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UTILIZATION OF DIFFERENT TYPES OF CERVICAL CANCER SCREENING TEST

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Abstract: **Cervical cancer is one most common cancer occurring in women. There are different types of cervical cancers screening test, cervical cancer is one of the leading cancer among women all over the world, cervical cancer is the most common female cancer worldwide. one women die of cervical cancer every two minutes, This cancer has managed to create a burden is significant across all cultures and economics, however in NIGERIA this disease is still killing up to 8000. women annually. It is also one of the most common cancer of woman that can be detect and treated completely at precancerous stages. STD is main cause of cervical cancer and also due to the Human Papillomavirus (HPV). mainly HPV-16 and HPV-18. It continues to be major public health troubles for female in India. The incidence of cervical cancer is 55-59 years and a considerable proportion of women report in the late stage of disease. Prophylactic vaccines against HPV-16 and 18 therapeutic vaccines are used against cervical cancer. Other epidemiological risk factor are premature at sexual activity ,Teenage pregnancy. Family past, Oral contraceptive.This article ,explain history of cervical cancer, histopathological variety, risk factor, avoidance, treatment and Drug approved to prevent cervical cancer .The most common type of cervical cancer is called Squamous cell carcinoma .Vaccine is helpful only in people who have no previous infection with HPV.**

Keywords: **Carcinoma Cervix., Rural Cervical Cancer, Single Lifetime Cytological Screening, Human Papillomavirus Treatment, Prevention, Sexually Transmitted Diseases.**

1. INTRODUCTION

Cancer of the cervix is a malignant tumor of the cervix (the lower part of the uterus) and it is a major public health problem throughout the world. Globally, cervical cancer is a major cause of cancer-related morbidity and mortality in women (1). Cervical cancer is an important reproductive health problem. It is a preventable disease of significant public health concern especially in developing countries like Nigeria. It is the third most common cancer worldwide and the second most common cancer and leading cause of death from cancer among Young girls in developing countries (2). It continues to be the second commonest female cancer worldwide after breast carcinoma with an estimated 500,000 new cases and 250,000 deaths occur worldwide annually but majority (80%) occurred in developing countries (3). Among different types of cancer, cervical cancer is regarded as the common cancer-related cause of death among women, and it can be prevented through regular screening programs (4). Cervical carcinoma is still the most common cancer of women on the African continent. Worldwide increase in mortality rate at 50% was mainly because of late presentation, advanced stage of disease and absence of a functioning screening process. The etiological link between human papilloma virus (HPV) infection and cervical cancer has been well established and a number of high-risk HPV genotypes have been identified. HPV infection is the most common sexually transmitted infection (STI) in the world today up to 80% of sexually active females will harbor HPV at some point in their lives. The majority of women will experience natural elimination of HPV infection because of an intact immune system. Persistent infection with a high risk type HPV puts women at high risk to develop precursors of cervical cancer or carcinoma itself. Perception, from the context of the study is the organization, identification, and interpretation of sensory information in order to represent and understand the presented information, or the environment (5). Perception also includes how people respond to the information. People can think that perception is a process where they take in sensory information from their environment and use that information in order to interact with the environment. Perception allows us to take the sensory information in and make it into something meaningfull (6). Perception depends on complex functions of the nervous system, but subjectively seems

mostly effortless because this process happens outside conscious awareness . Utilization can be stated as a critical evaluation by health workers of health-care services provided to patients that are made especially for the purpose of controlling costs and monitoring quality of care. Then, cancer screening aims to detect cancer before symptoms appear. This may involve blood tests, urine tests; DNA tests other tests, or medical imaging (7). It may involve mass screening or population screening (screening everyone, usually within a specific age group). The benefits of screening in terms of cancer prevention, early detection and subsequent treatment must be weighed against any harm. In developed countries, it is estimated that more than half of women found to have cervical cancer have a history of no screening or infrequent screening (8). In Canada, Ontario Cervical Screening Program (9). stated that women tend to have a low level of education, to live in poverty, to be newcomers to the country, to be over 50 years of age. Globally, Parkin, Bray and Ferlay (10). underserved and lower socioeconomic status of populations bears the greatest burden of cervical cancer. African-American women are 50% more likely to be diagnosed with cervical cancer and twice as likely to die from the disease as Caucasian women. In addition, cervical cancer incidence and mortality for Hispanic women is higher than for non-Hispanic women in the USA (11). Although cervical cancer is largely preventable through regular Pap smear screening, also known as Working Group on the Evaluation of Cancer-Preventive Strategies stated that more than half of women diagnosed with cervical cancer have had no screening (12). One way to increase screening for the risk of cervical cancer among women who seldom or never get pap tests is to offer self-collection tests to test HPV by women at home and return to laboratory. A self-collection test, or selftest, collects HPV DNA using a device such as a vaginal swab, cytobrush, or vaginal lavage. There are many reasons why women in both developing and developed countries do not participate in cervical screening, such as lack of access to a health care provider (13). discomfort with physical examination, cultural and religious, or personal values that prohibit examination by a male physician. HPV DNA testing has the potential to reach under-screened populations with self-sampling methods. Self-sampling has proved to be reliable in screening for sexually

transmitted diseases in hard-to-reach populations; for example, self-administered tampons were shown to be both an acceptable and a sensitive method for detecting sexually transmitted diseases in women living in remote regions of Australia (14). Self-collected vaginal swabs produced reliable results and were acceptable to women in Southern Asia for the detection of reproductive tract infections(15).It is clear that more information on self-sampling for HPV DNA testing is needed. In theory, self-sampling has the potential to improve screening and follow-up rates in women who are never or seldom (>3 years between tests) screened by clinicians, thereby contributing to reduced mortality and morbidity from cervical cancer. Since the majority of women do experience natural elimination of HPV infection because of an intact immune system. Therefore, persistent infection of HPV puts women at high risk to develop precursors of cervical cancer or carcinoma itself and the idea of this study were adopted We provide an example of ethics dumping in three trials conducted from 1998 to 2015 in urban and rural areas India on testing for cervical cancer.

2. LITERATURE REVIEW

Donna e.s/anna,"et al (2011):-It is a preventable disease of significant public health concern especially in developing countries like Nigeria. It is the third most common cancer worldwide and the second most common cancer and leading cause of death from cancer among Young girls in developing countries the African continent. advanced stage of disease and absence of a functioning screening process. The etiological link between human papilloma virus (HPV) infection and cervical cancer has been well established and a number of high-risk HPV genotypes have been identified. African-American women are 50% more likely to be diagnosed with cervical cancer and twice as likely to die from the disease as Caucasian women (page.no-6,7)7pdf.

kunkule,r/pakale,r/jadhav,s"et al(2020):- 400 b.c. by the greek physician pericles hippocrates. by german scientist zur hausen where they discovered human papilloma virus (hpv) dna in cervical cancer and warts. in 1985 zur hausen, gissmann and their co-workers further identified the structure and sequence of HPV(page no-10,11)4pdf.

*md boggess j.f/ zolnoun d,"et al(2002)***:-**The goal of sampling for cytology purpose is to sample the transformation zone: that area of the cervix where physiologic transformation from the columnar cells lining the endocervical canal to the squamous cells covering the ectocervix occurs. Cervical dysplasia and cancers arise in the transformation zone. The transformation zone is easily sampled in younger women because it is on the surface of the cervix (page no-12)5pdf.

*claeys.p/ petitpierre.j,"et al (2006)***:-** this refi nement of conventional cytology was introduced in the mid-1990s and is increasingly used in high-resource settings. instead of smearing cervical cells on a slide, the provider transfers the specimen from a brush to a preservative solution. the specimen is sent to a laboratory where the slide is prepared. lbc is more expensive than conventional cytology and laboratory staff need to be specially trained. however, it appears to have a number of advantages over conventional methods(page. no-14)3book analysis.

md.gibb r.k/martens,m.g"et al(2011) **:-**the second major advance was liquid-based cytology (lbc). this review presents a wide range of data, discusses the strengths and weaknesses of the available information regarding pap technologies, and reviews the meta-analyses, which have examined the differences in clinical performance (page. no-17)4pdf

shapiro.k/ottolengh e.d,"et al(2006):- hpv dna-based tests currently require sophisticated and expensive laboratory equipment, although work is under way to develop a more affordable and less complicated test that can be carried out in lowerlevel settings. detection of high-risk hpv does not necessarily mean that precancer or cancer is present; it indicates simply that there is an hpv infection. as mentioned earlier, hpv infections are extremely common in women under 35 years, and most of them resolve spontaneously. when detection of hpv is used as a primary screening test, hpv dna testing can be done by trained providers at any level of the health care system, provided that there is an appropriate laboratory within a reasonable distance, and that reliable transport is available for specimens. clinic needs for hpv testing are the same as for pap smears and visual methods(page. No-18.19)4book analysis.

*Eifel p/klopp ah/Berek js,"et al(2019) :-*the most important risk factor for developing cervical cancer is infection with human papillomavirus (hpv). doctors can test for the high-risk hpv types that are most likely to cause cervical cancer by looking for pieces of their dna in cervical cells. the test can be done by itself (primary hpv test) or at the same time as a pap test1 (called a co-test). you won't notice a difference in your exam if you have both tests done(page.no-22)5pdf.

