Chapter 10: Cervical Cancer Screening Test Results

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

The lab will issue ONE cervical cancer screening result report which will include:

1- Pap test (cytology) interpretation,
2- High-risk human papillomavirus (hrHPV) triage test result*
Note: (HPV triage will only be included for ASCUS results in patients age 30 and over, and LSIL results in patients age 50 and over), and
3- Management of results complete with a follow-up recommendation and/or educational note.

NOTE: High-risk HPV **triage** testing and high-risk HPV **reflex** testing both refer to the same genotyping process outlined above.

SAMPLE CERVICAL CANCER SCREENING HISTORY:

CancerCare Manitoba
ActionCancerManitoba

Cervical Cancer Screening History

Patient name:	**Krista Smith**
Health number:	**123456789**
Date of birth:	
Age:	**30**

Date	Service	Detail	Clinician	Analyzing Lab
1 month ago	**Cytology**	**Result:** Atypical squamous cells of unknown significance ASC-US	Dr. Smith	Health Sciences Centre - Cytology
	HPV	**Overall result:** High Risk HPV Positive Type 16 Detected Type 18 Not detected Type Other Not detected		
9 months ago	**Cytology**	**Result:** Atypical Cells of Undetermined Significance AS-CUS **Recommendation:** Repeat Test in 6 months	Dr. Smith	Health Sciences Centre - Cytology
3 years ago	**Cytology**	**Result:** Negative for Intraepithelial Lesion or Malignancy	Dr. Smith	Health Sciences Centre - Cytology

1- Pap Test Interpretation

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 cytology specimen adequacy are:

a) Unsatisfactory for Evaluation
b) Satisfactory for Evaluation

a) 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.

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
- Infection

b) 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)

2- High-Risk Human Papillomavirus (hrHPV) Triage Result

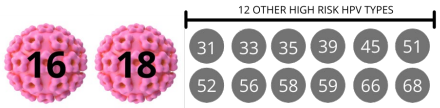
HPV reflex testing will be performed on the following low-grade cytological specimen interpretations:

- Atypical squamous cells of undetermined significance (ASCUS) in patients age 30 and over
- Low grade squamous intraepithelial lesion (LSIL) in patients age 50 and over

If any one of the following three genotyping sequences is **detected**, the HPV triage result will be **positive**.

1- HPV 16 (detected or undetected)
2- HPV 18 (detected or undetected)
3- HPV Other (detected or undetected)

HPV Other refers to the genotyping of 12 other hrHPV types as illustrated here:



The hrHPV triage result will be either:

- **Positive:** high-risk HPV is detected in any one or more of the (3) genotyping sequences (HPV16, HPV18, HPV Other)
- **Negative:** high-risk HPV is undetected in all (3) of the genotyping sequences (HPV16, HPV18, HPV Other)
- **Invalid:** The presence or absence of high-risk HPV could not be determined.

3- Management of Results

Each lab report will contain information about how to manage the results and may or may not include an educational note. The following table shows CervixCheck recommendations for follow-up of all Pap test interpretations and hrHPV results.

