

## **Diagnosis of Cervical Cancer**

### **Cervical Cancer Diagnosis: Overcoming Uncertainty with Knowledge and Support**

**Understanding the diagnosis of cervical cancer is crucial, as it empowers patients to make informed decisions about their treatment options**

Fig.1: A logo representing all the diagnosis methods in the form of a logo.

#### **Summary/Abstract:**

Cervical cancer is a type of cancer that is only found in females. As it originates in the cervix, which is a part of the female reproductive system that sits in the lower part of the uterus that connects to vagina.[4]

It is primarily caused by persistent infection by human papillomavirus (HPV). [4]

Cervical cancer diagnosis refers to the process of confirming the presence of cancerous or abnormal cells in the cervix.[4]

The main purpose of diagnosis is to detect cervical cancer early or identify abnormal cell changes before they develop into cancer.[4]

Diagnosis helps identify the presence of cervical cancer or abnormal cell changes early, allowing for timely intervention. Early detection can prevent the cancer from advancing, improving treatment outcomes and survival rates.[4]

Diagnosis is usually conducted after abnormal results are found in routine screening tests (e.g., Pap smear or HPV test).[4]

It may also be done if a patient shows symptoms of cervical cancer or has risk factors like a history of HPV infection or smoking.[4]

Some methods used in diagnosis include Pap Smear, HPV Test, Biopsy, Imaging Tests like MRI, Colposcopy, etc.[4]

After confirming the diagnosis, doctors assess the stage of the cancer, which helps determine treatment options such as surgery, radiation, or chemotherapy.

The patient may undergo additional tests to check if the cancer has spread to other parts of the body.[4]

Therefore, below are all the diagnosis methods given which are used in the present world so that the individuals can take prompt actions for the betterment of their health.  
[4]

### **Body:**

#### **Are Diagnosis and Detection two different terms?**

In the medical field, **diagnosis** and **detection** are terms often used interchangeably, but they represent distinct processes with different goals and methods. Understanding the difference is crucial for both healthcare professionals and patients, as these concepts play different roles in disease management and prevention.[12]

<b><u>Aspect</u></b>	<b><u>Diagnosis</u></b>	<b><u>Detection</u></b>
<b><u>Definition</u></b>	Diagnosis is the process of identifying a disease or condition based on symptoms, tests, and clinical evaluation.	Detection refers to the act of discovering or identifying the presence of a disease, condition, or abnormality, often at an early or asymptomatic stage.
<b><u>Purpose</u></b>	The goal of diagnosis is to establish the specific condition or disease a person has.	The purpose of detection is to identify whether a condition or disease exists, often before symptoms appear.
<b><u>Process</u></b>	Diagnosis involves analyzing symptoms, medical history, and diagnostic tests to understand the condition in detail.	Detection typically involves screening tools or tests to identify possible conditions or abnormalities.

<b><u>Scope</u></b>	Diagnosis is broader and focuses on understanding the nature and cause of symptoms or problems.	Detection is narrower, aimed at finding out if a disease or abnormality is present.
<b><u>Time Frame</u></b>	Diagnosis usually occurs after symptoms manifest, allowing for a comprehensive evaluation of the condition.	Detection often takes place before symptoms are evident, or at the earliest stage of the disease.
<b><u>Tools Used</u></b>	Common tools include a review of medical history, physical examination, lab tests, and imaging.	Detection methods often rely on screening tests, imaging, lab tests, and sometimes wearable devices.
<b><u>Example</u></b>	Diagnosing diabetes after observing high blood sugar levels and symptoms such as increased thirst or frequent urination.	Detecting early signs of diabetes through routine screening, even before symptoms like thirst or fatigue are noticeable.
<b><u>Outcome</u></b>	Diagnosis results in a specific and comprehensive understanding of the patient's condition.	Detection provides preliminary evidence of a possible disease, prompting further diagnostic evaluation.
<b><u>Application</u></b>	Diagnosis is used when a patient presents with symptoms or a suspected condition.	Detection is used in screening programs or preventive health measures to catch diseases early.

