

## **PREVENTING CERVICAL CANCER- THE HPV LINKAGE & VACCINATION**

A few days ago I was most privileged to be a member of a team doing a documentary on cervical cancer. Our star performer was a young woman aged 39 years with two children aged 14 and 11 years. Her problem started about three years ago when she noticed bloody discharge in her underwear(s) anytime she had sexual intercourse with the husband. She had also noticed increasing pain anytime she had sex with the husband. Indeed the normal moments of intimacy had now become an ordeal! After a few consultations she was diagnosed as having cancer of cervix and referred to a specialist at Korle-Bu for treatment. She also revealed that four other close family members had already succumbed to cancer but did not think so much of these incidents (she was young by then) until recently.

Last year at the cancer screening programme of the Cancer Society of Ghana (CSG), out of over a thousand (1000) women who presented for screening (cancer of the breast, cervix), only about a hundred (100) women got screened for cervical cancer. The procedure used was the Visual Inspection using Acetic Acid (V.I.A.). It involves virtually painting the cervix with vinegar and observing any changes of the cervix using a light source. This procedure has been demonstrated to be very effective and low-cost screening procedure for resource constrained settings (IARC 2005).

There were very few women who went through the Pap Smear Test (literally scraping the neck of the womb with a wooden spatula and sending over to the pathologist for interpretation) because it was far more expensive.

In fact, I also realized that many women were most comfortable with immediate results provided (on site) by the V.I.A. technique. Yet very few health centres in the country had specially trained people to undertake cervical cancer screening using the V.I.A. technique. At the time (of the cancer screening last year 2009) there three centres in the whole of the Greater Accra Region (Ridge Hospital, Tema General hospital and Amasaman hospital) with specially trained personnel to undertake cervical cancer screening using the V.I.A. technique.

About 500,000 cases of cervical cancer occur each year with over 270,000 deaths each year. Over 80% of these incidents occur in developing countries such as Ghana. Cervical cancer is the second most common cancer in women worldwide because majority of women lack access to cervical screening which can prevent up to 75% of cervical cancer.

### **Human Papilloma Virus (HPV)**

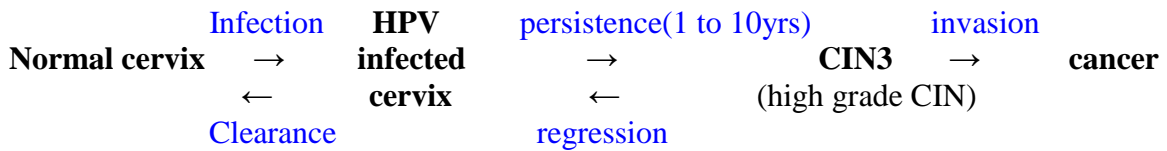
The discovery of the linkage between the human papilloma virus (HPV) and cervical cancer represented a major breakthrough in efforts aimed at controlling cervical cancer in the world. HPV is likely to be the number two (2) carcinogen after tobacco, accounting for 5% of human cancer, 10% of cancer in women and 15% of cancer in women in developing countries.

HPV DNA can be identified in virtually all (99.7%) cervical cancer. Indeed it is now generally regarded that any cervical cancer sample that tests negative for HPV is probably due to test limitations or quality of the specimen. In randomized controlled

trials, HPV-negative women have extremely low risk of subsequent development of cancer (Sankaranarayanan R. New Engl J Med 2009).

Genital HPV infection and HPV-associated cervical and other anogenital cancers are significant public health problems globally. HPV is the most common sexually transmitted viral infection and the lifetime risk of HPV infection is extremely high (hpvtoday.com). A large proportion of adolescents are exposed to HPV soon after first sex, even though about 90% of women with new HPV infections clear the infection within two years.

**Natural History of HPV & Cancer of Cervix**



Cancer of the cervix arises from a small area in the centre of the cervix (or neck of the womb) where a small exposed area of normal soft cells undergo a simple change to firm cells. The normal change occurs in all women of reproductive age. When the process becomes abnormal it leads to the development of abnormal cells that may over time become cancerous. The abnormal process is called cervical intraepithelial neoplasia (CIN)

There are so far over 100 types of HPVs (IARC 2005). Only a small number of HPV types inflict infections that have the potential to lead to cancers (cervix 95%, vulva 30%, vagina 65-90%, anus 80%, penis 40%, mouth 30%, oropharynx 30%). There are 15 types of HPV deemed to have high risk for anogenital cancer, with HPV 16 and 18 rated as possessing the greatest cancer risk (accounting for about 70% of all cervical cancers). The low-risk HPVs such as types 6 and 11 are most associated with benign genital warts and recurrent respiratory papillomatosis (RRP).

**Risk factors for HPV Infection & Progression from HPV Persistent Infection To Cancer**

Some identified risk factors are; number of sexual partners (including the number of partners of the male partner), early age at sexual initiation, tobacco smoking, long-term use of oral contraceptives, number of full-term pregnancies, herpes simplex virus-2 (HSV-2), Chlamydia trachomatis, HIV, immunosuppression (organ transplant recipients).

