

*Full Length Research Paper*

# **Awareness screening programme reduces the risk of cervical cancer in women**

**Jyotsna A. Saonere**

Department of Pharmacy, Government Polytechnic Gadge Nagar, Amravati 444603. (M. S.), India.  
E-mail: saonereja@yahoo.com. Tel: 9890922092.

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**Cervical cancer is a major health problem in the world today. Cervical cancer is a disease of young women and most commonly occurs around the mid 40's. It can affect a wide age range and women in their 20's may develop the disease. Worldwide cervical cancer is the fifth most deadly cancer in women. Cervical cancer is the malignant cancer of cervix uteri or cervical area. In the precancerous stage, readily detectable changes occur in the cells lining the surface of the cervix. This happens when normal cells in the cervix change into cancer cells. Human papillomavirus (HPV) infection is a necessary factor in the development of nearly all cases of cervical cancer. Pap smear screening can identify potentially precancerous changes. Treatment of high grade changes can prevent the development of cancer. Cervical cancer is the major risk in women today. Awareness screening programme, preventive vaccination and diet are preventive measures that reduce the incidence of cervical cancer. In developed countries, the widespread use of cervical screening programmes has reduced the incidence of invasive cervical cancer by 50% or more. In this article effort has been taken to discuss causes, symptoms, diagnosis, preventive vaccination and treatment and preventive measures discussed in details which would surely prove to be some help to decrease the risk of cervical cancer in women.**

**Key words:** Cervical cancer, cervix, human papillomavirus, pap smear, preventive measures.

## **INTRODUCTION**

Cervical cancer is malignant cancer of the cervix uteri or cervical area. It may occur with vaginal bleeding but symptoms may be absent until the cancer is in its advanced stages. Cervical cancer forms in the interior lining of the cervix, the junction of the vagina and uterus. It is the cancer of the neck or cervix of the womb. In the precancerous stage, readily detectable changes occur in the cells lining of the surface of the cervix. This happens when normal cells in the cervix change into cancer cells. This change normally takes several years to happen, but it can also happen in a very short period of time. Before the cells turn into cancer, abnormal cells develop on the cervix that can be found by a Pap test. If not treated, it can cause death. About 0.5 to 5.0% of cervical cancers occur in pregnant women and about one-third of women

are under 35 when given the diagnosis. The survival rates for the pregnant versus the non-pregnant woman are very similar. Invasive cancer of the cervix occurs when abnormally dividing cells, which arise in the outer layer (or epithelium), invade into the deeper tissue layers. The resulting mass of invading cells continues to divide and enlarge as it invades the surrounding tissue. Cells may break off from the primary tumor and spread via the lymphatic or blood vessels to distant sites. The size and degree of invasion of the cancerous tissue will determine the stage of the disease. Accurate staging of cervical cancer is vital in determining the optimum treatment.

Pap smear screening can identify potentially precancerous changes. Treatment of high grade changes can prevent the development of cancer. In developed countries, the widespread use of cervical screening programmes has reduced the incidence of invasive cervical cancer by 50% or more. Human papillomavirus (HPV) infection is a necessary factor in the development of

**Abbreviation:** HPV, Human papillomavirus.

nearly all cases of cervical cancer. HPV vaccine effective against the two strains of HPV that cause the most cervical cancer has been licensed in the U.S. and the EU. These two HPV strains together are currently responsible for approximately 70% of all cervical cancers. Since the vaccine only covers some high-risk types, women should seek regular pap smear screening, even after vaccination.

### Signs and symptoms

The early stages of cervical cancer may be completely asymptomatic; otherwise the following may be present: vaginal discharge containing blood, abnormal vaginal bleeding, pelvic pain, blood in urine, bowel symptoms, blood in stool, painful sex, unusual vaginal bleeding, unusual vaginal discharge, contact bleeding, vaginal mass, moderate pain during sexual intercourse, loss of appetite, weight loss, fatigue.

Symptoms of advanced cervical cancer may include: loss of appetite, weight loss, fatigue, pelvic pain, back pain, leg pain, single swollen leg, heavy bleeding from the vagina, leaking of urine or faeces from the vagina and bone fractures (Figure 1).

### TYPES OF CERVICAL CANCER

There are two main types of cervical cancer:

- (1) Squamous cell (epidermoid) comes from the outer portion of the cervix which protrudes into the vagina. Approximately 80 - 90% of cervical cancers are squamous cell carcinomas.
- (2) Adenocarcinoma comes from cells that make up glands in the cervix. It starts on the more "inner" portion of the cervix, from the same type of cells lining the uterus. Approximately 10% of cervical cancers are Adenocarcinoma.

