Pap Reports
What Now?

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As presented at the Calgary Health Region's
37th Annual Mackid Symposium:
Cancer Care in the Community (May 22, 2003)

Of all women undergoing Papanicolaou (Pap) smear testing, approximately 7% will be diagnosed with an abnormality requiring further followup or evaluation. It is in reporting on these evaluations that the Bethesda system comes into play (Table 1).

The Bethesda system for reporting results of cervical cytology was developed in 1988. This system was created to standardize all laboratory reporting. Modifications to this system initially occurred in 1991 based on actual laboratory and clinical experience. With the development of new technologies and, most importantly, research studies, a new terminology was developed in 2001.

Management guidelines have been developed from the consensus conference sponsored by the American Society for Colposcopy and Cervical Pathology and subsequently modified by the Canadian Colposcopy Society and Working Group for Cervical Cancer Screening Program for Alberta.

The recommendations for cervical screening are listed in Table 2.

What has changed?

Specimen adequacy

The term "satisfactory, but limited by" has been dropped due to confusion that caused unnecessary repeat testing. Longitudinal studies have shown no increased disease detection during followup of women whose specimens had neither endocervical, nor squamous metaplastic cells.

Specimens with more than 75% of epithelial cells obscured are unsatisfactory. Scant cellularity will also make the Pap smear unsatisfactory. As a result, a repeat Pap smear is necessary within a short interval. A longitudinal study showed that patients with an unsatisfactory Pap were significantly more likely to have squamous intraepithelial lesions (SIL) or cancer on followup than those with satisfactory negative Paps. There is an expectation that with the new terminology there will be a higher rate of "unsatisfactory" Paps.

General categorization

The general categorization is the cytopathologist's description of the cellular findings of a Pap smear as either normal or abnormal.

Table 1
Bethesda system 2001

Specimen type

- Indicate conventional Pap smear vs. liquid-based vs. other

Specimen adequacy

- Satisfactory for evaluation: Describe presence or absence of endocervical/transformation zone component and any other quality indicators
- Unsatisfactory for evaluation: Specify reasons (specimen rejected/not processed; specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormality)

General categorization (optional)

- Negative for intraepithelial lesion or malignancy
- Epithelial cell abnormality (specify as squamous or glandular)
- Other: See interpretation/result

Automated review

- If case examined by automated device, specify device and result

Ancillary testing

- Provide a brief description of the test methods and report results so that they are easily understood by clinicians

Interpretation/result

- Negative for intraepithelial lesion or malignancy (when there is no cellular evidence of neoplasia; state this in the general categorizaton or in the interpretation results section, whether or not there are organisms or other non-neoplastic findings)
- Organisms: Trichomas vaginalis; fungal organisms morphologically consistent with Candida sp.; shift in flora suggestive of bacterial vaginosis; bacteria morphologically consistent with Actinomyces sp.; cellular changes associated with HSV
- Non-neoplastic findings (optional to report): Reactive cellular changes, associated with inflammation, radiation, or IUDs; glandular cells status post-hysterectomy; atrophy, *etc*.
- Other: Endometrial cells in women 40 or older (specify if negative for squamous intraepithelial lesion)
- Epithelial cell abnormalities
    - Squamous cell: Atypical cells (of undetermined significance [ASC-US]; cannot exclude HSIL [ASC-H]); LSIL (encompassing HPV/mild dysplasia/CIN 1); HSIL (encompassing moderate and severe dysplaisa)
    - CIN 2 and CIN 3: With features suspicious for invasion
    - Glandular cell: Atypical (endocervical cells, endometrial cells, glandular cells, or NOS); Atypical (endocervical cells, favour neoplasia; glandular cells, favour neoplasia); endocervical adenocarcinoma in situ; adenocarcinoma (endocervical, endometrial, extrauterine, or NOS)
- Other malignant neoplasms (specify)

Educational notes and suggestions (optional)

- Suggestions should be concise and consistent with clinical followup guidelines published by professional organizations

HSV: Herpes simplex virus
IUD: Intrauterine contraceptive device
HSIL: High-grade squamous intraepithelial lesion
LSIL: Low-grade squamous intraepithelial lesion
CIN: Cervical intraepithelial neoplasia
HPV: Human papillomavirus
NOS: Not otherwise specified
sp.: Specimen

Table 2
Recommendations for cervical screening (Alberta)

Who should be screened?	How often?
1. All women aged 18 to 69 who are sexually active	Annually
2. Women over 69 who have never been screened	Every six to 12 months
3. Immunocompromised women	Annually
4. Women with a history of CIN or cervical malignancy	Annually
5. No screening for women who have had a hysterectomy for benign disease	

CIN: Cervical intraepithelial neoplasia

Table 3
Types of of epithelial cell abnormalities

ASC-US
- 0.1-0.2% risk of invasive cervical cancer
- 5-17% risk of biopsy-proven CIN 2/3

ASC-H
- 24-94% risk of biopsy-proven CIN 2/3

ASC-US: Atypical squamous cell of undetermined significance
ASC-H: Atypical squamous cell cannot exlude high-grade squamous intraepithelial lesion

The 2001 system changes "within normal limits" to "negative for intraepithelial lesion or malignancy" and "not within normal limits" to "epithelial cell abnormality."

