MAYO CLINIC LABORATORIES

Test Definition: DTPCO

ThinPrep with Human Papillomavirus (HPV) Co-Test-Diagnostic, Varies

Overview

Useful For

Detection and diagnosis of cervical carcinoma or intraepithelial lesions and the presence or absence of high-risk human papillomavirus (HR-HPV) in women over age 30 at risk for cervical neoplasia

Detecting high-risk HPV genotypes associated with the development of cervical cancer

Aids in triaging women with abnormal Pap smear results

Individual genotyping of HPV-16 or HPV-18 if present

Aids in triaging women with positive HR-HPV 16 and 18, but negative Pap smear results

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
TPDPC	Physician Interp Diagnostic	No	No
VHPV	HPV Vaginal Detect / Genotyping PCR	Yes	No
HPV	HPV with Genotyping, PCR, ThinPrep	Yes	No

Testing Algorithm

When this test is ordered, a ThinPrep Pap cytology diagnostic and human papillomavirus high-risk DNA detection with genotyping by polymerase chain reaction test will be performed at an additional charge.

If ThinPrep Pap results are abnormal, a pathologist will review the case at an additional charge.

Special Instructions

- Gyn-Cytology Patient Information

Method Name

ThinPrep Pap Cytology Screening by Light Microscopy/Real-Time Polymerase Chain Reaction

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

1. Mayo Clinic Laboratories' clients need prior laboratory approval to order Cytology testing.

2. Due to the transient nature of the human papillomavirus (HPV) in younger patients, **this test is not recommended for patients younger than 30 years of age**; order DTHPV / ThinPrep Diagnostic with Human Papillomavirus (HPV) Reflex, Varies for women, under the age of 30, with abnormal Pap smear results.

Necessary Information

1. An acceptable cytology request form must accompany specimen containers and include the following: Patient's name, medical record number, date of birth, sex, source (exact location and procedure used), date specimen was taken, name of ordering physician and pager number.

2. Submit any pertinent history or clinical information.

Specimen Required

Patient Preparation: For optimal interpretation, Papanicolaou smears should be collected near the middle of the menstrual cycle. No douching, lubricant use, and sexual intercourse for 24 hours prior to specimen collection.

Only 1 aliquot may be removed from PreservCyt sample vial prior to performing the ThinPrep Pap Test, regardless of the volume of the aliquot (maximum aliquot volume: 4 mL).

Submit only 1 of the following specimens:

Specimen Type: Cervical
Supplies: ThinPrep Media with Broom Kit (T056)
Collection Container/Tube: ThinPrep
Specimen Volume: 16 mL
Collection Instructions:
1. Obtain adequate sampling from cervix using a broom-like collection device. If desired, use lukewarm water to warm and lubricate the speculum. Insert the central bristles of the broom into the endocervical canal deep enough to allow the shorter bristles to fully contact the ectocervix. Push gently and rotate the broom in a clockwise direction 5 times.
2. Rinse the broom as quickly as possible into the PreservCyt solution vial by pushing broom into bottom of vial 10 times, forcing the bristles apart.
3. As a final step, swirl broom vigorously to further release material. Discard the collection device.
4. Tighten cap on vial so that the torque line on the cap passes the torque line on the vial.
5. **Specimen vial must be labeled with a minimum of 2 unique identifiers** (patient's name and medical record number or date of birth).
6. Bag ThinPrep specimens individually as they have a tendency to leak during transport.
7. Place labels on the vial and on the bag.

Specimen Type: Ectocervix and endocervix
Supplies: ThinPrep Media with Spatula and Brush Kit (T434)
Collection Container/Tube: ThinPrep

Specimen Volume: 16 mL
Collection Instructions:
1. Obtain an adequate sampling from the ectocervix using a plastic spatula. If desired, use lukewarm water to warm and lubricate the speculum. Select contoured end of plastic spatula and rotate it 360 degrees around the entire exocervix while maintaining tight contact with exocervical surface.
2. Rinse spatulas quickly as possible into the PreservCyt solution vial by swirling spatula vigorously in vial 10 times. Discard the spatula.
3. Next, obtain an adequate specimen from endocervix using an endocervical brush device. Insert the brush into the cervix until only the bottommost fibers are exposed. Slowly rotate one-quarter or one-half turn in 1 direction. **Do not over rotate.**
4. Rinse the brush as quickly as possible in the PreservCyt solution by rotating the device in the solution 10 times while pushing against the PreservCyt vial wall.
5. Swirl brush vigorously as final step to further release material. Discard the brush.
6. Tighten the cap so that the torque line on the cap passes the torque line on the vial.
7. **Specimen vial must be labeled with a minimum of 2 unique identifiers** (patient's name and medical record number or date of birth).
8. Bag ThinPrep specimens individually as they have a tendency to leak during transport.
9. Place labels on the vial and on the bag.