Russell ah/seiden mv/duska lr,"et al(2020):- many people confuse pelvic exams with pap tests. the pelvic exam is part of a woman's routine health care. during a pelvic exam, the doctor looks at and feels the reproductive organs, including the uterus and the ovaries and may do tests for sexually transmitted disease. pelvic exams may help find other types of cancers and reproductive problems(page.no-23)7pdf.

sankaranarayanan.r/budukh a.m/rajkumar.r"et al(2001):- cytology smears and treating precancerous lesions. It has been widely believed that invasive cervical cancer develops from dysplastic precursor lesions, progressing steadily from mild to moderate to severe dysplasia, then to carcinoma in situ, and finally to cancer. It now appears that the direct precursor of cervical cancer is high-grade dysplasia (page.no-24.25)4pdf.

dr:kaur.t/dr:shrisvastava.s,"et al(2016):- once cancer has been diagnosed, additional tests may be performed to determine whether or not the cancer has spread to other parts of the body. this is called staging. learning the stage of the cancer helps plan treatment options.tests that may be performed to determine whether cancer has spread include(page.no-26.30)7pdf.

*kunkule.r/pakale.r/jadhav.s"et al(2020)***:-** Approximately all cervical cancer cause by HPV. The climax age of cervical cancer is about 47 ages of years. HPV usually transmit through sexual contact, it can spread without sex, by skin-to-skin contact with infected area of body. HPV infection diagnosed in young women lasts from 8-13 months (page.no-31)3pdf

*kashyap.n m.sc nursing/sukhpal.k,"et al(2019)***:-** cervical cancer progresses slowly in the body. the known risk factors of developing cervical cancer are human papilloma virus (hpv), low socio-economic status, smoking, marrying before age 18 years, young age at the first coitus, multiple sexual partners, multiple sexual partners of spouse, and multiple childbirths. these factors raise the risk of developing cervical cancer. it has now been proven that hpv is the major causative factor of carcinoma of the cervix. hpv types 16, 18, 31, 33, and 45 are mostly related with invasive carcinoma of the cervix. most research studies show that an increasing number of steady partners and young age at first sexual intercourse increase the probability of developing cervical cancer(page. No-33.34.35)8pdf.

3. BACKGROUND HISTORY

Cervical cancer is the third most common cancer among women in the world leading to 90% deaths in low and middle income countries. About 96,922 new cervical cancer cases are diagnosed annually in India. cancer is one of the leading causes of adult deaths worldwide. Every year about 14 million new cancer cases are detected and 8 million people die of cancer. However, there is a marked difference in the distribution of cancer sites across different regions of the world. In contrast to developed countries, cervical cancer is a public health problem in developing countries like India, so much so that India alone accounts for one-quarter of the worldwide burden of cervical cancers. It is the one of the leading cause of cancer mortality, accounting for 17% of all cancer deaths among women aged between 30 and 69 years. It is estimated that cervical cancer will occur in approximately 1 in 53 Indian women during their lifetime compared with 1 in 100 women in more developed regions of the world,Cervical cancer is a major cause of cancer mortality in women and more than a quarter of, in spite of alarmingly high figures(16).

The first description of cervical cancer was found in 400 B.C. by the Greek physician Pericles Hippocrates. It was considered in curable at the time until. Some 2000 years later, the opinion of the pathogenic mechanism was recognized through pioneer work by an Italian surgeon. During in the mid 19 th century, Dr. Rigoni Stern noticed that the incidence of cervical cancer was rare among nuns (Rigoni-stern, 1842). All these work has indications that the causation of cervical cancer is linked with sexual intercourse. Hence cervical cancer was considered highly transmissible. Transmitting agents was only reported later in 1976 publication. by German Scientist Zur Hausen where they discovered human papilloma virus (HPV) DNA in cervical cancer and warts. In 1985 Zur Hausen, Gissmann and their co-workers further identified the structure and sequence of HPV. Further later discovery of HPV vaccine led to the milestone in curing the disease(17). Pathology Cervical cancer is characterized by the abnormal growth of cells in the cervix. Mostly at the region of the uterus that joins the vagina. It is a common cancer in women but mortality rate is reduced by using pap smear. Cervical cancer is common in developing countries.

Histopathological Types Of Cervical Carcinoma

1 In squamous epithelial cells of cervix 66% of squamous cells carcinoma are found.

2 The mucus producing glandular cells of endocervix adenoocarcinoma 28% cases are found.

3 Adenosquamous carcinoma and neuroendorine carcinoma are rarer types of carcinoma found in only 6% (18).

Epidemiology This cervical cancer was most important cancer among women in the past two decades. In India this incidence mostly occur in 55-59 years. This data in between 2009 and 2011 of Aizawl district in the north eastern part in India revealed the highest level of cervical cancer at an age adjusted rate of 24.3, followed by Barshi Expanded at 19.5 and Bangalore at 18.9(19).The common histological type of cancer, originates in the ectocervix is squamous cell carcinoma and that in the endocervix is adenocarcinoma. The entire populationbased registry has , a persistent surgein the age adjusted rates even in the absence of the control program. Cervical cancer rates among women in the 30 to 64 age group decreased by 1.8% per year on average but still accounted for 16 % of the total female cancer burden. In Odisha, cancer cervix was the second most common cancer with an increase of 3.1% from 2001 to 2011. In the southern part of India, the north eastern district of Tamilnadu show a disnictive pattern with a high incidence of cervical cancer(20). This may be attributed to a infection with human papilloma virus (HPV). The high burden of cervical cancer in south and south east Asian countries is due to a high prevalence of HPV (More than 10% in women aged more than 30 years) and due to lack of screening(21).