The category "benign cellular changes" has now been eliminated. The new system of reporting will not eliminate the term completely, but will place it in a separate descriptor so that the clinician will know whether herpes, trichomonas, or other infections are still present. What is important about this change is that cases with benign cellular changes will still be read out as negative for intraepithelial lesion and malignancy.

The "other" category has been created to place cells that are not intraepithelial lesions or malignant cells (*e.g.*, endometrial cells in a woman over 40 or cells from a tubal or ovarian carcinoma or sarcoma). In a woman younger than 40, the presence of endometrial cells is very unlikely to be associated with a malignant process, so they will not be mentioned on a Pap smear.

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Epithelial cell abnormalities

The 1988 Bethesda system included the term "atypical squamous cells of undermined significance"

(ASC-US). This term was used when the reactive changes on the Pap smear fell short of definitive diagnosis of SIL. In practice, pathologists reported a significant number of "ASC-US, not otherwise specified."

The focus in the 1988 classification was also on identifying all SIL, including LSIL, based on the view that all grades of SIL required colposcopy and treatment. There has now, however, been a shift regarding management of LSIL, as the majority represent a self-limiting human papilloma virus (HPV) infection.

There is now more emphasis on detection and treatment of histologically confirmed high-grade CIN. It is also logical for the atypical squamous cell (ASC) category to emphasize the importance of detecting HSIL.

ASC

ASC represents the most common abnormality on Pap smears, with a prevalence of 2.9% to 4.4%. The new Bethesda system classification subdivides these cells into two categories: ASC-US; and atypical squamous cells, which cannot exclude HSIL (ASC-H) (Table 3).

What's involved in management?

HSIL

Most patients with HSIL should be referred for colposcopy.

Glandular cell abnormalities

The intent of the Bethesda 2001 committee was to place more emphasis on atypical glandular cells because patients with that pathology are at significant risk for serious lesions.

The 2001 Bethesda system classifies glandular cell abnormalities into three categories (Table 4).

Table 4
Types of of glandular cell abnormalities

AGC (Either endocervical, endometrial, or not NOS)
- Much higher risk of cervical neoplasia than ASC or LSIL
- 9% to 54% have CIN
- 0% to 18% have AIS
- < 1% have invasive cancer

AGC NOS (Favour neoplasia [either endocervical or NOS])
- 9% to 14% have CIN 2, CIN 3, AIS, or invasive cancer

AIS (Endocervical)
- 48% to 69% have biopsy proven AIS
- 38% risk of invasive cervical adenocarcinoma

AGC: Atypical glandular cell
ASC: Atypical squamous cell
LSIL: Low-grade squamous intraepithelial lesions
CIN: Cervical intraepithelial neoplasia
AIS: Adenocarcinoma in situ

Colposcopy with electrocardiogram is recommended for women with all subcategories of AGC (with the exception of women with atypical endometrial cells, who should initially be evaluated with endometrial sampling). Endometrial biopsy should be performed in all women over 35 with AGC, and in younger women with AGC and unexplained vaginal bleeding.

If initial colposcopic workup does not identify invasive cancer, women with AGC favour neoplasia and endocervical AIS should have a cone biopsy.

If initial colposcopy workup does not identify invasive cancer, women with AGG NOS should have repeat Pap tests every six months until four consecutive "negative for intraepithelial lesion or malignancy" results are obtained.

What is the system's goal?

The goal of the Bethesda system 2001 was to incorporate new research data into the terminology to

improve communication of cytology results from the laboratory to the clinicians.

In Alberta, women with ASCUS LSIL should have repeat Pap smears every six months until four consecutive negative results are obtained. The only exception is immunosuppressed women who should be referred for colposcopy.

Trials are ongoing on the possible role for HPV testing in patients with ASC on cervical screening. The Digene HPV test, based on the hybrid capture II system, is commercially available to detect high-risk and low-risk HPV subtypes. This test has identified 90% of patients with high-grade dysplasia in a population of patients with ASCUS Pap smears, and may decrease the necessity for colposcopy.

What does the future hold?

Pap smear testing using liquid-based cytology (LBC) is more sensitive and specific in detecting cervical dysplasia, although the positive predictive value for malignancy is similar to conventional Pap smears. Two LBC systems, ThinPrep® and SurePath™ have been approved in Canada. The LBC system has the added advantage of allowing HPV testing. Dx

References available upon request—contact *The Canadian Journal of Diagnosis* at **diagnosis@sta.ca**.

Surf your way to...

1. The Canadian Society of Cervical Pathology and Colposcopy: *www.ifcpc.org/canadian.html*
2. The American Society for Colposcopy and Cervical Pathology: *www.asccp.org*