The Bethesda System 2001
Reporting System for Cervical Cytology

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Why use The Bethesda System 2001?

- **A single global reporting system facilitates international epidemiological research**
- **We now have greater understanding of the pre-invasive phase of cervical cancer.**
  - **LSIL(CIN1/HPV) = Acute viral infection**
  - **HSIL = HPV induced cx. cancer precursor**
- **TBS 2001 diagnostic categories better reflect patient management options**
  - **ASC-US = Repeat cytology or HPV testing**
  - **LSIL = Repeat cytology 6 months**
  - **HSIL = Colposcopy and Biopsy**
- **Reduced diagnostic categories improves inter- and intra-observer variability**

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Comparison of Reporting Nomenclature for Cervical Cytology

Papanicolaou System	Class I, II	Class IIIa		Class IIIb	Class IV	Class V	
		ASC-US		ASC-H			
WHO	Negative	Mild Dysplasia (CIN 1)	Moderate Dysplasia (CIN 2)	Severe Dysplasia (CIN 3)	CIS	Microinv. SCC	Invasive SCC
TBS 2001	Negative	LSIL	HSIL			HSIL (susp.for invasion)	SCC
		ASC-US	ASC-H				
		AGC(NOS), AGC(favor neoplastic)			AIS	Adenocarcinoma	

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SPECIMEN TYPE

Indicate conventional smear (Pap smear) vs. liquid based vs. other

SPECIMEN ADEQUACY

- Satisfactory for evaluation

  (*describe presence or absence of transformation zone component and any other quality indicators, e.g., partially obscuring blood, inflammation, etc.*)
- Unsatisfactory for evaluation … (*specify reason*)

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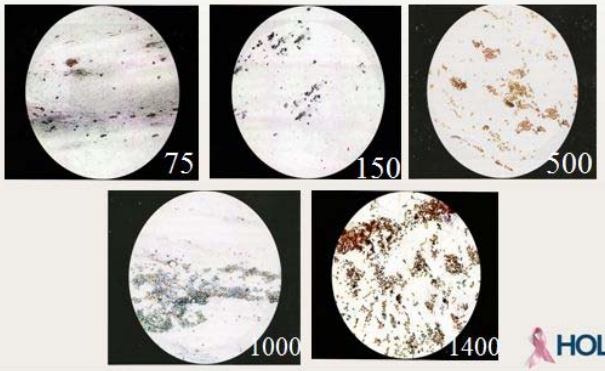
Conventional Pap Smear Specimen Adequacy

- Approx. 8,000 – 12,000 well preserved squamous cells
- An estimation based on reference images below



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ThinPrep® Pap Test Specimen Adequacy

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Cellular Composition for Adequacy

		FN20 eyepiece/ 10x obj.		FN20 eyepiece/ 40x obj.		FN22 eyepiece/ 10x obj.		FN22 eyepiece/ 40x obj.	
TP Diam mm	Area mm^2	# Fields @ FN20 10X	# Cells/Field for 5K Total	# Fields @ FN20 40X	# Cells/Field for 5K Total	# Fields @ FN22 10X	# Cells/Field for 5K Total	# Fields @ FN22 40X	# Cells/Field for 5K Total
20	314.2	100	50.0	1600	3.1	82.6	60.5	1322	3.8

- A minimum of 5000 well preserved squamous cells

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NEGATIVE FOR INTRAEPITHELIAL LESION OR MALIGNANCY (NILM)

- ORGANISMS:
  - *Trichomonas vaginalis*
  - Fungal organisms morphologically consistent with *Candida* spp
  - Shift in flora suggestive of bacterial vaginosis
  - Bacteria morphologically consistent with *Actinomyces* spp.
  - Cellular changes consistent with Herpes simplex virus

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NEGATIVE FOR INTRAEPITHELIAL LESION OR MALIGNANCY (NILM)

- OTHER NON NEOPLASTIC FINDINGS
  - Reactive cellular changes associated with
    - inflammation (includes typical repair)
    - radiation
    - intrauterine contraceptive device (IUD)
  - Glandular cells status post hysterectomy
  - Atrophy
- OTHER
  - Endometrial cells (*> 40 years of age*)

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EPITHELIAL CELL ABNORMALITIES

SQUAMOUS CELL

- Atypical squamous cells
  - of undetermined significance (ASC-US)
  - cannot exclude HSIL (ASC-H)
- Low grade squamous intraepithelial lesion (LSIL) encompassing: HPV/CIN 1
- High grade squamous intraepithelial lesion (HSIL) encompassing: CIN 2 and CIN 3/CIS
  - with features suspicious for invasion
- Squamous cell carcinoma

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Atypical Squamous Cells of Undetermined Significance (ASC-US)

- Atypical cells falling short of LSIL (CIN 1, HPV)
- USA median laboratory reporting rate 4.3% [1]
- Conventional Pap Range 0.3% - 8.2%
- Management
  - Reflex HPV Testing if using LBC
  - Repeat Cervical Cytology in 6 months
- Risk of HSIL on biopsy = 10% [2]

