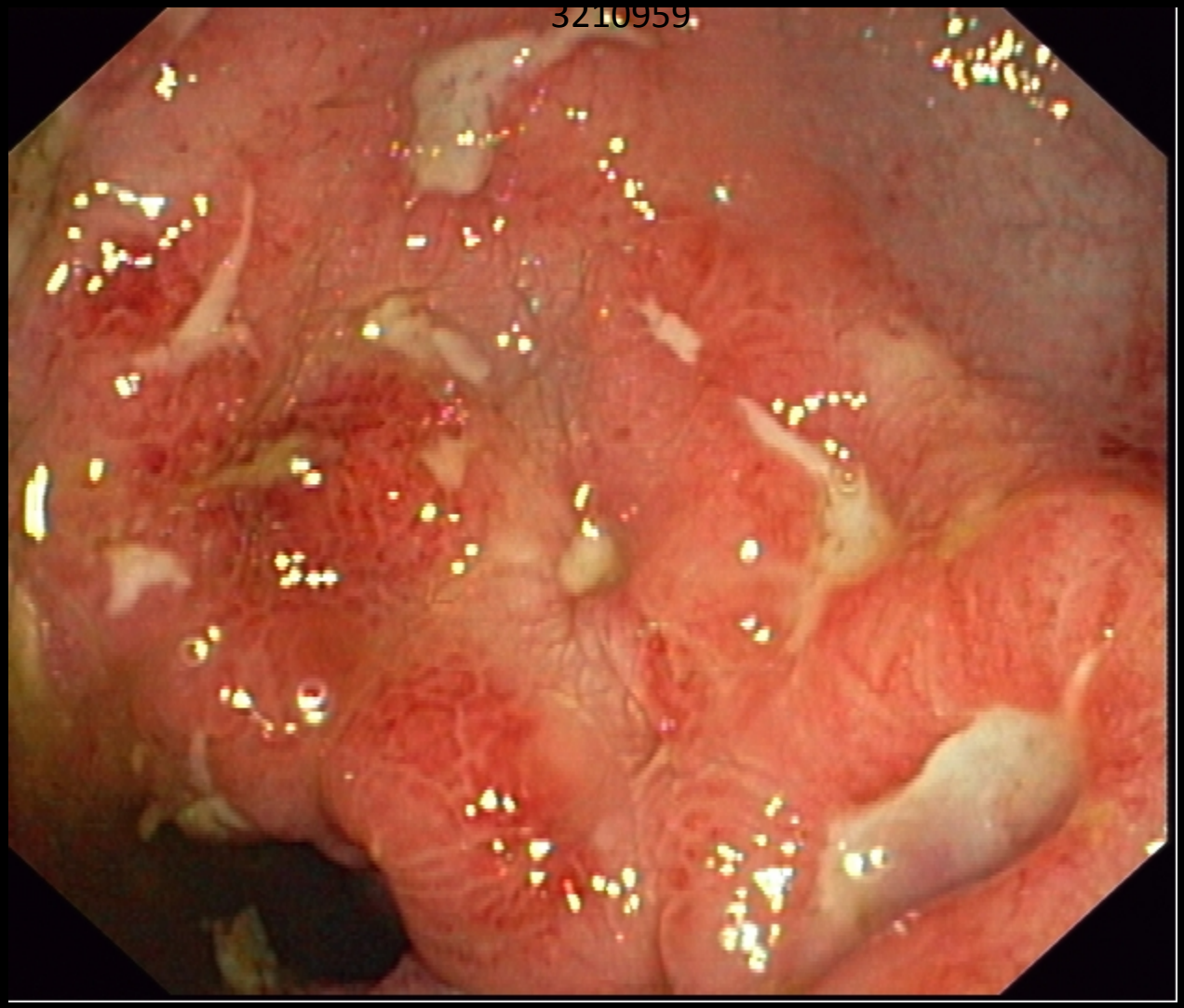
- Proctitis/SOA's
- HIV/Anal intraepithelial neoplasia
- Anus carcinoom

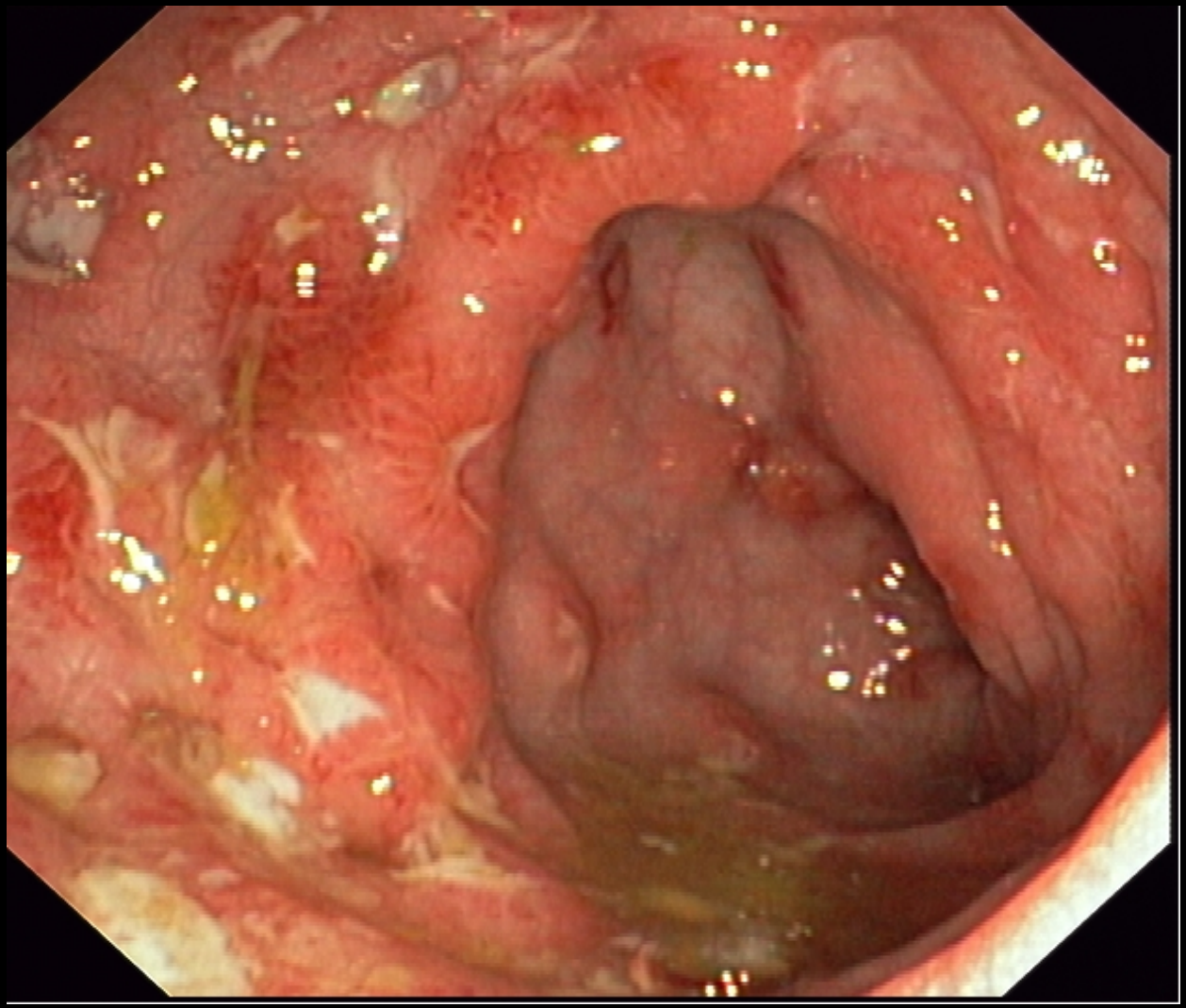

MSM

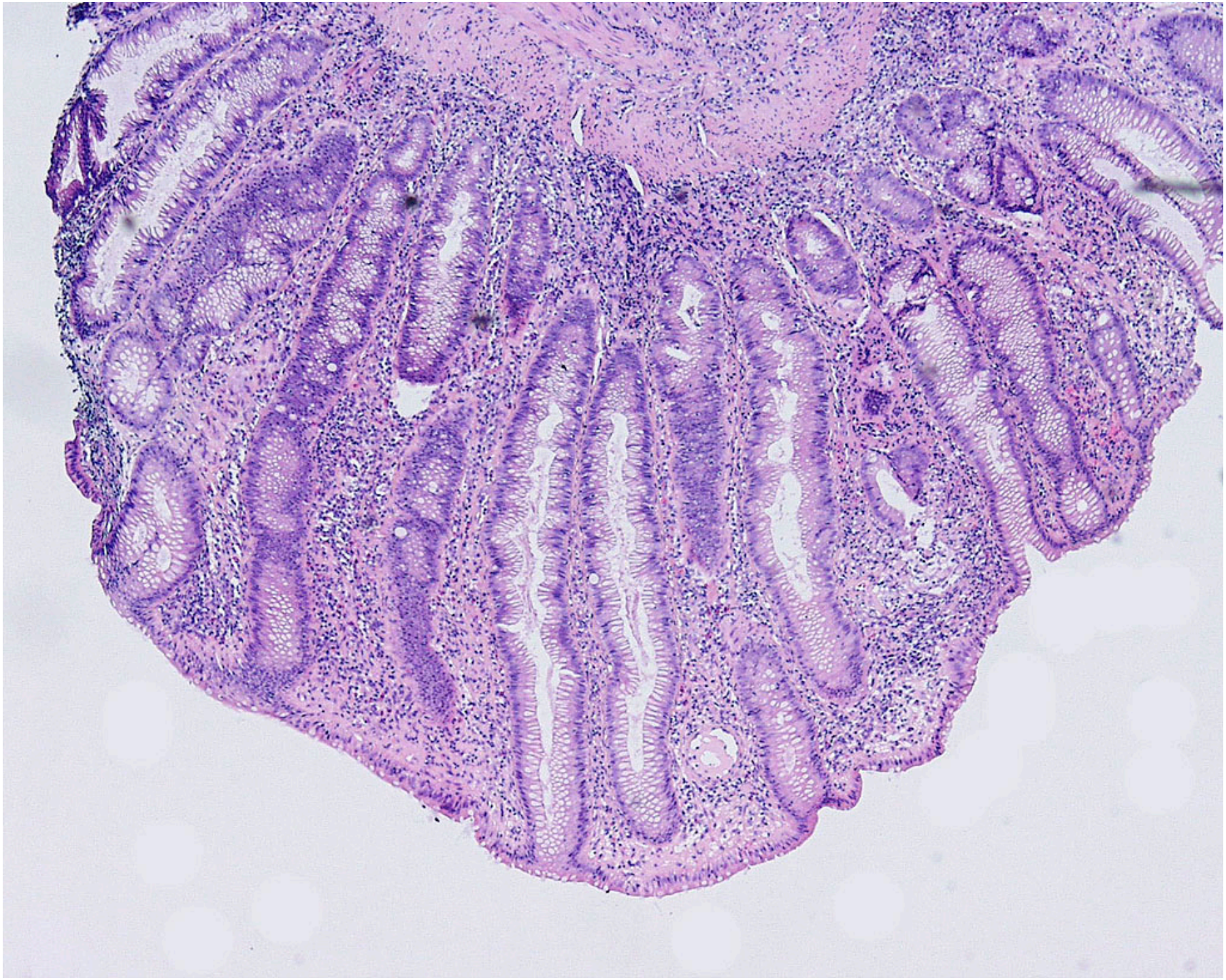
35 –year old man

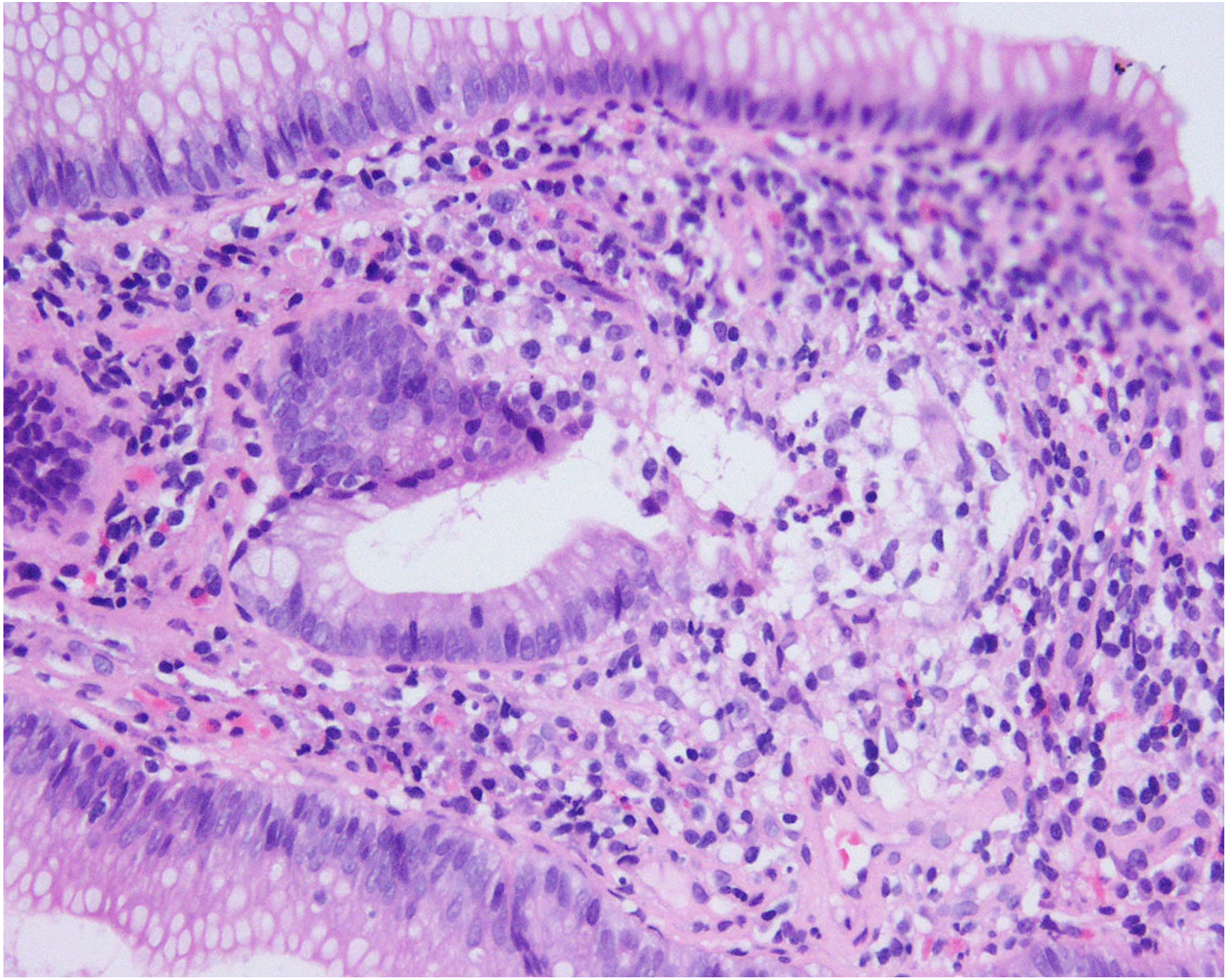
- since two days: pain on defecation
  rectal discharge
  blood in stools
  defecation : 15 x