Forms
Gyn-Cytology Patient Information (T601)

Specimen Minimum Volume
See Specimen Required

Reject Due To

SurePath vial	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)	42 days	THIN PREP
	Refrigerated	42 days	THIN PREP

Clinical & Interpretive

Clinical Information
The majority (>99%) of cervical epithelial neoplasms are the result of human papillomavirus (HPV) infection. High-risk HPV (HR-HPV) types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) can result in both low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL), as well as invasive carcinoma.(1,2) Patients with both negative cytology and negative HPV have been shown to be at extremely low risk for cervical neoplasia.(1,2)

For women 30 years and older who have received a negative Pap smear test and concurrent negative HPV results, the American Cancer Society (ACS) and American College of Obstetricians and Gynecologists (ACOG) recommendations for cervical screening state that physicians may lengthen the screening interval to 3 years when using the combined tests. Patients deemed to be at high risk by the clinician should still be screened more frequently.

The presence of HR-HPV types in cervical specimens identifies a subgroup of patients with a greater likelihood of having a high-grade squamous intraepithelial lesion. Current guidelines for follow-up of a cytology-negative/HPV-positive patient recommend repeat HPV testing in 12 months.(2)

Persistent infection with HPV is the principal cause of cervical cancer and its precursor cervical intraepithelial neoplasia (CIN).(1-3) The presence of HPV has been implicated in more than 99% of cervical cancers worldwide. HPV is a small, nonenveloped, double-stranded DNA virus, with a genome of approximately 8000 nucleotides. There are more than 118 different types of HPV and approximately 40 different HPVs that can infect the human anogenital mucosa. However, data suggest that 14 of these types (HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) are considered high risk for the development of cervical cancer and its precursor lesions. Furthermore, HPV types 16 and 18 have been regarded as the genotypes most closely associated with progression to cervical cancer. HPV-16 is the most carcinogenic and is associated with approximately 60% of all cervical cancers, while HPV-18 accounts for approximately 10% to 15% of cervical cancers.(4-6)

Although persistent infection with HR-HPV is necessary for the development of cervical cancer and its precursor lesions, only a very small percentage of infections progress to these disease states. Sexually transmitted infection with HPV is extremely common, with estimates of up to 75% of all women being exposed to HPV at some point. However, almost all infected women will mount an effective immune response and clear the infection within 2 years without any long-term health consequences. An infection with any HPV type can produce CIN although this also usually resolves once the HPV infection has been cleared.

In developed countries with cervical cancer screening programs, the Pap smear has been used since the mid-1950s as the primary tool to detect early precursors to cervical cancer. Although it has decreased the death rates due to cervical cancer dramatically in those countries, the Pap smear and subsequent liquid-based cytology methods require subjective interpretation by highly trained cytopathologists and misinterpretation can occur. Cytological abnormalities are primarily due to infection with HPV; however, various inflammatory conditions or sampling variations can result in false-positive cytology results. Triage of an abnormal cytology result may involve repeat testing, colposcopy, and biopsy. A histologically confirmed high-grade lesion must be surgically removed or ablated in order to prevent the development of invasive cervical cancer.

DNA testing by polymerase chain reaction has become a standard, noninvasive method for determining the presence of a cervical HPV infection. Proper implementation of nucleic acid testing for HPV may increase the sensitivity of cervical cancer screening programs by detecting high-risk lesions earlier in women 30 years and older with normal cytology and reduce the need for unnecessary colposcopy and treatment in patients 21 and older with cytology results showing atypical squamous cells of undetermined significance).

Recent data suggest that individual genotyping for HPV types 16 and 18 can assist in determining appropriate follow-up testing and triaging women at risk for progression to cervical cancer. Studies have shown that the absolute risk of CIN-2

or worse in HPV-16 and HPV-18 positive women is 11.4% (95% CI 8.4%-14.8%) compared with 6.1% (95% CI, 4.9%-7.2%) of women positive for other HR-HPV genotypes and 0.8% (95% CI, 0.3%-1.5%) in HR-HPV negative women.(7) Based in part on these data, the American Society for Colposcopy and Cervical Pathology (ASCCP) now recommends that HPV 16 and 18 genotyping be performed on women who are positive for HR-HPV but negative by routine cytology. Women who are found to be positive for HPV-16 or HPV-18 may be referred to colposcopy, while women who are negative for genotypes 16 and 18 may have repeat cytology and HR-HPV testing in 12 months.(4)

Reference Values

ThinPrep PAPANICOLAOU
Satisfactory for evaluation. Negative for intraepithelial lesion or malignancy.

HUMAN PAPILLOMAVIRUS (HPV)
Negative for HPV genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68

Interpretation

Cytology:
Standard reporting, as defined by the Bethesda System is utilized.

Human papillomavirus (HPV):
A positive result indicates the presence of HPV DNA due to 1 or more of the following genotypes: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68.

A negative result indicates the absence of HPV DNA of the targeted genotypes.

For patients with atypical squamous cells of undetermined significance (ASC-US) Pap smear result and who are positive for high-risk HPV (HR-HPV), consider referral for colposcopy, if clinically indicated.

For women aged 30 years and older with a negative Pap smear result, but who are positive for HPV-16 or HPV-18, consider referral for colposcopy, if clinically indicated.

