Protocol for the Reporting of Cervicovaginal Cytology Specimens

Version: 1.0.0.0
Protocol Posting Date: June 2022
The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

This protocol may be used for the following:

Procedure	Description
Cervicovaginal cytology	Includes broom, spatula, and endocervical brush collection methods
Specimen Type	**Description**
PAP stained cervicovaginal cytology	

The following should NOT be reported using this protocol:

Specimen
Non-cervicovaginal cytology specimens

Authors
Sana O. Tabbara, MD*; George G. Birdsong, MD; Christine N. Booth, MD; Jennifer Brainard, MD; Stuart E. H. Cameron, MD; James Dvorak; Abha Goyal, MD; Lananh Nguyen, MD; Kaitlin Sundling, MD, PhD.
With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.
* Denotes primary author.

Accreditation Requirements
The use of this case summary is recommended for clinical care purposes but is not required for accreditation purposes. The core and conditional data elements are routinely reported. Non-core data elements are indicated with a plus sign (+) to allow for reporting information that may be of clinical value.

Includes The Bethesda System (TBS) 2014 terminology for reporting cervicovaginal cytology specimens.

Summary of Changes

v 1.0.0.0

- New Protocol

Reporting Template

Protocol Posting Date: June 2022
Select a single response unless otherwise indicated.

CASE SUMMARY: (Protocol for the Reporting of Cervicovaginal Cytology Specimens)
This case summary may be useful for clinical care purposes but is not required for accreditation purposes. Core data elements are bolded to help identify routinely reported elements. (Note A)

PATIENT INFORMATION

Age: _____

Gender (Note B)
___ Male
___ Female
___ Other (specify): _____

Collection Date: _____

Date of Last Menstrual Period (if applicable): _____

Indication for Examination
___ Screening, routine
___ Screening, high-risk
___ Diagnostic
___ Reflex cytology following positive primary HPV screening result

Prescription Drugs (select all that apply)
___ None
___ Unknown
___ Hormone replacement therapy (estrogen / progesterone)
___ Androgen therapy
___ Oral contraceptive drugs
___ Chemotherapeutic agents
___ Other (specify): _____

Clinical History (select all that apply)
___ Unknown
___ Pregnant
___ Post-partum
___ Hysterectomy
  ___ Total
  ___ Supracervical
___ Prior radiation therapy
___ Diethylstilbesterol (DES) exposure
___ Intrauterine device (IUD)
___ Post-menopausal bleeding

___ Abnormal bleeding
___ Vaginal discharge
___ Other (specify): _____

History of Dysplasia or Malignancy
___ Unknown
___ Negative
___ Positive
  ___ Abnormal Pap tests / Dysplasia, NOS
  ___ Low-grade squamous intraepithelial lesion (LSIL)
  ___ High-grade squamous intraepithelial lesion (HSIL)
  ___ Endocervical adenocarcinoma in situ (AIS)
  ___ Squamous cell carcinoma
  ___ Adenocarcinoma
  ___ Other (specify): _____
  ___ Carcinoma, NOS

High-Risk Human Papillomavirus (HPV) History (select all that apply)
___ Unknown
___ Negative
___ Positive for high risk
___ Positive genotype 16
___ Positive genotype 18
___ Positive for genotype 16/18
___ Positive for genotype 18/45
___ Other high-risk types (specify, if known): _____
___ Date of first positive (if available): _____
___ Date of most recent HPV testing: _____

HPV Vaccination History (Note C)
___ Unknown
___ Unvaccinated
___ Vaccinated
  +___ Completed
  +___ Incomplete
  +___ Quadravalent
  +___ Nonavalent
  +___ Other (specify): _____

+Human Immunodeficiency Virus (HIV) Status
___ Unknown
___ Negative
___ Positive
___ Positive but undetected