The different subtypes of adenocarcinoma are:

- (i) Endocervical cervical cancer
- (ii) Clear cell cervical cancer
- (iii) Mucinous adenocarcinoma
- (iv) Adenosquamous cervical cancer is a mixed cell type having features of both squamous cell carcinomas and Adenocarcinoma.
- (v) Glassy cell carcinoma of the cervix is also called poorly differentiated adenosquamous carcinoma.
- (vi) Sarcoma arises from the fat, cartilage, or muscle cells.

The types of cervical sarcoma include:

- (i) Stromal sarcoma

- (ii) Embryonal rhabdomyosarcoma
- (iii) Sarcoma botryoides
- (iv) Leiomyosarcoma

Rare types of cervical cancer includes:

- (i) Lymphoma: Primary cervical lymphoma is rare with less than 60 cases reported as at 2005. The extent of disease, size of primary tumor and type of lymphoma are significant prognostic features.
- (ii) Neuroendocrine cervical cancer is a rare, aggressive tumor which is often under or misdiagnosed.
- (iii) Small cell cervical cancer
- (iv) Carcinoid tumor
- (v) Melanoma of the cervix. Careful evaluation is important to determine if the lesion originated in the cervix, or migrated (metastasized) from elsewhere in the body.
- (vi) Adenoid cystic carcinoma of the cervix. Generally presents in the elderly age group and in early-stage.

### STAGES OF CERVICAL CANCER

#### Stage 0

Stage 0 cervical cancer is also known as cervical carcinoma in situ. It is found only in the top layer of cells in the tissue that lines the cervix.

#### Stage I

Stage I (stage 1) cervical cancer is found only in the cervix. Stage I is divided into stages IA and IB, based on the amount of cancer that is found.

Stage IA cervical cancer indicates a very small amount of cancer that can only be seen with a microscope is found in the tissues of the cervix. The cancer is not deeper than 5 millimeters and not wider than 7 millimeters.

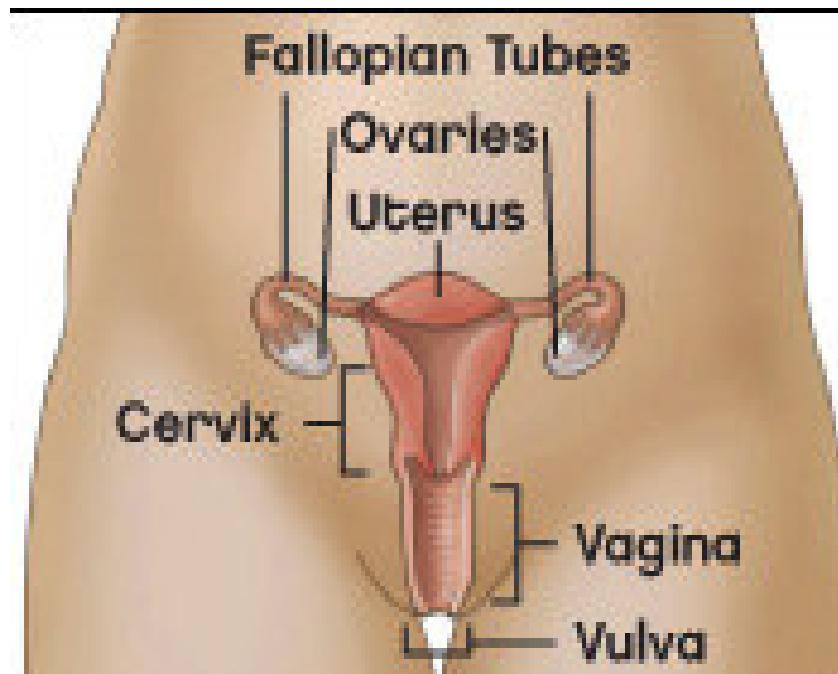
Stage IB cervical cancer is still within the cervix and either: can only be seen with a microscope and is deeper than 5 millimeters or wider than 7 millimeters; or can be seen without a microscope and may be larger than 4 centimeters.

#### Stage II

Stage II (stage 2) cervical cancer extends beyond the cervix into nearby tissues. It extends to the upper part of the vagina. The cancer does not invade the lower third of the vagina or the pelvic wall (the lining of the part of the body between the hips).

Stage IIA cervical cancer has spread beyond the cervix to the upper two thirds of the vagina but not to tissues around the uterus.