- since 5 years: HIV-infection: CD4 > 400.10_6/L
- recent visit Thailand: amebiasis + giardiasis


3210959

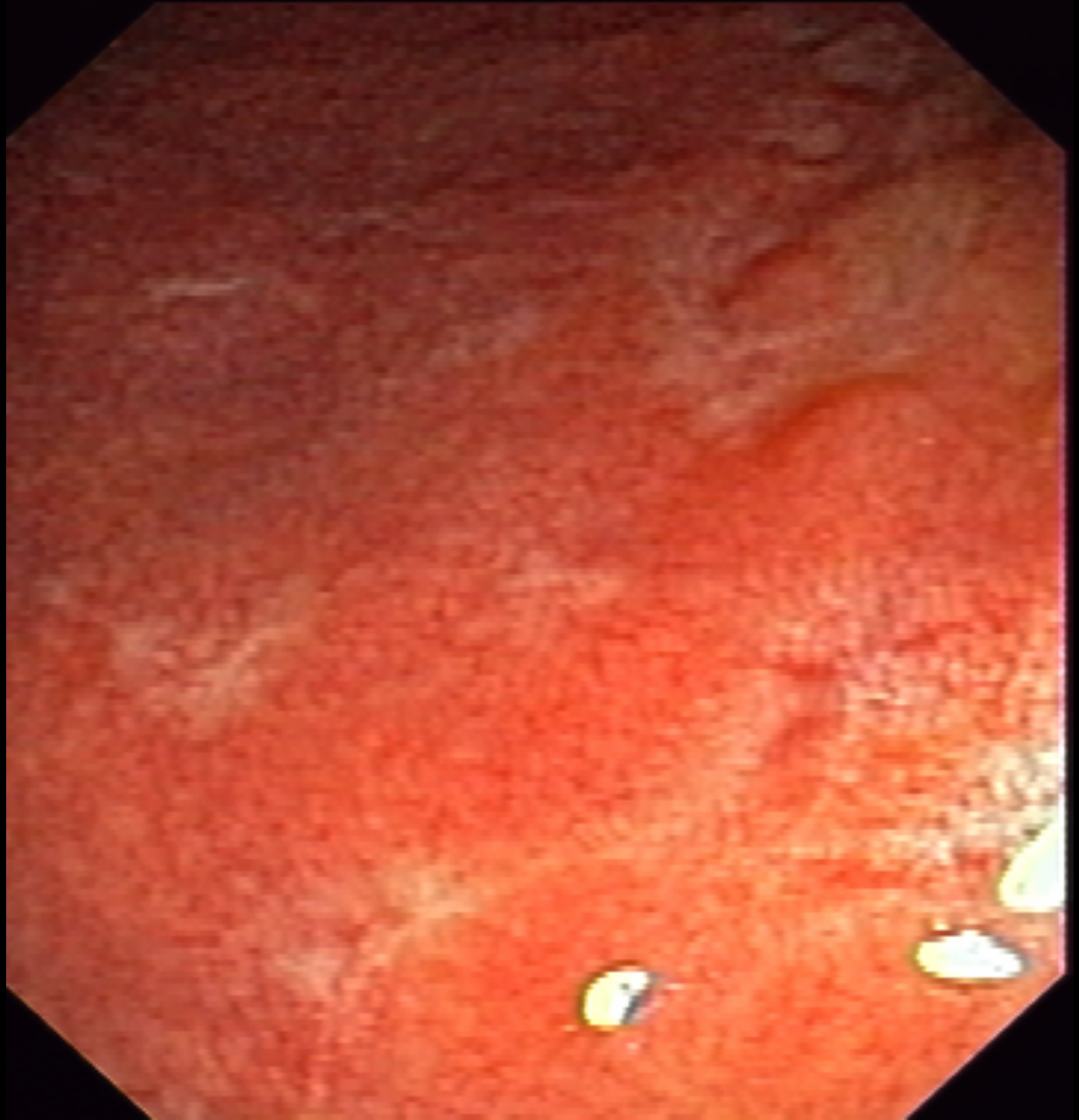






3210959

after treatment



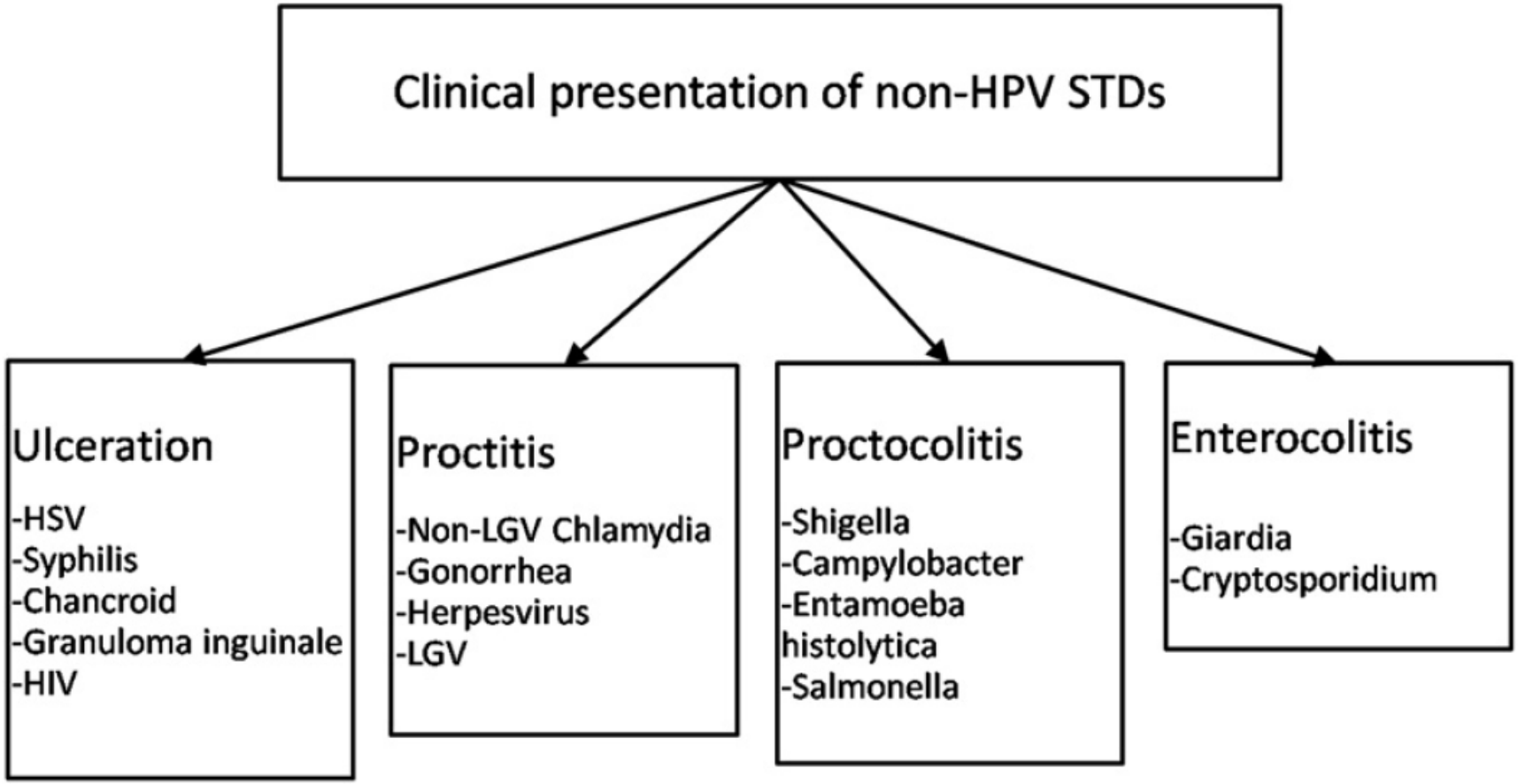


Fig. 1. Common causes of non-HPV sexually transmitted diseases. Refer to www.cdc.gov for an exhaustive review of sexually transmitted diseases.

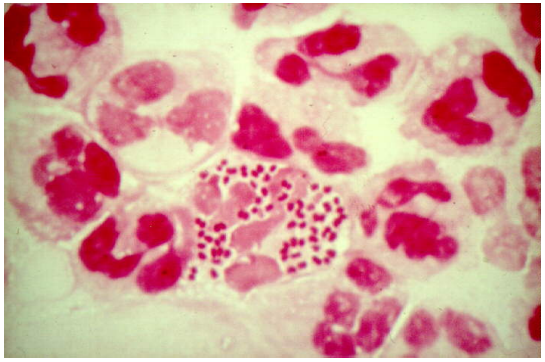
Lee,2010

infectious proctitis

STD

N.gonorrhoea	*30 %*
C.trachomatis	*19 %*
HSV-2	*16 %*
T.pallidum	*2 %*
Co-infection	*10 %*

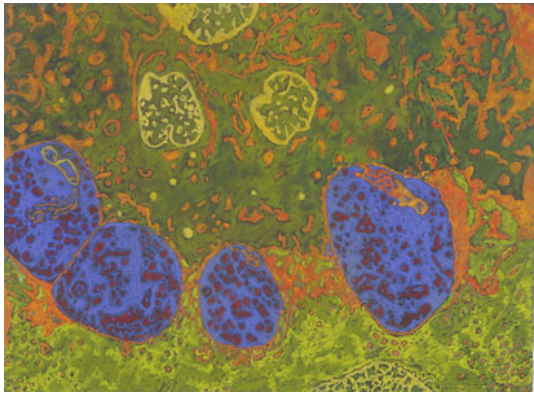
PROCTITIS
gonorrhoea

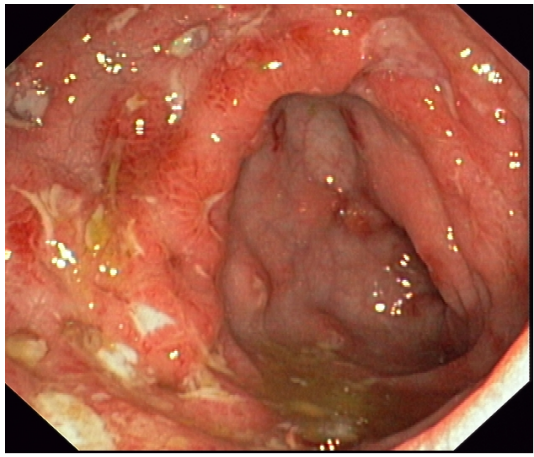


- Incubationtime: 5 – 7 days
- Mild complaints:mucopurulent discharge
- Proctoscopy: superficial proctitis,no ulcers
- D: gramstaining / culture

- TH: ceftriaxone 125 mg im. 99% healing

PROCTITIS
C.trachomatis





1. Non-LGV: mild
   superficial proctitis
   no ulcers
2. LGV-type: severe complaints
   bloodloss
   severe proctitis,ulcers
   granulomas

D: serology,culture,PCR

TH: doxycycline,2dd 100 mg 7-10 days

Stary,2008

Lymphogranuloma venereum outbreak in Europe

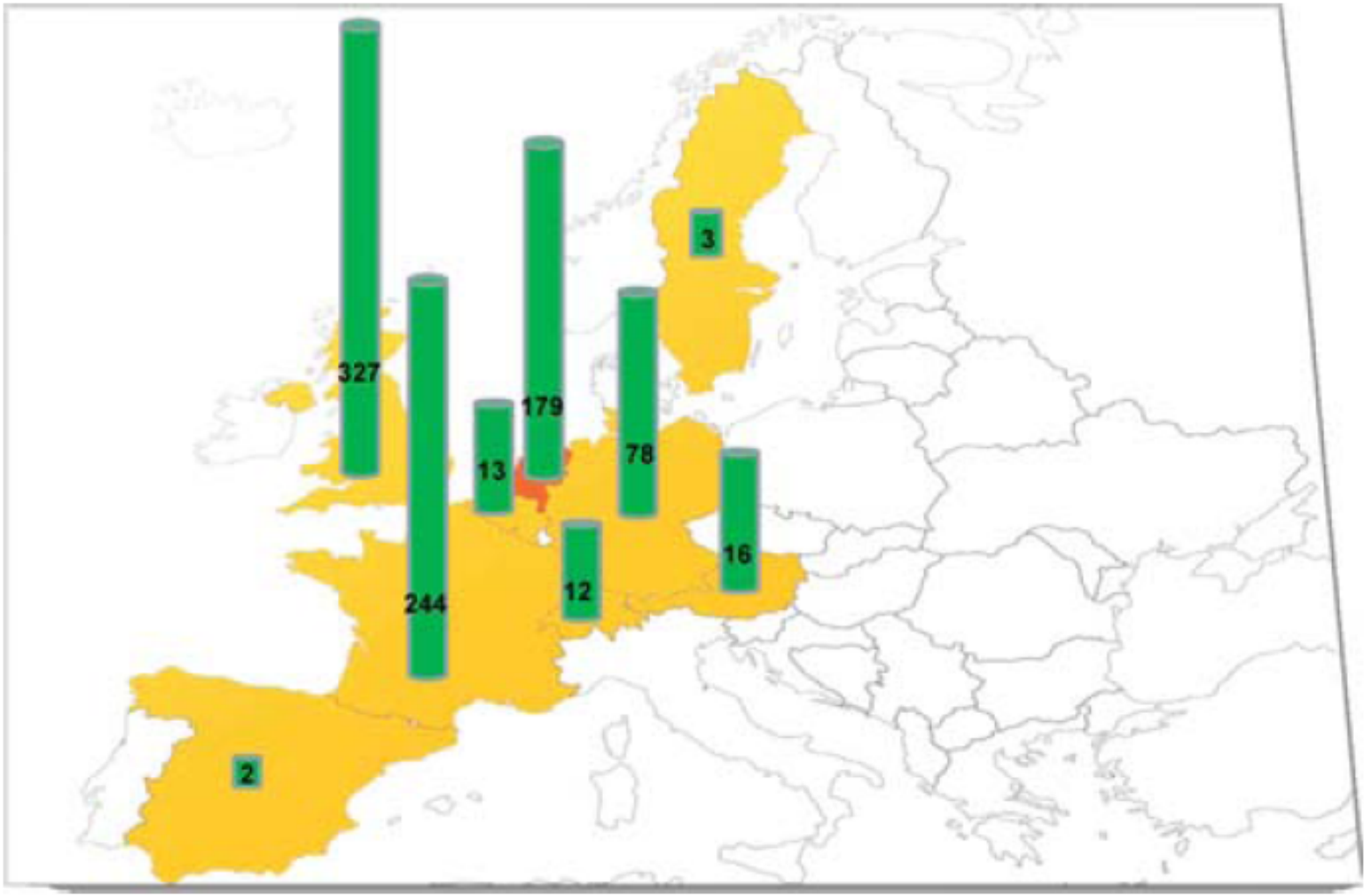


Figure 2: Spread of LGV in Europe. Graphic showing published numbers of patients with LGV in various countries.