PREANALYTICAL EXAMINATION OF THE SPECIMEN

Source
___ Cervical
___ Vaginal
___ Other (specify): _____

+Sampling Device
___ Broom
___ Spatula / Endocervical Brush
___ Unknown
___ Other (specify): _____

Test(s) Ordered
___ Pap test only
___ Cotesting
___ Reflex cytology following positive primary HPV screening result

Gross Description (select all that apply)
___ Number of conventional smear slides: _____
___ Liquid-based in fixative
Color (specify): _____
Approximate Volume: _____ ml
___ Other (specify): _____

Preparation Type
___ Conventional
___ Liquid-based ThinPrep
___ Liquid-based SurePath
___ Other (specify): _____

Number of Slides Prepared (specify): _____

+Liquid-based Imaging System Type
___ ThinPrep Imaging System
___ BD FocalPoint GS
___ Other (specify): _____

INTERPRETATION

Specimen Adequacy (Note D)
___ Satisfactory for evaluation
Quality Indicators
___ Transformation zone present
___ Transformation zone absent
___ Not applicable
___ Cannot be determined

___ Unsatisfactory for evaluation
  ___ Processed and examined
    ___ Insufficient squamous cellularity
    ___ Obscuring blood
    ___ Obscuring inflammation
    ___ Obscuring acellular material
    ___ Other (specify): _____
  ___ Not processed (explain): _____

Results (select all that apply)
___ Negative for intraepithelial lesion or malignancy (NILM)
___ Negative for squamous intraepithelial lesion
  +Non-Neoplastic Cellular Variations (select all that apply)
  ___ Squamous metaplasia
  ___ Keratotic changes
  ___ Tubal metaplasia
  ___ Atrophy
  ___ Pregnancy-associated changes
  ___ Other (specify): _____
  Reactive Cellular Changes (Note E)
  ___ Present
    +___ Inflammation (includes typical repair)
    +___ Lymphocytic (follicular) cervicitis
    +___ Radiation
    +___ Intrauterine device (IUD)
    +___ Glandular cells status post-hysterectomy
    +___ Other (specify): _____
  ___ Absent
___ Squamous cell abnormalities
  Squamous Cell Abnormalities
  ___ Atypical squamous cells - undetermined significance (ASC-US)
  ___ Atypical squamous cells cannot exclude HSIL (ASC-H)
  ___ Low-grade squamous intraepithelial lesion (LSIL)
  ___ High-grade squamous intraepithelial lesion (HSIL)
  ___ High-grade squamous intraepithelial lesion (HSIL) with features suspicious for invasion
  ___ Squamous cell carcinoma
  ___ Other (specify): _____
___ Glandular cell abnormalities
  Glandular Cell Abnormalities
  ___ Atypical endocervical cells (NOS or specify): _____
  ___ Atypical endometrial cells: _____
  ___ Atypical glandular cells (NOS or specify): _____
  ___ Atypical glandular cells, favor neoplastic
  ___ Atypical endocervical cells, favor neoplastic
  ___ Endocervical adenocarcinoma in situ
  ___ Endocervical adenocarcinoma
  ___ Endometrial adenocarcinoma

___ Extrauterine adenocarcinoma
___ Adenocarcinoma NOS
___ Other (specify): _____
___ Other malignant neoplasms (specify): _____

Other Significant Findings (select all that apply)
___ Endometrial cells present (in patients 45 years of age or older)
___ Trichomonas vaginalis
___ Fungal organisms morphologically consistent with Candida species
___ Shift in flora suggestive of bacterial vaginosis
___ Bacteria morphologically consistent with Actinomyces species
___ Cellular changes consistent with herpes simplex virus
___ Cellular changes consistent with cytomegalovirus
___ Other (specify): _____
___ None identified

ANCILLARY TESTING
Please complete all available test results associated with the current Pap test

HR-HPV (select all that apply)
___ Not performed
___ Negative
___ Positive (not otherwise specified)
___ Positive for genotype 16
___ Positive for genotype 18
___ Positive for genotype 18/45
___ Positive for other high-risk types (specify): _____
___ Positive for unknown subtype
___ Pending at the time of cytologic evaluation