Stage IIB cervical cancer has spread beyond the cervix to the upper two thirds of the vagina and to the tissues



**Figure 1.** Female reproductive system

around the uterus.

### Stage III

Stage III (stage 3) cervical cancer extends to the lower part of the vagina. It also may have spread to the pelvic wall and nearby lymph nodes.

Stage IIIA cervical cancer has spread to the lower third of the vagina but not to the pelvic wall.

Stage IIIB cervical cancer has spread to the pelvic wall and/or the tumor has become large enough to block the ureters (the tubes that connect the kidneys to the bladder). This blockage can cause the kidneys to enlarge or stop working. Cancer cells may also have spread to lymph nodes in the pelvis.

### Stage IV

Stage IV (stage 4) cervical cancer has spread to the bladder, rectum, or other parts of the body.

Stage IVA cervical cancer has spread to the bladder or rectal wall and may have spread to lymph nodes in the pelvis.

Stage IVB has spread beyond the pelvis and pelvic lymph nodes to other places in the body, such as the abdomen, liver, intestinal tract, or lungs.

### RECURRENT

Recurrent cervical cancer indicates that the cancer was

initially treated but has returned after a period of time during which it could not be detected. The cancer may show up again in the cervix or in other parts of the body.

### CAUSES

#### What causes cervical cancer?

We do not know exactly what causes cervical cancer, but certain risk factors are believed to have an effect. Medical history and lifestyle - especially sexual habits - play a role in a woman's chances of developing cervical cancer. The most significant risk factors are:

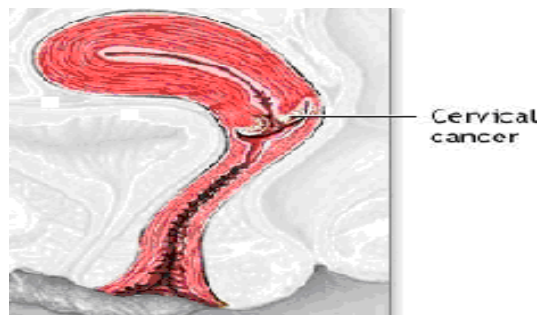
- (1) Human Papillomavirus (HPV)
- (2) Sexual history
- (3) Various other risk factors have also been identified.

#### Human papillomavirus (HPV)

Human papillomavirus (HPV) is a virus that can infect:

- (1) The genital tract
- (2) The external genitals
- (3) The area around the anus

HPV has nothing to do with HIV, the virus that causes AIDS. There are 46 genetic types of HPV, but not all are dangerous. Only certain types of HPV, which can be



**Figure 2.** Cervical cancer

transmitted from one person to another during sexual contact, increase the risk of cell dysplasia (abnormal cell growth) and/or progression to cervical cancer (Figure 2).

The virus cancer link works by triggering alterations in the cells of the cervix, which can lead to the development of cervical intraepithelial neoplasia, which can lead to cancer.

The HPV types that produce genital warts (lesions that are raised and bumpy, or flat and almost impossible to see) are different from those that cause cervical cancer. However, women who have a history of genital warts have almost twice the risk of an abnormal pap smear as other women with Human papillomavirus infection.

More than 150 types of HPV are acknowledged to exist (some sources indicate more than 200 subtypes). Of these, 15 are classified as high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73 and 82), 3 as probable high-risk (26, 53 and 66) and 12 as low-risk (6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81 and CP6108), but even those may cause cancer. Types 16 and 18 are generally acknowledged to cause about 70% of cervical cancer cases. Together with type 31, they are the prime risk factors for cervical cancer.

### **Sexual history**

A woman has a higher-than-average risk of developing cervical if she:

1. Have had multiple sexual partners
2. Began having sexual relations before the age of 18
3. Has a partner who has had sexual contact with a woman with cervical cancer

### **Other risk factors**

It is probable that other factors contribute to cervical cancer, such as:

#### **Poverty**

Women who are poor may not have access to medical

services that detect and treat precancerous cervical conditions. When such women develop cervical cancer, the disease usually remains undiagnosed and untreated until it has spread to other parts of the body. Women who are poor are often undernourished and poor nutrition can also increase cervical cancer risk.

Pap test history- Not having regular Pap tests increases the chance of unrecognized cervical cancer. Between 60 and 80% of women with newly diagnosed cervical cancer have not had a Pap test in at least five years.

#### **Tobacco use**

Women who smoke are about twice as likely to develop cervical cancer as women who do not. The more a woman smokes - and the longer she has been smoking - the greater the risk.