It also needs to be stressed that there is high mother-to-child transmission of hpv types 6 & 11 related disorders (90%) such as genital warts and recurrent respiratory papillomatosis RRP). There is however very low transmission from mother-to-child for hpv 16 & 18.

Public awareness and education is key to the successful control of HPV infection. People should know that HPV is very common and most people will have had an infection at one time or another in their lives. HPV is sexually transmitted. It can be caught by any skin-

to-skin sexual contact and not just sexual intercourse. Condoms are therefore less protective for HPV. The majority of HPV infections have no symptoms and most people will never know they have it. HPV infections usually go away on their own, but can sometimes persist for many years without any symptoms (Tristram et al, 2006).

The foregoing highlight the increasing trend towards integrating HPV testing into cervical screening programmes. HPV testing will facilitate HPV triage by improving detection of high-grade cervical intraepithelial neoplasia (CIN) and thereby avoid unnecessary investigation of HPV negative women. HPV testing is sensitive as a test of cure after treatment of high-grade CIN. Primary HPV screening is known to be very sensitive but less specific and can therefore be combined with cytology triage of HPV positive women.

**Screening Practices in the European Union (Antilla et al, Br. J. Cancer 2004)**

Country	Age(yrs)	Interval	Lifetime Pap Smears
Denmark	23-59	3 yrs	13
France	20/25 - 65	3 yrs	14 - 17
Germany	20 - 85+	1 yr	~ 65
Finland	30 - 60	5 yrs	7
Iceland	20 - 69	2 yrs	25
Italy	25 - 64	3 yrs	14
Luxembourg	15+	1 yr	~ 70
Netherlands	30 - 60	5 yrs	7
UK	25 - 64 YRS	3 - 5 yrs	8 - 13

It is clear also that the production of HPV vaccines represent a crucial breakthrough in the global fight against cervical cancer. Ideally the vaccines must be administered early in life on account of the natural history of HPV infection. Consequently a large number of European countries including the U.K. have recommended HPV vaccination.

In the U.K. 12-14 year-old girls will be vaccinated with a catch-up to age 18 phased over 3 years. Italy (12-year-old girls), Belgium (10 - 13-year-olds), Austria (to pre-adolescents), Germany (12 - 17-year-old girls, Switzerland (11 - 14-year-olds), France (14-year-olds with catch-up for women up to 23 years).

There are currently two licensed HPV prophylactic vaccines based on virus-like particles (VLPs), namely Gardasil® and Cervarix™. Both vaccines have a common goal of preventing disease associated with the two most prevalent HPV types (-16 and -18) associated with the risk of progression to cervical cancer. Gardasil also offers additional protection against warts.

## Comparison of Commercial HPV Virus-Like Particles (VLP) Vaccines

	<b>Gardasil</b>	<b>Cervarix</b>
Manufacturer	Merck	GSK
VLP Types	6/11/16/18	16/18
Dose of L1 Protein	20/40/40/20 mg	20/20 mg
Producer Cells	Saccharomyces cerevisiae (bread yeast) expressing L1	Trichoplusia ni (Hi 5) Insect cell line infected With L1 recombinant baculovirus
Adjuvant	225 mg Aluminium Hydroxyphosphate sulphate	500 mg Aluminium hydroxide + 50 mg 3-O-deacylated-4O Monophosphoryl lipid A
Injection Schedule	0, 2, 6 months	0, 1, 6 months

HPV L1 VLP vaccines provide protection for at least 5 years after full immunization.

### HPV Vaccination in Developing Countries- Experiences From Hepatitis B

A 3 dose HPV vaccine schedule currently costs over US\$120.00. The high cost is a major barrier for the rapid introduction and widespread use of HPV vaccine in immunization programmes in resource-constrained settings.

It will be extremely difficult for the public health to consider implementing HPV vaccine at this cost when entire vaccine antigens used for infant vaccination in developing countries cost less than US\$5.00 per child. This is because these infant vaccines are produced mainly in developing countries such as India, South Africa, South Korea, Brazil, etc.

As result only persons who can afford these vaccines can get access to them. It is an area that is seriously under consideration by the Global Alliance for Vaccines and Immunization (GAVI). My own experiences from the Pharmaceutical Society's Hepatitis B campaign indicate that when people understand the issues at stake it is very easy for them to make informed decisions. As a result parents of school children quickly agreed to the screening and vaccination of their wards against hepatitis B infection. A number of organizations willingly invited our teams for screening and vaccination because management and staff understood clearly the issues involved. The same model can be applied to HPV.

We would however need to ensure the use of standard HPV test kit to avoid some of the controversies encountered with hepatitis B screening programmes.

You will recall that I was inspired to compose this piece while assisting in the production of a documentary on cervical cancer. Our star performer has a daughter who is only 11 years old. It is clear that given her mother's experiences it is crucial for her to be protected against cervical cancer.

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