MANAGEMENT OF RESULTS

Pap test interpretation	Management
Negative for intraepithelial lesion or malignancy (NILM)	Routine screening with a Pap test in 3 years.
Atypical squamous cells of undetermined significance (ASCUS) hrHPV = high-risk human papillomavirus	**21 to 29 years of age** Repeat Pap test in 6 months → **Negative** → Repeat Pap test in 6 months → **Negative** → Routine screening Repeat Pap test in 6 months → **Negative** → Repeat Pap test in 6 months → **Abnormal** → Refer for colposcopy Repeat Pap test in 6 months → **Abnormal** → Refer for colposcopy **30 years of age and older** Lab automatically tests the same specimen for hrHPV → hrHPV negative → Routine screening Lab automatically tests the same specimen for hrHPV → hrHPV positive → Refer for colposcopy Lab automatically tests the same specimen for hrHPV → hrHPV invalid → Repeat Pap test in 6 months
Low-grade squamous intraepithelial lesion (LSIL)	**21 to 49 years of age** Repeat Pap test in 6 months → **Negative** → Repeat Pap test in 6 months → **Negative** → Routine screening Repeat Pap test in 6 months → **Negative** → Repeat Pap test in 6 months → **Abnormal** → Refer for colposcopy Repeat Pap test in 6 months → **Abnormal** → Refer for colposcopy **50 years of age and older** Lab automatically tests the same specimen for hrHPV → hrHPV negative → Routine screening Lab automatically tests the same specimen for hrHPV → hrHPV positive → Refer for colposcopy Lab automatically tests the same specimen for hrHPV → hrHPV invalid → Repeat Pap test in 6 months
Atypical glandular cells (AGC)	Refer for colposcopy and endocervical curettage. If patient is 35 years of age and older or has abnormal bleeding, colposcopy should also include an endometrial biopsy.
Atypical squamous cells, cannot rule out high-grade (ASC-H)	Refer for colposcopy.
High-grade squamous intraepithelial lesion (HSIL)	Refer for colposcopy.
Atypical endocervical cells	Refer for colposcopy.
Atypical endometrial cells	Refer for endometrial biopsy.
Benign endometrial cells	If patient has abnormal bleeding: refer for endometrial biopsy. If patient does not have abnormal bleeding and is - less than 45 years of age: continue routine screening - 45 years of age and older: refer for endometrial biopsy
Adenocarcinoma in situ (AIS)	Refer for colposcopy.
Squamous carcinoma, adenocarcinoma, other malignant neoplasms	Refer for colposcopy.
Unsatisfactory	Repeat Pap test in 3 months. If persistent (2 consecutive or 2 within 12 months) unsatisfactory result due to "obscuring blood" or "obscuring inflammation," refer for colposcopy.
Absence of transformation zone cells	Screen according to cytology result.

NOTE: All cytological abnormal results in immunocompromised or HIV positive individuals should be referred for colposcopy (includes LSIL and ASCUS cytology results).

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EDUCATIONAL NOTE

RESULT	WHAT DOES IT MEAN?	WHAT SHOULD I DO?
hrHPV POSITIVE	One or more types of high-risk HPV that are linked to high-grade lesions and cervical cancer has been detected. This patient is at higher risk for cervical cancer. **It does not necessarily mean your patient has cervical cancer or will get cervical cancer.** Colposcopy is required to determine if treatment is necessary.	**Notify patient. Refer patient to colposcopy.** Visit our website for a list of colposcopy services in Manitoba.
hrHPV NEGATIVE	High-risk HPV was not detected and the risk for cervical cancer in the next three years is very low.	**Return patient to routine screening.**
hrHPV INVALID	The presence of absence of high-risk HPV could not be determined.	**Notify patient. Repeat Pap test in 6 months.**

Colposcopy Referral

To make a colposcopy referral, refer to the Colposcopy Services in Manitoba (pdf) list to make a direct referral to a colposcopy clinic. In the referral include:

- Patient name, address, date of birth, PHIN, phone number
- Referring doctor or nurse practitioner name, clinic name, address, phone, fax
- Reason for referral
- Lab report for the most recent Pap test indicating colposcopy is needed
- CervixCheck screening history (request from CervixCheck using the *Request for Cervical Cancer Screening Histories* (pdf) form)

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.

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 vial is improperly labeled
- The specimen vial is not labeled with sufficient personal identification
- Discrepancy of information between the specimen vial 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 individuals eligible for cervical cancer screening should be screened every three years.	Important Information

Talking to Clients about Abnormal Results

Abnormal cervical cancer screening 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 an HCP communicates an abnormal result can impact the client's perspective and subsequent psychological response. Before you communicate abnormal results:

1- Review chapter 2 sections entitled:
   a. Natural History
   b. Risk Factors for HPV and Cervical Cancer
2- Review the suggestions below 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.