#### **Eating habits**

A diet that doesn't include ample amounts of fruits and vegetables can increase a woman's risk of developing cervical cancer.

#### **Weakened immune system**

A woman whose immune system is weakened has a higher-than-average risk of developing cervical lesions that can become cancerous. This includes women who are HIV-positive (infected with the virus that causes AIDS). It also includes women who have received organ transplants and must take drugs to suppress the immune system so that the body won't reject the new organ.

#### **Hormonal medications**

Some experts suggest that hormones in oral contraceptives (birth control pills) can make women more susceptible to Human Papillomavirus (HPV). At least one study has indicated that taking birth control pills significantly increases a woman's risk of developing HPV-related genital warts. Other research suggests that using oral contraceptives for five years or longer slightly elevates a woman's risk of developing cervical cancer, especially if she began taking the Pill before the age of 25.

#### **Diethylstilberstrol (DES)**

A rare type of cervical cancer has been diagnosed in a small number of women whose mothers took diethylstilbestrol (DES), a medicine that was once used to prevent miscarriage.

**Douching**

Because douching may destroy natural antiviral agents normally present in the vagina, women who douche every week are more apt to develop cervical cancer than women who do not.

**Chemical exposure**

Women who work on farms or in the manufacturing industry may be exposed to chemicals that can increase their risk of cervical cancer. Cervical cancer is very common in women who are positive for human immunodeficiency virus (HIV). HIV can compound the effects of Human Papillomavirus (HPV), causing cervical changes to progress more rapidly into cervical cancer than they otherwise might

**PATHOPHYSIOLOGY**

The presence of strains 16, 18 and 31 of Human Papillomavirus (HPV) is the prime risk factor for cervical cancer and Walboomers et al. (1999) reported that the presence of HPV is a necessary condition for the development of cervical cancer. A virus cancer link with HPV has been found to trigger alterations in the cells of the cervix, leading to the development of cancer. The E6 gene introduced by the virus inhibits the p53 gene, the central cellular switch for apoptosis (the process by which damaged cells kill themselves). The mitosis rate accelerates and the cell accumulates more DNA damage that makes it capable of invading other tissues.

**Cofactors**

The American Cancer Society provides the following list of risk factors for cervical cancer: human papillomavirus (HPV) infection, smoking, HIV infection, chlamydia infection, dietary factors, hormonal contraception, multiple pregnancies, exposure to the hormonal drug diethylstilbestrol (DES) and a family history of cervical cancer. There is a possible genetic risk associated with HLA-B7. Despite the development of an HPV vaccine, some researchers argue that routine neonatal male circumcision is an acceptable way to lower the risk of cervical cancer in their future female sexual partner. Others maintain that the benefits do not outweigh the risks and/or consider the removal of healthy genital tissue from infants to be unethical as it cannot be reasonably assumed that a male would choose to be circumcised. There has not been any definitive evidence to support the claim that male circumcision prevents cervical cancer, although some researchers say there is compelling epidemiological evidence that men who have been

circumcised are less likely to be infected with HPV. However, in men with low-risk sexual behaviour and monogamous female partners, circumcision makes no difference to the risk of cervical cancer.

**DIAGNOSIS****Biopsy procedures**

While the Pap smear is an effective screening test, confirmation of the diagnosis of cervical cancer or pre-cancer requires a biopsy of the cervix. This is often done through colposcopy, a magnified visual inspection of the cervix aided by using a dilute acetic acid (e.g. vinegar) solution to highlight abnormal cells on the surface of the cervix.

Further diagnostic procedures are loop electrical excision procedure (LEEP) and conization, in which the inner lining of the cervix is removed to be examined pathologically. These are carried out if the biopsy confirms severe cervical intraepithelial neoplasia.

**Colposcopy**

If abnormal cells are found in a smear test or liquid-based cytology, you may be referred for a colposcopy to have a biopsy

**Hot conisation**

Large loop excision of the transformation zone (LLETZ) or LEEP -This is often used to remove the area of the cervix that contains the abnormal cells, which can then be examined under a microscope in the laboratory. The area of the cervix where abnormal cells are most likely to develop is known as the transformation zone. LLETZ is usually carried out under local anaesthetic.

**Cold knife cone biopsy**

If the abnormal area can't be seen properly with the colposcope, you may have a cone biopsy. This is often done under local anaesthetic, although you may need a general anaesthetic and an overnight stay in hospital. A small cone-shaped section of the cervix, that is aimed to be large enough to remove any abnormal cells, is taken for examination under a microscope by a pathologist. Various methods can be used to do this.