HR-HPV Test Platform
___ BD Onclarity TM HPV Assay
___ Hologic Cervista
___ Hologic Aptima
___ Qiagen Digene Hybrid Capture 2 (HC2)
___ Roche cobas 4800
___ Roche cobas 6800/8800
___ Laboratory-developed method
___ DNA
___ RNA
___ Other (specify): _____
___ Other (specify): _____

+Neisseria gonorrhoeae
___ Negative
___ Positive

+Chlamydia trachomatis
___ Negative
___ Positive

+Trichomonas vaginalis
___ Negative
___ Positive

+Herpes Simplex Virus (HSV) (select all that apply)
___ Negative
___ Positive (not otherwise specified): _____
___ Positive for HSV-1
___ Positive for HSV-2

+Immunocytochemistry (select all that apply)
___ P16: _____
___ Ki-67: _____
___ Other (specify): _____

+Other Tests Performed (specify): _____

+Concurrent Biopsy
___ Yes
___ No

COMPUTER-ASSISTED INTERPRETATION OF CERVICAL CYTOLOGY
+Specify Device: _____
+Specify Results: _____

COMMENTS

Comment(s): _____

Explanatory Notes

A. Introduction

The aim of this protocol is to improve the completeness, clarity, and portability of Pap test reporting, while being mindful of the wide range of practice settings in which the data in the report is generated and disseminated. This report includes the Bethesda System for reporting Cervical Cytology[1] which is widely used standardized terminology and incorporate clinical and ancillary testing results that have already been integrated into daily practice, as outlined in the ASCCP guidelines.[2] It also takes into consideration the introduction of additional testing recommendations and modalities in the future.[3,4]

The protocol is based upon input from past and present members of the CAP Cytopathology Committee and prepared in conjunction with the CAP Pathology Electronic Reporting Committee.

This reporting format is meant to replace the final report and will be adapted to laboratory information systems to facilitate utilization and provide more easily reproducible and extractable data. The construction of this protocol does allow for the insertion of pertinent additional information when available. It may be used as a guide for trainees and pathologists who may only perform a limited number of Pap tests in their practice. The committee hopes this is a first step in providing a general framework for more standardized quality Pap reporting practice.

The content of the protocol represents the consensus opinion of the CAP Cytopathology Committee and the CAP Pathology Electronic Reporting Committee. It is the Committees' recommendation that all available elements be included.

References

1. Nayar R, DC Wilbur, Eds The Bethesda System for Reporting Cervical Cytology, 3rd. edition. New York, NY: Springer 2015.
2. Perkins RB, Guido RS, Castle PE, et al. *2019* ASCCP Risk-Based Management Consensus Guidelines for abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis* 24: 102–131, 2020
3. Fontham ETH, Wolf AMD, Church TR, et al. Cervical Screening for Individuals at Average Risk: 2020 Guideline Update from the American Cancer Society. *Cancer J Clin* 2020, 0:1-26 c 2020 American Cancer Society
4. US Preventive Services Task Force. Screening for Cervical Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2018;320(7):674–686. doi:10.1001/jama.2018.10897

B. Gender

In cervical cancer screening, it is important to recognize the importance of using inclusive gender terminology within the pathology report. Individuals at risk for cervical cancer may identify as women, men, or other non-binary or gender fluid terms.

Laboratory information systems should accurately convey the patient's gender identity on reports. At minimum, a nonbinary option such as "Other" is recommended to be included, ideally allowing the patient to self-describe their gender identity. Laboratory information systems may also record the sex assigned at birth, which would be kept separately from the gender identity.[1] Ideally, patients would be offered the opportunity to update this information at any time they choose, such as through an online patient portal or at appointments. If pronouns are used in the pathology report, "they/them/theirs" pronouns are

recommended if patient-identified pronouns are not indicated. Care should be taken not to assume "she/her/hers" pronouns on Pap test reporting.