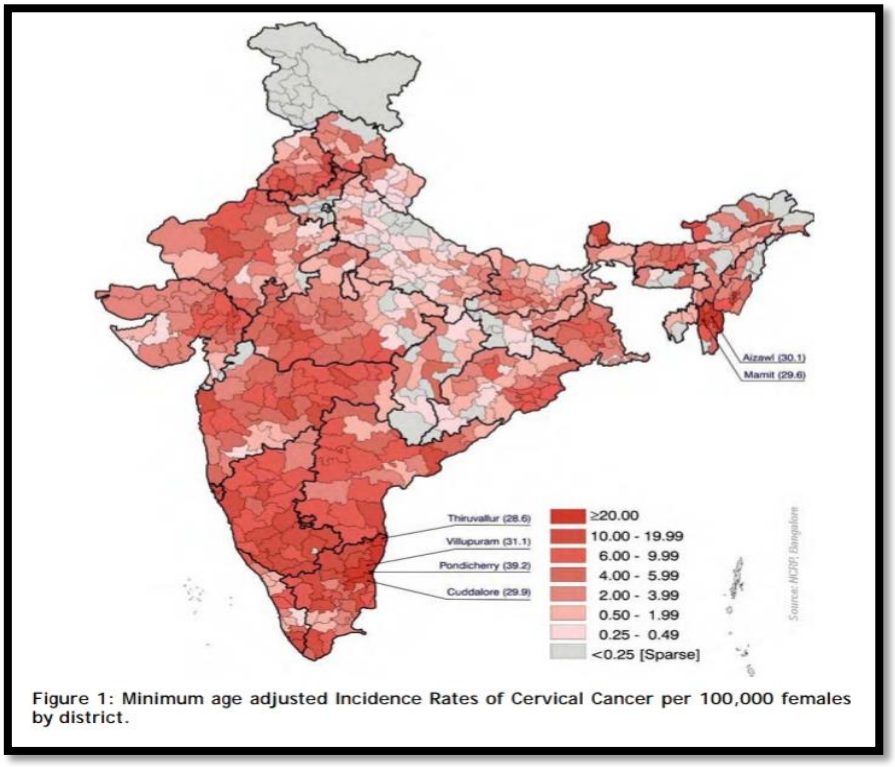


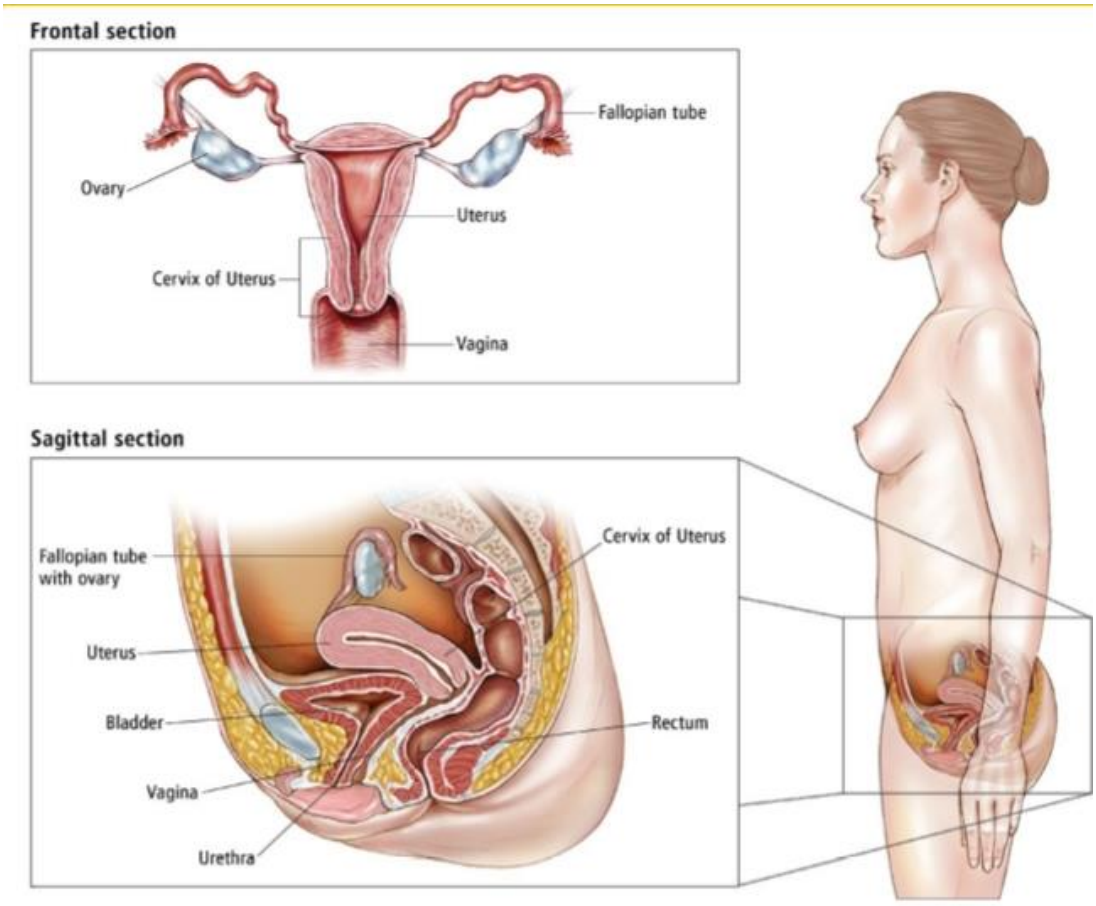
Figure 1: Minimum age adjusted Incidence Rates of Cervical Cancer per 100,000 females by district.

WHAT IS THE FUNCTION OF THE CERVIX

The cervix is the lower, narrow part of a woman's uterus. The uterus holds the growing fetus during pregnancy. The cervix connects the uterus to the vagina and, with the vagina, forms the birth canal**.**

WHAT IS A CERVICAL CANCER SCREENING

Cervical cancer is a disease in which healthy cells on the surface of the cervix change, grow out of control, and form a mass of cells called a tumor. At first, the changes in a cell are abnormal, not precancerous. Research shows these cells can become precancerous and may change into cancer over time. This phase of the disease is called dysplasia. If the precancerous cells change into cancer cells and spread deeper into the cervix or to other tissues and organs, the disease is called cervical cancer(22). The 2 main types of cervical cancer are squamous cell carcinoma and adenocarcinoma. Cervical cancers can often be prevented by having regular Pap tests to find and treat pre cancers early.



METHODS OF CERVICAL CANCER SCREENING TEST

1 Cytological.

- Conventional Pap Smear.
- Liquid-based cytological (LBC).
- Automated cytological screening.

2 HPV testing.

- Visual inspection with acetic acid (VIA).

3 The pap (papanicolaou) test.

4 Cervical intraepithelial neoplasia (CIN).

PAP SMEAR/ CYTOLOGY

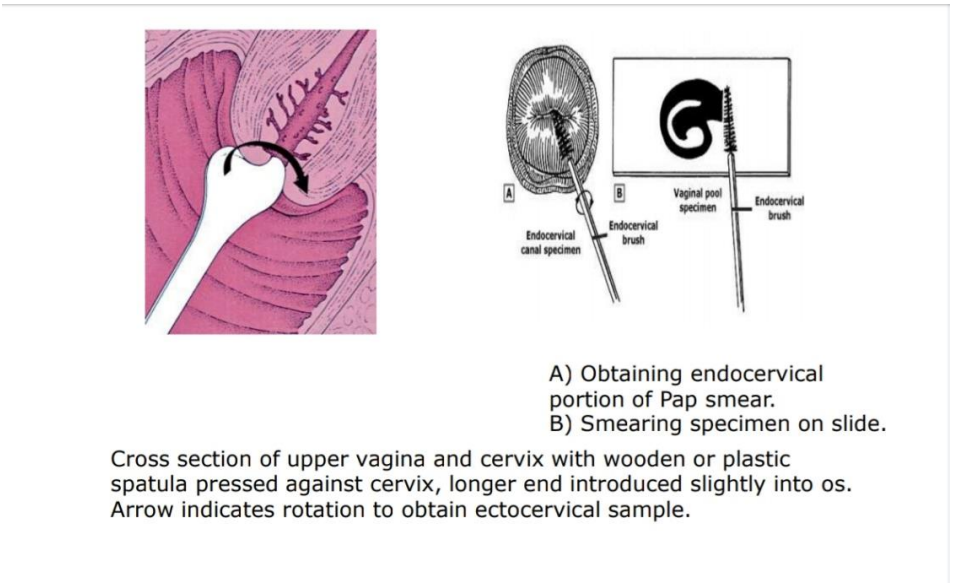
- The Papanicolaou test, also known as Pap smear, was developed in the 1940s by Georgios

Papanikolaou.

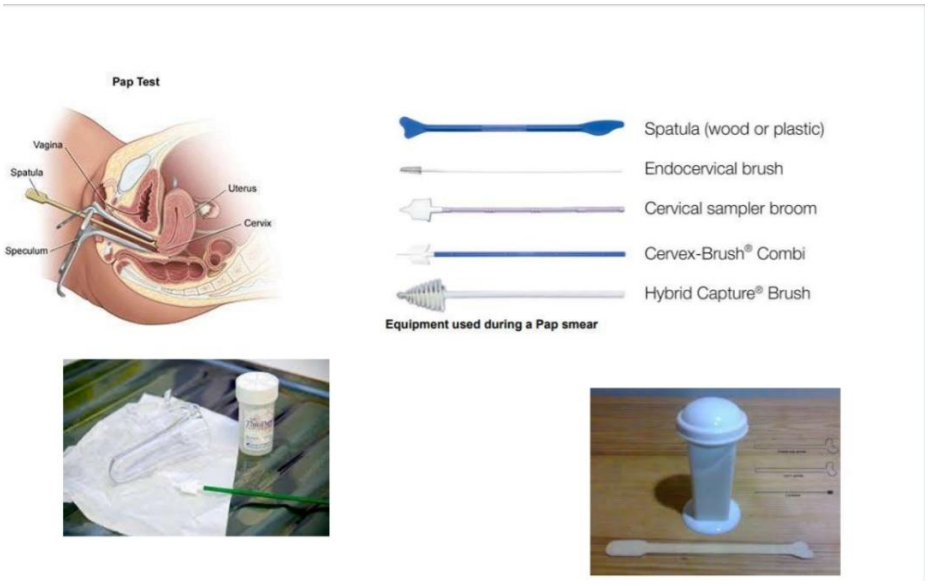
- It involves exfoliating cells from the transformation zone of the cervix to enable examination of these cells microscopically for of cancerous or precancerous lesions detection.

- Two types: conventional and liquid base cytology

For conventional Pap smears, the ectocervical spatula is smeared and the endocervical brush is rolled uniformly onto a single slide promptly after obtaining the specimens(23). The slide is then rapidly fixed to avoid air-drying; the usual fixatives are either ethyl ether plus 95 percent ethyl alcohol or 95 percent ethyl alcohol alone(24). If spray fixatives are used, the spray should be held at least 10 inches away from the slide to prevent disruption of cells by the propellant.



