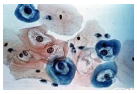
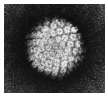
Diagnostic and Staging of HPV-associated Tumours

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Background

Incidence anal SCC:

1.6 /100'000

National Cancer Institute

4 / 100'000 (1973-78)

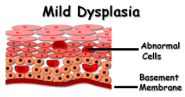
21 / 100'000 (1996-1999)[1]

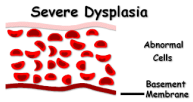
35 / 100'000 (HIV- MSM)

70 / 100'000 (HIV+ MSM)[2,3]

[1] Cress RD. **Prev Med**. 2003 [2] Melbye M. **Lancet** 1994 [3] Goedert JJ. **Lancet** 1998

Background





- **Anal intraepithelial neoplasia (AIN I-III)** : precursor of anal cancer
- **High-grade AIN (AIN II/III)**
- **LSIL/HSIL:** Low/high grade squamous intraepithelial lesion
- (Carcinoma in situ (AIN III))

Diagnosis

Cytology

Bethesda Criteria:

-Normal
-ASCUS
-LSIL
-HSIL
-Cancer

Anal Pap Smear

to detect anal dysplasia of any grade

	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)
De Ruiter[1] *et al.*	87	16	70	37
Palefsky[2] *et al.*	81	63	95	46
Fox[3] *et al.*	83	38	33	86
Nahas[4] *et al.*	61	60	64	56

[1] DeRuiter A et al. Genitourin Med 1994; 70:22-5
[2] Palefsky et al. JAIDSHR 1997; 14:415-22
[3] Fox PA et al. SexTransm Infect 2005; 81:142-6
[4] Nahas CSR et al. DCR 2009; 52:1854-63

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Anal Pap Smear

Sensitivity/Specificity (for HSIL/ anal cancer)

Patients with anal condylomata referred to surgery (n=319)

	Sensitivity (%)	Specificity (%)
HIV-neg. MSM	89	23
HIV-pos. MSM	93	58
MSM (entire)	90	33

Schlecht HP et al. CID 2010; 51:107-10

Anal Pap Smear

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Anal Pap Smear

Correlation between cytology and histology for HSIL

HIV-pos. MSM	**p<0.001**
HIV-neg. MSM	p=0.353

Schlecht HP et al. CID 2010; 51:107-10

Anal Pap Smear

Cytology (for AIN2+)

– Cross-sectional, 401 HIV+MSM

	Sensitivity (%)	Specificity (%)
ASCUS threshold	82	39
HSIL threshold	21	91
Oncogenic HPV	100	16

Cervical PAP testing for women: Sensitivity of 50% at a threshold of ASCUS to detect CIN2+[2]

[2]Cuzick J et al. Int J Cancer 2006;119:1095-1101 Salit IE et al. AIDS 2010; 24:1307-13

Anal Pap Smear

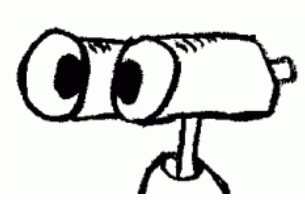
Cytology (for AIN2+)

– Cross-sectional, 401 HIV+MSM

	PPV (%)	NPV (%)
ASCUS threshold	31	88
HSIL threshold	45	78
Oncogenic HPV	28	100

Salit IE et al. AIDS 2010; 24:1307-13

High-Resolution Anoscopy (HRA)



Diagnosis

50% of AIN are missed without the use of HRA

Watson AJ et al. **ANZ J Surg** 2006

To screen or not to screen?

HIV+MSM

Any abnormal cytological finding

→ **HRA and biopsy**

Cranston RD et al. Int J STD AIDS 2007; 18:77-80

To screen or not to screen?

