Test Definition: SHPV

Human Papillomavirus (HPV) DNA Detection with Genotyping, High-Risk Types by PCR, SurePath, Varies

Overview

Useful For

Detection of high-risk (HR) genotypes associated with the development of cervical cancer

An aid in triaging women with abnormal Pap smear test results

Individual genotyping of human papillomavirus (HPV)-16 and/or HPV-18, if present

This testing is intended for use in clinical monitoring and management of patients. It is **not intended** for use in medical-legal applications.

Method Name

Real-Time Polymerase Chain Reaction (PCR)

NY State Available

Yes

Specimen

Specimen Type

Varies

Necessary Information

Specimen source, collection date, and patient identifiers are required.

Specimen Required

Supplies: Cobas PCR Media Tube w/Cap (T945)
Specimen Type: Cervical (endocervical or ectocervical) or vaginal
Specimen Volume: 3.0 mL
Collection Instructions:
1. Aliquot 3 mL SurePath specimen into Cobas PCR Media Tube w/Cap tube.
2. Bag specimens individually as they have a tendency to leak during transport.
3. Place labels on the vial and on the bag.

Forms

If not ordering electronically, complete, print, and send a Microbiology Test Request (T244) with the specimen.

Specimen Minimum Volume

1 mL

Reject Due To

SurePath enriched cell pellet	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Persistent infection with human papillomavirus (HPV) is the principal cause of cervical cancer. The presence of HPV has been implicated in more than 99% of cervical cancers worldwide, including both cervical squamous cell carcinoma and cervical adenocarcinoma. Before the development of invasive cancer, HPV infects the squamous mucosa cells and/or the glandular cells of the endocervix, leading to clonal expansion and morphologic changes. While the HPV-infected cells are restricted to their normal anatomic location, these changes are classified as cervical intraepithelial neoplasia (CIN). The severity of the morphologic changes and the degree to which those changes resemble the morphology of an invasive carcinoma are used to "grade" CIN. In general, high-grade CIN more closely resembles invasive carcinoma morphologically. HPV can also infect other mucosal cells in the anogenital region, such as the vaginal mucosa, leading to the development of HPV-associated intraepithelial neoplasia as well as invasive carcinoma not involving the cervix itself, although this is less common.

Human papillomavirus 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 can infect the human anogenital mucosa. Only a very small percentage of patients who are exposed to HPV will develop CIN. Of those patients, only a small percentage will progress to invasive cervical cancer. Sexual transmission of 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 long-term health consequences. Both high-risk HPV genotypes (especially HPV-16 and 18), as well as persistent HPV infection (eg, an infection that is not cleared by the patient's immune system over time), are associated with an increased chance of progressing to high-grade CIN and invasive cancer.

Data suggest that certain HPV genotypes (eg, HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) are high risk (HR) 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.

In developed countries with cervical cancer screening programs, the Pap smear has been used since the mid-1950s as the primary tool to morphologically detect CIN, the precursor to cervical cancer. Pap smear screening has decreased death rates due to cervical cancer dramatically, since in many cases CIN can be treated and eliminated (eg, by local excision) before it progresses to invasive carcinoma. Although Pap smears and other liquid-based cytology methods have many advantages, they also have limitations: they require subjective interpretation by a highly trained cytopathologist and misinterpretation can occur, morphologic changes that resemble HIV-associated CIN can be caused by other conditions (eg, inflammation), and Pap smear does not sample every cell within the cervix/anogenital region potentially leading to falsely negative results. Perhaps most importantly, Pap smear does not differentiate between HPV genotypes that are high or low risk for progression to cervical cancer and it does not detect very early infections, which may lack a morphological phenotype.

Nucleic acid (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:
1) increase the sensitivity of cervical cancer screening programs by detecting high-risk lesions earlier in women 30 years and older with normal cytology and
2) reduce the need for unnecessary colposcopy and treatment in patients 21 years and older with cytology results showing atypical squamous cells of undetermined significance.

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/or 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. Based in part on these data, the American Society for Colposcopy and Cervical Pathology now recommends that HPV 16/18 genotyping be performed on women who are positive for HR-HPV, but negative by routine cytology/Pap smear. Women who are found to be positive for HPV-16 and/or -18 may be referred to colposcopy, while women who are negative for genotypes 16 and/or 18 may have repeat cytology and HR HPV testing in 12 months.