**Blood tests**

A sample of blood is taken to check the number of blood

cells and to see how well your kidneys and liver are working.

### **Chest x-ray**

This is to check that your lungs and heart are healthy.

### **Examination under anaesthetic (EUA)**

This is an examination of the vagina and cervix under a general anaesthetic. It allows the doctor to examine you thoroughly without it being uncomfortable. The doctor may also take a look into your bladder and the lower end of your large bowel (the colon and rectum) to see if the cancer has spread. In this scan, several x-rays are taken of the pelvic area and fed into a computer. This builds up a detailed picture of the size and position of the cancer. This test is similar to a CT scan, but uses magnetism instead of x rays to build up cross-sectional pictures of your body.

### **Pelvic ultrasound test**

This test may be used to measure the size and position of the cancer. Ultrasound is completely painless and only takes a few minutes.

Alternatively, a probe (like a tube) may be placed in your vagina to produce an ultrasound picture of your pelvis. This can be uncomfortable, but is not painful and only takes a few minutes

## **PREVENTION**

### **Awareness**

Cervical cancer is nearly 100% preventable; the occurrence of deaths from cervical cancer has declined significantly. Cervical cancer is preventable and curable if it is detected early by providing information on how to prevent this deadly disease cervical cancer. Screening younger women is an important strategy that can actually prevent cervical cancer from developing almost 100% of the time. Furthermore, when cervical cancer is detected at its earliest stage, the 5 year survival rate is more than 90%. Educating the people for cervical cancer by arranging screening program, providing information about the causes, risk, symptoms of cervical cancer and idea about the preventive measures by proper diet and changing life style can reduces the risk of cervical cancer. Routine Pap smear and HPV test is necessary for the women of age above 30 positive Pap smear test in precancerous stage reduces the risk of progressive development of cervical cancer by providing examination and possible preventive treatment.

### **Screening**

The widespread introduction of the Papanicolaou test, or

Pap smear for cervical cancer screening has been credited with dramatically reducing the incidence and mortality of cervical cancer in developed countries. Abnormal Pap smear results may suggest the presence of cervical intraepithelial neoplasia (potentially premalignant changes in the cervix) before a cancer has developed, allowing examination and possible preventive treatment. Recommendations for how often a Pap smear should be done vary from once a year to once every five years. Until recently the Pap smear has remained the principal technology for preventing cervical cancer.

The HPV test is a newer technique for cervical cancer triage which detects the presence of human papillomavirus infection in the cervix. It is more sensitive than the Pap smear (less likely to produce false negative results), but less specific (more likely to produce false positive results) and its role in routine screening is still evolving. Since more than 99% of invasive cervical cancers worldwide contain HPV, some researchers recommend that HPV testing be done together with routine cervical screening. But, given the prevalence of HPV (around 80% infection history among the sexually active population) others suggest that routine HPV testing would cause undue alarm to carriers. HPV testing can reduce the incidence of grade 2 or 3 cervical intraepithelial neoplasia or cervical cancer detected by subsequent screening tests among women 32 – 38 years old according to a randomized controlled trial. The relative risk reduction was 41.3%. For patients at similar risk to those in this study (63.0% had CIN 2 - 3 or cancer), this leads to an absolute risk reduction of 26%. 3.8 patients must be treated for one to benefit (number needed to treat = 3.8).

### **Preventive vaccination**

#### ***HPV vaccine***

HPV vaccines are targeted at girls and women of age 9 to 26 because the vaccine only works if given before infection occurs; therefore, public health workers are targeting girls before they begin having sex. The use of the vaccine in men to prevent genital warts and interrupt transmission to women is initially considered only a secondary market. In an address at the 4th International Public Conference on Vaccination in October 2009, Dr. Diane Harper, lead researcher for the HPV vaccines, stated that Gardasil and Cervarix will do little to reduce cervical cancer rates. She also stated that no efficacy trials for children under 15 have been performed.

### **Condoms**

Condoms offer some protection against cervical cancer. Evidence on whether condoms protect against HPV infection is mixed, but they do provide protect against genital warts and the precursors to cervical cancer. They

also provide protection against other STDs, such as HIV and Chlamydia, which are associated with greater risks of developing cervical cancer. Condoms may also be useful in treating potentially precancerous changes in the cervix. Exposure to semen appears to increase the risk of precancerous changes (CIN 3) and use of condoms helps to cause these changes to regress and helps clear HPV. One study suggests that prostaglandin in semen may fuel the growth of cervical and uterine tumours and that affected women may benefit from the use of condoms.