While this form is developed specifically for cervical and vaginal sources (of natal organs), it is also recognized that patients with a neovagina are also at risk of HPV infection, and Pap test screening is recommended.[2,3] Neovaginal specimens may be considered non-gynecologic in origin; however, many aspects of this reporting form may still apply. A neovaginal specimen source should be specifically indicated, when known to the collecting clinician.

References

1. Gamelin M. *Guide to LGBTQ+ Inclusive Forms.* Accessed January 17, 2022. https://denverptc.org/resource.php?id=231
2. Grosse A, Grosse C, Lenggenhager D, Bode B, Camenisch U, Bode P. Cytology of the neovagina in transgender women and individuals with congenital or acquired absence of a natural vagina. *Cytopathology*. 2017;28(3):184-191. doi:10.1111/cyt.12417
3. Garcia MM. Cancer screening in the transgender population: a review of current guidelines, best practices, and a proposed care model. *Transl Androl Urol*. 2020;9(6):2771-2785. doi:10.21037/tau-20-954

C. HPV Vaccination

Human papillomavirus (HPV) is a common sexually transmitted viral infection that affects multiple sites, commonly the reproductive organs. In females, the virus causes cancer of the cervix, vulva, and vagina whereas in males, it causes cancer of the penis. For both genders, it causes cancer of the anus and oropharynx. HPV infection also causes benign lesions, such as anogenital warts and respiratory papillomatosis. Although there are many types of HPV, studies have identified key genotypes associated with disease. HPV 16 and 18 are two specific genotypes associated with cancer and are considered high risk types.[1]

Currently, there are three vaccines approved by the United States Food and Drug Administration. Nonavalent, (Gardasil 9, 9vHPV), quadrivalent, (Gardasil 4, 4vHPV), and bivalent (Cervarix, 2vHPV). All three vaccines protect against high risk HPV types 16 and 18 with specific targets to the L1 protein. Quadrivalent vaccine includes additional targets to HPV 6 and 11. Nonavalent vaccine includes targets to HPV 6, 11, 31, 33, 45, 52, and 58. Nonavalent vaccine is only distributed in the United States. Both bivalent and nonavalent vaccines are distributed in Canada and all three are distributed in Europe.[2]

The recommended dosing for the vaccination is based on the patient's age at administration and patient's history.[3] Two doses are required for patients who received the first dose before they turn 15. Three doses are required for a) patients who received two doses less than 5 months apart when they are between 9 and14 years old OR b) patients are between 9 and 26 years old with weakened immune systems. Vaccination is not recommended for patients older than 26 years old.

References

1. Human Papillomavirus (HPV) Vaccination: What Everyone Should Know. https://www.cdc.gov/vaccines/vpd/hpv/public/index.html

2. European Medicine Agency, Human papillomavirus vaccines, Cervarix, Gardasil, Gardasil 9, Silgard. https://www.ema.europa.eu/en/documents/referral/hpv-vaccines-article-20-procedure-assessment-report_en.pdf
3. National Advisory Committee on Immunization (NACI). Update on Human Papillomavirus (HPV) Vaccines. An Advisory Committee Statement (ACS). *Canada Communicable Disease Report*. January 2012;Volume 38, ACS-1:1-62.

D. Specimen Adequacy

Adequacy criteria were set forth in The Bethesda System (TBS)[1] to provide criteria and protocols to promote the consistent assessment of the adequacy of cervical and anal cytology specimens. In the absence of such criteria, individual laboratories would need to develop their own adequacy criteria which would probably lead to greater inconsistency in the percent of cases flagged as unsatisfactory or suboptimal across laboratories.