(a)



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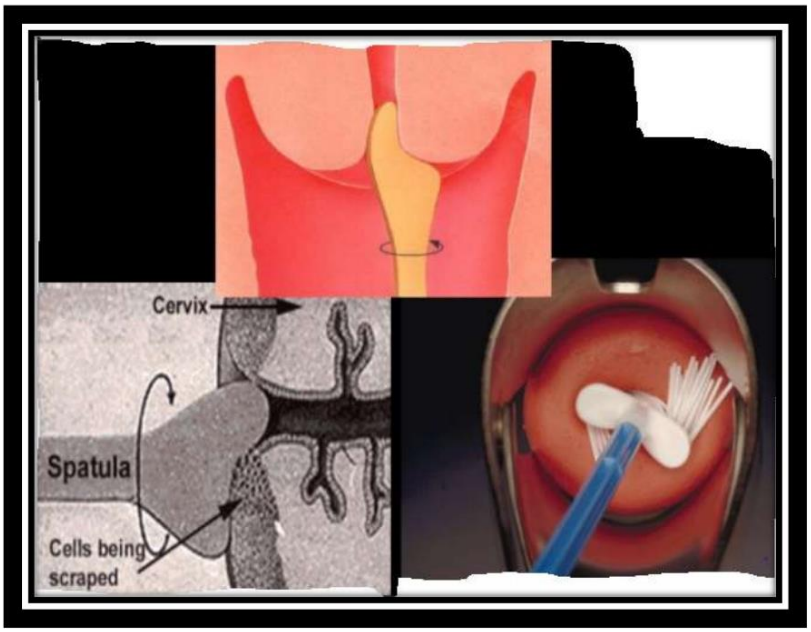
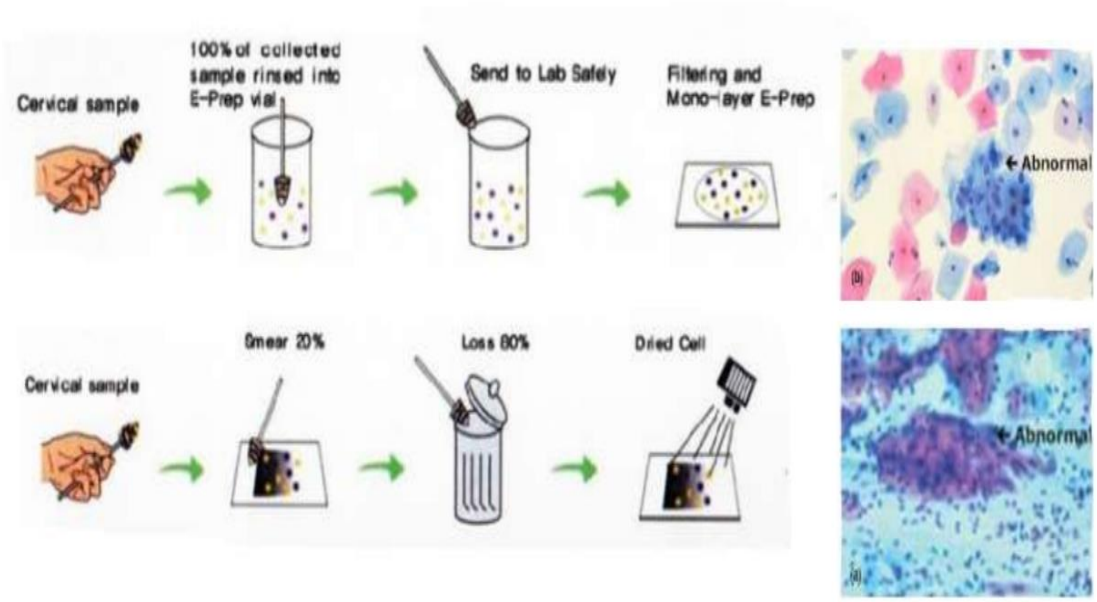


(c)

LIQUID BASE CYTOLOGY (LBC)

- The principle behind LBC is that instead of smearing the spatula across slide, it is rinsed in a vial of preservative solution. In the Lab the suspension is centrifuged and passed through a filter to create a slide with a monolayer preparation of thin layer of cells on a slide. Two technologies for LBC preparation are Sure Path and Thin Prep.
- It also allows the possibility of other tests such as HPV testing from the same sample.
- Liquid based cytology leads to significant reduction of unsatisfactory rate. LBC samples offered better clarity, uniform spread of smears, less time for screening and better handling of hemorrhagic and inflammatory samples(25). LBC had equivalent sensitivity and specificity to CPS. 2013 Aug; 24,- 254-63. DOI: 10.1111/cyt.12037. Pub 2017 Jan 21.



(a)

CONVENTIONAL PAP smear	Liquid base cytology
•Heterogeneous •—Graphic cell localization •—300-500 cells/slide •—Variable fixation •—Thick uneven groups •—need frequent focusing •—Dirty background •—Variable preservation •—False Negative rates higher than 50%. Compromised by the presence of blood, mucous, obscuring inflammation, scant cellular material and air-drying artefact.	•—Homogeneous •—Random cell presentation •—50-70 cells/slide •—Uniform fixation •—Uniform thin layer •—Not single cell, mono layers •—Clean background •—Well preserved cells •—Increases disease detection 65%. This method preserves the cells and minimizes cell overlap, blood, mucus, and inflammation. It creates a mono-layer, a layer one cell thick, with no overlapping cells. FDA approved-ThinPrep and Sure Path

(b)

- **AUTOMATED PAP SMEARS**

To reduce errors by using computerized analysis to evaluate Pap smear slides.

1 Autocyte

2 AutoPap**.**

THE HPV TESTING

Doctors can now test for the HPV (high-risk or carcinogenic types) that are most likely to cause cervical cancer by looking for pieces of their DNA in cervical cells. The test can be done by itself or at the same time as the Pap test, with the same swab or a second swab.

The best way to find cervical cancer early is to have regular screening tests. The tests for cervical cancer screening are the HPV test and the Pap test. These tests can be done alone or at the same time (called a co-test). Regular screening has been shown to prevent cervical cancers and save lives. The most important thing to remember is to get screened regularly, no matter which test you get.

Early detection greatly improves the chances of successful treatment and can prevent any early cervical cell changes from becoming cancer(26). Being alert to any signs and symptoms of cervical cancer can also help avoid unnecessary delays in diagnosis,

A screening test is a test done on people who are healthy and without symptoms, to identify those with a higher chance of getting a particular disease. A cervical cancer screening test can determine if a cervix is normal or not. It can detect early signs of disease before a woman has symptoms, when treatment can prevent the disease from developing.

HPV DNA testing: Molecular tests can detect DNA from cancer causing HPV types in vaginal or cervical smears collected using a small brush or swab, either by trained providers or by women by themselves.

• Nearly 100% of cervical cancer cases test positive for HPV.

• International Agency for Research on Cancer (IARC) has classified 12 HPV types as group 1 carcinogens (i.e, oncogenic or high risk): HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59.

• Molecular technologies for the detection of HPV DNA can be broadly divided into amplified and non-amplified and main techniques of each category are the hybrid capture 2 (HC2) assay and polymerase chain reactions (PCR).

DNA/RNA TEST TECHNIQUE NAME

Test	Technique	Name
DNA	Direct genome detection	Hybrid Capture 2 careHPV test
	Amplification	GP5+/GP6+ bio PCR-EIA Cervista HPV HR
	Amplification and genotyping of HPV-16 and HPV-18	Cervista HPV 16/18 Cobas HPV test Xpert HPV abbott Real time high risk HPV assay Papillo check
RNA	Amplification of E6/E7 proteins	Aptima HPV assay PreTect HPV-Proofer HPV
	Monoclonal antibodies	AVantage HPV E6 test

(a)

Test	Technique	Name
DNA	Direct genome detection	Hybrid Capture 2 careHPV test
	Amplification	GP5+/GP6+ bio PCR-EIA Cervista HPV HR
	Amplification and genotyping of HPV-16 and HPV-18	Cervista HPV 16/18 Cobas HPV test Xpert HPV abbott Real time high risk HPV assay Papillo check
RNA	Amplification of E6/E7 proteins	Aptima HPV assay PreTect HPV-Proofer HPV
	Monoclonal antibodies	AVantage HPV E6 test

(b)

- **HYBRID CAPTURE II KIT (HC II. QIAGEN INC. USA)**

• Approved by FDA frequently used.

• Gold standard HPV test**.**

• Detects whether a person is infected with one or more of the 13 high-risk HPV viral types (types16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68).

• Routine screening test with Pap testing above 30 year.

2 HPV DNA- PCR testing (HPV typing): Isolated HPV types could be detected. The PCR based assay is based on target amplification and care must be taken to avoid contamination. Its advantage is that it allows identification of different types of HPV and can discriminate between multiple infections(27).it is expensive, time-consuming and laborious , not suited to be applied as a mass screening test.

3 Cervista : single amplification method , using cleavase enzymes , 14 HR HPV can be detected.

4 Cobas 4800 HPV (Roche) : detect 16 and 18 individually and other HR HPV.

5 Aptima (Gene probe now Hologic) : Detects 14 HR HPV types by detecting mRNA. Has Increased specificity, useful for HPV triage**.**