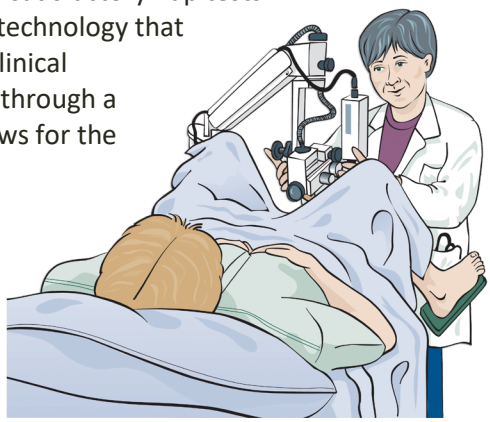
10. Provide the client with a copy of CervixCheck's 'What you need to know about preventing cervical cancer booklet.'

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:

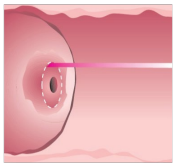
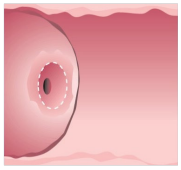
- Epithelial density (white epithelium)
- Vascular patterns (punctation, etc.)

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

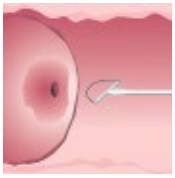
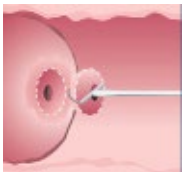
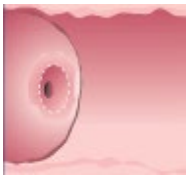


If a high-grade lesion is identified involving the cervix, it can be treated by one of the following methods:

- **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.

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

Dysplasia terminology	CIN terminology	2014 Consensus Statements (current)
Normal	Normal	Negative
Mild dysplasia or atypia	CIN 1	Low-grade squamous intraepitheleal lesion (LSIL)
Moderate dysplasia or atypia	CIN 2	High-grade squamous intraepitheleal lesion (HSIL)
Severe dysplasia or atypia	CIN 3	
Carcinoma in-situ	CIN 3	
Dysplasia NOS	CIN NOS	Squamous intraepitheleal lesion (SIL), Ungraded
Adenocarcinoma in-situ (AIS)		High-grade adenocarcinoma intraepithelial lesion
Invasive carcinoma	Invasive carcinoma	Superficially Invasive Squamous Cell Carcinoma (SISCCA)
		Invasion

Remember: The colposcopy impression refers to the colposcopist's visual estimate and is not the biopsy result. By a colposcopist stating their impression prior to the histology report, they 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 Biopsy 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, it is recommended that an annual screening interval is adhered to because of a high-grade histology result.

EXAMPLE 3:

July 1, 2017

Colposcopy:

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

July 1, 2017

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

Human Papillomavirus (HPV): Frequently Asked Questions

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. (2019). Laboratory Standards January 2019.pdf (cpsm.mb.ca). Winnipeg: Manitoba.

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

1. How are Pap test results interpreted? 2. What is the recommended management for all abnormal cytology results? 3. What is the recommended management for high-risk HPV results? 4. What is the difference between a cytology interpretation and a histopathology result?	Chapter 10 Self-Test

References

[1] Nayar, R. & Wilbur, D. (2015). The Pap Test and Bethesda 2014: Retrieved on February 11, 2016 from: https://www.karger.com/Article/Pdf/381842

[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.

[3] Mitchell H, Medley G. (1991). Longitudinal study of women with negative cervical smearsaccording to endocervical status. Lancet 337: 265-7.

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

[5] Mitchell H, Medley G. (1995). Differences between Papanicolaou smears with correct andincorrect diagnoses. Cytopathology 6: 368-75.

[6] O'Sullivan JP, A'Hern RP, Chapman PA, et al. (1998) A case-control study of true-positive versus false-negative cervical smears in women with cervical intraepithelial neoplasia (CIN) III. Cytopathology 9: 155-61.

[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.

[8] Killough et al. (1988). Correlation between sytodiagnosis and the presence of endocervical or squamous metaplastic cells in gynecologic smears. *Acta Cytol* 32:758.

[9] Boon, Mathilde E & Albert J.J. Suurmeijer (1993). The Pap Smear. The Netherlends: Colombn Press Leyden.

[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.