Chapter 10: Pap Test Results

Learning Objectives	On completion of this section, the learner will be able to: 1. Identify how Pap test results are interpreted and the reasons for normal and abnormal results. 2. Describe the appropriate follow-up for each Pap result using the CervixCheck Screening Guidelines.

The Bethesda System[1]

The terminology for reporting cervical cytology is based on The Bethesda System which is the internationally recognized reporting standard.

Specimen Adequacy

The two categories of specimen adequacy are:

1. Unsatisfactory for Evaluation
2. Satisfactory for Evaluation

1. Unsatisfactory for Evaluation

Unsatisfactory for Evaluation indicates that:

- The specimen was processed and examined but was unsatisfactory for evaluation because of obscuring factors (excessive RBCs, WBCs or mucous) or insufficient epithelial cells or cytolysis.

The reason the Pap test was considered *Unsatisfactory for Evaluation* will be indicated in the report.

Unsatisfactory Pap tests are mostly due to:

- cervical sampling errors, or
- specimen collection issues (refer to chapter 9 to review Pap test sampling techniques).

The following table identifies and describes each reason for Unsatisfactory Pap test results:

Unsatisfactory due to:	Description
Mainly endocervical cells only	Only cells from the endocervix are visible.
Excessively thick cell preparation for adequate cytological evaluation	The sample was likely not spread uniformly across the slide (where conventional cytology is in use), such that the sample appears lumped together or "thick."
Acellularity	Not enough cells were collected to interpret the sample.
Insufficient epithelial cells	Not enough cells were collected to interpret the sample.
Obscuring inflammation	There is a presence of infection and/or necrosis (dying cells, usually due to disease) in the sample.
Obscuring blood	The presence of blood in the sample makes it inadequate for interpretation.
Lubricant or other foreign material	Other foreign material, i.e. lubricant exists on the sample making it difficult to interpret.
Mechanical distortion	The sample is inadequate for interpretation due to broken down cells (i.e. from too much pressure applying the sample to the slide). This reason is typically only seen where conventional cytology has been used.

Factors associated with the client may also produce Unsatisfactory Pap tests results. These include:

- Intercourse within 24 hours of Pap test
- Douching or vaginal medication used 24 hours before Pap test
- Menses
- Infection

2. Satisfactory for Evaluation

The diagnostic categories are:

- Negative for Intraepithelial Lesion or Malignancy
- Epithelial Cell Abnormality
- Other

Negative for Intraepithelial Lesion or Malignancy
Where there is no cellular evidence of neoplasia, Pap tests are interpreted as Negative for Intraepithelial Lesion or Malignancy. Clients with negative results can typically continue with routine screening.

Epithelial Cell Abnormality
Pap tests interpreted as Epithelial Cell Abnormality include both those that:

- represent cervical carcinoma, and
- have changes considered to indicate increased risk of cervical carcinoma.

Changes indicative of increased risk for cervical carcinoma are reported as:
Squamous Cell

- Atypical squamous cells (ASC)
  - of undetermined significance (ASC-US)
  - cannot exclude HSIL (ASC-H)
- Low-Grade Squamous Intraepithelial Lesion (LSIL)
- High-Grade Squamous Intraepithelial Lesion (HSIL)
- Squamous cell carcinoma

Glandular Cell

- Atypical
  - glandular cells (AGC)
  - endocervical cells
  - endometrial cells
- Endocervical adenocarcinoma in Situ (AIS)
- Adenocarcinoma
  - Endocervical
  - Endometrial
  - Extrauterine
  - Not otherwise specified (NOS)

Management of Cytology Results

The following table shows CervixCheck recommendations for follow-up of all Pap test results:

CYTOLOGY RESULTS	MANAGEMENT
Negative	Routine screening every 3 years The absence of transformation zone is not a reason to repeat a Pap test earlier than the recommended interval
Unsatisfactory	Repeat Pap test in 3 months If persistent (2 consecutive, or 2 within 12 months) unsatisfactory due to "obscuring blood" or "obscuring inflammation," refer for colposcopy
ASC-US Atypical squamous cells of undetermined significance **LSIL** Low-grade squamous intraepithelial lesion	Repeat Pap test in 6 months Negative → Repeat Pap test in 6 months → Negative → Routine screening Abnormal → Colposcopy Abnormal → Colposcopy
ASC-H Atypical squamous cells, cannot rule out high-grade **HSIL** High-grade squamous intraepithelial lesion	Refer for colposcopy
AGC Atypical glandular cells	Refer for colposcopy and endocervical curettage • If woman is ≥ 35 years of age or has abnormal bleeding, refer for endometrial biopsy
Atypical endocervical cells	Refer for colposcopy
Atypical endometrial cells	Refer for endometrial biopsy
Benign endometrial cells	< 45 years of age: In the absence of abnormal bleeding, woman can continue routine screening ≥ 45 years of age: If woman is postmenopausal and/or has abnormal bleeding, refer for endometrial biopsy
AIS (Adenocarcinoma in situ)	Refer for colposcopy and endocervical curettage
Squamous carcinoma, adenocarcinoma, other malignant neoplasms.	Refer for colposcopy and oncology
Absence of transformation zone cells	Screen according to cytology result. The absence of transformation zone is not a reason to repeat a Pap test earlier than the recommended interval
Rejected specimen	Repeat Pap test in 3 months Inform woman repeat is not due to abnormal cytology

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Other Results

Absence of Transformation Zone Cells

The decision to repeat a Pap test should be based on the cytology diagnosis and not the presence or absence of transformation zone cells. Screen according to the cytology result.	Important Information

Sufficient sampling of the transformation zone (TZ) include an adequate number of squamous and endocervical cells (EC) or metaplastic cells or dysplastic cells.

Lack of TZ/EC on a Pap test is often seen in postmenopausal and pregnant clients. In the absence of these clinical scenarios, the lack of TZ/EC may indicate improper screening technique.

Studies show that dysplastic/SIL cells are more likely to be present on Pap tests where TZ/EC are present.[2] However, retrospective cohort studies have shown that women with Pap tests lacking TZ/EC are not more likely to have squamous lesions on follow-up than are women with EC. [3 4] Finally, retrospective case-control studies have failed to show an association between false negative interpretations of Pap tests and lack of TZ/EC.[5 6] Cross-sectional studies have consistently demonstrated a higher percentage of cytological abnormalities in conventional Pap tests with evidence of TZ sampling than those without.[4 7 8 9] Longitudinal studies have not shown an increased risk of high-grade lesions or cancer in women with Pap tests lacking TZ sampling.[5 10 11]

Clients with Pap test results that are “Negative for Intraepitheleal Lesion or Malignancy”, and report an “absence of transformation zone cells,” do not need a repeat Pap test - the client may remain in routine screening **unless**:

- They have had a previous Pap test result that is ≥High-Grade and does not have three subsequent negative Pap tests, with at least one that has TZ/EC,
- They have ever had a previous Pap test result that is AGC,
- They have had a positive HPV test within 12 months,
- The HCP cannot see the entire cervix upon visual inspection,
- They are immunocompromised, and/or

- They have an insufficient screening history (lack of routine screening every 3 years).

A Pap test that lacks TZ/EC in clients who have persistent postcoital bleeding (PCB) or intermenstrual bleeding (IMB) should be referred to colposcopy or gynecology.

Rejected Specimen
A specimen may be rejected for one of the following reasons:

- The specimen is improperly labeled
- The specimen is not labeled with sufficient personal identification
- Discrepancy of information between the specimen and the requisition
- Where conventional cytology is used, the slide is broken beyond repair
- The specimen is received without accompanying requisition

Limitations of Pap Test Results

A false negative result occurs when the Pap test fails to detect an abnormality that is present on the cervix. False negatives occur because either:

1. abnormal cells are not present on the slide due to limitations of cervical sampling and Pap test preparation, or
2. the laboratory did not identify abnormal cells in the Pap test.

Repeat screening at regular intervals is necessary to provide adequate lifetime protection from cervical cancer. Most sexually active clients should be screened every three years.	Important Information

Talking to Clients about Abnormal Pap Test Results

Abnormal Pap test results are common. One in four women will have an abnormal Pap test result in her lifetime.[12] The psychological impact of having an abnormal result varies between clients. How a HCP communicates an abnormal result can impact the client's perspective and subsequent psychological response. Below are some suggestions for how to communicate abnormal Pap test results:

EDUCATE

1. Inform the client that their Pap test result is abnormal, meaning that the Pap test has detected abnormal cell changes on the cervix. Abnormal cell changes are caused by the HPV virus.

2. In rare circumstances, and often over a long period of time, abnormal changes caused by HPV can become cancerous.

3. Reassure the client that their abnormal result is most likely not cancer.

4. Normalize HPV. Reassure the client that HPV is very common. Three out of four people will have at least one HPV infection in their lifetime. Most infections will disappear on their own.