1. Eversole GM et al. Arch Path Lab Med, Mar 2010
2. Wright T et al, NCCN 2002

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Low-Grade Squamous Intraepithelial Lesion (LSIL)

- Incorporates diagnoses HPV and CIN1, mild dysplasia
- USA median laboratory reporting rate 2.5% [1]
- Conventional Pap Range 0.3% - 6.7%
- Management
  - Repeat Cervical Cytology in 6, 12 months or colposcopy
- Risk of HSIL on biopsy = 15%-30% [2]

1. Eversole GM et al. Arch Path Lab Med, Mar 2010
2. Moscicki AB et al. JAMA, 2001

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Atypical Squamous Cells – cannot exclude HSIL (ASC-H)

- Atypical cells present where HSIL cannot be excluded
  - Cells usually scant
- USA median laboratory reporting rate 0.3% [1]
- Conventional Pap Range 0.1% - 2.0%
- Management
  - Colposcopy and Biopsy
- Risk of HSIL on Biopsy = 24 – 94% [2]

1. Davey D et al. Arch Path Lab Med, Nov 2004
2. Wright T et al, NCCN 2002

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High-Grade Squamous Intraepithelial Lesion (HSIL)

- Incorporates diagnoses CIN2 (moderate dysplasia) and CIN3 (severe dysplasia)
- USA median laboratory reporting rate 0.5% [1]
- Conventional Pap Range 0.1% - 2.0%
- Management
  - Colposcopy and Biopsy
- Risk of HSIL on biopsy = 92-98% [2]

1. Eversole GM et al. Arch Path Lab Med, Mar 2010
2. Belinson J et al. Gyn Onc 2001

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Squamous Cell Carcinoma

- The conventional Pap smear has proven very effective at reducing incidence of Squamous Cell Carcinoma
- Many pathologists utilise verbiage such as *"High grade epithelial abnormality, cannot exclude Squamous Cell Carcinoma"*

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EPITHELIAL CELL ABNORMALITIES

GLANDULAR CELL

- Atypical
  - endocervical cells (exceeds reactive, reparative)
  - endometrial cells
  - glandular cells
- Atypical
  - endocervical cells, favor neoplastic (just short of AIS)
  - glandular cells, favor neoplastic
- Endocervical adenocarcinoma in situ (AIS)
- Adenocarcinoma
  - endocervical
  - endometrial
  - extrauterine

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Atypical Glandular Cells (AGC)

- Endocervical
- Endometrial
- Glandular

} Exceeds diagnosis of reactive, reparative change

- USA median reporting rate 0.2% [1]
- Management
  - Colposcopy plus endocervical sampling
  - Women >35 (with abn. bleeding or atypical endom.) = colposcopy plus endocervical & endometrial sampling
- Risk of HSIL, AIS, or Ca on Biopsy = 9 - 41% [2]

1. Davey D et al. Arch Path Lab Med, Nov 2004
2. Wright T et al, NCCN 2002

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Atypical Glandular Cells – Endocervical

- May reflect the presence of reparative/regenerative process or cervicitis
- Typically used for cases of repair with atypia

Atypical Glandular Cells – Endocervical

- May reflect the presence of endometrial hyperplasia or proliferative endometrium
- Typically used when endometrial cells are present in peri- or post-menopausal patients not on HRT
- Cells may appear cytologically benign

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Atypical Glandular Cells – favour neoplastic

- Endocervical
- Glandular

} Falling short of definitive diagnosis of AIS or neoplasia

- Total AGC USA median laboratory reporting rate 0.2% [1]
- Management
  - Colposcopy and Endocervical Sampling, Cone Biopsy (cold knife)
- Risk of HSIL, AIS, or Ca on Biopsy = 27-96% [2]

1. Davey D et al. Arch Path Lab Med, Nov 2004
2. Wright T et al, NCCN 2002

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Adenocarcinoma in situ (AIS)

- AIS median laboratory reporting rate 0.01% [1]
- Not easily identified [2]
- Management
  - Colposcopy and Endocervical Sampling, Cone Biopsy (cold knife)

1. Davey D et al. Arch Path Lab Med, Nov 2004
2. Renshaw A. Arch Path Lab Med, Feb 2004

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Endocervical Adenocarcinoma

- Now account for 15-20% of invasive cervical cancer
- Endocervical adenocarcinoma have increased 4 fold since the 1970's

Endometrial Adenocarcinoma

- Incidental finding on Pap test
- Improved sensitivity and specificith with the ThinPrep Pap Test

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Summary

- **Recommendations for Specimen Adequacy**
- **Precancerous lesion division reflect current understanding of HPV infection**
  LSIL, HSIL
- **Recommendation for Atypical cells**
  ASC-US, ASC-H, AGC

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