## **When is Diagnosis for Cervical cancer done?**

Cervical cancer is often diagnosed when the patients' cancer has progressed enough to cause noticeable symptoms, or during routine screening procedures. It is crucial to identify the condition at an early stage, as it is highly treatable when detected early. Diagnosis can be done at various points depending on the stage of the cancer and the symptoms presented.[5]

### **o Early cancer stage Symptoms:**

Vaginal bleeding after sex, menopause or vaginal discharge containing blood and odor or periods that are longer and pelvic pain.[5]

### **o Advanced cancer stage symptoms:**

Difficulty, pain and blood in urination, swelling of legs, pain in the abdomen bleeding from rectum during bowel activity.[5]

(A reference can be given for the symptoms of cervical cancer in detail)

## **Traditional Diagnostic Methods:**

Traditional diagnostic methods refer to the practices and techniques used by doctors to diagnose medical conditions before the arrival of modern technologies and laboratory tests. These methods often rely on clinical skills, observation, patient history, physical examination, and sometimes natural remedies or treatments.

### **1. Screening Methods:**

- **Pap test (Papanicolaou test):**

- o It is a procedure to collect cells from the cervix so that they can be observed under microscope. A doctor usually uses a speculum and a spatula to slightly open vagina and take the cells from the exocervix.[10]

- o It is the most successful screening method but also has a limitation. As it involves examination of results using naked eyes, hence human errors are possible.[10] [2]

- **HPV Testing:**

- o An [HPV test](#) looks for cervical Human Papillomavirus (HPV) infection. It detects high-risk types of HPV that are more likely to cause pre-cancers

and cancers of the cervix. But an HPV test cannot detect pre-cancer or cancer itself.[9]

- o It is recommended that a *primary HPV test* is the preferred test for cervical cancer screening for people 25-65 years of age.[9]
- o An HPV test can be done either by itself (**primary HPV testing**) or at the same time as the Pap test (**co-testing**).[9]
- o E6 and E7 are proteins found on high-risk types of HPV viruses. Some HPV tests work by checking a sample for mRNA E6/E7. If the results of an HPV test say that mRNA E6/E7 was detected, it means the test is positive for HPV. Not all HPV tests look for these proteins. Some tests work by looking for the DNA of specific types of high-risk HPVs.[9][2](A reference can be given to learn more)

Fig.2: The image is illustrating the screening method being performed.

## 2. Colposcopy:

It is a follow-up method for abnormal Pap smears to provide a closer examination.

In this method the doctor inserts a Colposcope (a magnifying tool) and a tool using which he gently opens the vagina to observe the cervix for any abnormalities. [2]

Fig.3: The image is illustrating the process.

## 3. Visual Inspection with Acetic Acid (VIA):

Acetic acid is applied to the cervix so that the abnormal cells can be seen if any, which turns white when exposed to the acid.[2]

This method is simple and affordable and is accessible even in resource-poor environments. [2]

## 4. Biopsy:

Biopsy is a procedure in which a sample of tissue is removed from the cervix for the pathologists to examine the cells under a microscope for any signs of cancer.

These processes are mostly done in doctors clinic under the influence of local anesthesia. [2]

Ø **Methods:**

○ **Punch Biopsy**

- A procedure where a small, round piece of tissue is removed from the cervix using a sharp, hollow circular instrument for diagnosis.
- Sometimes several different areas are checked using this method. [2]

Ø **Criteria:**

**Punch Biopsy is typically chosen when:**

- o The abnormal area is **small** and located on the external part of the cervix.[2]
- o The goal is to **take a small tissue sample** for diagnosis, without the need to remove a larger portion of tissue.[2]
- o It is a quicker, less invasive procedure, usually done in a doctor's office.[2]

