The Pap Test: Cervical Changes and Further Testing

Did you have a recent Pap smear that showed abnormal changes in the cells of your cervix or a positive HPV test and you need further testing? This article will help you understand the Pap and HPV test results and the most likely plan for follow up.

What is a Pap Test?

The Pap test, also called a "Pap smear" was introduced as a screening test for cervical cancer in 1943 by Dr. George Papanicolaou, for whom the test is named. The Pap test involves taking cells from the cervix, which is located at the top of the vagina, using a small brush or other tool. The sample is sent to a laboratory where it is examined for abnormal appearing cervical cells. A small percentage of abnormal cells can become cancer.

In many women, providers also use a test to detect Human Papilloma Virus (HPV) in conjunction with the pap test for cervical cancer screening. The large majority of cervical cancers are caused by certain "high-risk" strains of HPV. This test looks for these high-risk types of HPV in the cervical cells. This gives your provider more information about a possible cause of an abnormal pap result and helps to determine next steps.

When should cervical cancer screening be done?

All women should begin cervical cancer screening, beginning at age 21 using the following methods:

- **Age 21-29**: Pap testing done every 3 years. HPV testing is used only to follow up abnormal Pap results.
- **Age 30-65**: Pap testing and HPV test done every 5 years. Alternatively, a woman could have a Pap test alone every 3 years.
- **Over age 65**:
  - Women who have had 3 normal Pap results in a row, or 2 co-tests - Pap & HPV, in the last 10 years with the last test done within the last 5 years, can stop testing all together.
  - Women who have had a history of a serious cervical pre-cancer should continue to be tested for 20 years after that diagnosis, even if this continues past age 65.
- **Women who have had their uterus & cervix removed for reasons not related to cervical cancer and have no history of cervical cancer or pre-cancer do not need testing. If the hysterectomy was done as treatment for pre-cancer, you should have screening for 20 years after the surgery or follow the guidelines that your provider gives you.
- **Women who have had the HPV vaccination should still have Pap testing per the above guidelines.**

Some women, because of their history, may need to have a different screening schedule for cervical cancer. Please see the ACS document, Cervical Cancer Prevention and Early Detection for more information.

How is the screening done?

During the gynecologic examination, a speculum is inserted into the vagina so that the cervix and vagina can be seen. The doctor or nurse inserts a cotton-tipped swab or small brush into the cervical opening (cervical os) to sample endocervical cells (which come from the area most at risk for cervical cancer).

Normal vaginal discharge contains cells that are shed from the cervix and uterus. Samples of these cells are taken for the Pap test. For this reason, you should not douche, have vaginal intercourse, use tampons or vaginal medication for 48 hours before the Pap test is done.

The samples are sent to a pathologist for detailed examination under a microscope. A report is sent to your doctor with a
classification of the test results and a description of the cell changes. It can take up to three weeks to receive your results. An HPV test, looking for certain strains of the HPV virus associated with cervical cancer, can also be sent using the same sample.

**Process of Cervical Changes**

The cervix is the part of the uterus that extends into the vagina. There are two types of cells that line the cervix, one lines the outer cervix (portio) and another lines the inner cervix (endocervix). There is a distinct junction between the two cell types called the transformation zone. The Pap test is taken from this area because this where dysplasia (pre-cancer) and cancer most often arise.

Two common changes in cells are metaplasia and dysplasia.

**Metaplasia** - Metaplasia is generally described as a process of cell growth or cell repair that is benign (not cancerous). This process normally occurs in unborn babies, during adolescence, and with the first pregnancy. Studies have shown that metaplasia is present in more than one half of all women at some point in their development. This is a normal finding and does not indicate cancer.