### Smoking avoidance

Carcinogens from tobacco increase the risk for many cancer types, including cervical cancer and women who smoke have about double the chance of a non-smoker to develop cervical cancer.

### Nutrition

#### *Fruits and vegetables*

Higher levels of vegetable consumption were associated with a 54% decrease risk of HPV persistence. Consumption of papaya at least once a week was inversely associated with persistent HPV infection.

1. Vitamin A: There is weak evidence to suggest a significant deficiency of retinol can increase chances of cervical dysplasia, independently of HPV infection.
2. Vitamin C: Risk of type-specific, persistent HPV infection was lower among women reporting intake values of vitamin C in the upper quartile compared with those reporting intake in the lowest quartile.
3. Vitamin E: HPV clearance time was significantly shorter among women with the highest compared with the lowest serum levels of tocopherols, but significant trends in these associations were limited to infections lasting  $\leq 120$  days. Clearance of persistent HPV infection (lasting  $> 120$  days) was not significantly associated with circulating levels of tocopherols. Results from this investigation support an association of micronutrients with the rapid clearance of incident oncogenic HPV infection of the uterine cervix.

A statistically significantly lower level of alpha-tocopherol was observed in the blood serum of HPV-positive patients with cervical intraepithelial neoplasia. The risk of dysplasia was four times higher for an alpha-tocopherol level  $< 7.95 \mu\text{mol/l}$ .

4. Folic acid: Higher folate status was inversely associated with becoming HPV test-positive. Women with higher folate status were significantly less likely to be repeatedly HPV test-positive and more likely to become test-negative. Studies have shown that lower levels of antioxidants coexisting with low levels of folic acid

increases the risk of CIN development. Improving folate status in subjects at risk of getting infected or already infected with high-risk HPV may have a beneficial impact in the prevention of cervical cancer. However, another study showed no relationship between folate status and cervical dysplasia.

### Carotenoids

Higher circulating levels of carotenoids were associated with a significant decrease in the clearance time of type-specific HPV infection, particularly during the early stages of infection ( $\leq 120$  days). The likelihood of clearing an oncogenic HPV infection is significantly higher with increasing levels of lycopenes. A 56% reduction in HPV persistence risk was observed in women with the highest plasma [lycopene] concentrations compared with women with the lowest plasma lycopene concentrations. These data suggests that vegetable consumption and circulating lycopene may be protective against HPV persistence.

### CoQ10

Women who had either CIN or cervical cancer had markedly lower levels of CoQ10 in their blood and in their cervical cells than the women who were

### Prognosis

Prognosis depends on the stage of the cancer. With treatment, the 5-year relative survival rate for the earliest stage of invasive cervical cancer is 92% and the overall (all stages combined) 5-year survival rate is about 72%. These statistics may be improved when applied to women newly diagnosed, bearing in mind that these outcomes may be partly based on the state of treatment five years ago when the women studied were first diagnosed.

With treatment, 80 to 90% of women with stage I cancer and 50 to 65% of those with stage II cancer are alive 5 years after diagnosis. Only 25 to 35% of women with stage III cancer and 15% or fewer of those with stage IV cancer are alive after 5 years.

According to the International Federation of Gynecology and Obstetrics, survival improves when radiotherapy is combined with cisplatin-based chemotherapy.

As the cancer metastasizes to other parts of the body, prognosis drops dramatically because treatment of local lesions is generally more effective than whole body treatments such as chemotherapy.

Interval evaluation of the patient after therapy is imperative. Recurrent cervical cancer detected at its earliest stages might be successfully treated with surgery, radiation, chemotherapy, or a combination of the three. Thirty-five % of patients with invasive cervical

cancer have persistent or recurrent disease after treatment.

Average years of potential life lost from cervical cancer are 25.3 (SEER Cancer Statistics Review 1975-2000, National Cancer Institute (NCI)). Approximately 4,600 women were projected to die in 2001 in the US of cervical cancer (DSTD) and the annual incidence was 13,000 in 2002 in the US, as calculated by SEER. Thus the ratio of deaths to incidence is approximately 35.4%.

Regular screening has meant that pre cancerous changes and early stage cervical cancers have been detected and treated early. Figures suggest that cervical screening is saving 5,000 lives each year in the UK by preventing cervical cancer. About 1,000 women per year die of cervical cancer in the UK.

Regular two-yearly pap tests can reduce the incidence of cervical cancer by up to 90% in Australia and save 1,200 Australian women dying from the disease each year.