5. Use "What you need to know about preventing cervical cancer" booklet (available at cancercare.mb.ca/screening/resources) to help explain the meaning of the result and the recommended follow-up.

CHECK FOR UNDERSTANDING

6. Ensure the client understands the information you have provided her and clarify any misunderstanding.

7. Remind the client that most clients who have abnormal Pap test results and who have follow-up tests and/or treatment will never get cancer of the cancer.

8. Address any fears/barriers that may prevent them from following up on the recommended course of action.

PROVIDE RESOURCES

9. Clients can contact CervixCheck, CancerCare Manitoba for more information.

10. Provide the client with a copy of CervixCheck's 'What you need to know about preventing cervical cancer booklet.'

Colposcopy[13]

Clients with high-grade and persistent low grade/unsatisfactory Pap tests results are referred to colposcopy. Colposcopy is a technology that has been used for several decades to identify sub-clinical abnormalities of the cervix. The cervix is magnified through a binocular scope with a high intensity light. This allows for the identification of abnormalities based upon:

- Epithelial density (white epithelium)
- Vascular patterns (punctation, etc.)

Using these parameters, an area of abnormality can be identified in order to direct a tissue biopsy.

If a high-grade lesion is identified involving the cervix, it can be treated by one of the following methods:

- Laser surgery uses an intense, narrow beam of energy to vapourize the abnormal area.
- LEEP (loop electro surgical excision procedure) Excision uses an electrical wire loop to remove the abnormal cervical tissue.
- Cone biopsy involves the removal of a cone-shaped piece of tissue either for treatment or for diagnosis when a high-grade lesion is suspected but not seen at colposcopy.

To see colposcopy images, as well as carcinoma and other abnormalities of the cervix, please see the Pap Test Learning Module video presentation on "At your cervix: What's normal anyways?"

Terminology for cervical histopathology specimens has changed over time. Squamous abnormalities have generally been reported using terms including "dysplasia", "cervical intraepithelial neoplasia" (CIN) and "squamous

intraepithelial lesions". In 2014, the Pan-Canadian Cervical Screening Network (Canadian Partnership Against Cancer) reported on and published Canadian consensus statements for reporting histopathology specimens from the cervix and vagina[14]. Manitoba histo-pathology labs have adopted these consensus statements. The following table provides the current cervical histopathology nomenclature with comparison to previous reporting terminology.

Cervical histopathology nomenclature correlations

<table>
<tr><th>Dysplasia terminology</th><th>CIN terminology</th><th>2014 Consensus Statements (current)</th></tr>
<tr><td>Normal</td><td>Normal</td><td>Negative</td></tr>
<tr><td>Mild dysplasia</td><td>CIN 1</td><td>Low-grade squamous intraepitheleal lesion (LSIL)</td></tr>
<tr><td>Moderate dysplasia</td><td>CIN 2</td><td rowspan="3">High-grade squamous intraepitheleal lesion (HSIL)</td></tr>
<tr><td>Severe dysplasia</td><td>CIN 3</td></tr>
<tr><td>Carcinoma in-situ</td><td>CIN 3</td></tr>
<tr><td>Dysplasia NOS</td><td>CIN NOS</td><td>Squamous intraepitheleal lesion (SIL), Ungraded</td></tr>
<tr><td>Adenocarcinoma in-situ (AIS)</td><td></td><td>High-grade adenocarcinoma intraepithelial lesion</td></tr>
<tr><td rowspan="2">Invasive carcinoma</td><td rowspan="2">Invasive carcinoma</td><td>Superficially Invasive Squamous Cell Carcinoma (SISCCA)</td></tr>
<tr><td>Invasion</td></tr>
</table>

Remember: colposcopic impression refers to the colposcopist's visual estimate and is not the biopsy result. By a colposcopist's stating their impression prior to the histology report, s/he can participate in Quality Assurance to assist their clinical continued medical education. The **biopsy** result will provide the diagnosis upon which to base follow-up management.

EXAMPLE 1:

Colposcopy:		
	Impression	HSIL CIN 2
		HSIL CIN 3
	Biopsy	Low-Grade Squamous Intraepitheleal Lesion (LSIL)
	ECC	Endocervical Curettage Biospy Definitely Not Done
	Repeat Colp.	Follow-up in 6 months

INTERPRETATION:
While the **impression** is high-grade; the **biopsy** reveals a low-grade histopathology result that does not require treatment. Most LSIL will resolve without treatment. Upon discharge from colposcopy a screening interval of every 3 years (routine screening is recommended.