For women aged 30 years and older with a negative Pap smear, positive HR-HPV test result, but who are negative for HPV-16 and HPV-18, consider repeat testing by both cytology and a HR-HPV test in 12 months.

Cautions

The Pap test is a screening test for cervical cancer with inherent false-negative results. A negative human papillomavirus (HPV) test or Pap smear result does not preclude the presence of carcinoma or intraepithelial lesion. The false-negative rates of the Pap test range from 15% to 30%.

The cobas HPV test detects DNA of the high-risk types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. This test does not detect DNA of HPV low-risk types (eg, 6, 11, 42, 43, 44) since these are not associated with cervical cancer and its precursor lesions.

The cobas HPV test is not recommended for evaluation of suspected sexual abuse.

Prevalence of HPV infection in a population may affect performance. Positive predictive values decrease when testing

populations with low prevalence or individuals with no risk of infection.

Infection with HPV is not an indicator of cytologic high grade intraepithelial lesion (HSIL) or underlying high-grade cervical intraepithelial neoplasia (CIN), nor does it imply that CIN2-3 or cancer will develop. Most women infected with 1 or more high-risk HPV (HR-HPV) types do not develop CIN2-3 or cancer.

A negative HR-HPV result does not exclude the possibility of future cytologic HSIL or underlying CIN2-3 or cancer.

Clinical Reference

1. Lorincz AT, Richart RM: Human papillomavirus DNA testing as an adjunct to cytology in cervical screening programs. Arch Pathol Lab Med. 2003 Aug;127(8):959-968
2. Wright TC Jr, Schiffman M: Adding a test for human papillomavirus DNA to cervical-cancer screening. N Engl J Med. 2003 Feb 6;348(6):489-490
3. Solomon D, Davey D, Kurman R, et al: The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA. 2002 Apr 24;287(16):2114-2119
4. Saslow D, Solomon D, Lawson HW, et al: American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. J Low Genit Tract Dis. 2012 Jul;16(3):175-204
5. Walboomers JM, Jacobs MV, Manos MM, et al: Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol. 1999 Sep;189(1):12-19
6. de Sanjose S, Quint WG, Alemany L, et al: Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. Lancet Oncol. 2010 Nov;11(11):1048-1056
7. Wright TC Jr, Stoler MH, Sharma A, Zhang G, Behrens C, Wright TL: Evaluation of HPV-16 and HPV-18 genotyping for the triage of women with high-risk HPV positive, cytology-negative results. Am J Clin Pathol. 2011 Oct;136(4):578-586
8. Massad LS, Einstein MH, Huh WK, et al: 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis. 2013 Apr;17(5 Suppl 1):S1-S27
9. Sherman ME, Lorincz AT, Scott DR, et al: Baseline cytology, human papillomavirus testing, and risk for cervical neoplasia: a 10-year cohort analysis. J Nat Cancer Inst. 2003 Jan 1;95(1):46-52

Performance

Method Description

A ThinPrep Pap specimen is collected, processed on a T2000 or T5000 processor, and stained with a Pap stain. Cases are examined microscopically and those with appropriate cytologic diagnoses are referred for human papillomavirus (HPV) testing if the patient is 21 or older.(Instruction manuals: ThinPrep 2000 System Operator's Manual. Hologic; MAN-02585-001 Rev. 006, 02/2017; ThinPrep 5000 Processor Operator's Manual. Hologic; MAN-02203-001 Rev. 002, 2016)

The cobas HPV test targets and detects nucleic acid from the L1 region of the HPV genome using real-time polymerase chain reaction (PCR) technology. The cobas HPV test is used for the in vitro qualitative detection of 14 high-risk HPV types commonly associated with cervical cancer. The assay is able to specifically assess for the presence or absence of HPV genotypes 16 and 18, while concurrently detecting the remaining 12 high-risk types (31, 33, 35, 39, 45, 51, 52, 56,

58, 59, 66 and 68). The cobas HPV test is used in conjunction with the cobas 4800 System. The cobas 4800 System comprises the cobas x 480 instrument and cobas z 480 analyzer that fully automates the cobas HPV from sample extraction through amplification, detection, and data reduction.(Procedure manual and package insert: cobas HPV test. Roche Diagnostics; version 05641268001-01EN, 10/2018)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
5 to 8 days

Specimen Retention Time
14 days after report issued

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
88142
G0123 (for government payers)
87626 (if appropriate)
87626 (if appropriate)
88141 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
DTPCO	ThinPrep w/HPV Co-Test-Diagnostic	101822-5

Result ID	Test Result Name	Result LOINC® Value
71331	Interpretation	59465-5
71332	Participated in the Interpretation	No LOINC Needed
71333	Report electronically signed by	19139-5
71334	Addendum	35265-8
71335	Gross Description	22634-0
CY002	Pap Test Source	19763-2
CY003	Clinical History	22636-5
CY004	Menstrual Status (LMP, PM, Pregnant)	8678-5
CY005	Hormone Therapy/Contraceptives	8659-5
71579	Disclaimer	62364-5
71825	Case Number	80398-1