Specimen Cellularity

Cellularity thresholds are based on limited scientific evidence. One study has suggested that liquid-based preparations (LBP) with fewer than 5000-20,000 cells may have a higher risk of being false negative (FNP),[2,3] however this has not been confirmed. TBS states that an LBP from a woman with a cervix should have an estimated minimum of 5000 well-preserved, well-visualized, nucleated squamous cells to be considered adequate.[1] This threshold is provided to promote the usage of consistent criteria across laboratories however, it is not meant to be rigidly applied. Exceptions to this guideline are women with a history of chemo or radiation therapy for cancer, or who are post-hysterectomy or post-menopausal with atrophic changes. The patient's history must be taken into account in assessing adequacy, but specimens with less than or equal to 2000 cells should usually be considered unsatisfactory.

Cytologists should not attempt to manually count cells to determine cellularity.[1] The cellularity of LBP can be estimated by counting the number of cells in multiple high-power fields (HPFs), usually 40X, across the diameter of the preparation. The two commercially available LBPs, ThinPrep (Hologic), and SurePath (BD) deposit the cells in circles of different diameters and have different cellular densities. ThinPrep deposits cells in a 20 mm diameter circle whereas the SurePath circle is 13 mm. The number of cells/HPF that correspond to the 5000 cell minimum is therefore different. This number is also affected by the field number (FN) of the eyepieces of the microscope. Table 1 displays the number of cells/HPF for different combinations of eyepiece field number, objective power, and circle diameter.[1]

Table 1. Guidelines for Estimating Cellularity of Liquid-Based Preparations

FN20 eyepiece/10X objective			
Prep. diameter (mm)	**Area (mm2)**	**Number of fields at FN20, 10X**	**Number of cells/field for 5K total**
13	132.7	42.3	118.3
20	314.2	100	50
FN20 eyepiece/40X objective			
Prep. diameter (mm)	**Area (mm2)**	**Number of fields at FN20, 40X**	**Number of cells/field for 5K total**
13	132.7	676	7.4
20	314.2	1600	3.1
FN22 eyepiece/10X objective			
Prep. diameter (mm)	**Area (mm2)**	**Number of fields at FN22, 10X**	**Number of cells/field for 5K total**
13	132.7	34.9	143.2
20	314.2	82.6	60.5
FN22 eyepiece/40X objective			
Prep. diameter (mm)	**Area (mm2)**	**Number of fields at FN22, 40X**	**Number of cells/field for 5K total**
13	132.7	559	9
20	314.2	1322	3.8

FN=field number.

Conventional preparations should contain a minimum of 8000-12,000 well-preserved, well-visualized cells. As with LBP, cellularity should be estimated and not considered a rigid threshold. It is not necessary to count cells on conventional preparations. Cellularity can be estimated by comparing representative fields with the computer edited reference images in the Bethesda System for Reporting Cervical Cytology.[1]

Endocervical/Transformation Zone Component

TBS states that an adequate T-zone sample requires at least 10 well preserved endocervical or squamous metaplastic cells, singly or in clusters. The presence of a transformation zone or endocervical component (T-zone) is not necessary for a specimen to be considered adequate. Theoretically, it might be expected that the risk of an FNP specimen would be elevated if a T-zone component were absent since squamous intraepithelial lesions are thought to arise in the T-zone. Some studies have shown that endocervical cells are more likely to be present in specimens with squamous intraepithelial lesions,[4,5,6] however other studies have shown that specimens which lack endocervical cells are not significantly more likely to be FNP, and in fact, some studies show a trend toward a lower risk of FNP.[7,8,9,10,11] While these observations may be somewhat confusing, the co-presence of endocervical cells and dysplastic cells in specimens does not by itself indicate that specimens which lack endocervical cells have a higher risk of being FNP. Nevertheless, the presence of the T-zone component is considered an important quality indicator. Lack of endocervical cells indicates that the endocervical region has not been well sampled, possibly increasing the risk of missing an endocervical lesion such as adenocarcinoma-in-situ or adenocarcinoma.[1]