Reference Values

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

Interpretation

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

For patients with atypical squamous cells of undetermined significance Pap smear test result and who are positive for high-risk (HR) HPV, consider referral for colposcopy, if clinically indicated.
A negative result indicates the absence of HPV DNA of the targeted genotypes.

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

For women 30 years and older with a negative Pap smear test result, 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 cobas human papillomavirus (HPV) test is US Food and Drug Administration (FDA)-approved for cervical/endocervical samples collected in PreservCyt (ThinPrep) media. Other sample types (eg, vaginal) collected in media, such as SurePath, are not considered FDA-approved sources; however, verification studies have been completed in compliance with CLIA-regulations by Mayo Clinic Laboratories.

Prolonged storage (>42 days) of clinical samples in SurePath media may impact the detection of high-risk (HR) HPV, especially if the amount of nucleic acid present in the sample is initially at a low concentration. Therefore, samples should be submitted for testing as soon as possible following collection.

Cervical specimens often show visibly detectable levels of whole blood as a pink or light brown coloration. These specimens are processed normally on the cobas systems. If concentrations of whole blood exceed 10% (dark-red or brown coloration) in PreservCyt solution, there is a likelihood of obtaining a false-negative result.

The cobas HPV test performance has been validated with PreservCyt specimens that have been treated with up to 5% glacial acetic acid for removal of red blood cells. Addition of glacial acetic acid over 5% in PreservCyt specimens prior to HPV testing would invalidate the cobas HPV Test results.

Human beta-globin amplification and detection is included in cobas HPV to differentiate HPV negative specimens from those that do not exhibit HPV signal due to insufficient cell mass in the specimen. All HPV negative specimens must have a valid beta-globin signal within a pre-defined range to be identified as valid negatives.

The cobas HPV test detects DNA from high-risk genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. This test does not detect DNA of low-risk HPV types (eg, 6, 11, 42, 43, 44), which are not associated with invasive cervical cancer and its precursor lesions. Low-risk HPV types are associated with noninvasive genital warts and laryngeal papillomatosis.

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 high-grade cervical intraepithelial neoplasia (CIN), nor does it indicate that a high-grade intraepithelial lesion (eg, HSIL or CIN2-3) or cancer will develop. Most women infected with 1 or more HR HPV types do not develop CIN2-3 or cancer.

A negative HR HPV result does not exclude the possibility of a patient developing a high-grade intraepithelial lesion (eg, HSIL or CIN2-3) or cancer in the future.

Clinical Reference

1. US Preventive Services Task Force, Curry SJ, Krist AH, et al. Screening for cervical cancer: US Preventive Services Task

Force Recommendation Statement. JAMA. 2018;320(7):674-686. doi:10.1001/jama.2018.10897
2. Poljak M, Balencak AO, Cuschieri K, Bohinc KB, Arbyn M. 2023 global inventory of commercial molecular tests for human papillomaviruses (HPV). J Clin Viro. 2024:172;105671
3. 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. 2020;24(2):102-131. doi:10.1097/LGT.0000000000000525

Performance

Method Description

The cobas HPV (human papillomavirus) test is a qualitative real-time polymerase chain reaction (PCR) test that detects 14 high-risk HPV genotypes. The test uses primers to define a sequence of approximately 200 nucleotides within the polymorphic L1 region of the HPV genome. A pool of HPV primers present in the Master Mix is designed to amplify HPV DNA from 14 high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). An additional primer pair targets the human beta-globin gene (330 base pair amplicon) as an internal control to monitor the entire sample preparation and PCR amplification process. Fluorescent oligonucleotide probes bind to polymorphic regions within the sequence defined by these primers. The test utilizes a low titer positive and a negative control.(Package insert: cobas HPV: Qualitative nucleic acid test for the cobas 5800/6800/8800 Systems. Roche Diagnostics, Inc; Rev. 2.0, 09/2024)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

3 to 6 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

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 modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

87626
G0476 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SHPV	HPV with Genotyping, PCR, Surepath	77378-8

Result ID	Test Result Name	Result LOINC® Value
SS018	Specimen Source	31208-2
36003	HPV High Risk type 16, PCR	61372-9
36004	HPV High Risk type 18, PCR	61373-7
36005	HPV other High Risk types, PCR	77375-4