- **CLINICAL UTILITY OF HPV TESTING.**

1 HPV DNA testing as a primary screening test

2 Combined screening with HPV DNA plus cytology

3 HPV DNA testing in the triage of equivocal (ASCUS) or low-grade (LSIL) cytologic findings.

4 HPV DNA testing for follow-up post-treatment .

5 HPV DNA testing of self-collected vaginal samples .

- **VISUAL INSPECTION WITH ACETIC ACID (VIA).**

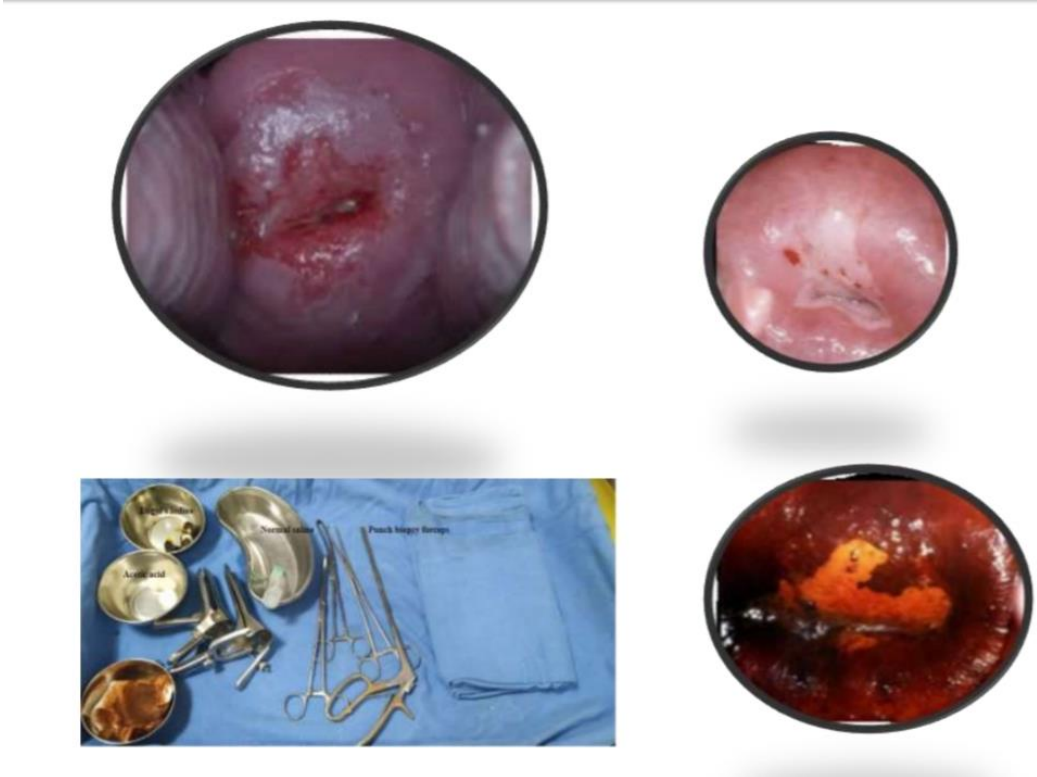
Involves naked-eye inspection of the cervix one minute after application of a 3–5% solution of acetic acid using a cotton swab or a spray(28).

- Test positivity is based on the appearance of acetowhite areas in the transformation zone, close to the squamocolumnar junction or the os.

Effects of acetic acid: 1. Coagulates the proteins of the nucleus & cytoplasm: protein opaque & white.

1 Dehydrates the cells: cytoplasmic volume is reduced & the reflection is increased.

2 Duration: appears after 20 seconds and disappears after 2 minutes.



THE PAP (PAPANICOLAOU) TEST

- The Pap test is a procedure used to collect cells from the cervix so that they can be looked at in the lab to find cancer and pre-cancer.
- When Cervical Screening Test Results are Abnormal.
- The first step in finding cervical cancer is often an abnormal HPV or Pap test result. This will lead to further tests, which can diagnose cervical cancer.
- The Pap test is a procedure that collects cells from the cervix so that they can be looked at closely in the lab to find cancer and pre-cancer.
- The health care professional first places a speculum inside the vagina. The speculum is a metal or plastic instrument that keeps the vagina open so that the cervix can be seen clearly. Next, using a small spatula or brush, a sample of cells and mucus is lightly scraped from the exocervix (see illustration in What is Cervical Cancer(29). A small brush or a cotton-tipped swab is then inserted into the opening of the cervix to take a sample from the endocervix . If your cervix has been removed (because you had a trachelectomy or hysterectomy) as a part of the treatment for a cervical cancer or precancer, the cells from the upper part of the vagina (known as the vaginal cuff) will be sampled. The samples are then looked at in the lab.
- Although the Pap test has been more successful than any other screening test in preventing a cancer, it's not perfect. One of the limitations of the Pap test is that the results need to be examined by the human eye, so an accurate analysis of the hundreds of thousands of cells in each sample is not always possible. Engineers, scientists, and doctors are working together to improve this test.[30], Because some abnormalities may be missed (even when samples are looked at in the best labs), it's best to have this test regularly as recommended by the American Cancer Society guidelines.

Making your Pap tests more accurate.

You can do several things to make your Pap test as accurate as possible.

Try not to schedule an appointment for a time during your menstrual period. The best time is at least 5 days after your period stops.

Don't use tampons, birth-control foams or jellies, other vaginal creams, moisturizers, or lubricants, or vaginal medicines for 2 to 3 days before the Pap test.

Don't douche for 2 to 3 days before the Pap test. Don't have vaginal sex for 2 days before the Pap test.

A pelvic exam is not the same as a Pap test.

Many people confuse pelvic exams with Pap tests.The pelvic exam is part of a woman's routine health care. During a pelvic exam, the doctor looks at and feels the reproductive organs, including the uterus and the ovaries and may do tests for sexually transmitted disease. Pelvic exams may help find other types of cancers and reproductive problems. A Pap test can be done during a pelvic exam , but sometimes a pelvic exam is done without a Pap test. A Pap test is needed to find early cervical cancer or pre-cancers so ask your doctor if you had a Pap test with your pelvic exam.

- **How Pap test results are reported**

The most widely used system for describing Pap test results is the Bethesda System (TBS). There are 3 main categories, some of which have sub-categories:

● Negative for intraepithelial lesion or malignancy.

● Epithelial cell abnormalities.

● Other malignant neoplasms.

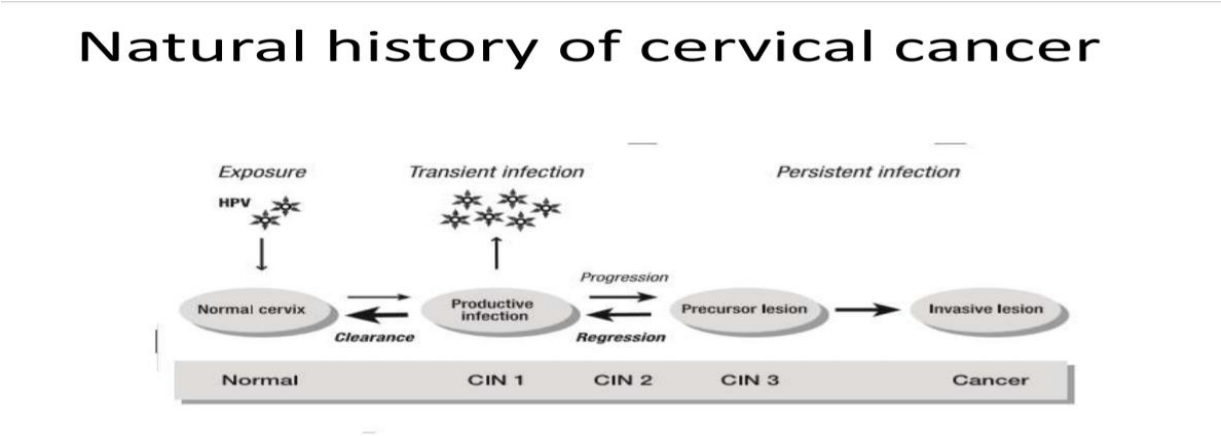
You may need further testing if your Pap test showed any of the abnormalities below. See Work-up of Abnormal Pap Test Results.

CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)

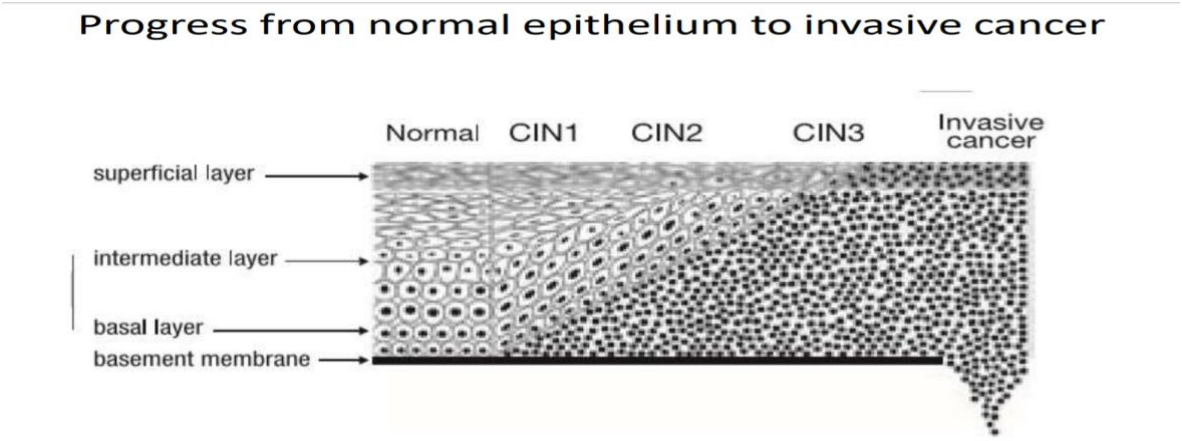
Cervical intraepithelial neoplasia (CIN) refers to the histological diagnosis of a spectrum of changes in squamous epithelium known to be precursors of invasive squamous cell carcinoma (31).