Sexually Transmitted Diseases, February 2008, Vol. 35, No. 2, p.203–208
DOI: 10.1097/OLQ.0b013e31815abb08

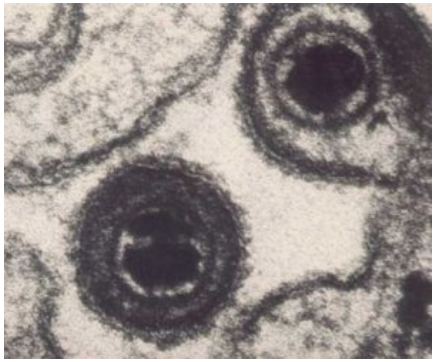
Lymphogranuloma Venereum Proctitis in Men Who Have Sex With Men Is Associated With Anal Enema Use and High-Risk Behavior

HENRY J. C. DE VRIES, MD, PHD,*‡ AKKE K. VAN DER BIJ, MD, PHD,† JOHAN S. A. FENNEMA, MD, PHD,† COLETTE SMIT, MD,†‖ FRANK DE WOLF, MD, PHD,‖ MARIA PRINS, PHD,†§ ROEL A. COUTINHO, MD, PHD,†§¶ AND SERVAAS A. MORRÉ, PHD#**††

TABLE 4. Multivariate Multinomial Logistic Regression Model of 32 Men With LGV Proctitis (LGVP), 16 Men With Gonorrheal Proctitis (GOP), 29 Men With a Non-LGV Chlamydia Proctitis (Non-LGV Chlamydial Proctitis), Compared With 24 Men With a Proctitis of Unknown Etiology (PUE), Reference Group)* (STI Outpatient Clinic Amsterdam, August 2004 to April 2006)

Group	Risk Factor	Odds Ratio (95% CI)	*P*
CTP	Use of toys	0.3 (0.1–1.5)	0.1
	Use of enemas	8.7 (1.6–46.7)	0.01
	Sex at a sex party	1.6 (0.3–9.8)	0.6
	Sex with HIV-positive partners	0.7 (0.2–2.5)	0.5
GOP	Use of toys	0.4 (0.08–2.5)	0.4
	Use of enemas	3.1 (0.5–20.4)	0.2
	Sex at a sex party	1.0 (0.1–8.2)	1.0
	Sex with HIV-positive partners	1.3 (0.3–5.4)	0.7
LGVP	Use of toys	0.07 (0.01–0.4)	0.004
	Use of enemas	31.1 (5.4–180.3)	0.000
	Sex at a sex party	7.6 (1.2–47.1)	0.03
	Sex with HIV-positive partners	2.8 (0.7–11.3)	0.1

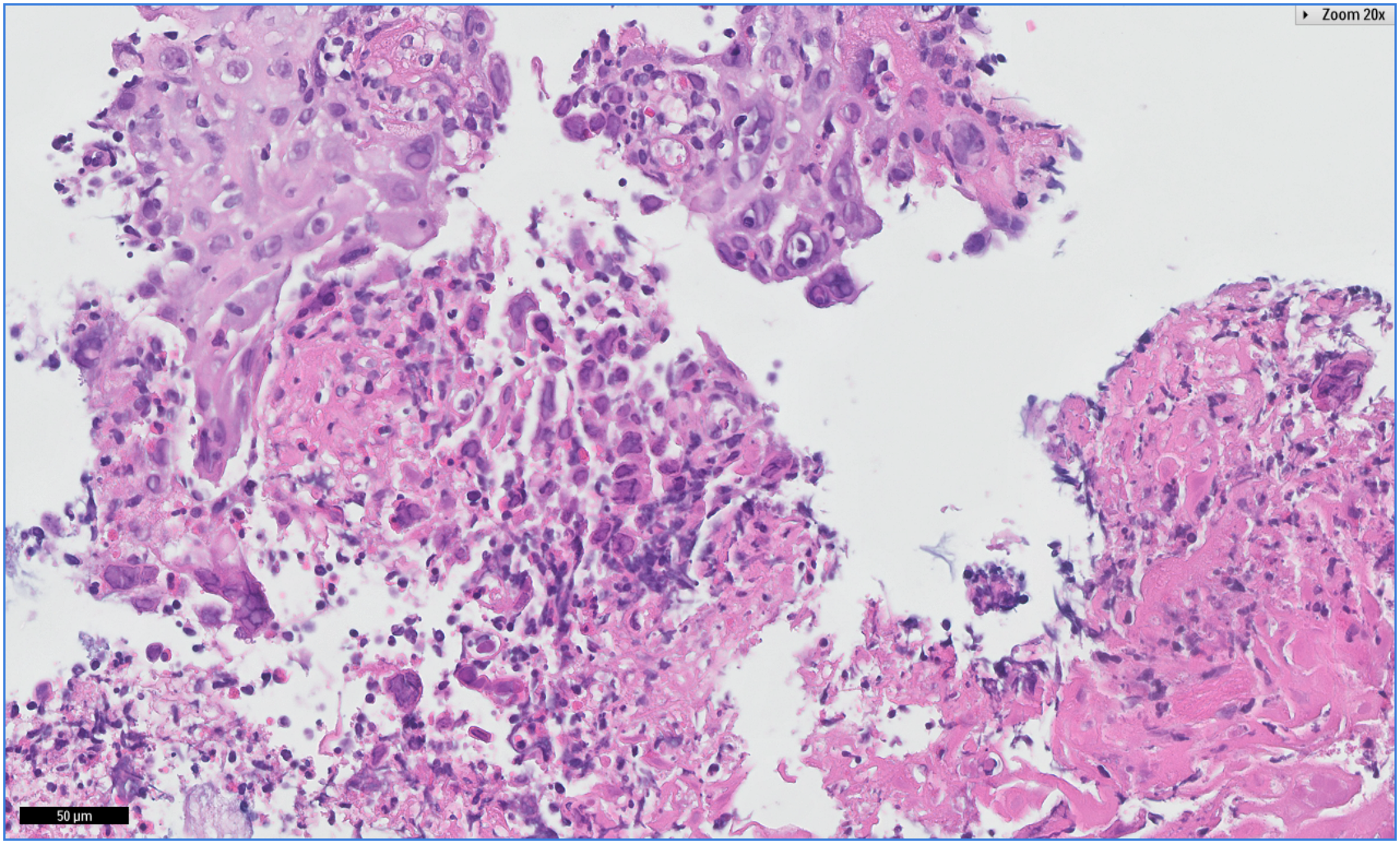
PROCTITIS HSV

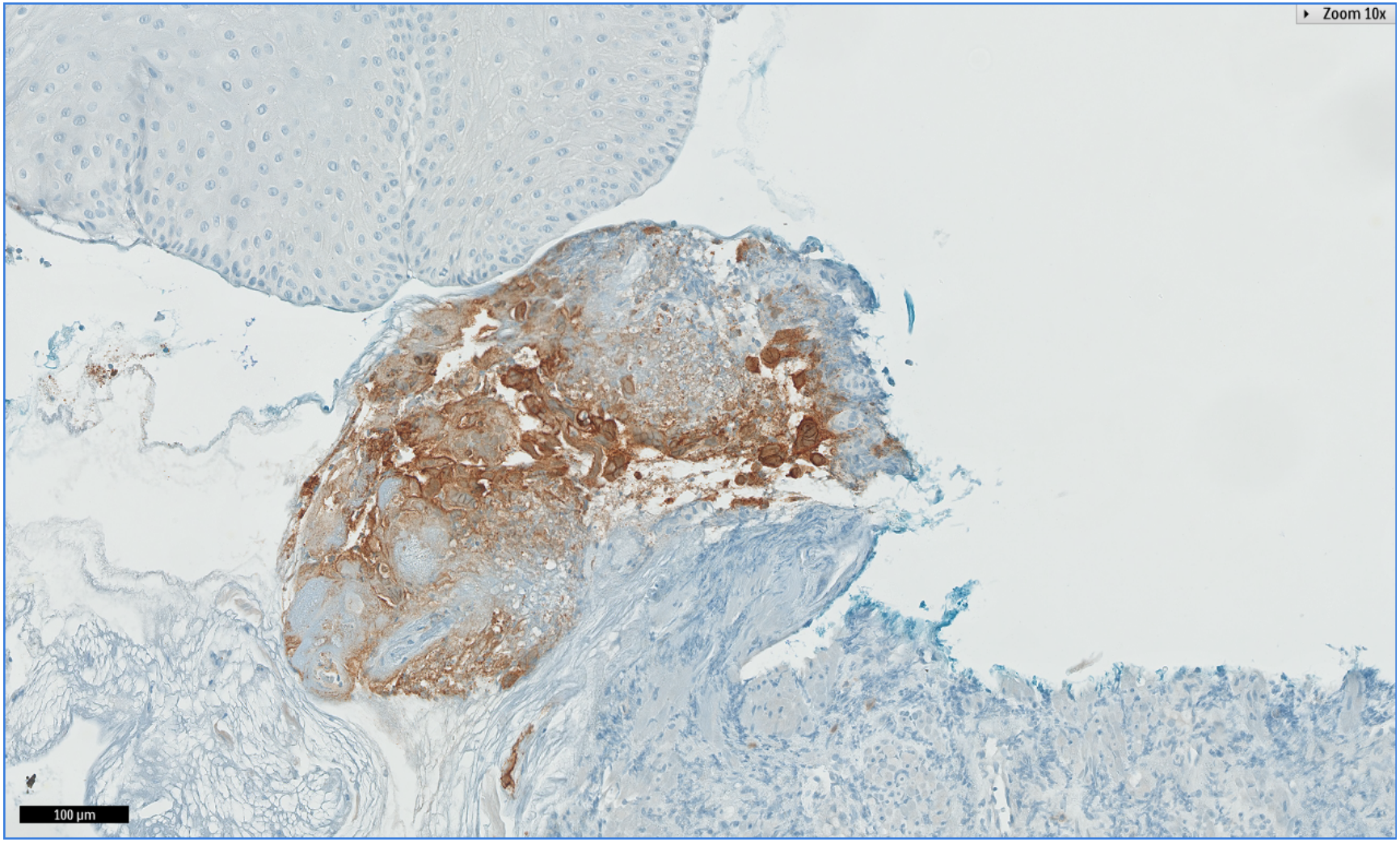


- 70 % HSV 2
- also perianal disease
- severe complaints
- impotence,sacral paresthesias
- fever
- perianal and rectal lesions: ulcers