## EPIDEMIOLOGY

Worldwide, cervical cancer is the fifth most deadly cancer in women. It affects about 16 per 100,000 women per year and kills about 9 per 100,000 per year. In the United States, it is only the 8th most common cancer of women. In 1998, about 12,800 women were diagnosed in the US and about 4,800 died.

Among gynecological cancers it ranks behind endometrial cancer and ovarian cancer. The incidence and mortality in the US are about half those for the rest of the world, which is due in part to the success of screening with the Pap smear. The incidence of new cases of cervical cancer in the United States was 7 per 100,000 women in 2004.

In the United Kingdom, the incidence is 9.1/100,000 per year (2005), similar to the rest of Northern Europe and mortality is 3.1/100,000 per year (2006) (Cancer Research UK Cervical cancer statistics for the UK). With a 42% reduction from 1988 - 1997 the NHS implemented screening programme has been highly successful, screening the highest risk age group (25 – 49 years) every 3 years and those ages 50 – 64 every 5 years.

In Canada, an estimated 1,300 women will be diagnosed with cervical cancer in 2008 and 380 will die. In Australia, there were 734 cases of cervical cancer (2005). The number of women diagnosed with cervical cancer has dropped on average by 4.5% each year since organized screening began in 1991 (1991 - 2005). Worldwide it is estimated that there are 473,000 cases of cervical cancer and 253,500 deaths per year.

## Surgery

For localized disease confined to the cervix, surgery is

the treatment of choice. Radiotherapy is equally effective but tends to carry more side-effects. Surgery involves a vaginal or abdominal hysterectomy. Vaginal hysterectomy is removal of the uterus and cervix through the vagina. It is the less traumatic of the two but may be difficult in those with other gynaecological problems or obese patients. Abdominal hysterectomy involves surgical removal of the uterus, upper part of the vagina, ligaments and connective tissues that hold the uterus in place via an incision in the abdomen. Pelvic lymph nodes are also frequently resected and an oophorectomy and salpingectomy may be required.

Surgical approaches may lead to a number of long-term complications, particularly if radiotherapy is utilised as well. The radical trachelectomy is a specialised surgical procedure which allows preservation of the body of the uterus for young women with early-stage cervical cancer. This is a relatively new approach and data is being collected to establish its role (Plante and Roy, 2001).

## Cryosurgery

A metal probe cooled with carbon dioxide is placed directly on the cervix. This kills the abnormal cells by freezing them. Cryosurgery is used to treat pre-invasive cervical cancer (stage 0), but not invasive cancer.

## Laser surgery

A focused laser beam, directed through the vagina, is used to vaporize (burn off) abnormal cells or to remove a small piece of tissue for study. Laser surgery is used to treat pre-invasive cervical cancer (stage 0). It is not used to treat invasive cancer.

## Conization

A cone-shaped piece of tissue is removed from the cervix. This is done using a surgical or laser knife (cold knife cone biopsy) or using a thin wire heated by electricity (the loop electrosurgical, LEEP or LEETZ procedure). A cone biopsy may be used to diagnose the cancer before additional treatment with surgery or radiation. It can also be used as the only treatment in women with early (stage IA1) cancer who want to preserve their ability to have children (fertility).

## Hysterectomy

This is surgery to remove the uterus (both the body of the uterus and the cervix) but not the structures next to the uterus (parametria and uterosacral ligaments). The



vagina and pelvic lymph nodes are not removed. The ovaries and fallopian tubes are usually left in place unless there is some other reason to remove them

### **Radical hysterectomy and pelvic lymph node dissection**

For this operation the surgeon removes more than just the uterus. Also removed are the tissues next to the uterus (parametria and uterosacral ligaments), the upper part (about 1 inch) of the vagina next to the cervix and some pelvic lymph nodes (pea-sized collections of immune system tissue). Another surgical approach is called laparoscopic-assisted radical vaginal hysterectomy. This operation combines a radical vaginal hysterectomy with a laparoscopic pelvic node dissection. Laparoscopy allows the inside of the abdomen and pelvis to be seen through a tube inserted into very small surgical incisions.

Robot-assisted laparoscopic surgery is also sometimes used to perform radical hysterectomies. However, this way of treating cervical cancer is still relatively new and its ultimate role in treatment is still being studied.

Sexual impact of hysterectomy: Radical hysterectomy does not change a woman's ability to feel sexual pleasure. Although the vagina is shortened, the area around the clitoris and the lining of the vagina remains as sensitive as before. A woman does not need a uterus or cervix to reach orgasm. When cancer has caused pain or bleeding with intercourse, the hysterectomy may actually improve a woman's sex life by stopping these symptoms.