**Dysplasia** - In dysplasia, there is an increase in the number of cells formed, which do not mature as expected. This changes the inside of the cell. The higher the grade of dysplasia found on the cervix, the more likely that it will progress to invasive cancer. For this reason, dysplasia is thought of as a "pre-cancerous" condition. Dysplasias are nearly 100% curable if managed appropriately. Although some mild dysplasias (LSIL) will regress without treatment, it is not possible distinguish between dysplastic areas of the cervix that will return to normal and dysplastic areas which will progress and ultimately become cancer. In turn, these results require further testing.

**Causes of Cervical Cell Changes**

Inflammation often results in a mildly abnormal Pap test, resulting in the diagnosis of ASCUS in the Bethesda System or changes consistent with Human Papilloma Virus (HPV) infection. An inflamed cervix may appear red, irritated, or eroded. Some of the common causes of cervical inflammation are:

- Bacteria (from an infection)
- Viruses, especially herpes infections and condyloma cuminata (warts)
- Yeast or monilia infections
- Trichomonas infections
- Pregnancy, miscarriage, or abortion
- Chemicals (for example, medications)
- Hormonal changes

When the inflammation is treated, repair of the tissues through metaplasia usually will follow. In several months, a repeat Pap test will often then be normal.

**Classification of Squamous Cells on the Pap Test**

Several different classification schemes have evolved over the years for characterizing Pap test results. Unfortunately, this is a continuing source of confusion. The most commonly used classification scheme is the Bethesda System.

- **ASC** - atypical squamous cells. This is the most common abnormal finding in Pap tests. In fact, of the over 50 million Pap tests each year, only 3.5 million are abnormal, and only about ten thousand women are diagnosed each year with invasive cervical cancer. The Bethesda System divides this category into two groups:
  - **ASC-US** - atypical squamous cells of undetermined significance. The squamous cells do not appear completely normal, but doctors are uncertain about what the cell changes mean. Sometimes the changes are related to HPV infection, but they can also be caused by other factors such as pregnancy. For women who have ASC-US, her cells may then be tested for the presence of high-risk HPV. If HPV is present, colposcopy (see below) will usually be done. Alternatively, the pap test may be repeated in 6 months, and if normal, she may resume the usual schedule of
screening. If a woman has ASC-US on her pap with a negative test for high-risk subtypes of HPV, a pap and HPV test may just be repeated in one year without further testing.

- **ASC-H** - atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion. Intraepithelial refers to cells on the surface of the cervix. ASC-H cells do not appear normal, but doctors are uncertain about what the cell changes mean. However, there is a possibility that a pre-cancerous lesion is developing, so a colposcopy is recommended.

- **LSIL** - low-grade squamous intraepithelial lesion; this is the earliest pre-cancerous lesion. LSILs may be referred to as mild dysplasia or as cervical intraepithelial neoplasia type 1 (CIN-1). Although many LSIL lesions will resolve on their own, there is no way to predict which ones will resolve, so doctors will typically perform a colposcopy.

- **HSIL** - high-grade squamous intraepithelial lesion. HSILs are more abnormal looking than LSILs and have a higher likelihood of progressing to cancer. HSILs include lesions that in other classification systems may be referred to as moderate or severe dysplasia, carcinoma in situ, and/or CIN-2 and CIN-3. A finding of HSIL necessitates a colposcopy.

- **Squamous cell carcinoma** is the most advanced category. This means that abnormal cervical squamous cells have invaded into the cervix. A finding of squamous cell carcinoma requires further testing and treatment. Keep in mind, when women undergo appropriate screening, most of the time, abnormalities in the cervix are detected and treated before they have had the chance to progress to cervical cancer.