D: culture, IF staining

TH: acyclovir 5dd 400 mg - 10 days


Zoom 20x
50 µm

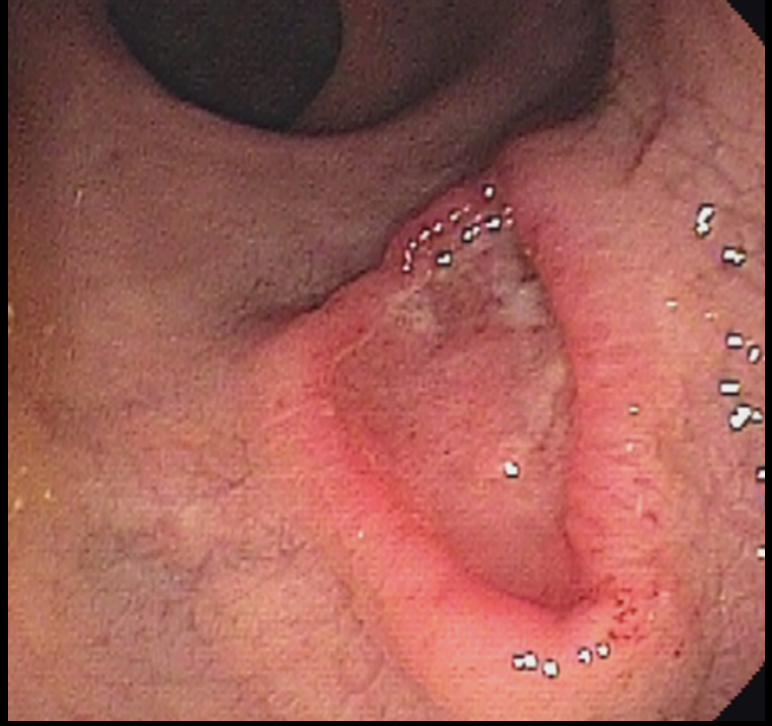

Zoom 10x
100 µm

PROCTITIS
t.pallidum

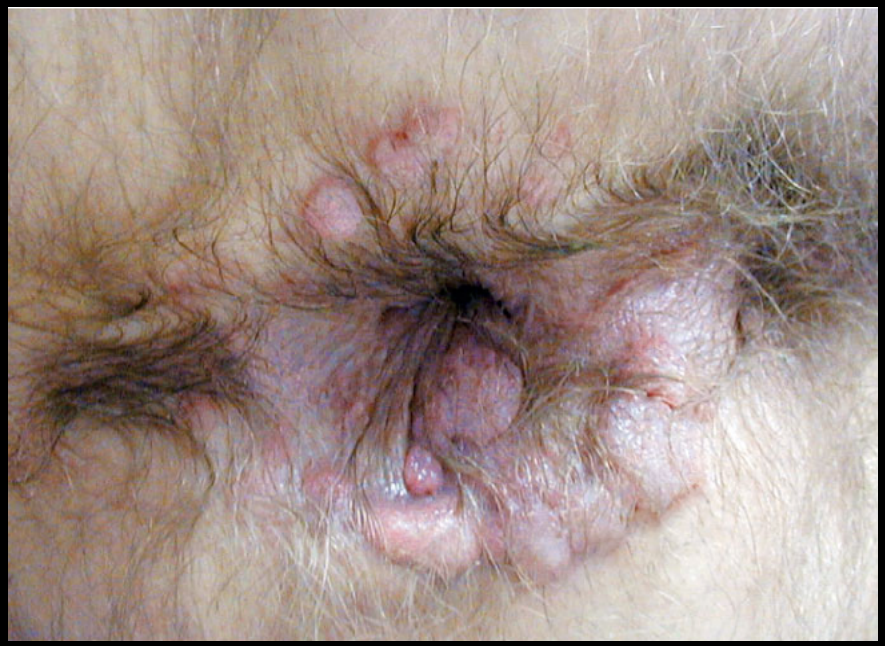
1. Syphilis I : 2-6 weken na anale sex
   pijnloos,jeuk,bloedverlies
   scherp gedemarkeerde ano-
   rectale lesie met geindureerde
   randen (lijkt fissuur !)
2. Syphilis II: rectale massa,condylomata
   lata

D: serologie,biopt (zilverkleuring0

TH: penicilline: 2,4 Milj.units im



Syphilis I



Condylomata Lata of Secondary Syphilis

Syphilis II

Josip Begovac, M.D., Ph.D.
Davorka Lukas, M.D., Ph.D.

University Hospital
for Infectious Diseases
10 000 Zagreb, Croatia

Table 1 Sexually Transmitted Proctitides: Cause, Diagnosis, and Treatment

Voth, 2007

Cause	Diagnosis	Treatment (First Line)
N. gonorrhoeae	Culture, Thayer-Martin	Cefixime/ceftriaxone
C. trachomatis	LCR/PCR	Azithromycin/ doxycycline
T. pallidum	Darkfield examination	Penicillin G
Herpes simplex	Tzanck preparation	Symptomatic (+/− acyclovir)

LCR, ligase chain reaction; PCR, polymerase chain reaction.

When infectious proctitis is diagnosed

HIV testing is mandatory !

HIV infection

- 1982 - 1996: pre - HAART
- 1996 - 2004: post - HAART:

  mortality ↓
  infections ↓

  KS ↓
  NHL ↓
  Anus carcinoma ↑

AMC Amsterdam
1982 - 1992

- AIDS patients: 606
- data available: 550

- male homosexuals: 487
- male heterosexuals: 40
- female: 23

AIDS
gastrointestinal disease

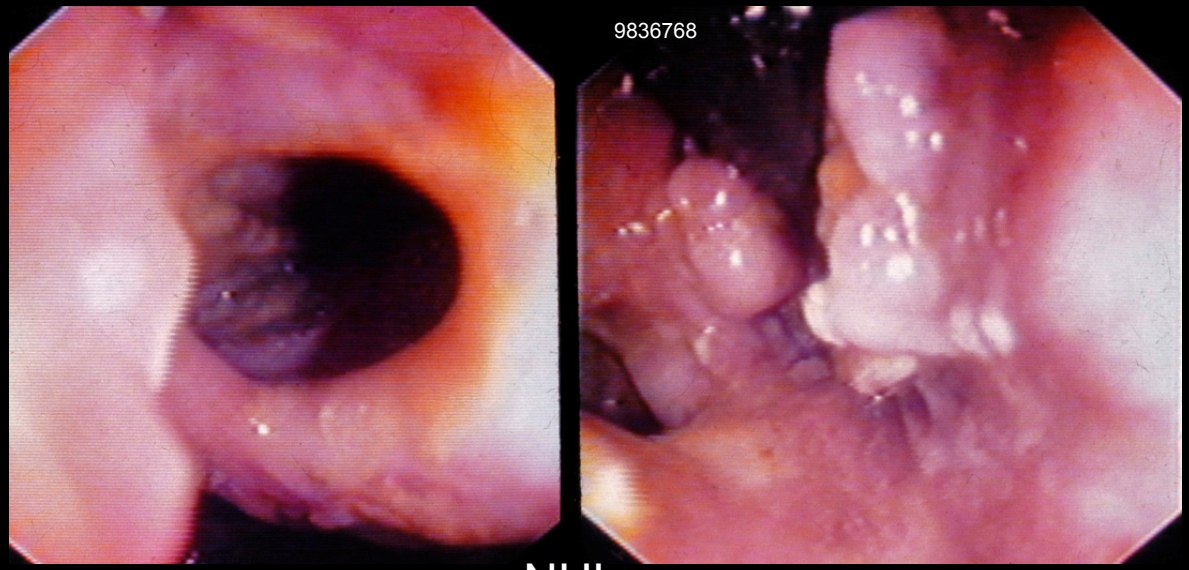
- Diarrhea 44 %
- Dysphagia 32 %
- KS 29 %
- Anal disease 18 %
- Hepatobiliary disease 19 %

AIDS
dysphagia/odynophagia

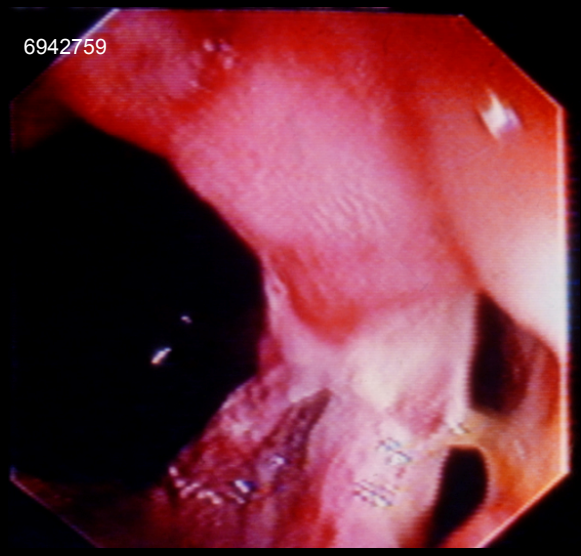
Oesophagitis:

- Candida 50 %
- CMV 25 %
- HSV 10 %
- multiple causes 25 %

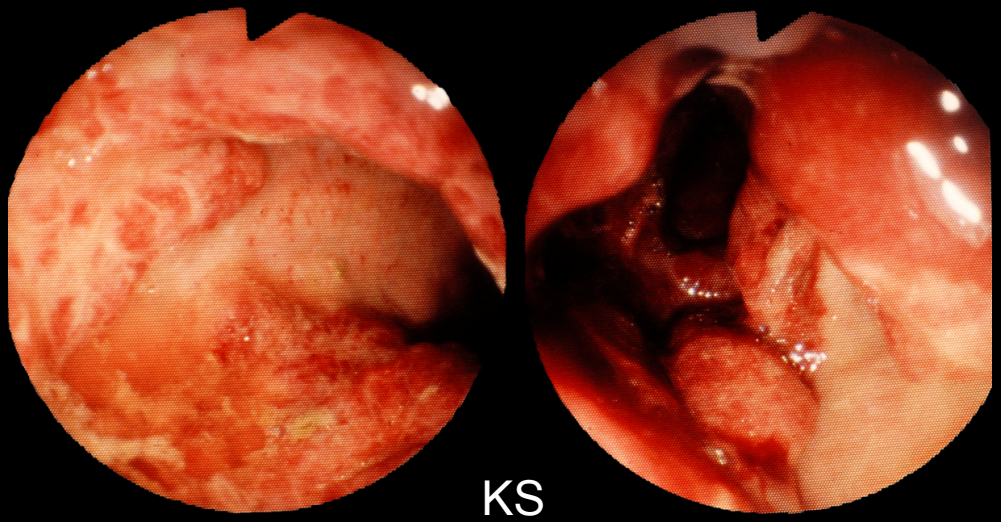
Bonacini,1991



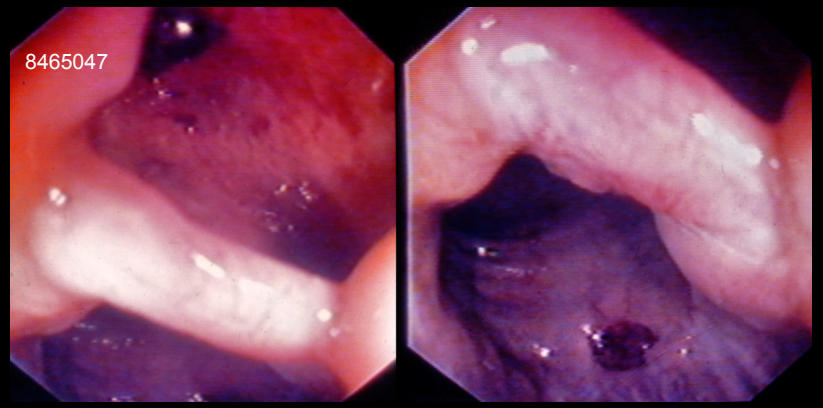
NHL



CMV+HSV-2



KS



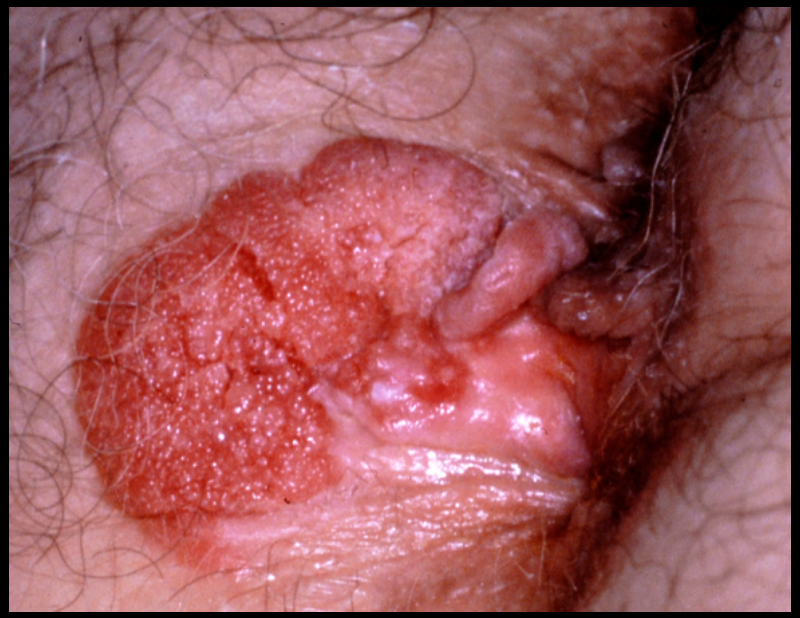
HSV

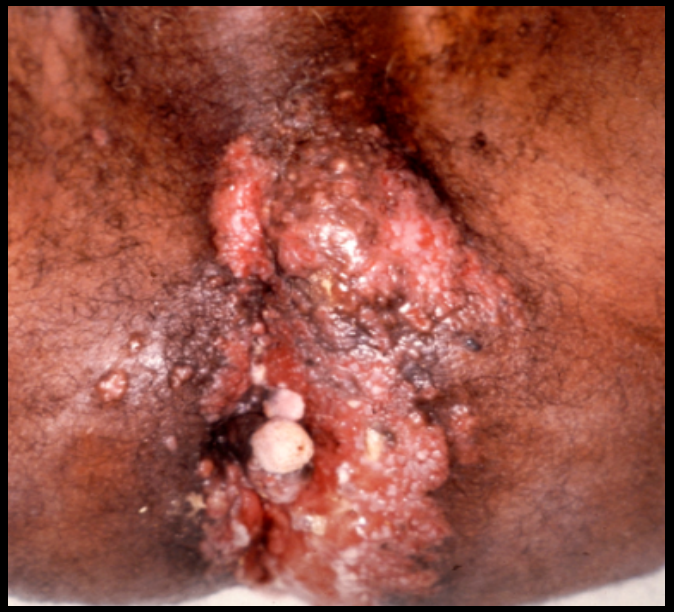
AIDS ANORECTAL DISEASE

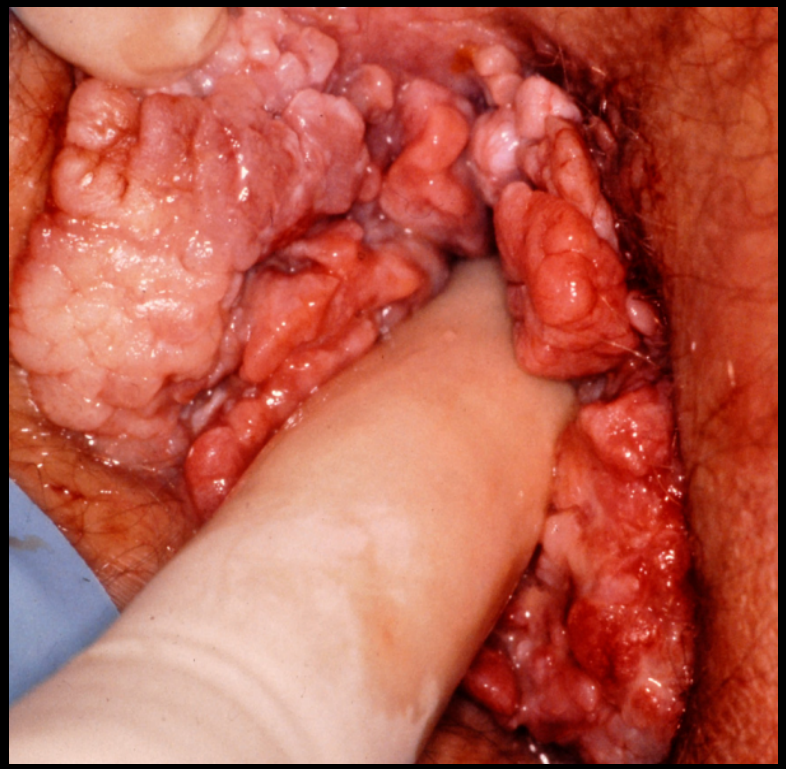
HIV HAART-era

- After 1996 impressive decrease HIV-related morbidity and mortality
- HIV has become a chronic disease
- Aging HIV patient
- New causes of morbidity