Earlier disease model - precursor lesions, progressing from mild to moderate to severe dysplasias to carcinoma in situ (CIS) and then to cancer. The current cervical carcinogenesis model includes 3 steps of.

• HPV infection, progression to high grade **preinvasive lesions and invasion.**



(a)



(b)

Pathological finding of of CIN

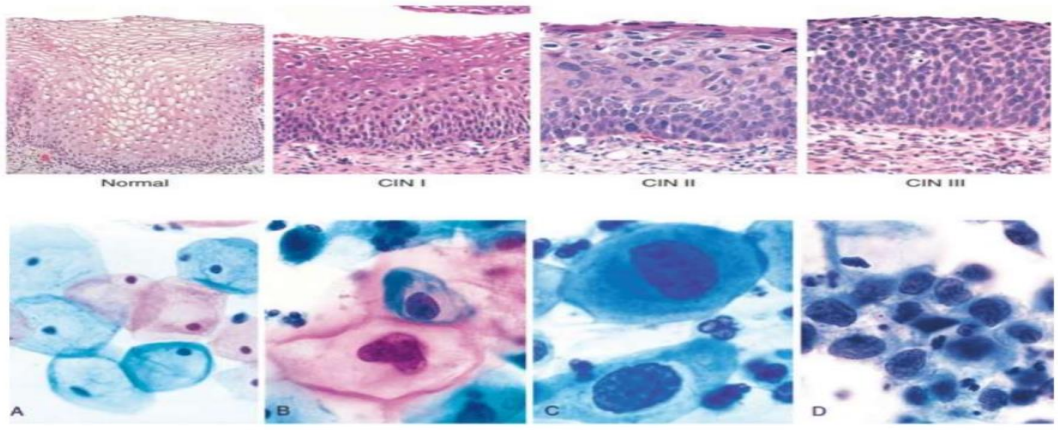
CIN 1 (flat condyloma. Koilocytosis. mild dysplasia) LSIL.

• Neoplastic. basaloid cells and mitotic figures occupy the lower third of the epithelium.

• These lesions frequently show marked HPV cytopathic effects including perinuclear halos, multinucleation and nuclear membrane irregularities, and hyperchromasia (e.g., "koilocytosis").

- CIN 2 (moderate dysplasia): neoplastic basaloid cells and mitotic figures occupy the lower two thirds of the epithelium.
- CIN 3 (severe dysplasia; carcinoma in situ): HSIL.

The characteristic histological feature of CIN 3 is the presence of neoplastic basaloid cells and mitotic, occupy the full thickness of the epithelium. These cells have high. nuclear: cytoplasmic ratios, with scant cytoplasm and dense, hyper chromatic nuclei having. coarse clumped chromatin and irregular nuclear outlines.

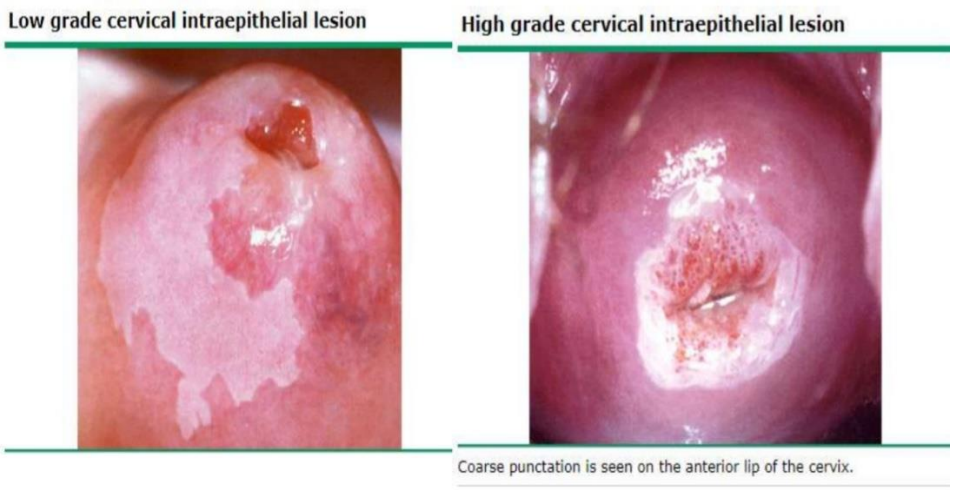


(c)

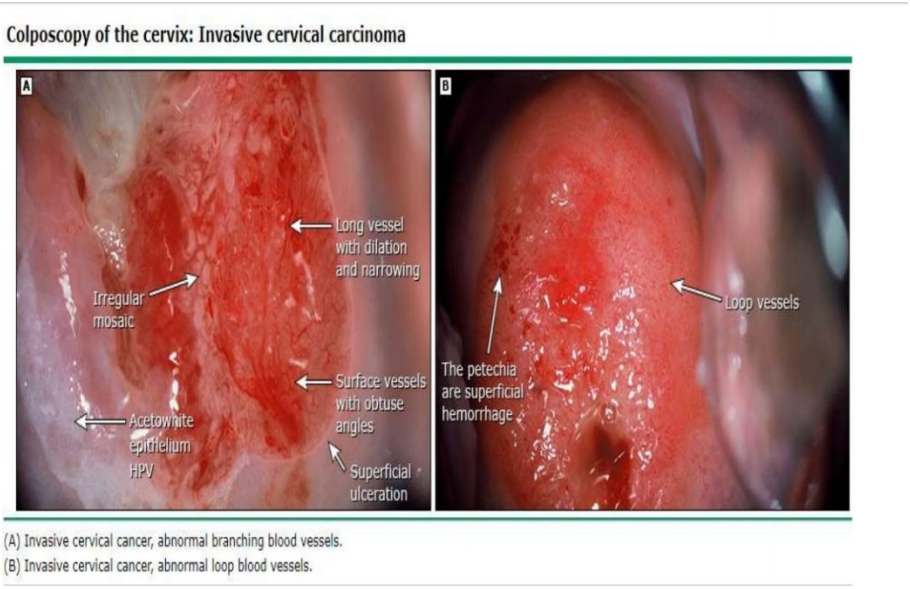
Prognosis of untreated CIN lesions

	Regression	Persistence	Progression to CIN3	Invasive cancer
CIN 1	60%	40%	10%	1%
CIN2	40%	40%	20%	5%
CIN3	32%	56%		>12%

(d)



(a)



(b)

CLINICAL SYMPTOM

• No symptom majority of cases

• Post coital bleeding

• Spoting

• Abnormal vaginal discharge.

STAGES OF CERVICAL CANCER

(DEVIDE INTO FOUR TYPES),

- STAGES-1. Cancer is confined to the cervix.
- STAGES -2.Cancer at this stage includes the cervix and uterus, but has not soread to the pelvic wall or the lower portion of the vagina.
- STAGES-3.Cancer at this stage has moved beyond the cervix and uterus to the pelvic wall or the lower portion of the vagina.
- STAGES-4. At this stage, cancer has spread to nearby organs, such as the bladder or rectum, or it has spread to other areas of the body, such as the lumgs, liver or bones.

Overview of FIGO stages related to management and Prognosis

Stage 0. Carcinoma in situ, cervical intraepithelial neoplasia Grade III.

Carcinoma in situ, cervical intraepithelial neoplasia Grade III. This is not considered invasive cancer,

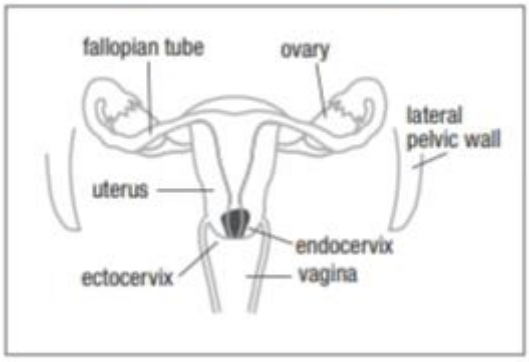
since the lesion has not gone beyond the basement membrane. .

Stage I. Carcinoma confi ned to the cervix. Extension to the uterus is disregarded.

- IA. Microinvasive carcinoma, strictly confi ned to the cervix. Can only be diagnosed by microscopy(32). it is not clinically visible.
- Stage IA1: Stromal invasion no greater than 3.0 mm in depth and not more than 7.0 mm in horizontal spread. 5-year survival with optimal treatment: ~98%.
- Stage IA2: Stromal invasion of more than 3.0 mm but not more than 5.0 mm in depth and with horizontal spread of 7.0 mm or less. 5-year survival with optimal treatment: ~95%.

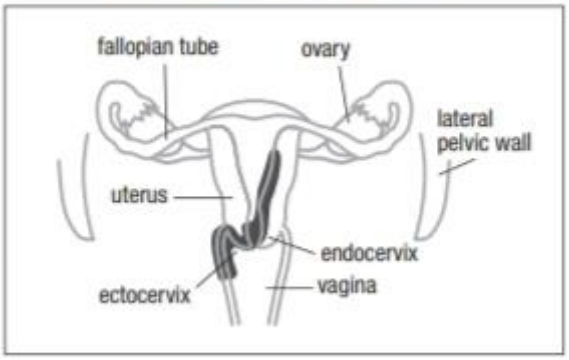
- IB: Carcinoma strictly confi ned to the cervix and clinically visible; or a microscopic lesion greater than IA2 (Figure 6.1).
- IB1: Clinically visible lesion 4.0 cm or less in greatest dimension. 5-year survival with optimal treatment: ~85%.
- IB2: Clinically visible lesion more than 4.0 cm in greatest dimension. 5-year survival with optimal treatment: ~75%.