○ **Endocervical Curettage (ECC)**

- A procedure where curette (spoon shaped tool) is used to remove small amounts of cells from the cervical lining for diagnosis. [2]

Ø **Criteria:**

**ECC is recommended when:**

- o The abnormality is found in the **inner part of the cervix (the endocervical canal)**, which is hard to reach with other biopsy methods.[2]
- o The doctor needs to **scrape small tissue samples** from the lining of the cervix for diagnosis.[2]

- **LEEP (Loop Electrosurgical Excision Procedure)**

- A thin wire loop through which current is passed is used to remove tissue from the cervix.
- This method is used for diagnosis as well as used to remove the early staged cancer or precancer. [2]

Ø Criteria:

**LEEP** is typically chosen when:

- o There are **precancerous or early cancer cells** that need to be removed, not just diagnosed.[2]
- o The doctor wants to **remove abnormal tissue** and get a sample for diagnosis at the same time.[2]
- o It's used when a larger area needs to be treated, and it helps prevent the spread of cancerous cells.[2]

- **Cone Biopsy**

- It is a surgery in which a large, cone shaped piece of tissue is removed from cervix for diagnosis and may also be used to remove the early staged cancer or precancer (conization).[2]

Ø Criteria:

**Cone Biopsy** is often recommended when:

- o **There is a larger area of abnormal tissue** on the cervix, and a bigger tissue sample is needed for diagnosis.[2]
- o **Early-stage cancer or precancerous cells** are suspected. The cone-shaped tissue removed can help treat and diagnose these conditions.[2]

- o **Other methods have not provided enough information** or a more thorough sample is required to confirm the diagnosis.[2]

## 5. Imaging Techniques for Staging:

### o **Ultrasound:**

The process uses ultrasound which bounces back from the internal organs or tissues and makes echoes. These echoes form the picture of the body called sonogram.[2]

### o **PET-CT Scan :**

The process combines both the images from the positron emission tomography (PET) and computed tomography (CT) scans on the same machine to make a more detailed image of the area. This type of scan is mostly done on people already having cervical cancer.

For PET scan sugar is injected in vein due to which the malignant tumor cells appear brighter than the other cells as they consume more sugar. The scanner, scans the body and form the images.[2]

### o **MRI (Magnetic Resonance Imaging):**

The process uses magnet, radio waves which bounce back from the tissues making echoes and a computer which collects these echoes for making a series of pictures of internals. [2]

- o **Intravenous urography (IVP):** is an x-ray of the urinary system taken after a special dye is injected into a vein. This test can find abnormal areas in the urinary tract, caused by the spread of cervical cancer. The most common finding is that the cancer has blocked the ureters. IVP is rarely used for patients with cervical cancer because CT and MRI are also good at finding abnormal areas in the urinary tract, as well as others not seen with an IVP.[2]

- o **CT scan:** The process uses x-rays to show your body parts like bones, soft tissues, etc. more clearly than standard x-rays. It shows the size, shape and location of the tumor and even blood vessels which feed the tumor without having to cut the patient.[2]



## **Newly Emerging Diagnostic Methods:**

Newly emerging diagnostic methods refer to innovative, advanced, or developing techniques and tests that are being introduced or refined to improve the diagnosis of diseases, especially in fields like cancer detection. The listed methods below are new and advanced as they provide:

- Earlier detection
- More accurate staging
- Minimally invasive treatments
- Advanced imaging techniques

### **o HPV DNA Test (Screening test):**

A laboratory test in which cells are scraped from the cervix to look for DNA of human papillomaviruses (HPV). HPV can cause abnormal tissue growth (for example, warts) and other changes to cells.[9]

The method is available as a diagnostic method in hospitals and widely used in clinical practice as a screening tool to detect the presence of high-risk HPV strains .It is used alongside a Pap smear in routine cervical cancer screening.[9]

- **Sentinel Lymph Node Biopsy:**

Sentinel lymph node biopsy has been widely studied and clinically used for many types of cancer.