Obscuring Factors

Excessive blood or inflammation may obscure epithelial cells in Pap tests. A specimen should be deemed unsatisfactory when more than 75% of the squamous cells are obscured unless abnormal cells are

identified. If 50-75% of cells are obscured, a comment describing the specimen as partially obscured should be added following the satisfactory term. The percentage of cells obscured, not the area of the slide, is what is assessed. Minimal cellularity criteria should also be applied.[1]

Interfering Substances

Excessive blood or lubricants that contain carbomers or carbopol polymers can interfere with ThinPreps by clogging the filter thereby reducing the cellularity of the specimen.[12,13] Some specimens which are unsatisfactory due to blood can be successfully reprocessed utilizing dilute glacial acetic acid.[14,15] The unsatisfactory rate can be reduced by 50% or more with this technique, but it interferes with some types of HPV tests. Interfering substances have little or no effect on SurePath specimens.[16,17,18]

References

1. Birdsong G, Davey D. Specimen Adequacy. In: Nayar R, Wilbur D, editors. The Bethesda System for Reporting Cervical Cytology; Definitions, Criteria, and Explanatory Notes. Third ed. New York: Springer; 2015. p. 1-28.
2. Bolick DR, Kerr J, Staley BE, et al. Effect of cellularity in the detection rates of high grade and low grade squamous intraepithelial lesions. *Acta Cytol.* 2002;46:922-3.
3. Martin-Hirsch P, Lilford R, Jarvis G, Kitchener HC. Efficacy of cervical-smear collection devices: a systematic review and meta-analysis. *Lancet*. 1999;354(9192):1763-70.
4. Baer A, Kiviat NB, Kulasingam S, Mao C, Kuypers J, Koutsky LA. Liquid-based Papanicolaou smears without a transformation zone component: should clinicians worry? *Obstet Gynecol.* 2002;99(6):1053-9.
5. Bos AB, van Ballegooijen M, Elske van den Akker-van Marle M, Hanselaar AG, van Oortmarssen GJ, Habbema JD. Endocervical status is not predictive of the incidence of cervical cancer in the years after negative smears. *Am J Clin Pathol.* 2001;115(6):851-5.
6. Kivlahan C, Ingram E. Papanicolaou smears without endocervical cells. Are they inadequate? *Acta Cytol.* 1986;30(3):258-60.
7. Mitchell H, Medley G. Longitudinal study of women with negative cervical smears according to endocervical status. *Lancet.* 1991;337(8736):265-7.
8. Mitchell HS. Longitudinal analysis of histologic high-grade disease after negative cervical cytology according to endocervical status. *Cancer.* 2001;93(4):237-40.
9. Mintzer M, Curtis P, Resnick JC, Morrell D. The effect of the quality of Papanicolaou smears on the detection of cytologic abnormalities. *Cancer.* 1999;87(3):113-7.
10. Vooijs PG, Elias A, van der Graaf Y, Veling S. Relationship between the diagnosis of epithelial abnormalities and the composition of cervical smears. *Acta Cytol.* 1985;29(3):323-8.
11. Studeman KD, Ioffe OB, Puszkiewicz J, Sauvegeot J, Henry MR. Effect of cellularity on the sensitivity of detecting squamous lesions in liquid-based cervical cytology. *Acta Cytol.* 2003;47(4):605-10.
12. Feit TD, Mowry DA. Interference potential of personal lubricants and vaginal medications on ThinPrep pap tests. *J Am Board Fam Med.* 2011;24(2):181-6.
13. Lin SN, Taylor J, Alperstein S, Hoda R, Holcomb K. Does speculum lubricant affect liquid-based Papanicolaou test adequacy*? Cancer cytopathology.* 2014;122(3):221-6.
14. Bentz JS, Rowe LR, Gopez EV, Marshall CJ. The unsatisfactory ThinPrep Pap Test: missed opportunity for disease detection? *American Journal of Clinical Pathology.* 2002;117(3):457-63.
15. Haack LA, O'Brien D, Selvaggi SM. Protocol for the processing of bloody cervical specimens: glacial acetic acid and the ThinPrep Pap Test. *Diagn Cytopathol.* 2006;34(3):210-3.