Figure 6.1 Cervical cancer stage IB



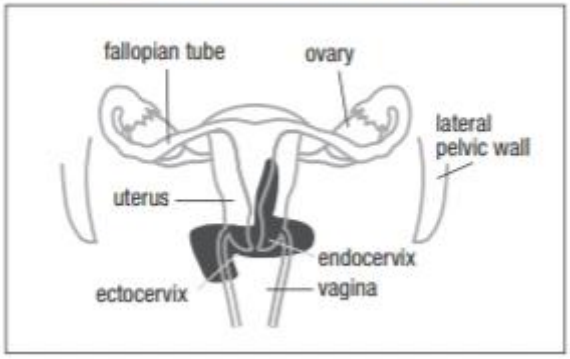
- Stage II: Carcinoma confined to the cervix. Extension to the uterus is disregarded.
- IIA: Spread beyond the cervix, including upper two-thirds of the vagina(33).but not to tissues around the uterus (parametrical) (Figure 6.2). 5-year survival with optimal treatment: ~75%.

Figure 6.2 Cervical cancer stage IIA



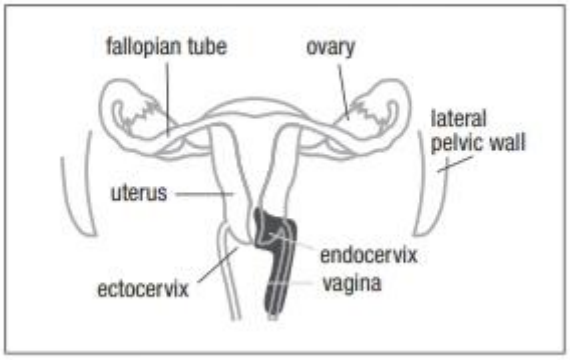
- IIB: Spread beyond the cervix, with parametrial invasion, but not as far as the pelvic wall or the lower third of the vagina (Figure 6.3). 5-year survival with optimal treatment: ~65%.

Figure 6.3 Cervical cancer stage IIB



- Stage III: Tumour extends to pelvic wall or involves lower third of the vagina, or causes hydronephrosis or non-functioning kidney.
- IIIA: Invasion of the lower third of the vagina, with no extension to the pelvic wall (Figure 6.4). 5-year survival with optimal treatment: ~30%.

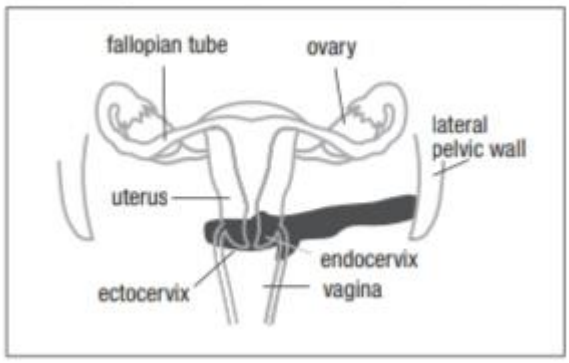
Figure 6.4 Cervical cancer stage IIIA



- IIIB: Extension to the pelvic wall, or hydronephrosis or nonfunctioning kidney (Figure 6.5).

5–year survival with optimal treatment: ~30%.

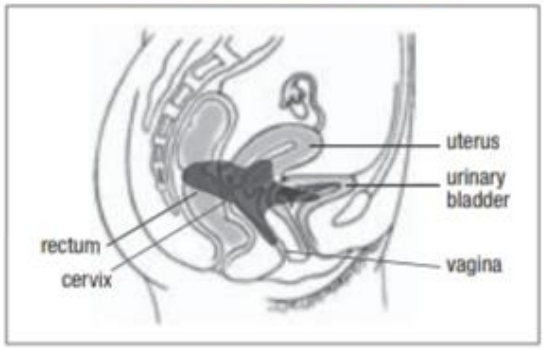
Figure 6.5 Cervical cancer stage IIIB



- Stage IV: Tumour has spread
- IVA: Spread to involve the mucosa of the bladder or rectum (Figure 6.6).

  5-year survival with optimal treatment: ~10%.

Figure 6.6 Cervical cancer stage IVA

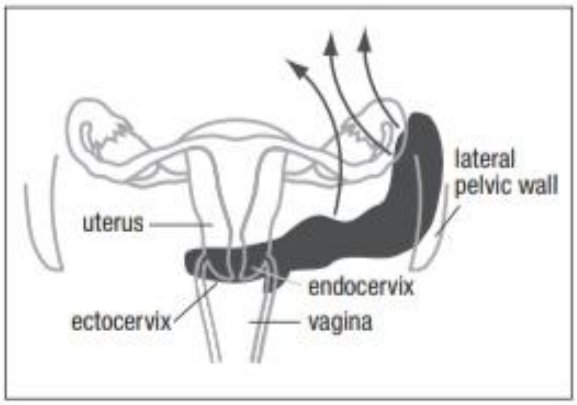


- IVB: Spread to distant organs

, such as extrapelvic lymph nodes, kidneys, bones, lungs, liver and brain

(Figure 6.7). 5-year survival with optimal treatment: <5%.

Figure 6.7 Cervical cancer stage IVB



After cervical cancer has been diagnosed, tests are done to find out if cancer cells have spread within the cervix or to other parts of the body.

The process used to find out if cancer has spread within the cervix or to other parts of the body is called staging. The information gathered from the staging process determines the stage of the disease. It is important to know the stage in order to plan treatment.

The following tests and procedures may be used in the staging process:

- CT scan (CAT scan):- A procedure that makes a series of detailed pictures of areas inside the body, taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerized tomography, or computerized axial tomography.(34).

- PET scan (positron emission tomography scan):- A procedure to find malignant tumor cells in the body. A small amount of radioactive glucose (sugar) is injected into a vein. The PET scanner rotates around the body and makes a picture of where glucose is being used in the body. Malignant tumor cells show up brighter in the picture because they are more active and take up more glucose than normal cells do.

- MRI (magnetic resonance imaging):-A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body. This procedure is also called nuclear magnetic resonance imaging (NMRI).

- Ultrasound exam:-A procedure in which high-energy sound waves (ultrasound) are bounced off internal tissues or organs and make echoes. The echoes form a picture of body tissues called a sonogram. This picture can be printed to be looked at later.

- Chest x-ray:- An x-ray of the organs and bones inside the chest. An x-ray is a type of energy beam that can go through the body and onto film, making a picture of areas inside the body.

- Lymph node biopsy:-The removal of all or part of a lymph node. A pathologist views the lymph node tissue under a microscope to check for cancer cells.

- Cystoscopy:-A procedure to look inside the bladder and urethra to check for abnormal areas. A cystoscope is inserted through the urethra into the bladder. A cystoscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue samples, which are checked under a microscope for signs of cancer.

- Laparoscopy:- A surgical procedure to look at the organs inside the abdomen to check for signs of disease. Small incisions (cuts) are made in the wall of the abdomen and a laparoscope (a thin, lighted tube) is inserted into one of the incisions. Other instruments may be inserted through the same or other incisions to perform procedures such as removing organs or taking tissue samples to be checked under a microscope for signs of disease.

- Pretreatment surgical staging:- Surgery (an operation) is done to find out if the cancer has spread within the cervix or to other parts of the body. In some cases, the cervical cancer can be removed at the same time. Pretreatment surgical staging is usually done only as part of a clinical trial.

- The results of these tests are viewed together with the results of the original tumor biopsy to determine the cervical cancer stage.

RISK FACTOR OF CERVICAL CANCER

Oncogenic human papillomaviruses (HPVs) are widely implicated with the development of cervical cancer Other risk factors such as early age of marriage, multiple sexual partners, multiple pregnancies, poor genital hygiene and lack of awareness, may be involved in modifying the risk of developing cervical cancer in women.(35). The worldwide prevalence of HPV infection is high (9-13%) and is the most common sexually transmitted infection, with no specific treatment.

Mostly Genital HPV infections are asymptomatic and unapparent and studies indicate that nearly all cervical cancer cases are caused by genital infection with specific high-risk HPV types. With use of the cervical smear Pap test or VIA, or application of effective HPV-DNA detection procedures, precursors of cervical cancer can be easily detected and successfully treated at an early stage.(36). Thus, cervical cancer can be easily prevented with regular screening programmes.

- Infection with HPV.
- Not getting regular pap tests- begin testing at age 21.
- Illnesses that weaken your immune system (HIV).
- Smoking.
- Diet.
- Multiple sexual partners throughout one's lifetime.
- Chlamydia (STIs.)
- Poverty.
- Family history.
- DES (diethyl-stilbestrol).