ANAL CANCER







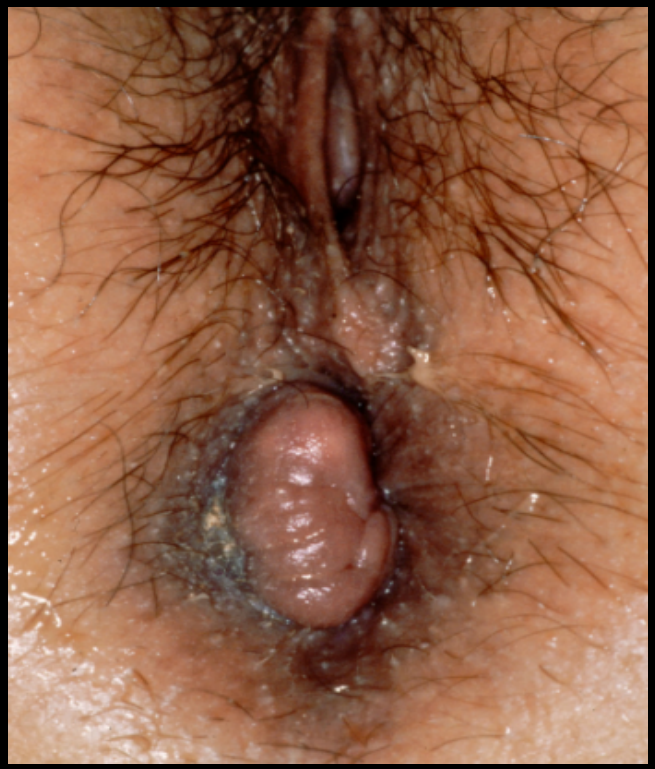


TABLE 1. RISK FACTORS FOR ANAL CANCER.

Strong evidence

Human papillomavirus infection (anogenital warts)
History of receptive anal intercourse
History of sexually transmitted disease
More than 10 sexual partners
History of cervical, vulvar, or vaginal cancer
Immunosuppression after solid-organ transplantation

Moderately strong evidence

Human immunodeficiency virus infection
Long-term use of corticosteroids
Cigarette smoking

Ryan,NEJM,2000

Anal Cancer and HIV+

- 2008 US Patel et al:
  RR 43 for anal cancer in HIV+ patients

  RR increased between 1992-2003: 19 → 48 → 72

- 2008 France Piketty et al:
  1992-2004: RR 11 → 40

- Incidence anal cancer HIV+ MSM San Diego:
  0 (1991) → 224 per 100.000/yr (2000)
  RR 352 (95% CI 186-669)

Pre-cursor lesion: AIN

- AIN: Anal Intraepithelial Neoplasia
- Premalignant
- AIN 1, AIN 2, AIN 3
- Oncogenic HPV: Human Papilloma Virus
- HPV 16 & 18

HPV and AIN in HIV+ MSM

- Palefsky et al 2005 (San Francisco, n= 357)

  HIV+ MSM:
  - 95% anal HPV, 88%>1 HPV-type
  - 81 % AIN of any grade
  - 52% high grade AIN (AIN 2 or 3)
  - High grade AIN: 98% HPV-positive

AIN progression

- 50 % van AIN I → AIN II/III (2-4 yr)
- AIN 2/3: regression is unusual
- Progression of CIN (Cervical Intraepithelial Neoplasia) McCredie et al 2008: inadequate treatment of CIN III: 31,3% cervixca.

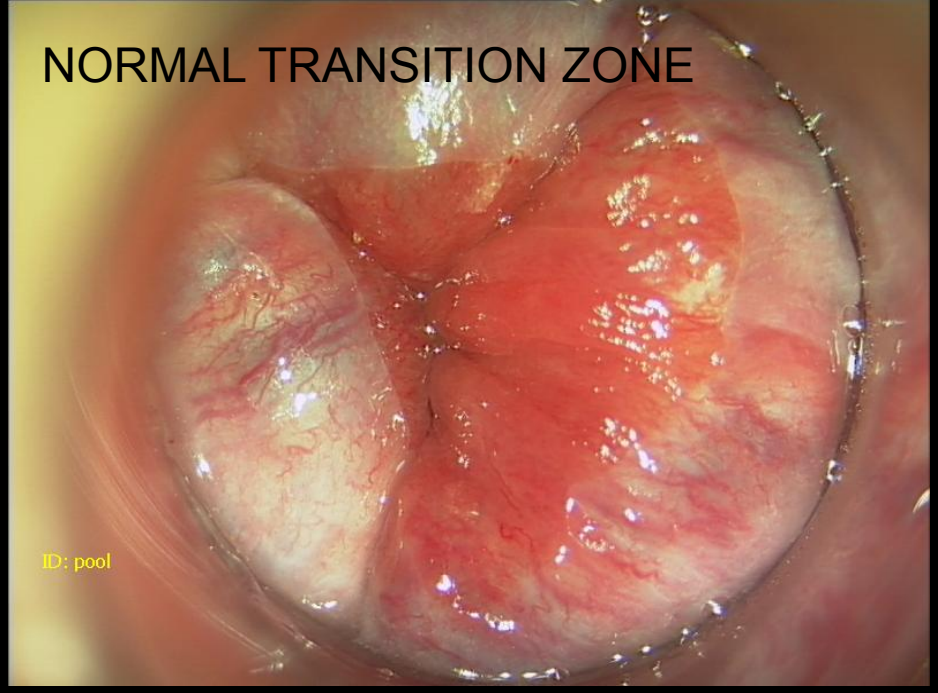
AIN diagnostics

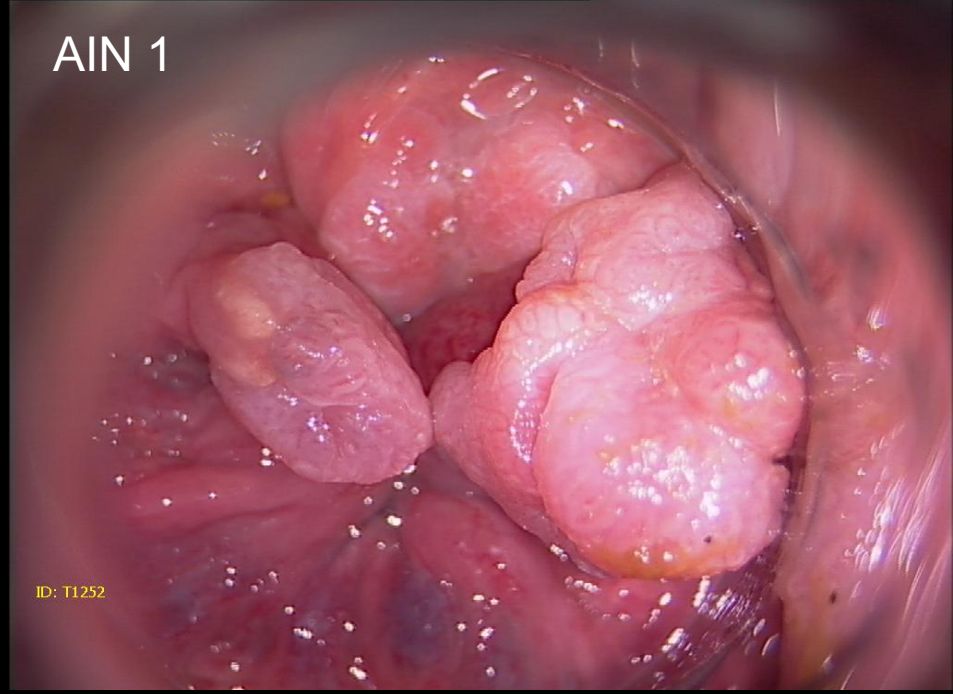
- Anal cytology
  Sensitivity: 69-93%
  Specificity: 32-59%
  → Comparable to cervical cytology

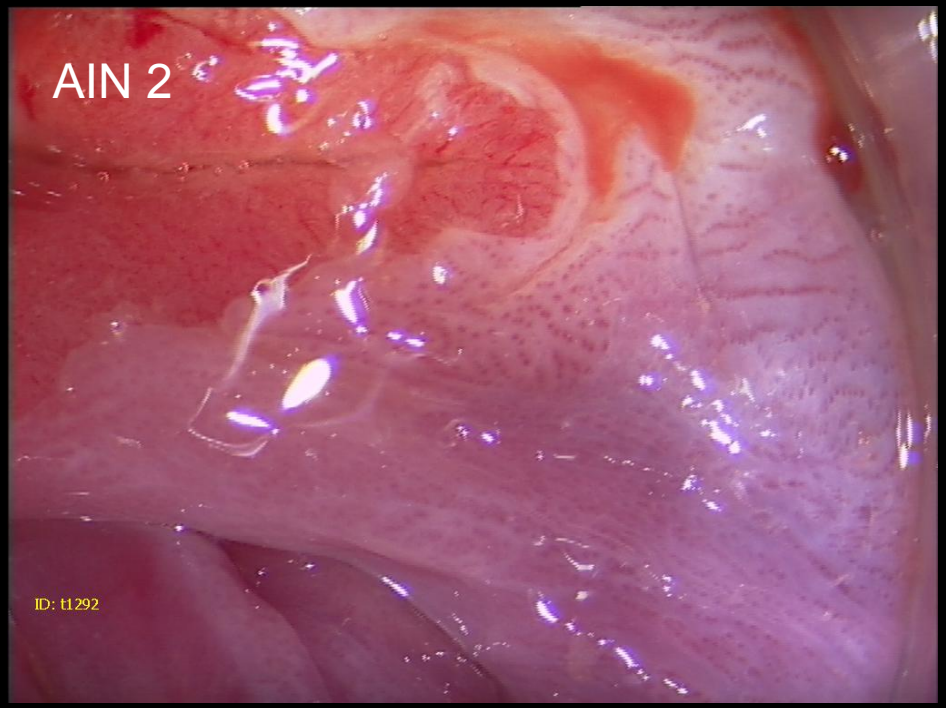
- High Resolution Anoscopy: Proctoscopy + Colposcopy
  1. Application acetic acid 5%
  2. Inspection of distal rectum, transformation zone and anal canal at 30-fold magnification
  3. Biopsy in case of suspect lesions