**Classification of Glandular Cells on the Pap Test**

Glandular cells, which produce mucus, are found in the opening of the cervix and in the uterus. Abnormalities in these cells are more difficult to classify. Glandular cells that are seen on the Pap test most commonly come from the endocervix (area closest to the uterus). However, other glandular epithelial surfaces in the female reproductive tract may shed cells that are visible on the Pap test. Endometrial cells may also appear on Pap tests and reveal underlying abnormalities. Because the female reproductive tract is open to the abdominal cavity via the Fallopian tubes, occasionally, cells from the ovary, Fallopian tubes, peritoneum or other abdominal organs may be seen on the Pap smear. Glandular cells on the the Pap test are classified as follows:

- Endometrial cells, cytologically benign, in a postmenopausal woman
- Atypical glandular cells (AGC, formerly AGUS) that should be qualified further, if possible, as to whether a reactive or neoplastic process is favored. A finding of AGC will typically be followed by a colposcopy and possibly also endometrial sampling.
- Endocervical Adenocarcinoma
- Endometrial Adenocarcinoma
- Extraterine Adenocarcinoma (e.g. ovarian, Fallopian tube, pancreas, etc.)
- Adenocarcinoma, not otherwise specified (i.e. unknown primary site)

**HPV DNA TEST**

The HPV test can be used for screening or as a next step after an abnormal pap test result. There are over 150 types of HPV, but only 30 types are thought to be "high-risk" for causing various types of cancer. Two of these types (16 & 18) are known to cause over 70% of cervical cancers. The HPV test looks for the highest risk types of HPV in the same sample used for the pap test. The results of the HPV test along with the pap test and your age and health will determine what the next steps will be.

**Colposcopy: The next diagnostic step**

All abnormal Pap smear result often requires further evaluation. If the abnormality is minor (i.e. inflammation, or HPV changes) your healthcare provider may choose to repeat the Pap test in a few months, as your own immune system may "clear" the HPV infection and a follow up Pap be normal. If the abnormalities have persisted or worsened, colposcopy is indicated. Colposcopy will enable your physician or nurse to make a more accurate diagnosis.

**Colposcopy** - A coloscope is a lighted microscope that is used to magnify the cervical tissue during a pelvic examination. The coloscope is used to visualize abnormal areas of the cervix and vagina that are too small to see with the naked eye. The
entire transformation zone must be seen. The colposcopic examination is an office procedure and may be a bit more uncomfortable than a routine pelvic examination because of the pressure from the speculum lasting longer than a typical Pap test. The test takes 5 to 10 minutes to perform. During the examination, the examiner may take small samples of cervical tissue (biopsies), which are later examined by a pathologist. These diagnostic biopsies will guide further management.

From the examiner's perspective

From the patient's perspective

**Treatment Options for Cervical Dysplasia**

**Cone Biopsy** - A cone biopsy (also called cold knife cone biopsy) is a minor operation, which is usually performed in an outpatient surgical facility. In the operating room, the physician removes a small cone shaped tissue sample from your inner cervix. This tissue is sent to a pathologist for detailed examination under a microscope. This procedure does not remove any of your reproductive organs and should have little impact on your future ability to become pregnant. If only dysplasia is found in the cone specimen, then often no additional treatment will be required. However, if invasive cancer is discovered, additional treatment (i.e. surgery or radiation therapy) is indicated. Therefore, a cone biopsy may be considered as therapeutic (if all of the dysplasia is removed) or diagnostic (if it discovers a worse problem that requires additional treatment).

**Loop Electrosurgical Excision Procedure (LEEP)** - The LEEP procedure is similar to a cone biopsy in that it removes a tissue sample from your cervix, which is then examined, under a microscope, by a pathologist. It may also be called a LLETZ (large loop excision of the transformational zone). The LEEP procedure uses a low voltage, electric wire to cut away the abnormal area and has the advantage of being easily performed in the office with local anesthesia. However, the LEEP procedure and cone biopsy are not equivalent and your physician will recommend which is the best option, depending on your case.

**Cryosurgery** - Cryosurgery is another treatment option that can be performed in the doctor's office. During the procedure, the doctor freezes and thereby destroys the dysplasia on your cervix. You may notice a brief unpleasant cold sensation during the freezing procedure. A disadvantage of cryosurgery is that no specimen is obtained for the pathologist to examine in order to exclude the possibility of invasive cancer.

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