USE FOR (C.C.S.) SAMPLING INSTRUMENTS

(a)

(b)

(c)

PRIMARY SCREENING MODALITY

HPV	Cytology	VIA
1.Alone for primary screening is recommended in women aged 30 years and older. Also preferred method of co-testing 2. high sensitivity and negative predictive value, and this allows safe prolongation of the screening intervals. 3. primary hrHPV screening detected approximately 50% more CIN3+ as compared to cytology,	1. Most commonly used screening test for detecting cervical preinvasive and invasive lesions of the cervix. 2.Reporting done by Bethesda system (Recent 2014). 3. Results of cervical cytology cannot be used to make a definitive diagnosis or start treatment, except when it is HSIL. 4. Further evaluation with colposcopy and or biopsy.	1.ASCO and WHO both recommend VIA for basic settings, feasible method to initiate mass screening in resource-poor settings 2.In limited-resource settings VIA should be done at least one to three times in a lifetime.

CERVICAL CANCER SCREENING GUIDELINES

	ACS, ASCCP, ASCP	FOGSI, WHO
Below 21 year	No screening	-
21-29 year	cytology alone every 3 yrs	• with good resources setup-starts with age 25 year, •limited resources setup-after 30 year
30- 65 year	HPV and Cytology "Cotesting" every 5 years (Preferred) Cytology alone every 3 years (Acceptable)	•preferably be screened with primary HPV testing or • combined cytology and HPV testing ("co-testing") every five years. •If HPV testing is not available, cytology alone/VIA is an acceptable modality and should be repeated every three years.
>65year	No screening following 3 consecutive negative prior screens screening can be discontinued in women with consistent negative results in the last 15 years. Treatment for CIN 2+, screening for 20 years following the time of treatment recommended.	
HIV positive & Immune suppressed	Annually	
After TAH (if cervix removed)	No screening, If hysterectomy for benign reasons, unless there is a history of previous CIN	
follow up in women with CIN in hysterectomy HPE report	need to be screened with HPV at 6 months and 18 months	
After HPV vaccination	Screening as per age specific guidelines	

as the preferred test for cervical cancer screening for people 25-65 years of age. (*A primary HPV test is an HPV test that is done by itself for screening. The US Food and Drug Administration has approved certain tests to be primary HPV tests.)

Some HPV tests are approved only as part of a co-test, when the HPV test and the Pap test are done at the same time to screen for cervical cancer. Because a primary HPV test may not be an option everywhere, a co-test every 5 years or a Pap test every 3 years are still good options.

All the screening tests (primary HPV test, co-test, and Pap test) are good at finding cancer and pre-cancer. The primary HPV test is better at preventing cervical cancers than a Pap test done alone and does not add more unnecessary tests, which can happen with a co-test. The most important thing to remember is to get screened regularly, no matter which test you get.

The result of the HPV test, along with your past test results, determines your risk of developing cervical cancer. If the test is positive, this could mean more follow-up visits, more tests to look for a pre-cancer or cancer, and sometimes a procedure to treat any pre-cancers that might be found. Because there are many different follow-up or treatment options depending on your specific risk of developing cervical cancer, it is best to talk to your healthcare provider about your screening results in more detail, to fully understand your risk of cervical cancer and what follow-up plan is best for you. For more information, see the American Cancer Society.

PREVENTION

Avoid smoking and avoid using oral contraceptive for long time

- It is also can be prohibited by avoiding hazard factor and by getting regular pap test (papnicolaou test) also known as Pap smear.[37]
- A vaccine is a most important avoidance for cervical cancer.
- Avoid many sexual partners during sex.
- Change in life style or eating habbits.
- Avoiding other risk factors like early marriage/ child bearing and smoking,

SYMPTOMS OF CERVICAL CANCER

Women with early cervical cancers and pre-cancers usually have no symptoms. Symptoms often do not begin until the cancer becomes larger and grows into nearby tissue. When this happens, the most common symptoms are:

Abnormal vaginal bleeding, such as bleeding after vaginal sex, bleeding after menopause, bleeding and spotting between periods, or having (menstrual) periods that are longer or heavier than usual. Bleeding after douching may also occur(38).

- An unusual discharge from the vagina the discharge may contain some blood and may occur between your periods or after menopause.
- Pain during sex.
- Pain in the pelvic regionSigns and symptoms seen with more advanced disease can include:
- Swelling of the legs.
- Problems urinating or having a bowel movement.
- Blood in the urine.

These signs and symptoms can also be caused by conditions other than cervical cancer. Still, if you have any of these symptoms, see a health care professional right away. Ignoring symptoms may allow the cancer to grow to a more advanced stage and lower your chance for successful treatment.

For the best chances for treatment to be successful, don't wait for symptoms to appear. Have regular screening tests for cervical cancer.

TREATMENT

Cervical cancer treatment options include surgery, radiotherapy, chemotherapy, or combinations of these.Deciding on the kind of treatment depends on several factors, such as the stage of the cancer, as well as age and overall state of health.

Treatment for early-stage cervical cancer, when the cancer remains within the cervix, has a good success rate. The further a cancer spreads from its original area, the lower the success rate tends to be.

EARLY-STAGE OPTIONS

Surgery is a common treatment method when the cancer has not spread from the cervix. Radiation therapy may help after surgery if a doctor believes that cancer cells might be present inside the body.

Radiation therapy may also reduce the risk of recurrence (cancer coming back). If the surgeon wants to shrink the tumor to make it easier to operate, the person may receive chemotherapy although this is not a very common approach.

Treatment for advanced cervical cancer

When the cancer has spread beyond the cervix, surgery is not usually an option.

Doctors also refer to advanced cancer as invasive cancer, because it has invaded other areas of the body. This type of cancer requires more extensive treatment, which will typically involve either radiation therapy or a combination of radiation therapy and chemotherapy.

In the later stages of cancer, healthcare professionals provide palliative therapy to relieve symptoms and improve quality of life.

RADIATION THERAPY

Shar

e on PinterestDoctors commonly use radiation therapy to treat advanced forms of cervical cancer.

Some doctors refer to radiation therapy as radiation oncology or XRT.

It involves the use of beams of high-energy X-rays or radiation to destroy cancer cells.

When the treating doctor aims radiation at the pelvic area, it may cause the following side effects, some of which may not emerge until after the treatment is over:

- Diarrhea
- Nausea
- Upset stomach

- Bladder irritation
- Narrowing of the vagina
- Interrupted menstrual cycle
- Early menopause

DRUGS USED TO TREAT CERVICAL CANCER

DRUG NAME	BRAND NAME
CISPLATIN.	PLATINOL, PLATINOL-AQ.
CARBOPLATIN.	PARAPLATIN.
TOPOTECAN.	HYCAMTIN.
BEVACIZUMB.	AVASTIN, MVASI(39).
CYCLOPHOSPHAMIDE.	IFEX

4. RESULTS

The Pap test and HPV test are screening tests, not diagnostic tests. They cannot tell for certain if you have cervical cancer. An abnormal Pap test or HPV test result may mean more testing is needed to see if a cancer or a pre-cancer is present. The tests that are used include colposcopy (with biopsy), endocervical scraping and cone biopsies.

Finding cervical cancer often starts with an abnormal HPV (human papillomavirus) or Pap test result. This will lead to further tests, which can diagnose cervical cancer or pre-cancer.

If there is a diagnosis of invasive cancer, your doctor should refer you to a gynecologic oncologist, a doctor who specializes in cancers of women's reproductive systems.

Because there are many different follow-up or treatment options depending on your specific risk of developing cervical cancer, it is best to talk to your healthcare provider about your screening results in more detail, to fully understand your risk of cervical cancer and what follow-up plan is best for you.

.Medical history and physical exam First:-

The doctor will ask you about your personal and family medical history. This includes information related to risk factors and symptoms of cervical cancer. A complete physical exam will help evaluate your general state of health. You will have a pelvic exam and maybe a Pap test if one has not already been done. In addition, your lymph nodes will be felt to see if the cancer has spread (metastasis).

This chapter presents the results of our systematic review on three main issues:-

Screening among women who are 65 years of age and older or who have had a hysterectomy, technologies for cervical cytology and testing the human papilloma virus (HPV) as a part of cervical cancer screening.

5. CONCLUSIONS

Cytology based screening for cervical cancer is undoubtedly one of the major success stories in the history of medicine and since its inception it has emerged as the gold standard for cervical cancer screening in the developed countries.

In recent years several newer technologies have been developed to try and overcome the acknowledged limitations of conventional PAP SMEAR TESTING, HPV TESTING, LBC, and CIN to improve its sensitivity, specificity and predictive values. It is however very clear that we cannot adopt these technologies as a routine until we provide robust evidence in favor of these.

technics by conducting large multi institutional studies. A major challenge for the countries of the third world is to formulate a screening program that is based upon available resources and which is easily available to a large section of society, particularly the rural populations. It is also important to set clear and realistic long term goals. With the active participation of medical personnel, paramedical workers and the local population, a cost effective screening program for cervical cancer needs to be formulated and implemented.

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