Two techniques exist for detecting sentinel nodes in cervical cancer, which are Blue dye and gamma probe with radioactive isotope (99mTc). Moreover, lymphoscintigraphy has many advantages over the stain method. Detecting the sentinel node is performed via laparoscopy or laparotomy; [11]

Fig.4: The image illustrates this method as it is used to diagnose metastatic lymph node cancer.

The method is available in clinical practice.[11]

This technique is well-established and commonly used for various cancers, including cervical cancer, to identify whether cancer has spread to the lymph nodes. The methods of detecting sentinel nodes (Blue Dye, Gamma Probe, Lymphoscintigraphy) are all clinically available.[11]

### **Dye Stain:**

This method involves injecting blue dyes like isosulfan blue, patent purple-blue, or methylene blue around a tumor, where they are absorbed by the lymphatic system within 5 to 15 minutes and remain for up to 60 minutes. Hence screening is done to observe and metastasis into lymph nodes. High dye levels injected into the tumor or vessels can cause excessive background signal, reducing diagnostic accuracy. In large tumors with necrosis, the dye may leak into the vagina through the cervical canal, but using a long spinal needle and controlling dye infiltration can improve precision. The dye is mostly eliminated through the biliary ducts, but side effects such as blue urine, allergic reactions, and severe reactions when mixed with anesthetics have been reported.[11]

### **Injection of radioactive isotopes:**

$^{99m}\text{Tc}$ -nanocolloid are injected to detect sentinel lymph nodes in cervical cancer using dynamic photography and a gamma probe. This process usually takes 20 to 30 minutes to track lymphatic drainage and identify hot lymph nodes, which are distinguishable from their background. The accuracy of this method depends on factors like the radioactive material's dosage, time between injection and surgery, and the type of gamma probe used.[11]

### **Lymphoscintigraphy:**

Lymphoscintigraphy, compared to dye staining, offers more precise lymph node location and reduces surgical bleeding risks, but is more expensive and time-consuming. The combined method, which uses both dye and radioisotope, has shown to be highly sensitive, with laparoscopy offering higher detection and sensitivity rates than laparotomy.[11]

- **Bone Scan:**

Bone metastasis in cervical cancer is rare.

Bone scan should be an investigation of choice for screening patients of carcinoma cervix with symptoms suggestive of metastasis in all stages of the disease. Bone scan is the most sensitive method for detection of bone metastasis.[2][4]

The method is available in clinical practice. Bone scans are routinely used to detect bone metastasis in cancer patients, including those with cervical cancer. [2][4]

#### o **PET/MRI Combination:**

Below is a real case scenario to prove that PET/MRI Combination is advanced and better than the previous methods.

A Philips Ingenuity TF PET/MRI machine was used and  $^{18}\text{F}$ -FDG 3.7-7.4 MBq/kg a solution was injected into the elbow vein, and a pelvic PET/MRI scan was performed 48-72 mins later, including pelvic PET image acquisition, a rapid 3D T1WI gradient-echo MR sequence (atMR) scan, and pelvic MR scan.

The PET/MRI had a higher diagnostic accuracy for cervical cancer than the PET/CT, MRI, and CT indicating that the PET/MRI is more effective at identifying the clinical stages of cervical cancer.[2][4]

The method is available in clinical practice..

While it is available in some hospitals, it is still considered a newer, more advanced technique and may not yet be standard practice in all medical centers.[2][4]

#### o **Oncogenic Biomarker Tests:**

It is now widely accepted that p16<sup>INK4A</sup> is a sensitive and specific marker of squamous and glandular dysplastic cells of the cervix and also a surrogate marker of high risk human papillomavirus, suggesting a valuable adjunctive test in cervical cancer screening. Hence it's in testing process to use it as a diagnosis method for cervical cancer.[2][4]

This method is still in clinical trials or early clinical use.