HIV+MSM

Any abnormal cytological finding

→ HRA and biopsy

Positive predictive value: 95%

Cranston RD et al. Int J STD AIDS 2007; 18:77-80

Screening

Digital rectal examination and anal cytologic screening annually

HIV+MSM	**any patient**
HIV-MSM	any patient with a **history of anogenital condyloma**
Women	with **abnormal cervical and/or vulvar histology**

New York State Department of Public Health AIDS Institute. Clinical Guidelines. Accessed September 25, 2010

High-resolution Anoscopy

Because high prevalence of AIN2+ in HIV+MSM and

the suboptimal test characteristics

→ **HRA as first-line screening strategy**

Nahas CSR et al. DCR 2009; 52:1854-63
Salit IE et al. AIDS 2010; 24:1307-13

High-resolution Anoscopy

Cost-effectiveness study

401 HIV+MSM

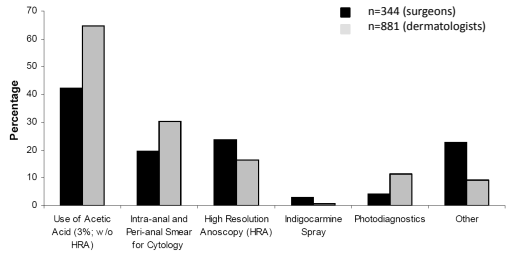
1. **Direct** use of HRA
2. HRA **if cytology abnormal**
3. HRA **if oncogenic HPV**

→ Direct use of HRA most cost-effective to detect AIN II/III

Lam JM et al. AIDS 2010, *ahead pf print*

Diagnosis: International Survey

What is your strategy for **anal cancer screening?**



Dindo D et al. Colorectal Dis. 2010.

Anal Cancer

Carcinoma of anal **margin**
- 15%
- m:w = 3:1
- Median age 50 yrs

Carcinoma of anal **canal**
- 85%
- m:w = 1:2-3
- Median age 60 to 70 yrs

Anal Cancer

T1: Tumor <2cm
T2: Tumor 2-5cm
T3: Tumor >5cm
T4: Infiltration von angrenzenden Organen

N1: perirektaler LK-Befall
N2: einseitige inguinale LK
einseitige LK der A. iliaca
N3: beidseitige LK perirektal,inguinal,iliakal

M1: Fernmetastasen

Symptoms of Anal Cancer

- **Anal lump**
- **Palpable inguinal lymph nodes**

- Incontinence
- Change of stool habits
- Pain
- Fistula

Diagnosis

- Inspection
- Palpation (DRE; Inguina!)
  - BUT: 50% of pos. NII <5mm![1]
- Proctoscopy

[1]**Glynne-Jones R** et al. Ann Oncology 2010

Lymph Node Metastases

- Ca of anal **margin**

  - **T1**(<2cm) **0%**[2]
  - **T2**(2-5cm) **23-24%**[1,2]
  - **T3**(>5cm) **30-67%**[1,2]

[1]ML. Welton , The ASCRS Textbook of Colon and Rectal Surgery, Springer 2007
[2]Barry W. Feig, M.D. Anderson surgical Oncology Handbook, sec. Edition,1999

Lymph Node Metastases

- Ca of anal **canal**

– **T1**(<2cm)	**0%**
– **T2**(2-5cm)	**8%**
– **T3**(>5cm)	**29%**
– **T4**	**35%**

ML. Welton , The ASCRS Textbook of Colon and Rectal Surgery, Springer 2007

Staging

- **PET/CT**[1]
  - **In up to 24% positive LN (PET-CT) in pat. with neg. nodes in CT**
- **Endosonography**[2]
  - Up to 100% Sensitivity
  - Correct T-stage in 66% of pat.
- **MRI**[2]
  - 89% sensitivity for locoregional disease
  - In 50% correct T-stage
  - less sensitivity concerning N-stage (cf. PET-CT)

[1]Glynne-Jones R et al. Ann Oncology 2010
[2]Otto SD et al, J Gastrointest Surg 2009

Conclusion

Cytology and HRA novel tools for diagnosis of AIN

Effectiveness yet to be determined

Guidelines still lacking