EXAMPLE 2:

Colposcopy:		
	Impression	Low-Grade Squamous Intraepitheleal Lesion (LSIL)
	Biopsy	HSIL CIN 2
	Treatment	LEEP Excision

INTERPRETATION:
While the **impression** is low grade; the **biopsy** reveals a high-grade result and treatment is recommended. Upon discharge from colposcopy a screening interval, it is recommended that an annual screening interval is adhered to because of a high-grade histology result.

EXAMPLE 3:

Screening & Colposcopy History (reverse chronology)

Spec/Service Date	Name	Health Number	Date of Birth	Service Provider	Cytology/Colposcopy
A 2017-Jul-01	DUCK, Daisy	987654321	1972-03-17	LOTOCKI, Robert, 1997	17-008285

Associated Cytology:

Colposcopy:		
	Impression	HSIL CIN 2
	Biopsy	Low-Grade Squamous Intraepitheleal Lesion (LSIL)
	ECC	Endocervical Curettage Biospy Definitely Not Done
	Repeat Colp.	Follow-up in 6 months

A 2017-Jul-01	DUCK, Daisy	987654321	1972-03-17	Health Sciences Centre-Cytology	HSC20170701
LOTOCKI ROBERT		ACF WOMENS HEALTH			

Cytology: **Atypical Squamous Cells Cannot Exclude a High Grade Squamous Intraepithelial Lesion ASC-H**

INTERPRETATION:

Although the cytology result from July 1, 2017 is ASC-H (a high-grade result) and the colposcopy **impression** is HSIL CIN 2 (high-grade), the **biopsy** is an LSIL. The biopsy confirms this is a low-grade histopathology result that does not require treatment. Most LSIL will resolve without treatment. Upon discharge from colposcopy result that does not require a more frequent screening interval than every 3 years (routine screening).

	Recommended Reading

CervixCheck Resources
Screening Guidelines
What you need to know about preventing cervical cancer booklet

Solomon, D., Davey, D., Kurman, R., Moriarty, A., O'Connor, D., Prey, M., Raab, S., Sherman, M., Wilbur, D., Wright, T., & Young, N. (2002). The 2001 bethesda system terminology for reporting results of cervical cytology. *JAMA*, 287(16): 2114-2119.

The College of Physicians and Surgeons of Manitoba. (2013). *Manitoba laboratory standards.* Winnipeg: Manitoba.

Contemporary Clinical Questions on HPV-Related Diseases and Vaccination: 2nd Edition

	Chapter 10 Self-Test
1. How are Pap test results interpreted? 2. What are reasons for Unsatisfactory Pap tests? 3. What is the recommended management for all abnormal cytology results? 4. Why does a false negative Pap test result occur?	

References

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[2] Vooijs PG, Elias A, Vander Graaf Y, Veling S.(1985). Relationship between the diagnosis of epithelial abnormalities and the composition of cervical smears. Acta Cytol 29: 323-8.

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[4] Kivlahan C, and Ingram E. (1986). Papanicolaou smears without endocervical cells. Are they inadequate? Acta Cytol 30: 258-60.

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[7] Elias A., Linthorst G., Bekker B., Vooijs PG. (1983). The significance of endocervical cells in the diagnosis of cervical epithelial changes. *Acta Cytol,* May-June;27(3):225-9.

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[10] Anita B. Bos, et al. (2001). Endocervical status is not predictive of incidence of cervical cancer in the years after negative smears. *American Journal of Clinic* Pathology, 115:851-855.

[11] Siebers, A.G. De Leeuw, Verbeek, A.L.M., & A.G.J.N. Hanselaar (2003). Prevalence of squamous abnormalities in women with a rectn smear without andocervical cells is lower as compared to women with smears with endocervical cells. *Cytopathology* 14:58-65.

[12] Manitoba Cervical Cancer Screening Program. (2008). Rates of cervical dysplasia. Manitoba: CancerCare Manitoba.

[13] From Alberta Medical Association. (2003). Guideline for screening for cervical cancer: Revised. Adapted with permission.

[14] Dr. C. Meg McLachlin on behalf of the Pan-Canadian Cervical Screening Initiative Working Group (2014). “Reporting on histopathology specimens from the cervix and vagina: consensus statements from the Pan-Canadian Cervical Screening Initiative. Canadian Journal of Pathology, Winter 2013-2014.