While it shows promise, the use of biomarkers like p16INK4A as a routine diagnostic method for cervical cancer is not yet widespread in clinical practice and remains in the research or trial phase.[2][4]

### **Prognosis:**

If you are diagnosed with cervical cancer, you might want to know how serious the cancer is and your survival rate. The likely outcome or course of a disease is called prognosis. [7]

Ø It depends on many factors:

- The stage of cancer (size of tumor). [7]

#### Ø Staging (FIGO Staging System):

Classifies the extent of the cancer based on clinical findings, imaging, and biopsy results. [1]

#### Stages:

- **Stage I:** Confined to the cervix.[1]
- **Stage II:** Spread beyond the cervix but not to the pelvic wall or lower vagina.[1]
- **Stage III:** Spread to the pelvic wall, lower part of the vagina, or causing kidney problems.[1]
- o **Stage IV:** Spread to distant organs.[1]

(A reference can be given about the types

<https://www.cancer.gov/types/cervical/stages>)

- The type of cervical cancer (adenocarcinoma or squamous cell carcinoma)[7]

Cervical cancers are named after the type of cell where the cancer started.

Ø The two main types are:

- o **Squamous cell carcinoma:** Most cervical cancers (up to 90%) are squamous cell carcinomas. These cancers develop from cells in the ectocervix. [4]

- o **Adenocarcinoma:** Cervical adenocarcinomas develop in the glandular cells of the endocervix. Clear cell adenocarcinoma, also called clear cell carcinoma or mesonephroma, is a rare type of cervical adenocarcinoma. [4]
- Your age and general health[7]
- Whether the cancer is newly diagnosed or recurred.[7]
- Other diseases like HIV or you are immunocompromised(low immunity).[7]

### **Reference:**

- [1] <https://www.bmj.com/content/bmj/335/7623/765.full.pdf> (bmj-335-7623-cr-00765)
- [2] <https://www.cancer.gov/types/cervical/diagnosis> (cervical cancer Diagnosis)
- [3] <https://www.cancer.gov/types/cervical/stages> (cervical cancer stages)
- [4] <https://www.cancer.gov/types/cervical> (What is cervical cancer)
- [5] <https://cancer.gov/types/cervical/symptoms> (cervical cancer symptoms)
- [6] <https://www.cancer.gov/types/cervical/screening> (cervical cancer screening)
- [7] <https://www.cancer.gov/types/cervical/survival> (prognosis and survival rates)
- [8] <https://www.cancer.gov/types/cervical/stages> (cervical cancer stages)
- [9] <https://www.cancer.org/cancer/types/cervical-cancer/detection-diagnosis-staging/screening-tests/hpv-test.html>
- [10] <https://www.cancer.org/cancer/types/cervical-cancer/detection-diagnosis-staging/screening-tests/pap-test.html>
- [11] <https://pmc.ncbi.nlm.nih.gov/articles/PMC5804466/> (sentinel lymph nodes in cervix)
- [12] <https://www.ncbi.nlm.nih.gov/books/NBK230925/>

## Images:

Fig.1: The image is made using chatgpt.

The image below illustrates all these methods for diagnosis in the form of a logo.