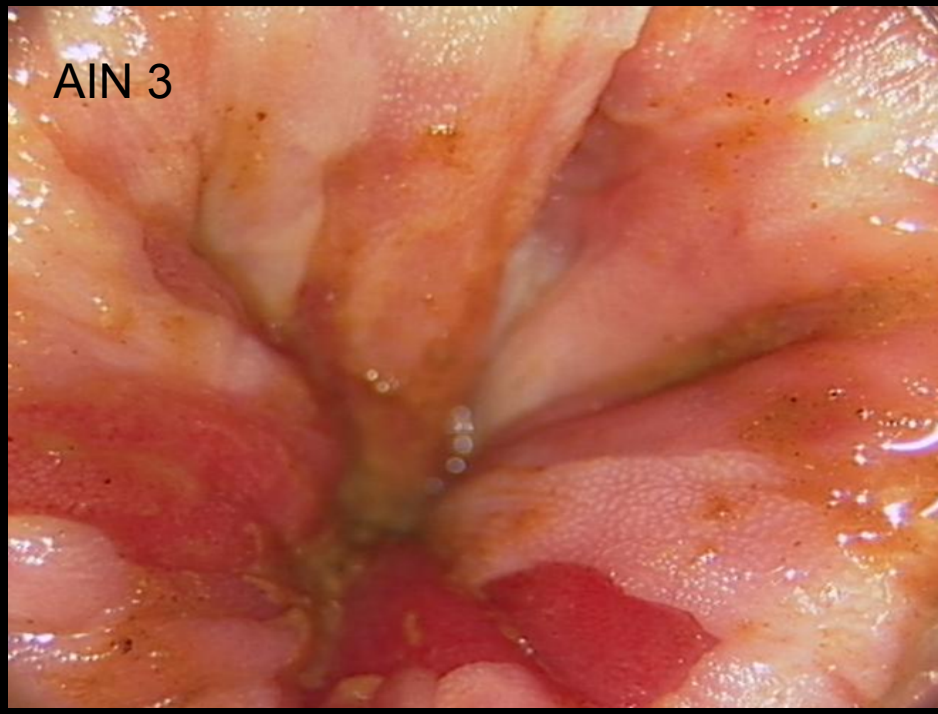
High Resolution Anoscopy

Olivier Richel


NORMAL TRANSITION ZONE
ID: pool


AIN 1
ID: T1252


AIN 2
ID: t1292


AIN 3

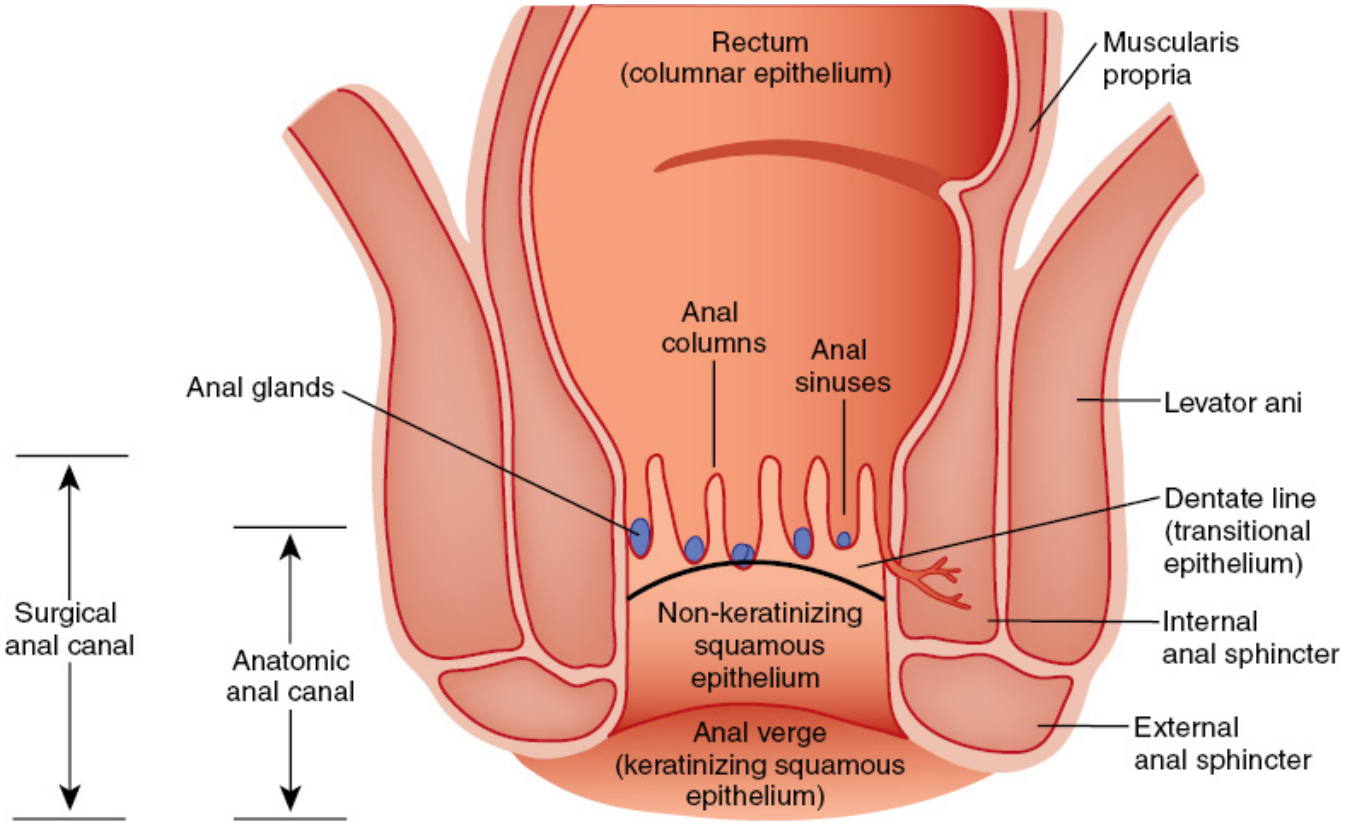
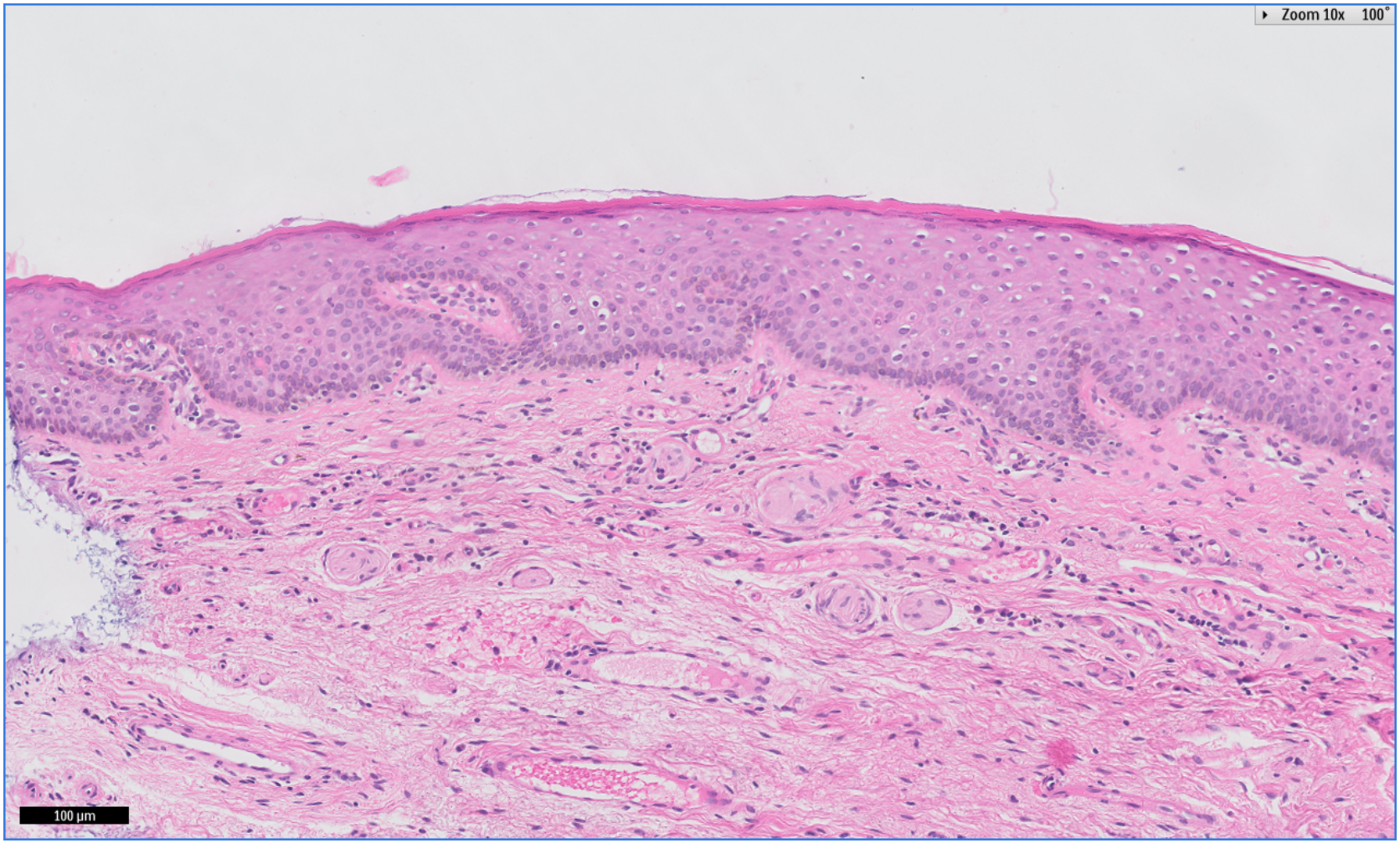
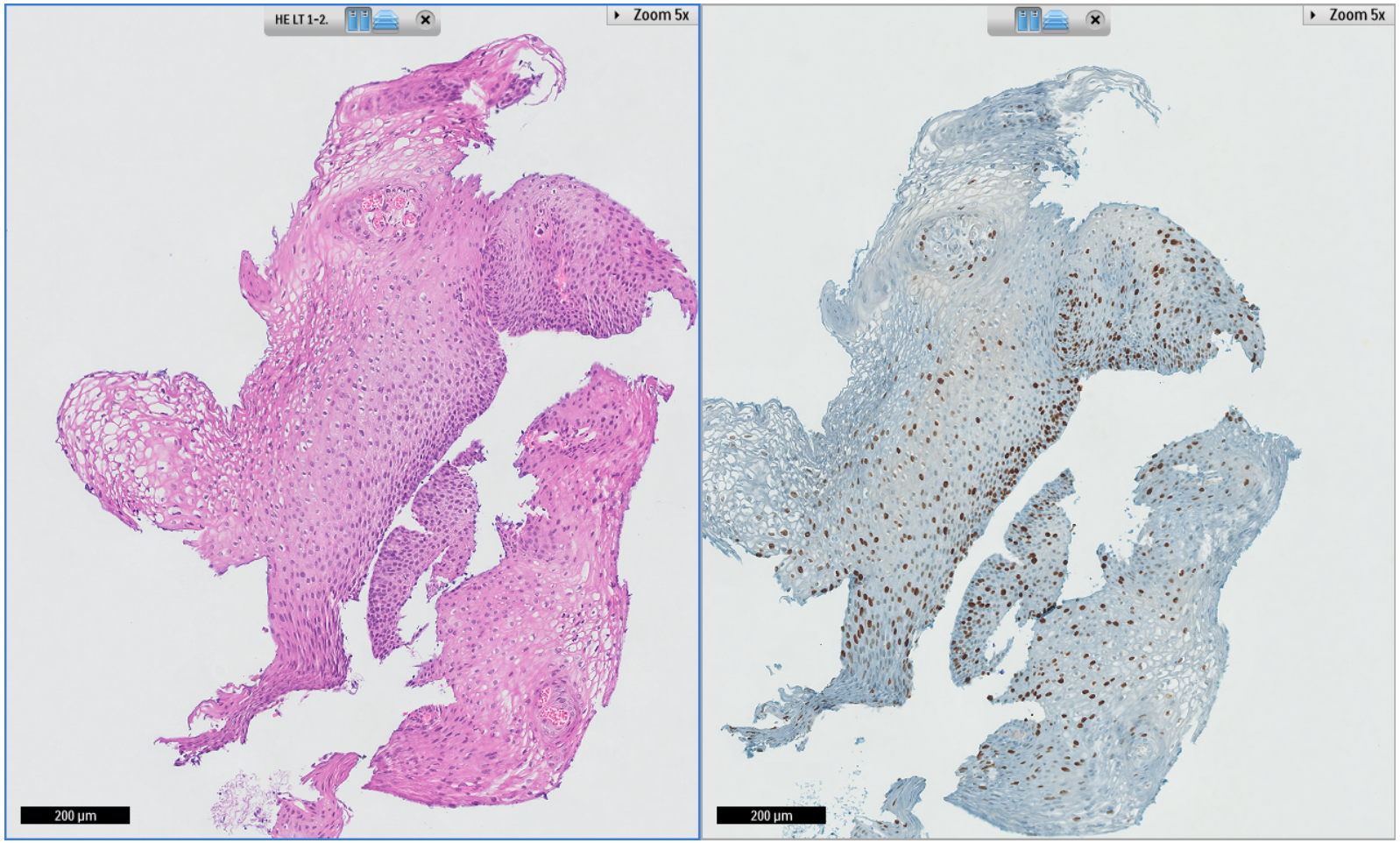
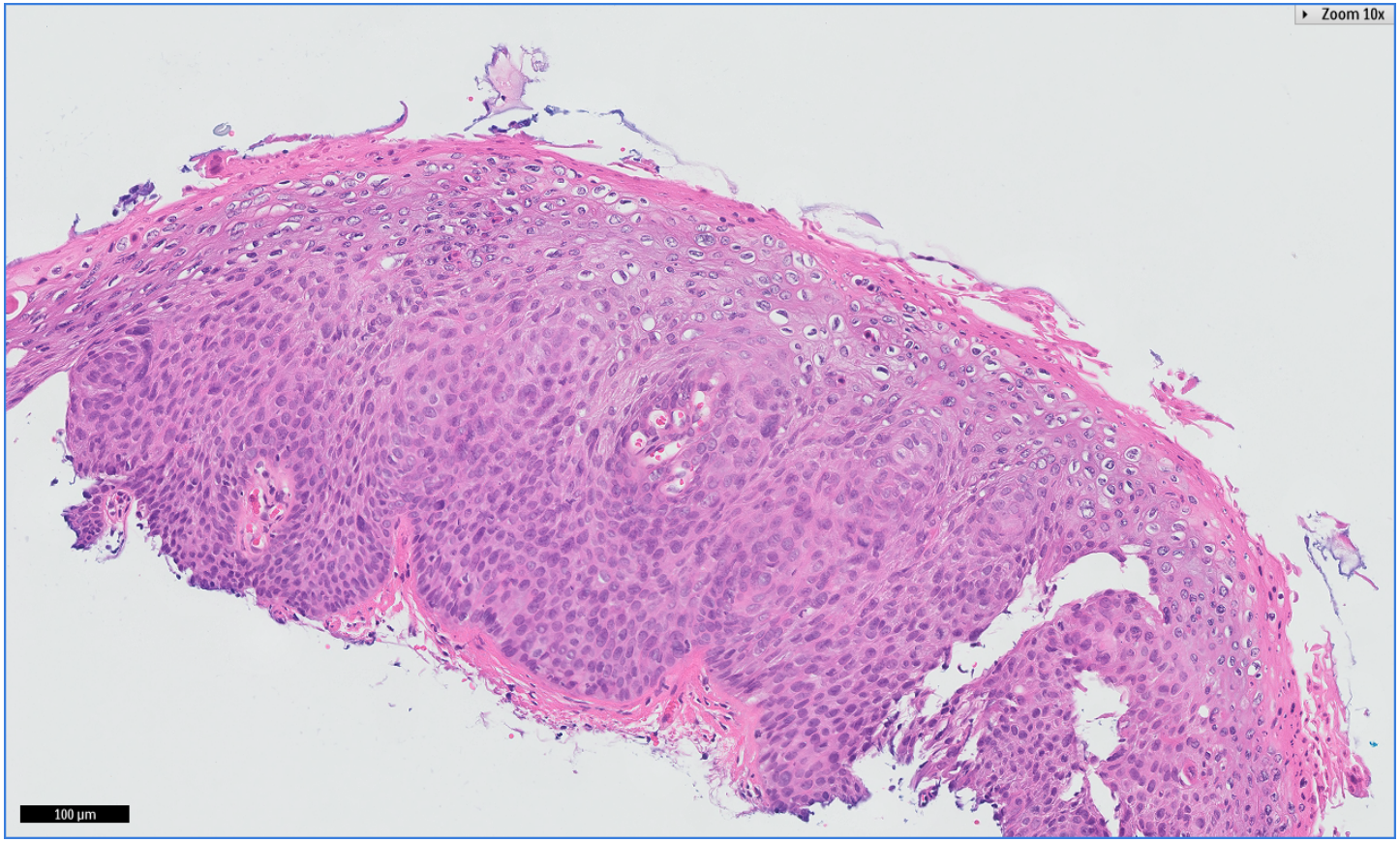
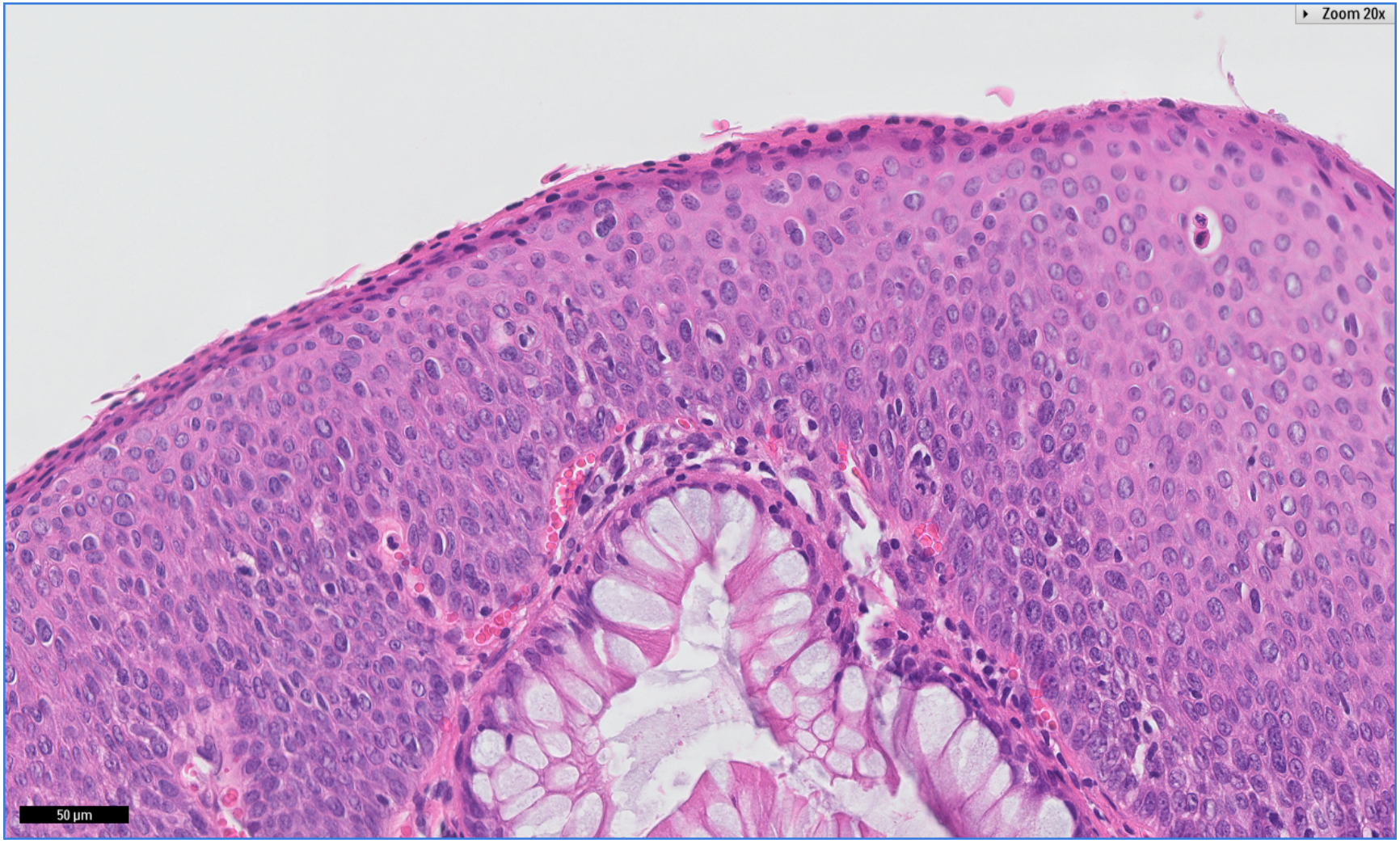