16. Kenyon S, Sweeney BJ, Happel J, Marchilli GE, Weinstein B, Schneider D. Comparison of BD Surepath and ThinPrep Pap systems in the processing of mucus-rich specimens. *Cancer Cytopathol.* 2010;118(5):244-9.
17. Owens CL, Peterson D, Kamineni A, Buist DS, Weinmann S, Ross TR, et al. Effects of transitioning from conventional methods to liquid-based methods on unsatisfactory Papanicolaou tests: results from a multicenter US study. *Cancer Cytopathol.* 2013;121(10):568-75.
18. Sweeney BJ, Haq Z, Happel JF, Weinstein B, Schneider D. Comparison of the effectiveness of two liquid-based Papanicolaou systems in the handling of adverse limiting factors, such as excessive blood. *Cancer*. 2006;108(1):27-31.

E. Reactive Cellular Changes

The Bethesda 2014 classification system for cervical cytology includes the subcategory of “Reactive Cellular Changes” under the Pap test reporting category “Negative for Intraepithelial Lesion or Malignancy”.[1]

The cells in the Pap test can undergo reactive changes associated with inflammation (including typical repair and lymphocytic cervicitis), radiation, and changes associated with intrauterine contraceptive devices. These changes can be a part of normal reactive changes and do not represent dysplastic or precancerous changes.

The reactive cells seen in repair or associated with inflammation can show an increase in nuclear size, presence of nucleoli, binucleation, cytoplasmic vacuolization, and polychromasia. A majority of reactive cells are of metaplastic origin but can also be seen in mature squamous cells or columnar epithelial cells.[2] The nuclei are usually non-overlapping and have an even and uniform fine granular chromatin. Small perinuclear halos can also be present but do not have peripheral thickening. The reactive changes in repair are often cohesive sheets of enlarged cells that can form a “school of fish” appearance.

In lymphocytic cervicitis, a polymorphous population of lymphocytes is present and can be seen with or without tingible body macrophages.

The changes seen in radiation can include markedly enlarged cells which maintain a normal nuclear to cytoplasmic ratio. Binucleation or multinucleation is also commonly seen. Chronic radiation-induced cellular changes can be seen indefinitely in the Pap test.

Changes associated with intrauterine devices can be either endometrial or endocervical columnar cells that undergo irritation and then exfoliation. These cells can be in small groups or be seen as single cells with a clean background. The cytoplasm frequently has large vacuolization that may even displace the nucleus. Actinomyces-like organisms are frequently also seen.

Reactive cellular changes seen on a Pap test have been found to show an increased risk of CIN2-3 but no significant increased risk of cancer.[3] In some patients with a previous history of CIN, benign cellular changes (BCC) may be of some significance, however, in patients with no significant prior cervical abnormalities, a Pap test classified as BCC represents a reactive process.[4]

References

1. The Bethesda System for Reporting Cervical Cytology. 3rd edition

2. Marshall LM, Cason Z, Cabaniss DE, Lemos LB, Benghuzzi HA. Reactive cell change in cervicovaginal smears. *Biomed Sci Instrum.* 1997;33:298-304.
3. Moitry M, Jégu J, Averous G, et al. Reporting reactive cellular changes on smears among women who undergo cervical cancer screening: results of a cohort study after seven years of follow-up. *Eur J Obstet Gynecol Reprod Biol.* 2017;216:232-238. doi:10.1016/j.ejogrb.2017.07.032
4. Malik SN, Wilkinson EJ, Drew PA, Hardt NS. Benign cellular changes in Pap smears. Causes and significance. *Acta Cytol*. 2001;45(1):5-8. doi:10.1159/000327180