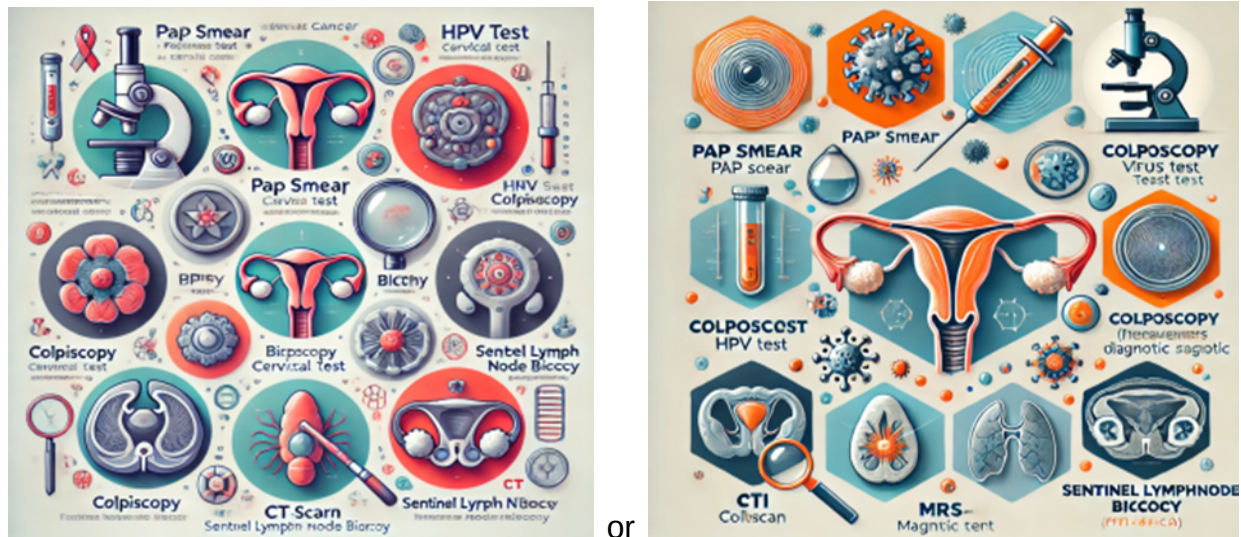


Fig.2: This image is taken from the site of the National cancer institute.

<https://www.cancer.gov/publications/dictionaries/cancer-terms/def/pap-smear>

The below figure illustrates the screening process being performed.

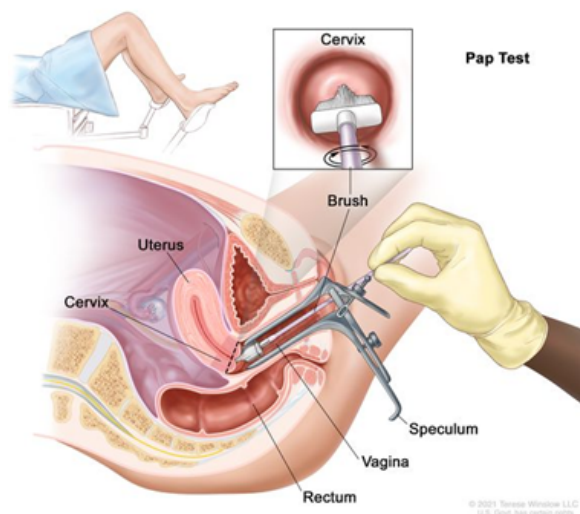


Fig.3: The image is taken from the site Cleveland Clinic.

<https://my.clevelandclinic.org/health/diagnostics/4044-colposcopy>

The image below illustrates the colposcopy method.

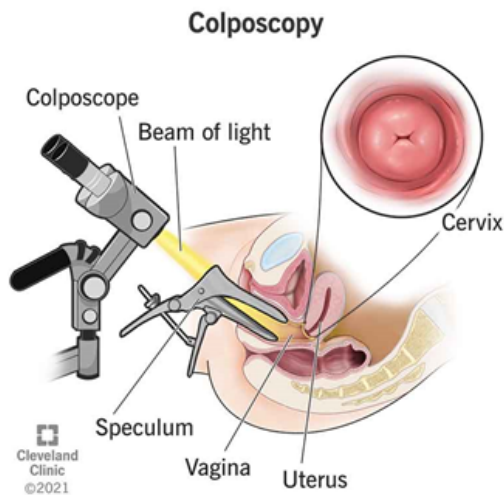


Fig.4: This image is taken from the site Gynecologic Oncology

<https://www.gynecologiconcology-online.net/article/S0090-8258%2821%2900512-6/fulltext>

The image illustrates the new method Sentinel Lymph Node Biopsy for diagnosis of the cancer to detect if its spreading .