FIGURE 28-1 Anatomic features of the anal canal.


Zoom 10x 100°
100 µm

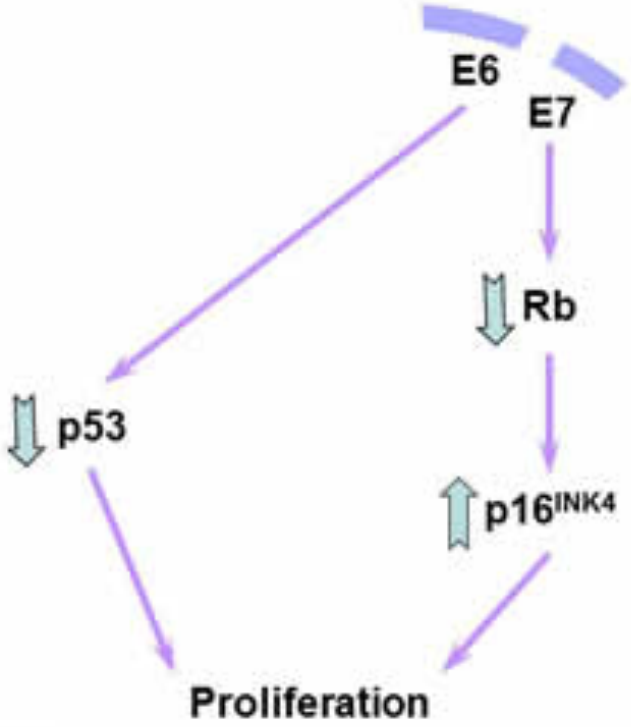

HE LT 1-2.
Zoom 5x
200 µm
Zoom 5x
200 µm


Zoom 10x
100 µm

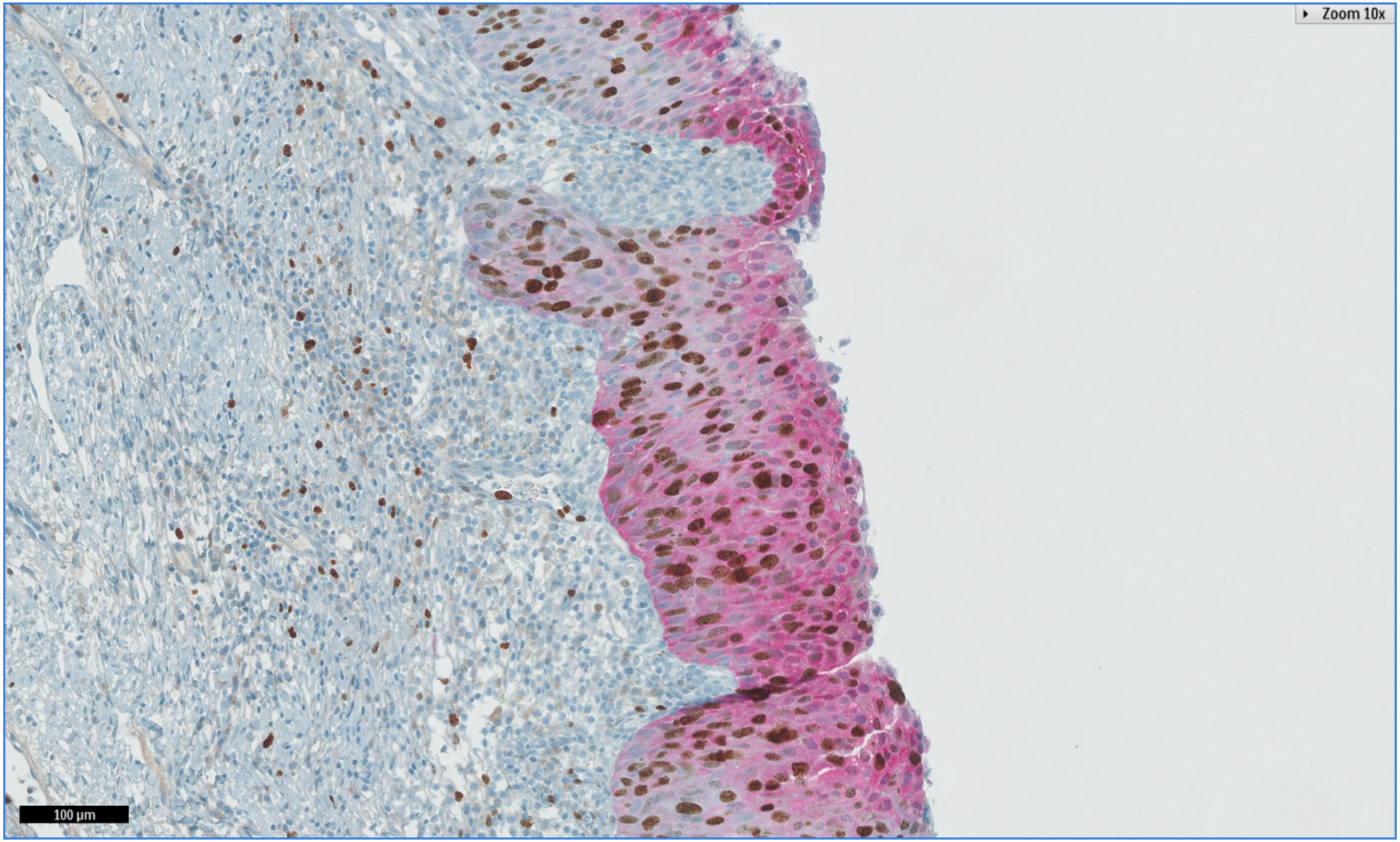

Zoom 20x
50 µm

MAYO CLINIC
Mayo Medical Laboratories

HPV in OPSCC Oncogenesis — Pathways



HPV Testing in Oropharyngeal Squamous Cell Carcinoma


Zoom 10x
100 µm

RICHTLIJN ANUSCARCINOOM 2013

Screening en preventie

- Standaard screening bij HIV+ mannen die seks hebben met mannen (MSM) of andere risicogroepen wordt niet aanbevolen.

- Diagnostiek en gradering van Anale Intraepitheliale Neoplasie (AIN) gebeurt op basis van histologisch onderzoek.

- Geen indicatie voor routinematig HPV analyse bij HIV+ MSM of andere risicogroepen.
- Een HIV-test is te overwegen

RICHTLIJN ANUSCARCINOOM 2013

Behandeling

Voorstadium, Anale Intraepitheliale Neoplasie (AIN)

- AIN1: jaarlijkse controle
- AIN2/3: bij voorkeur electro- of infraroodcoagulatie, eventueel Imiquimod
- (micro)invasief plaveiselcelcarcinoom: radicale locale excisie; indien niet mogelijk zonder mutilatie van de anale sfincter-complex :(chemo)radiotherapie

WHO classification* of tumours of the anal canal

Epithelial tumours

Premalignant lesions

Anal intraepithelial neoplasia (dysplasia), low grade

Anal intraepithelial neoplasia (dysplasia), high grade

Bowen disease

Perianal squamous intraepithelial neoplasia

Paget disease

Carcinoma

Squamous cell carcinoma

Verrucous carcinoma

Undifferentiated carcinoma

Adenocarcinoma

Mucinous adenocarcinoma

*Neuroendocrine neoplasms***

Neuroendocrine tumour (NET)

- NET G1 (carcinoid)
- NET G2

Neuroendocrine carcinoma (NEC)

- Large cell NEC

Small cell NEC

Mixed adenoneuroendocrine carcinoma

Mesenchymal tumours

Secondary tumours

* Morphology code of the International Classification of Diseases for Oncology (ICD-O). Behaviour is coded /0 for benign tumours, /1 for unspecified, borderline or uncertain behaviour, /2 for carcinoma in situ and grade III intraepithelial neoplasia, and /3 for malignant tumours.

** The classification is modified from the previous (third) edition of the WHO histological classification of tumours (691) taking into account changes in our understanding of these lesions. In the case of neuroendocrine neoplasms, the classification has been simplified to be of more practical utility in morphological classification.