### **Trachelectomy**

Most women with stage IA2 and stage IB are treated with hysterectomy. Another procedure, known as a radical trachelectomy, allows some of these young women to be treated without losing their ability to have children. This procedure removes the cervix and the upper part of the vagina and placing a "purse-string" stitch to act as an artificial internal opening of the cervix

### **Pelvic exenteration**

This is a more extensive operation that may be used to treat recurrent cervical cancer. In this surgery, all of the organs and tissues are removed as in a radical hysterectomy with pelvic lymph node dissection. This operation may also remove the bladder, vagina, rectum and part of the colon, depending on where the cancer has spread.

### **Radiotherapy**

Radiation therapy has been used successfully to treat

carcinoma of the cervix since the early 1900s. Adjuvant radiotherapy is utilised if there is a risk of residual disease postsurgery. Unfortunately, for the management of large cervical lesions the dose of radiation needed to achieve tumour control exceeds the dose tolerated by the normal tissues of the pelvis.

The most significant development in improving efficacy of radiotherapy is use of concurrent chemotherapy, which has been found to act as a radiosensitiser. The two treatments are thought to act synergistically via:

- Simultaneous activity of drug and radiation in different phases of the cell cycle and against different tumour subpopulations;
- Radiotherapy decreasing tumour cell repopulation;
- Increased tumour cell recruitment out of resting phase to responsive phases in the cell cycle;
- Inhibition of repair of sub-lethal radiation damage (Loizzi et al., 2003).

### **Chemotherapy**

Disseminated disease is primarily treated by chemotherapy. Survival rates and post recurrence is limited, about 30% of patients die of recurrent disease. Prognostic factors with a negative impact on survival include:

- Recurrence within a previously irradiated area;
- Young age;
- Poor performance status;
- Short time to progression from initial diagnosis (Eralp et al., 2003).

Cisplatin appears to be the most active chemotherapy agent, with response rates of about 20 %.

Chemotherapy has also been investigated in adjuvant and neoadjuvant settings, but there is no compelling data to support use of either routinely (Loizzi et al., 2003).

Systemic chemotherapy uses anti-cancer drugs that are injected into a vein or given by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment potentially useful for cancers that have spread to distant organs (metastasized).

Drugs most often used to treat cervical cancer include cisplatin, paclitaxel (Taxol<sup>®</sup>), topotecan, ifosfamide and fluorouracil (5-FU). If chemotherapy is chosen, you may receive a combination of drugs. Chemotherapy drugs kill cancer cells but also damage some normal cells, which can lead to side effects.

Chemotherapy side effects depend on the type of drugs, the amount taken and the length of time you are treated. Temporary side effects of chemotherapy might include:

- (1) Nausea and vomiting
- (2) Loss of appetite
- (3) Loss of hair

#### (4) Mouth sores

Because chemotherapy can damage the blood-producing cells of the bone marrow, the blood cell counts might become low.

This can result in an increased chance of infection (from a shortage of white blood cells) bleeding or bruising after minor cuts or injuries (because of a shortage of blood platelets) shortness of breath (due to low red blood cell counts)

Fatigue is also quite common and may be caused by low red blood cell counts, by other reasons related to the chemotherapy, or by the cancer itself.

Most side effects of chemotherapy (except premature menopause and infertility) disappear once treatment is stopped. Hair will grow back after treatment ends. Premature menopause can be treated with hormones.

For some stages of cervical cancer, chemotherapy is given to help the radiation work better. When chemotherapy and radiation therapy are given together, it is called concurrent chemo radiation. One option is to give a dose of cisplatin every week during radiation. This drug is given into a vein (IV) about 4 h before the radiation appointment. Another choice is to give cisplatin along with fluorouracil (5-FU) every 4 weeks during radiation. Other drug combinations are also used. Giving chemotherapy with radiation can improve the patient's outlook, but giving the two together also tends to have worse side effects. The nausea and fatigue are often worse. Diarrhea can also be a problem if chemotherapy is given at the same time as radiation. Problems with low blood counts can also be worse.

#### Conclusion

Cervical cancer is declining in incidence in the developed world and although no randomised trials have been performed, it is thought that the screening programme is responsible for this decline (Sedlacek, 2002). Treatment for advanced cancer remains problematic and has discouraging response rates. Management strategies must rely on early detection and screening through programmes that are also acceptable to women, who belong to minority ethnic groups and who are at high risk. Proper implementation of screening programme, education and preventive vaccines reduce the risk of cervical cancer to the greater extent in future.

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