WHO classification of Tumours of the Digestive System

Edited by Fred T. Bosman, Fátima Carneiro, Ralph H. Hruban, Neil D. Theise

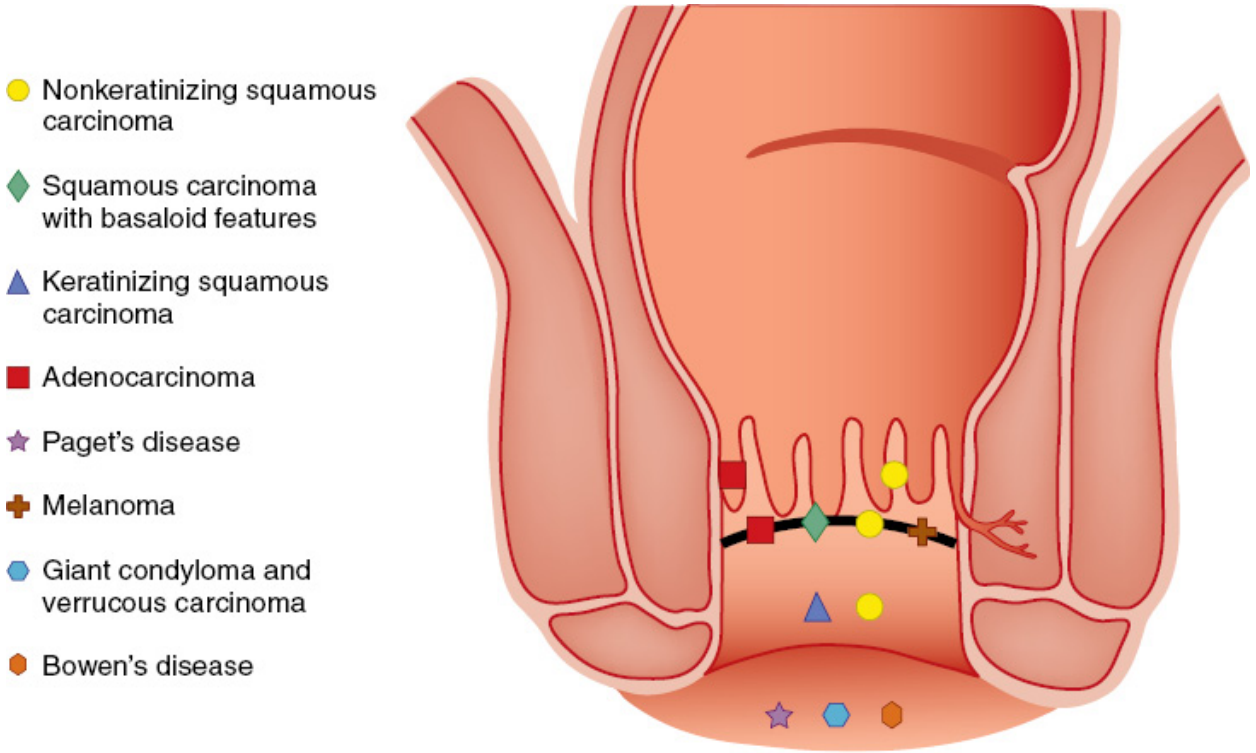
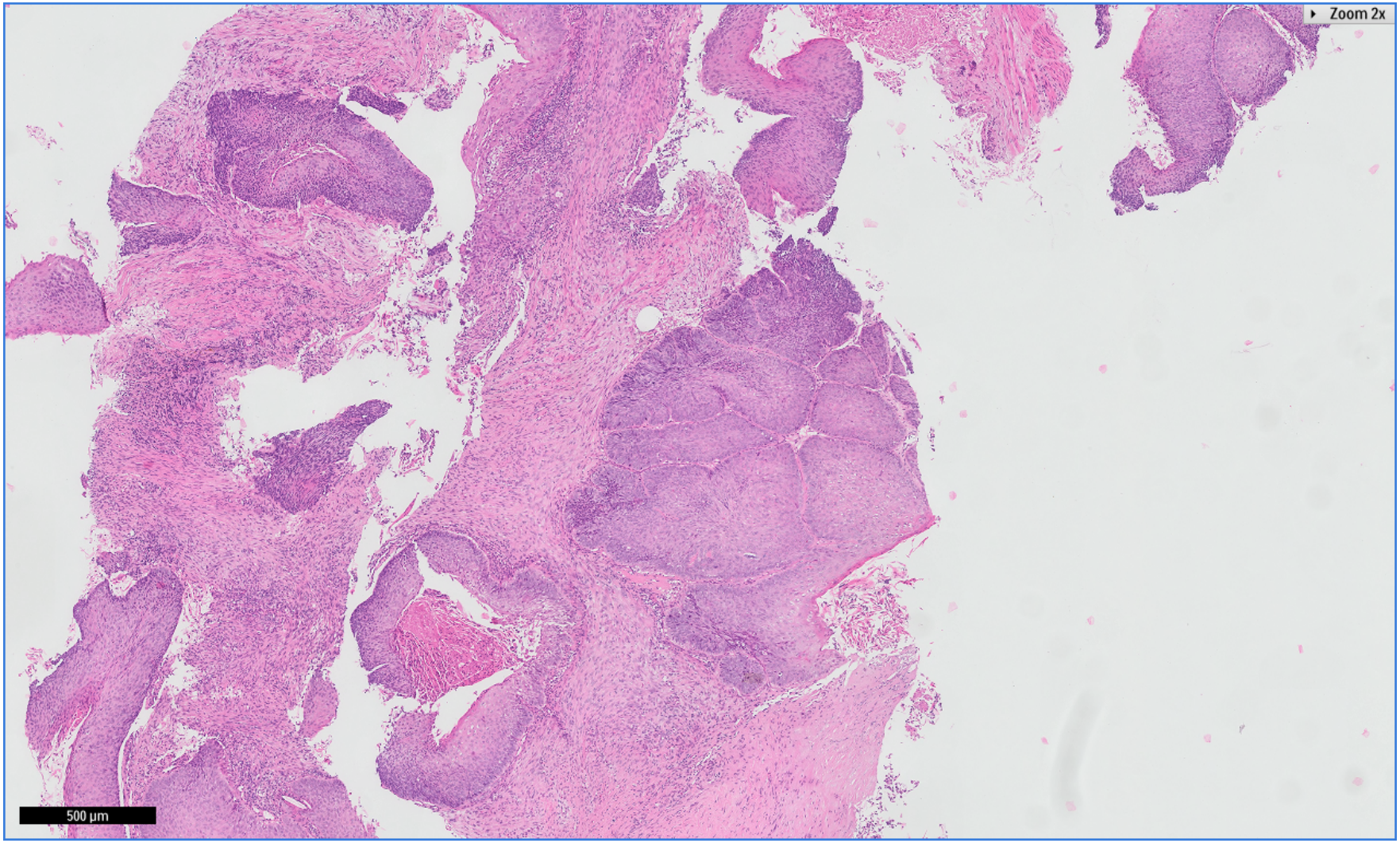
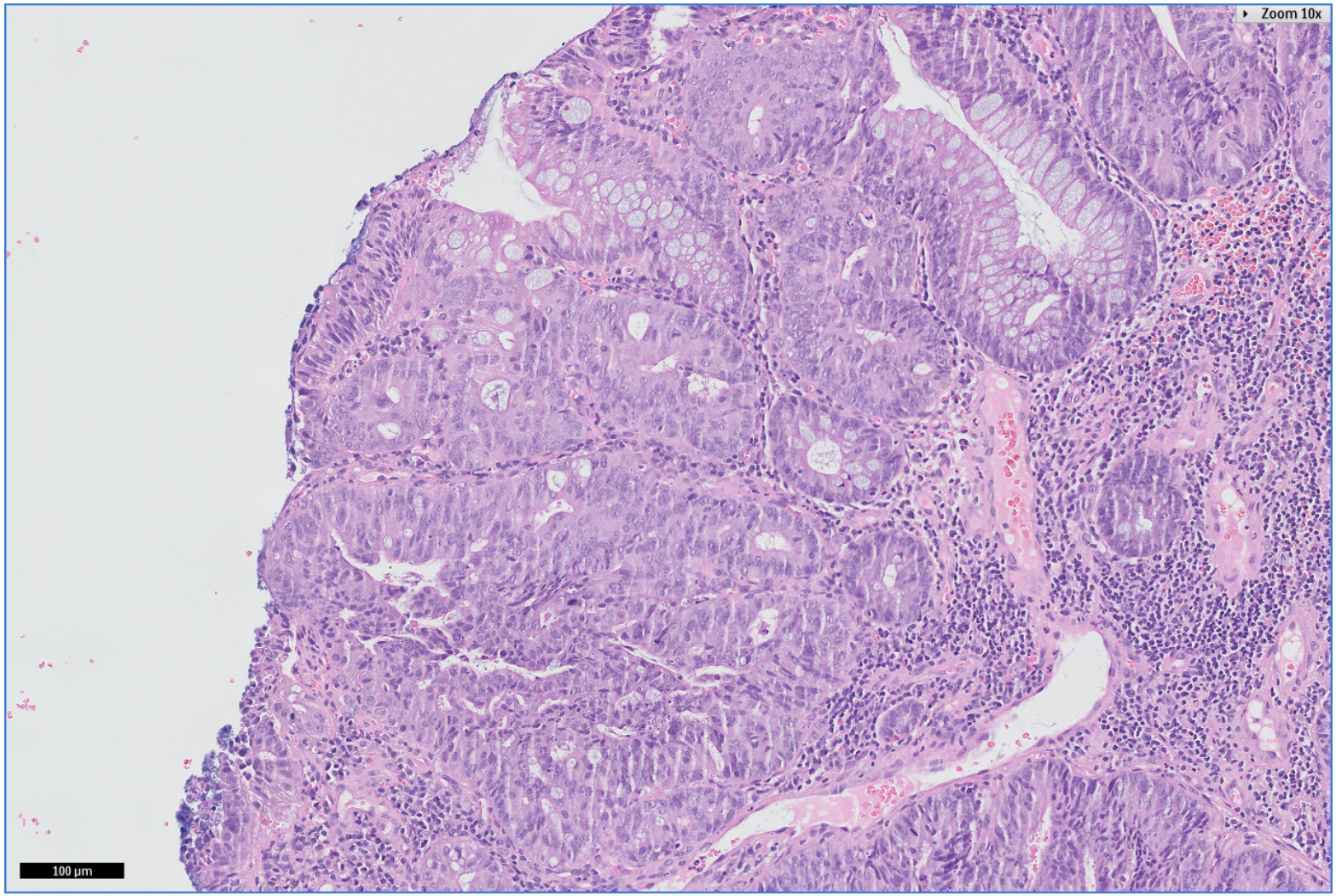
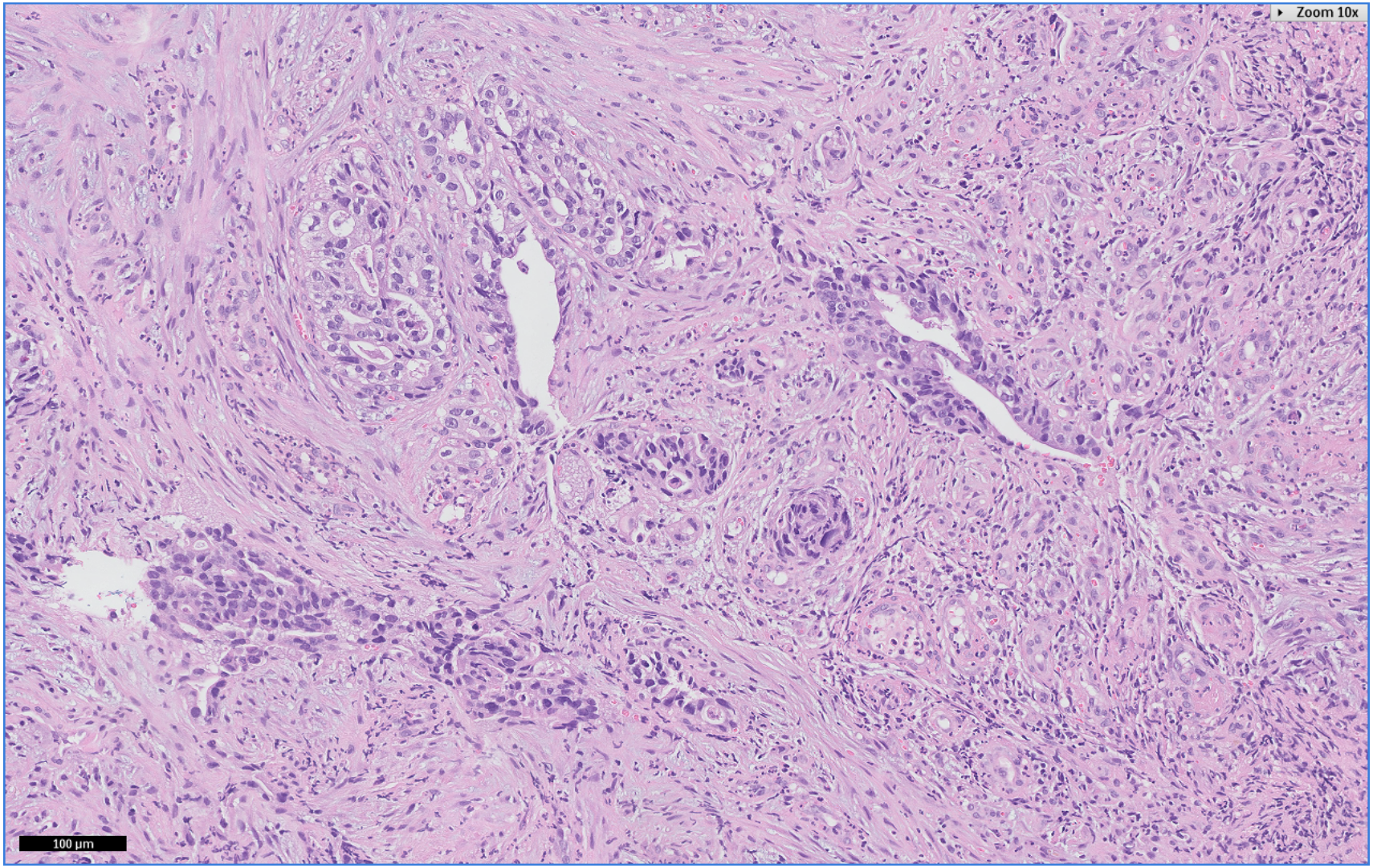


FIGURE 28-15 Most common locations of anal canal neoplasms.


Zoom 2x
500 µm


Zoom 10x
100 µm


Zoom 10x
100 µm

RICHTLIJN ANUSCARCINOOM 2013

Diagnostiek

- lichamelijk onderzoek en eventueel cytologie van de liesklieren middels dunne naald punctie
- geen routinebepaling van serologische tumormarkers
- ≥T2 : MRI heeft eventuele meerwaarde in de evaluatie van lokale en regionale tumoruitbreiding
- EAUS heeft alleen meerwaarde in ervaren handen, m.n. voor beoordeling transmurale uitbreiding
- FDG-PET kan nuttig zijn in de stadiëring en bij het uitwerken van een bestralingsplan; indien mogelijk steeds bevestigen met cytologisch of histologisch onderzoek

RICHTLIJN ANUSCARCINOOM 2013

Invasief plaveiselcelcarcinoom van de anus

- Curatieve chirurgie is beperkt tot een ruime locale excisie (> 1 cm marge) van oppervlakkig groeiende goed gedifferentieerde perianale tumoren, stadium cT1N0.
- Chemoradiotherapie is de behandeling van keuze voor de meeste patiënten met anuscarcinoom.
- MMC/5-FU is het voorkeurschema bij het niet-gemetastaseerde anuscarcinoom.
- Intensity-modulated radiotherapie (IMRT) of conformatie radiotherapie (CF-RT) heeft de voorkeur boven conventionele bestraling (CV-RT).
- Bij tumoren ≥ 1-2 cm, dan wel voor tumoren met aangetoonde regionale kliermetastasen, is het doelgebied voor bestraling de primaire tumor en de regionale kliergebieden